UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2020

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from_____ to_____

Commission File Number: 001-39620

PRAXIS PRECISION MEDICINES, INC.
(Exact Name of Registrant as Specified in its Charter)

Delaware	**47-5195942**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
One Broadway, 16th Floor Cambridge, MA	**02142**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: 617-300-8460

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	**PRAX**	**The Nasdaq Global Select Market**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of common stock held by non-affiliates of the registrant, based on the closing price of a share of common stock on October 16, 2020 as reported by the Nasdaq Global Select Market on such date was approximately $731.4 million. The registrant has elected to use October 16, 2020, which was the initial trading date on the Nasdaq Global Select Market, as the calculation date because on June 30, 2020 (the last business day of the registrant's most recently completed second fiscal quarter) the registrant was a privately held company. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

As of March 1, 2021, the registrant had 38,579,115 shares of common stock, $0.0001 par value per share, outstanding.

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SUMMARY OF THE MATERIAL AND OTHER RISKS ASSOCIATED WITH OUR BUSINESS

- We are a clinical-stage biopharmaceutical company and we have incurred significant losses since our inception. We anticipate that we will continue to incur significant losses for the foreseeable future.
- We will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product discovery and development programs or commercialization efforts.
- Our business substantially depends upon the successful development of PRAX-114, PRAX-944 and PRAX-562. If we are unable to obtain regulatory approval for, and successfully commercialize, PRAX-114, PRAX-944 or PRAX-562, our business may be materially harmed.
- Clinical development involves a lengthy, complex and expensive process, with an uncertain outcome. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials, which to date have primarily been conducted in Australia and New Zealand, may not satisfy the requirements of the FDA or comparable foreign regulatory authorities.
- Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following regulatory approval, if obtained.
- The markets for PRAX-114 for major depressive disorder and perimenopausal disorder, PRAX-944 for essential tremor, PRAX-562 for multiple rare neurological conditions and any other product candidates we may develop may be smaller than we expect.
- We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours, which may negatively impact our ability to successfully market or commercialize any product candidates we may develop and ultimately harm our financial condition.
- Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.
- We have entered into, and may enter into, license or other collaboration agreements that impose certain obligations on us. If we fail to comply with our obligations under such agreements with third parties, we could lose license rights that may be important to our business.
- Third-party claims of intellectual property infringement may prevent or delay our product discovery and development efforts.
- We expect to depend on collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.
- Business interruptions resulting from COVID-19 or a similar pandemic, epidemic or outbreak of an infectious disease in the United States or worldwide may adversely affect our business.
- The price of our stock may be volatile, and you could lose all or part of your investment.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements contained in this Annual Report on Form 10-K include, but are not limited to, statements about:

- the success, cost and timing of our product development activities and clinical trials;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates;
- the ability to license additional intellectual property relating to our product candidates from third parties and to comply with our existing license agreements and collaboration agreements;
- the ability and willingness of our third-party research institution collaborators to continue research and development activities relating to our product candidates;
- our ability to commercialize our products in light of the intellectual property rights of others;
- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates;
- the commercialization of our product candidates, if approved;
- our plans to research, develop and commercialize our product candidates;
- future agreements with third parties in connection with the commercialization of our product candidates and any other approved product;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates;
- the pricing and reimbursement of our product candidates, if approved;
- regulatory developments in the United States and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act, enacted in April 2012, or a smaller reporting company as defined in the Securities Exchange Act of 1934, as amended;
- the development of major public health concerns, including the novel coronavirus outbreak or other pandemics arising globally, and the future impact of it and COVID-19 on our clinical trials, business operations and funding requirements; and

- other risks and uncertainties, including those listed under the caption “Risk Factors.”

In some cases, you can identify forward-looking statements by terminology such as “may,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue” or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled “Risk Factors” and elsewhere in this Annual Report on Form 10-K. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K and have filed with the Securities and Exchange Commission as exhibits hereto completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this Annual Report on Form 10-K represent our views as of the date of this Annual Report on Form 10-K. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report on Form 10-K.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this Annual Report on Form 10-K, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors, including those discussed under the section titled “Risk Factors” and elsewhere in this Annual Report on Form 10-K.

PART I

Item 1. Business

BUSINESS

Company Overview

We are a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for central nervous system, or CNS, disorders characterized by neuronal imbalance. Normal brain function requires a delicate balance of excitation and inhibition in neuronal circuits, which, when dysregulated, can lead to abnormal function and disease. We are applying insights from genetic epilepsies to broader neurological and psychiatric disorders, using our understanding of shared biological targets and circuits in the brain. We apply a deliberate and pragmatic precision approach, leveraging a suite of translational tools including novel transgenic and predictive translational animal models and electrophysiology markers, to enable an efficient path to proof-of-concept in patients. Through this approach, we have established a broad portfolio, including multiple disclosed programs across CNS disorders, including depression, epilepsy, movement disorders and pain syndromes, with three clinical-stage product candidates. We expect multiple topline clinical trial readouts from all three programs in the next year and anticipate the launch of a new clinical development program in 2021. We intend to develop differentiated therapies that can deliver long-term benefits to human health by meaningfully impacting patients and society.

Our most advanced clinical program, PRAX-114, is an extrasynaptic GABAA receptor preferring positive allosteric modulator, or PAM, for the treatment of patients suffering from major depressive disorder, or MDD, and perimenopausal depression, or PMD. Together, these conditions affect more than 22 million people in the United States, many of whom are not responsive to or are underserved by current treatments. PRAX-114 is under development as a potentially differentiated treatment for a broad MDD population, as both a monotherapy and adjunctive therapy for both acute and maintenance treatment. We believe that PRAX-114 has several advantages relative to currently available therapies and product candidates in the GABAA PAM therapeutic class, including the potential for rapid and durable antidepressant effect across MDD symptoms, a wider therapeutic window, simple nightly dosing with or without a meal via tablet formulation and indication expansion opportunities. We have a multi-cohort, three-part Phase 2a clinical trial ongoing in Australia. Parts A and C of the trial are treating patients with MDD while Part B has focused on patients with PMD. For all parts of the trial, PRAX-114 was generally well-tolerated. In Parts A and C, we observed marked improvements in depression scores in MDD patients within two weeks of treatment that were maintained throughout the treatment period. We expect complete topline data from Part B of the trial in the second half of 2021. In October 2020, we submitted an Investigational New Drug application, or IND, to support the initiation of a Phase 2/3 clinical trial in the United States. At the end of the 30-day review period, the U.S. Food and Drug Administration, or the FDA, notified us that the IND was placed on full clinical hold pending the resolution of certain non-clinical pharmacology and toxicology matters. We subsequently interacted with the FDA to gain agreement on a path to initiate the clinical study, which included a proposal to submit available non-clinical data while other good laboratory practice, or GLP, reproductive toxicology studies were being completed. Based on this submission, the FDA removed the clinical hold in March 2021. We are operationally ready and intend to initiate the Phase 2/3 monotherapy MDD trial by the end of March 2021. If positive, the Phase 2/3 trial is intended to serve as one of two registrational trials required by the FDA to support clinical efficacy for monotherapy treatment of MDD, and we expect topline data in the first half of 2022. In addition to the Phase 2/3 monotherapy trial, we intend to initiate a Phase 2 dose range finding, or DRF, trial for adjunctive treatment of MDD in the third quarter of 2021 to provide controlled data to support advancing a Phase 3 adjunctive MDD trial and will further inform dose selection for the future Phase 3 monotherapy trial.

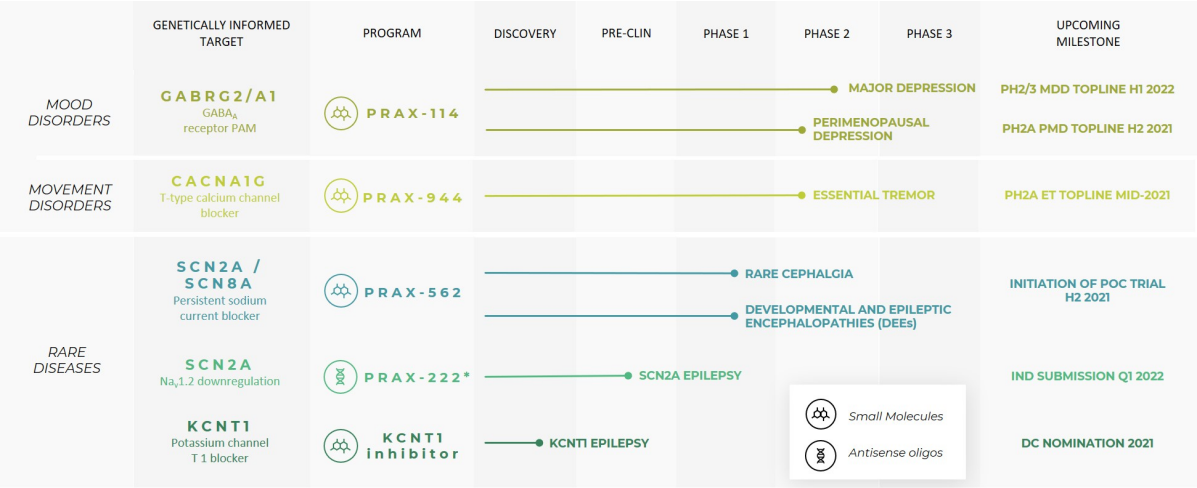
Our second clinical program, PRAX-944, is a potentially differentiated selective small molecule inhibitor of T-type calcium channels for the treatment of Essential Tremor, or ET. ET is a progressive and debilitating movement disorder with action tremor that significantly disrupts activities of daily living, with an estimated prevalence of up to seven million patients in the United States with only one approved pharmacotherapy that is poorly tolerated, resulting in high discontinuation rates. The condition can be debilitating enough that in severe cases, patients opt for invasive brain surgeries when pharmacotherapy fails. Successful development of T-type calcium channel modulators in ET likely requires a pharmacokinetic, or PK, profile with sustained exposure throughout the day and a blunted maximum drug concentration, or Cmax. We believe the therapeutic profile of PRAX-944 coupled with a modified release formulation allows the potential for PRAX-944 to be a differentiated therapy. We have evaluated the safety and tolerability of PRAX-944 in over 150 healthy volunteers in five separate clinical trials. We have studied the safety of PRAX-944 modified release formulation with titration up to 120mg/day and no maximum tolerated dose, or MTD, has been identified. We are currently conducting a Phase 2a proof-of-concept, open-label

trial, in ET patients. Preliminary site data from six participants in the low dose cohort showed tremor reduction, which compares favorably to the standard of care agents and historical placebo response. Based on the observed safety profile in the healthy volunteer titration study and the safety and preliminary efficacy data in ET participants administered up to 40mg daily, we have added a second cohort to the ongoing ET Phase 2a trial where patients will be titrated to a dose of up to120mg/day of PRAX-944. We have also included a randomized, double-blind, placebo-controlled withdrawal phase to this later cohort in the trial, where participants will either be maintained on their final open-label dose or switched to placebo. We plan to announce topline open-label safety, tolerability and efficacy data, for the high dose cohort, in mid-year 2021. In addition, we plan to start a Phase 1 trial to explore short titration schemes by mid-2021 and to initiate a Phase 2b randomized controlled trial in ET in late 2021.

Our most advanced rare disease product candidate and third clinical program, PRAX-562, is the first selective persistent sodium current blocker in development for the treatment of a broad range of rare, devastating CNS disorders, such as severe pediatric epilepsies and rare adult cephalgias. To date, PRAX-562 has demonstrated pharmacological activity in preclinical in-vivo models at generally well-tolerated doses. We initiated a Phase 1 trial of PRAX-562 in Australia to evaluate the safety, tolerability, PK and effects on an exploratory electroencephalography, or EEG, biomarker in up to 129 adult healthy volunteers. The single ascending dose, or SAD, portion up to the maximum planned dose has been completed with no dose limiting toxicities and the study has advanced to the multiple ascending dose, or MAD, phase. We anticipate initiating the first proof-of-concept trial in patients with rare adult cephalgias, including Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing, or SUNCT, Short-lasting Unilateral Neuralgiform headache with Autonomic symptoms, or SUNA, and Trigeminal Neuralgia, or TN, in the second half of 2021. The scope of the initial study has been expanded to include TN in addition to SUNCT and SUNA. In January 2021, the FDA granted rare pediatric disease designation for PRAX-562 for the treatment of SCN2A and SCN8A developmental epileptic encephalopathies, or SCN2A-DEE and SCN8A-DEE, respectively.

In addition to our clinical programs, our most advanced preclinical stage program is PRAX-222, an antisense oligonucleotide, or ASO, designed to decrease the expression levels of the protein encoded by the gene SCN2A in patients with gain-of-function, or GOF, mutations in epilepsy. The FDA has granted both rare pediatric disease and orphan drug designations for PRAX-222 for the treatment of SCN2A-DEE. We have one disclosed discovery program in development for KCNT1 related epilepsy and in March 2021 we have entered into an innovative research collaboration with The Florey Institute of Neuroscience and Mental Health to develop three additional novel ASOs for the treatment of patients with severe genetic epilepsies, including a novel approach targeting SCN2A loss-of-function, or LOF mutations.

Below is a summary of our portfolio of disclosed programs, addressing either broad psychiatric and neurologic conditions or rare diseases. We own global commercialization rights for all of our product candidates.



* PRAX-222 is a collaboration with Ionis Pharmaceuticals, or Ionis, and RogCon Inc. Ionis is eligible to receive royalties as a percentage of net product sales worldwide in the low-20s.

Our company was founded by scientific innovators Kiran Reddy, M.D., David Goldstein, Ph.D. and Steven Petrou, Ph.D., who have pioneered work to identify and characterize de novo mutations in several dozen genes believed to cause a number of forms of severe pediatric epilepsies. These genes regulate key neuronal circuits in the brain which, when dysregulated, can result in severe seizure phenotypes as well as comorbid developmental delays, cognitive deficits, sensory-motor issues and often early death. Further, based on our understanding of a body of preclinical and clinical evidence, we now believe that these genes also play critical roles in the predisposition to other more prevalent neurologic and psychiatric disorders, such as mood disorders, movement disorders, pain syndromes, autism, migraine and schizophrenia, making them attractive targets for therapeutic intervention for a wide range of CNS disorders.

We have attracted a talented team of scientists and researchers in genetics and biology, chemistry and translational medicine as well as business leaders with established track records of successfully executing innovative drug discovery and development programs. Our Chief Executive Officer, Marcio Souza, previously served as Chief Operating Officer at PTC Therapeutics, Inc. and was instrumental in the development and commercialization of multiple approved products while at NPS Pharmaceuticals, Inc., Shire Human Genetic Therapies Inc. and Sanofi Genzyme Corporation. Our Chief Medical Officer, Bernard Ravina, M.D., previously Chief Medical Officer at Voyager Therapeutics, Inc., is a neurologist and movement disorder specialist who brings decades of neurologic drug development experience from roles at Biogen, the University of Rochester and the NIH's Institute of Neurological Disorders and Stroke.

Our Approach

Each of our programs is based on four key principles that we believe will both increase the probability of success and allow us to efficiently translate insights into high-impact therapies for patients and society:

1. ***Focus on therapeutic targets identified through human genetics.*** Numerous CNS disorders are caused by an imbalance of excitation and inhibition in neuronal circuitry. By applying insights derived from the genetics of pediatric epilepsies, we have identified biological targets that we believe are implicated in determining neuronal excitability, not only in epilepsies, but also in a variety of more prevalent CNS disorders. For example, human genetics points to the relevance of the GABAergic system where mutations in $GABA_A$ receptors are associated with a number of rare pediatric epilepsies. The GABAergic system is also implicated in MDD, where enhancing $GABA_A$ activity is believed to be beneficial. As our understanding of the genetic underpinning of these disorders evolves, we plan to continually apply learnings to expand and advance our portfolio.
2. ***Utilize translational tools to validate the potential of our targets and product candidates.*** We leverage a number of translational tools to both confirm pharmacodynamic effects of our product candidates in the brain and establish on-mechanism effects, which we believe will result in an increased probability of success in the clinic. Our programs utilize target-specific EEG endpoints to serve as robust markers of pharmacological engagement of the drug target and novel transgenic animal models to assess the therapeutic activity of our molecules. We expect these tools, along with rigorous preclinical PK and pharmacodynamic characterization of our molecules will position us to more efficiently translate preclinical findings into clinical utility.
3. ***Pursue efficient, rigorous clinical development paths to proof-of-concept in humans***. Our development strategies are focused on defining efficient paths to demonstrate the safety and therapeutic activity of our programs in humans. We select indications that we believe will enable the early demonstration of desired effect in a relatively small patient sample and we focus on clinical endpoints that both minimize inter-patient variability and offer a clear connection between pharmacodynamic effects and clinical measures that are meaningful to patients, physicians and regulatory agencies. Our global network of contract research organizations, or CROs, and scientists affords us the flexibility to conduct research and development activities in diverse geographic locations to accelerate our development timelines and limit geographic risks.
4. ***Apply patient-centric development strategies.*** We pursue the development of candidates that address the treatment needs of patients and the treating community, including targeting the underlying disease pathology versus just symptom management. We intend to develop therapies that provide patients long-term relief from their disorders and significantly reduce the overall burden to patients and caregivers. Our development strategies are tailored to demonstrate these benefits.

Our Strategy

Our goal is to translate genetic insights into high-impact therapies for millions of people suffering from CNS disorders characterized by imbalance of neuronal excitation-inhibition. Key components of our strategy include:

- **Advance PRAX-114 in MDD and PMD toward regulatory approval and commercialization.** PRAX-114 is a potentially differentiated GABAA receptor PAM currently in Phase 2a development for the treatment of MDD and PMD. We observed marked improvements in depression scores in MDD patients within two weeks of treatment that were maintained throughout the treatment period. We are operationally ready and intend to initiate a Phase 2/3 trial in the United States and Australia by the end of March 2021. If positive, the Phase 2/3 trial in monotherapy MDD is intended to serve as one of two registrational trials required by the FDA to support clinical efficacy for the treatment of MDD, and we expect topline data in the first half of 2022. In addition to the Phase 2/3 monotherapy trial, we intend to initiate a Phase 2 DRF trial for the adjunctive treatment of MDD in the third quarter of 2021 to inform dose selection for Phase 3 monotherapy and provide controlled data to support advancing a Phase 3 adjunctive MDD trial. We are currently conducting a Phase 2a trial in Australia in PMD and expect to announce topline data in the second half of 2021. We intend to develop PRAX-114 in the United States and in other countries as both a monotherapy and adjunctive therapy for MDD and PMD for both acute and maintenance treatment. For a detailed description of the risks related to the development and commercialization of our product candidates, please refer to the section entitled “Risk Factors” in this Annual Report on Form 10-K.
- **Advance PRAX-944 in ET toward regulatory approval and commercialization.** PRAX-944 is a potentially differentiated selective small molecule inhibitor of T-type calcium channels in development for ET. During clinical development of PRAX-944, we have evaluated the safety and tolerability of PRAX-944 in over 150 healthy volunteers in five separate clinical trials. We have studied the safety of the PRAX-944 modified release formulation with titration up to 120mg/day and no MTD has been identified. We are currently conducting a Phase 2a proof-of-concept trial in Australia and New Zealand in ET patients. Preliminary site data from six participants of the low dose cohort showed tremor reduction, which seems to compare favorably to the standard of care agents and historical placebo response. Based on the observed safety profile and the ET participants administered up to 40mg daily, we have amended the ongoing ET trial to include a second cohort that will titrate in an open-label fashion up to 120mg daily. We have also included a randomized, double-blind, placebo-controlled withdrawal phase to the trial, where participants will either be maintained on their final open-label dose or switched to placebo. We plan to announce topline open-label safety, tolerability and efficacy data for the high dose cohort in mid-year 2021. In addition, we plan to start a Phase 1 trial to explore short titration schemes in mid-year 2021 and to initiate a Phase 2b randomized control trial in ET in late 2021. For a detailed description of the risks related to the development and commercialization of our product candidates, please refer to the section entitled “Risk Factors” in this Annual Report on Form 10-K.
- **Build a rare disease franchise.** We are advancing several programs for patients with rare diseases. We have six rare disease programs in our pipeline, including PRAX-562, which we believe represents the first selective persistent sodium current blocker in development for the treatment of a number of rare CNS diseases with limited or no treatment options. The current Phase 1 trial has completed the SAD portion up to maximum planned dose, with no dose limiting toxicities, and has advanced to MAD evaluation. We anticipate the initial proof of concept trial in patients to initiate in the second half of 2021. The clinical development plan for PRAX-562 encompasses exploring the broad potential for the mechanism of action in rare diseases through proof-of-concept trials in rare adult cephalgia patients and then expanding into a range of rare pediatric Developmental and Epileptic Encephalopathies, or DEEs. Given the overlapping biology, phenotypic presentation and clinical execution considerations, we believe that we can translate learnings for the treatment of DEEs across our portfolio with thorough knowledge to bring additional treatments to market. Our most advanced pre-clinical program is PRAX-222, an ASO for lowering the expression levels of the protein encoded by the gene SCN2A, in patients with GOF mutations of SCN2A epilepsy. In January 2021, the FDA granted rare pediatric disease designation for PRAX-562 for the treatment of SCN2A-DEE and SCN8A-DEE, and both rare pediatric disease and orphan drug designations for PRAX-222 for the treatment of SCN2A-DEE. Additionally, we have entered into an innovative research collaboration with The Florey Institute of Neuroscience and Mental Health to develop three novel ASOs for the treatment of rare epilepsy targets.
- **Maximize the value of our product candidates through select indication expansion.** All of our clinical stage product candidates address targets with therapeutic potential beyond their lead indications. As these programs advance through the clinic, we will pragmatically evaluate indication expansion and

consider subsequent clinical development that will expand the labels of our product candidates to encompass other compelling opportunities at a time when we determine to be most efficient.

- **Advance our understanding of genetics and neuronal imbalance to maintain our leadership and continue to build our pipeline.** Advances in the field of genetics continue to elucidate new insights into mutations that drive neuronal imbalance. Our team is deeply engaged in these efforts, which we believe will enable us to pursue a pipeline discovery and development strategy grounded in these learnings and coupled with our drug discovery, translational and clinical experience. As our knowledge base continues to grow, we believe our potential to deliver additional differentiated medicines for patients will grow as well.
- **Commercialize our products in the United States and globally.** To realize the full potential of our product candidates, we intend to build a sales and marketing infrastructure to reach prescribers in the United States. In order to capitalize on market opportunities outside the United States, we may pursue collaborations with reputable pharmaceutical companies that have established presences in key geographies.

BROAD PSYCHIATRY AND NEUROLOGY PROGRAMS

PRAX-114

We are developing PRAX-114, an extrasynaptic GABAA receptor preferring positive allosteric modulator, or PAM, for the treatment of patients suffering from MDD and PMD. PRAX-114 is a potentially differentiated treatment for a broad MDD population, as both a monotherapy and adjunctive therapy for both acute and maintenance use. We have a multi-cohort, three-part Phase 2a clinical trial ongoing in Australia. We observed marked improvements in depression scores in MDD patients in Parts A and C of this trial within two weeks of treatment that were maintained throughout the treatment period. We expect complete topline data from Part B of the trial for the treatment of patients suffering from PMD in the second half of 2021. In October 2020, we submitted an Investigational New Drug application, or IND, to support the initiation of a Phase 2/3 clinical trial in the United States. We are operationally ready and with the recent clearance of our IND we intend to initiate a Phase 2/3 monotherapy MDD trial in the United States and Australia by the end of March 2021. If positive, the Phase 2/3 trial is intended to serve as one of two registrational trials required by the FDA to support clinical efficacy for the monotherapy treatment of MDD, and we expect topline data in the first half of 2022. In addition to the Phase 2/3 monotherapy trial, we intend to initiate a Phase 2 DRF trial for the adjunctive treatment of MDD in the third quarter of 2021 to inform dose selection for a Phase 3 monotherapy trial and to provide controlled data to support advancing a Phase 3 adjunctive MDD trial.

There is significant unmet medical need in MDD and PMD with over 22 million individuals suffering from depressive symptoms in the United States. Current pharmacological interventions suffer from multiple shortcomings including slow onset of efficacy, low remission rates and side effects that limit patient compliance. PRAX-114 targets an increasingly well-understood neuronal circuit in the brain that we believe, when properly modulated, can result in a robust and rapid antidepressant effect with an advantageous safety and tolerability profile.

We believe that our PRAX-114 program has several advantages as compared to currently available therapies and product candidates in the GABAA PAM therapeutic class:

- **Planned Path to a Potential Broad MDD Label.** We have been diligently pursuing our strategy to advance PRAX-114 towards regulatory approval and commercialization to support a broad label in MDD that can be easily integrated into standard clinical practice. We intend to develop PRAX-114 in the United States and in other countries as both a monotherapy and adjunctive therapy for MDD for both acute and maintenance treatment. If positive, our planned Phase 2/3 trial is intended to serve as one of two registrational trials required by the FDA to support clinical efficacy for the monotherapy treatment of MDD. In addition to the Phase 2/3 monotherapy trial, we intend to initiate a dose range finding trial for the adjunctive treatment of MDD by the end of mid- 2021 to inform dose selection for Phase 3 and provide controlled data to support advancing a Phase 3 adjunctive MDD trial.

- **Wider Therapeutic Window.** We have determined that PRAX-114 is approximately 10-fold more selective PAM of the extrasynaptic form of GABAA receptors compared to the synaptic form. In healthy volunteers, we have observed PRAX-114 to markedly increase quantitative electroencephalography, or qEEG, power in the alpha and beta-frequency bands—unlike GABAA receptor PAMs that only modulate synaptic GABAA receptors, such as benzodiazepines, or that are equipotent at synaptic and extrasynaptic

receptors, such as allopregnanolone, which decreases power in the alpha frequency band. We believe these data suggest that PRAX-114 has a differentiated pharmacological profile to other GABAA PAMs at therapeutic doses due to the relatively selective activation of extrasynaptic GABAA receptors. By preferentially modulating extrasynaptic GABAA receptors, we believe PRAX-114 is able to uniquely activate the GABAergic target and has the potential to mediate antidepressant and anxiolytic activity without the significant sedation observed with less selective neuroactive steroids.

- **Simple Nightly Dosing.** We believe the ability to administer PRAX-114 and achieve targeted exposures, with or without food, is key for clinical and commercial success in MDD. This is also critical for a patient-centric therapy because many patients with depression suffer from appetite disturbances. We have observed fast absorption of PRAX-114 within one to three hours of dosing and a predictable PK profile across multiple trials. Based on clinical findings to date, PRAX-114 achieves reproducible overall exposure (*i.e.*, area under the concentration curve, or AUC) across a wide range of administration conditions, demonstrating consistent exposure when administered with or without food and at different times of day, whereas other GABAA PAM neuroactive steroids may require food to achieve therapeutic levels. While AUC is unaffected by administration conditions, nightly dosing has been demonstrated to reduce Cmax thereby enhancing the potential for improved tolerability.
- **Sustained Administration**. After consultation with the FDA and other stakeholders in MDD and PMD therapy, we designed our Phase 2/3 trial of PRAX-114 to include 28-day nightly dosing to evaluate patients at 14 days to assess the rapidity and robustness of response and 28 days to measure initial of effect. We believe that having a dosing paradigm consistent with the duration of depressive episodes and easily integrated into standard clinical practice will provide the most substantial benefit to patients in controlling their disease, further differentiating PRAX-114 from other GABAA PAMs.
- **Indication Expansion.** Based on the novel pharmacology of PRAX-114 and its generally well-tolerated profile in clinical trials to date and our knowledge of disorders related to MDD that may be treatable through the GABAA PAM mechanism, we believe PRAX-114 is suitable for potential development across a wide-range of indications in psychiatry and neurology, providing for potentially sizable expansion opportunities to explore in addition to MDD.

Major Depressive Disorder

Major Depressive Disorder, or MDD, is a chronic psychiatric condition causing severe impairments that interfere with the ability to carry out life activities. An MDD episode is characterized by a period of at least two weeks of persistent depressed mood and/or the loss of interest or pleasure in activities, accompanied by sleep and appetite disturbance, fatigue, concentration difficulty, cognitive impairment, feelings of guilt, psychomotor retardation or agitation and suicidal ideation. MDD is one of the most prevalent psychiatric disorders. In the United States, approximately 19 million adults, or 7% of the adult population suffer from MDD, with episodes lasting on average six to eight months. It is estimated that MDD affects more than 300 million people worldwide. Moreover, the prevalence of depression has increased during the COVID-19 pandemic in the US and globally. In the United States, depression symptoms have increased by more than 3-fold overall during the COVID-19 pandemic. The most dramatic increases are reported in moderate, moderately severe and severe depression symptoms, with a 2.6-fold, 3.7-fold, and 7.5-fold rise, respectively, relative to a pre-COVID-19 pandemic period.

MDD is a recurrent psychiatric condition that frequently requires long-term treatment, with the ultimate goal of achieving remission. MDD is associated with an elevated risk of suicide, underscoring the need for rapid and effective treatment. The most explored pharmacological mechanisms for treating MDD target monoamine neurotransmitters. Drugs in this class include selective serotonin reuptake inhibitors, or SSRIs, serotonin and norepinephrine reuptake inhibitors, or SNRIs, bupropion and atypical antipsychotic medications. SSRIs and SNRIs are associated with significant side effects, including weight gain, sexual dysfunction, drowsiness, nausea, insomnia and discontinuation syndrome. Atypical antipsychotics indicated for adjunctive treatment of insufficient clinical response are associated with weight gain, sexual dysfunction, metabolic syndrome and movement disorders. The side effect profile of current antidepressant standard of care negatively impacts treatment outcomes, quality of life and adherence in MDD patients.

Approximately seventy percent of MDD patients fail to achieve remission with first line treatment. Further, those patients that are responsive typically require approximately six to eight weeks of treatment to show a clinically meaningful response. Slow onset of action is a substantial unmet need in MDD, with some of the most commonly prescribed antidepressants showing a reduction in the Hamilton Depression Scale, or HAM-D, of approximately 6- to 8-points and a difference from placebo of approximately 1-2 points at Week 2 (Figure 1). Moreover, approximately

40% of patients on therapy discontinue treatment due to either a loss of response or adverse side effects. Finally, 33% of patients fail to respond after treatment with three or more different standard of care therapies.

Among the MDD patients who experience a response to treatment, the majority do not achieve remission. Even for patients deemed responsive, disease burden often persists through the presence of residual depression symptoms that lead to an ongoing negative impact on home, interpersonal and occupational functioning, as well as a significantly increased risk of relapse of the full depressive syndrome and worse comorbid outcomes, including suicide.

Despite the numerous and long-standing antidepressant treatment options, there continues to be an unmet need for antidepressants that provide rapid onset of effect, higher remission rates, efficacy throughout the depressive episode and an improved tolerability profile that is aligned with the clinical care and the course of MDD and its accompanying comorbid symptoms.

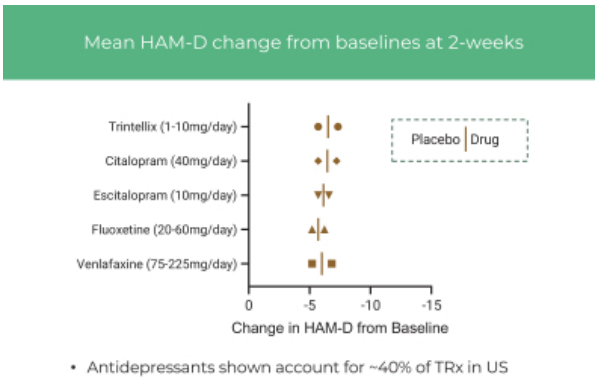


Figure 1. Reduction of HAM-D from baseline of commonly prescribed antidepressants and placebo at Week 2.

Perimenopausal depression

Perimenopause is the transition between the onset of hormonal and clinical features of menopause and the one-year period after the final menses. Perimenopause can last up to 10 years. Women with no lifetime history of major depression who have entered the perimenopause period are found to be twice as likely to develop significant depressive symptoms as women who have not entered the perimenopause period. Notably, the increased risk for depression during the perimenopausal transition has been observed to decline substantially after the final menstrual period.

There are over 30 million women in the United States between the ages of 45 and 59 years who are at risk of developing perimenopause symptoms, with an estimated three million developing mood symptoms such as depression, anxiety, irritability and suicidal ideation and behavior and an estimated 20 million women developing associated vasomotor symptoms or hot flushes. Notably, suicide rates are the highest among women 45 to 59 years of age and have increased by approximately 42% in recent decades.

Although primarily viewed as a reproductive transition, the symptoms of perimenopause are largely neuropsychiatric in nature. Neurological symptoms that emerge during perimenopause are indicative of disruption in multiple estrogen and progesterone-regulated systems such as thermoregulation, sleep, circadian rhythms and sensory processing and affect multiple domains of cognitive function. Perimenopausal depression also appears to impact the clinical symptomatology of menopause, with the presence of depression being associated with a greater degree of menopausal hot flushes than in women without perimenopausal depression.

There is substantial evidence that fluctuations in estrogen and progesterone, the precursor of the endogenous neuroactive steroid allopregnanolone, a GABAA receptor PAM, are in part responsible for the mood changes, hot flushes and other neurologic symptoms of perimenopause. Similar to MDD, SSRIs and SNRIs have shown limited efficacy in treating perimenopausal depression. There remains an unmet medical need for effective treatment of core depression symptoms and associated physical symptoms of menopause.

A GABAA receptor PAM, like PRAX-114, that potentiates the activity of endogenous neuroactive steroids on GABAA receptors, may offer broader therapeutic benefit compared to current standard of care antidepressants.

GABAA in depression

Gamma-aminobutyric acid, or GABA, is the principal neurotransmitter mediating neuronal inhibition in the brain. Neurons that produce GABA, known as GABAergic neurons, are present throughout the brain, representing between 20 percent and 40 percent of all neurons depending on the region. Their primary role is to balance and fine tune excitatory neurotransmission of various neuronal circuits. Whole-exome sequencing has identified GABAA receptor mutations as an important cause in a range of neurological conditions, underscoring their importance as central regulators of excitatory and inhibitory balance in the brain.

It is well established that GABAergic signaling is impaired in patients with MDD and other stress-related mood disorders. GABA levels, levels of the GABA synthesizing enzyme GAD67, as well as GABAA receptor levels, have been shown to be reduced in brains of patients with MDD. In addition, decreased GABAergic neuron function, most notably in the prefrontal cortex, has been documented in MDD patients and in preclinical animal models of depression. Endogenous neuroactive steroids, such as allopregnanolone and pregnanolone or synthetic derivatives thereof, such as PRAX-114, are known to potentiate the activity of GABAA receptors. Both human and animal data reveal an important role for neuroactive steroids in these GABAergic deficits and levels of endogenous neuroactive steroids are decreased in individuals with MDD and PMD.

Of particular relevance to the PRAX-114 program is the more recently established link between GABAergic signaling, neuroactive steroid levels and stress—a well-established risk factor for MDD and other mood disorders. In preclinical models, exposure to chronic stress leads to reduced neuroactive steroid biosynthesis and reduced GABAergic inhibition in depression-relevant brain circuits. This ultimately results in increased anxiety and depression-like behaviors. In particular, it has been shown that stress causes long-lasting loss of GABAergic inhibition in the amygdala, a brain region central to the stress response involved in controlling emotions. This reduced inhibition causes increased activity of the amygdala and is associated with an exaggerated stress hormone response.

We believe that enhancing modulation of GABAA receptors in patients with depression and anxiety has the potential to restore normal function in these circuits, leading to broad applications in mood and anxiety disorders.

GABAA receptors: The target of PRAX-114

PRAX-114 is a small molecule neuroactive steroid that acts as a positive allosteric modulator of GABAA receptors. Positive allosteric modulators, or PAMs, are substances that bind to a receptor, such as GABAA, to enhance that receptor's response to its endogenous ligand (or endogenous agonist). GABAA PAMs bind to a distinct site from endogenous GABA, an allosteric binding site, and do not activate the receptor in the absence of the GABA. Allosteric modulators are believed to have improved safety profiles and are less likely to result in tachyphylaxis, or decreasing drug response, as compared to agonists. GABA exerts its effects through binding to two types of GABAA receptors, synaptic and extrasynaptic receptors, which differ in their protein subunit composition, physical location on the cell surface and functional role in modulating neuronal circuits.

GABAA receptors are composed of five subunits which include two alpha, two beta and a fifth subunit (either gamma or delta) that is dependent on the type of receptor. Synaptic GABAA receptors, which are located in the synapse of neurons, contain a gamma subunit while GABAA receptors located outside of the synapse, referred to as extrasynaptic GABAA receptors, contain a delta subunit. Molecules that act as PAMs of only the synaptic GABAA receptor, such as benzodiazepines, bind to sites situated at the interface between the alpha and gamma subunits. Molecules that act as PAMs of both synaptic and extrasynaptic GABAA receptors, such as the neuroactive steroids allopregnanolone and PRAX-114, bind to sites situated at the interface between the alpha and beta subunits present in both types of receptors. The figure below displays the synaptic binding site for drugs such as benzodiazepines, and the distinct extrasynaptic and synaptic binding sites for neuroactive steroids, such as allopregnanolone and PRAX-114.

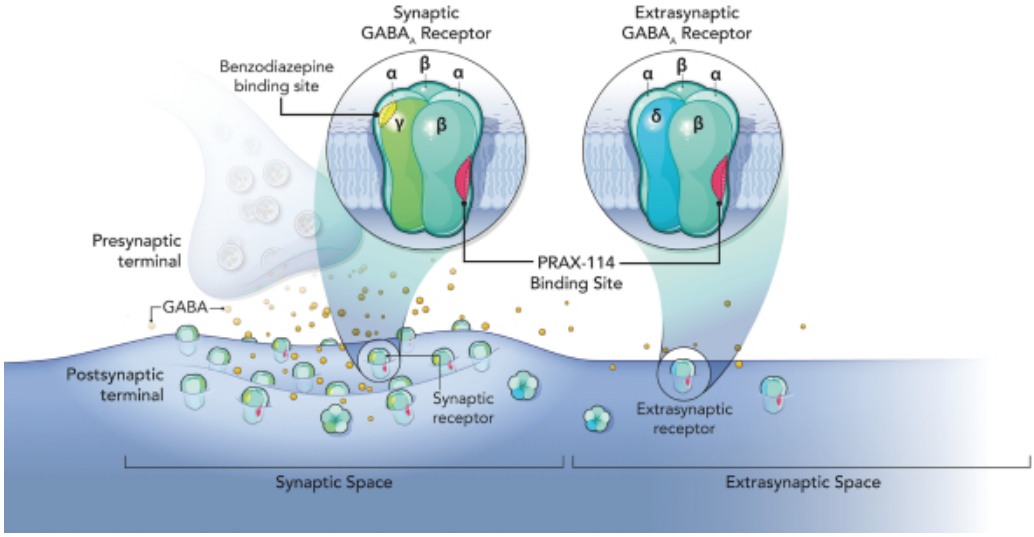


Figure 2. GABAA synaptic and extrasynaptic receptors differ in structure and function.

Synaptic and extrasynaptic GABAA receptors have distinct functions. Synaptic GABAA receptors are responsible for short-lasting, or phasic, inhibition of neurons in response to GABA release at the synapse. By contrast, extrasynaptic GABAA receptors drive continuous, or tonic, low-level inhibition of neurons in response to lower ambient levels of GABA outside of the synapse. While synaptic receptors can respond quickly to stimulation and network demand, extrasynaptic receptors have a broader modulatory role, serving to continuously modulate the overall excitability of neurons.

Molecules that act as PAMs of only the synaptic GABAA receptor, such as benzodiazepines and barbiturates, are used for sedation, sleep induction and anxiolysis, and have anticonvulsant and muscle relaxant properties. These drugs have potent and rapid onset of activity but have not demonstrated antidepressant effects.

Allopregnanolone is an endogenous neuroactive steroid and a PAM of both the extrasynaptic and synaptic GABAA receptors, which has been associated with antidepressant activity. However, allopregnanolone also has shown significant dose-limiting sedative activity, which we believe is likely mediated at least partially by its effects on synaptic GABAA receptors. Despite this limitation, a formulation of allopregnanolone has been approved and is marketed as Zulresso™ to treat post-partum depression.

The distinct effects mediated by these classes of GABAA PAMs suggest that modulation of extrasynaptic GABAA receptors is responsible for the antidepressant effects demonstrated by allopregnanolone. One of the goals for a next generation neuroactive steroid, such as PRAX-114, is to preferentially modulate extrasynaptic GABAA receptors while minimizing the sedative impact from modulation of synaptic GABAA receptors.

PRAX-114 preference for extrasynaptic GABAA receptors

To assess the relative potency *in-vitro* of PRAX-114-mediated GABAA receptor activation for synaptic and extrasynaptic receptors, we measured the peak current induced by a low concentration of GABA (2 µM) in the presence of increasing concentrations of PRAX-114 in Chinese Hamster Ovary, or CHO, cells expressing either extrasynaptic (α4ß3δ) or synaptic (α1ß2γ2) human GABAA receptors. In this model, PRAX-114 potentiates the GABA-activated current of both extrasynaptic and synaptic GABAA receptors, but was approximately 6.4-fold more potent in potentiating the extrasynaptic form of the receptor than the synaptic form based on the concentration that gives half-maximal response, or EC50. At a concentration that activates extrasynaptic GABAA receptors to the equivalent of full activation by the endogenous ligand GABA (~260 nM, 300% potentiation of 2µM GABA), PRAX-114 led to 10.5-fold greater potentiation of extrasynaptic GABAA receptors than synaptic GABAA receptors (29%) (Figure 3, Table 4).

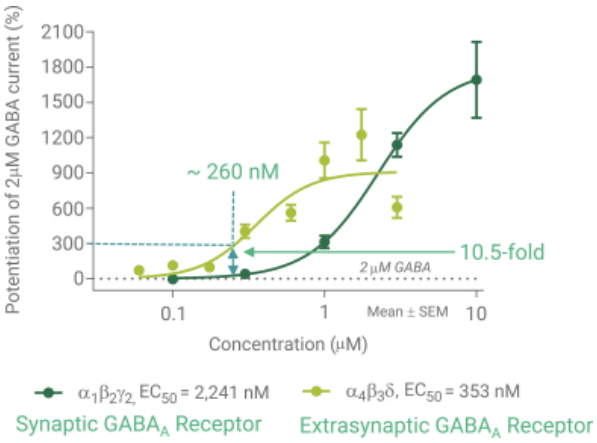


Figure 3. At 300% extrasynaptic GABAA receptor potentiation (equivalent to ~100% activation by endogenous agonist GABA), PRAX-114 led to 10.5-fold greater potentiation of extrasynaptic GABAA receptors than synaptic GABAA receptors (29%).

In the same assay, at the same level of extrasynaptic GABAA receptor potentiation (300%), other GABAA receptor PAM neuroactive steroids in development, or on the market, demonstrated only 0.4 to 2.6 fold greater potentiation of extrasynaptic GABAA receptors, which compares unfavorably to the 10.5 fold observed for PRAX-114 (Table 4). Based on these assay conditions, we believe that the differentiated preference at extrasynaptic GABAA receptors by PRAX-114 will allow it to achieve high levels of extrasynaptic GABAergic activation with improved tolerability.

	Dosing	α4β3δ % potentiation (Equivalent of full activation by GABA)	α1β2γ2 % potentiation	Fold potentiation α4β 3δ/α1β2γ2
PRAX-114	**Oral**	**300 %**	**29 %**	**10.5**
Zuranolone	Oral	300 %	117 %	2.6
Ganaxolone	IV, Oral	300 %	794 %	0.4
Zulresso™ (brexanolone)	IV	300 %	306 %	1.0

Table 4. Comparison of the degree of *in-vitro* GABAA receptor potentiation achieved by PRAX-114 and other neuroactive steroid GABAA PAMs. α4β3δ : extrasynaptic GABAA receptors, α1β2γ 2: synaptic GABAA receptors.

PRAX-114 clinical development in depression

We have initiated clinical development for PRAX-114 in mood disorders. To date, two Phase 1 clinical trials of PRAX-114 have been completed in healthy volunteers. These studies in 82 healthy volunteers showed PRAX-114 to be generally well-tolerated, with dose-dependent pharmacodynamic activities. In our ongoing Phase 2a clinical trial in Australia, we observed marked improvements in depression scores in MDD patients within two weeks of treatment that was maintained throughout the treatment period. We have also conducted a pharmacokinetics bridging study in healthy volunteers that confirmed our generally well-tolerated profile and consistency in exposure across a wide range of administration conditions including fed versus fasted and morning versus evening dosing. We are operationally ready and intend to initiate a Phase 2/3 trial in the United States and Australia by the end of March 2021. If positive, the Phase 2/3 trial is intended to serve as one of two registrational trials required by the FDA to support clinical efficacy for monotherapy treatment of MDD, and we expect topline data in the first half of 2022. In addition to the Phase 2/3 monotherapy trial, we intend to initiate a Phase 2 DRF trial for adjunctive treatment of MDD by mid-2021 to inform dose selection for the Phase 3 monotherapy trial and provide controlled data to support advancing a Phase 3 adjunctive MDD trial.

Phase 1 SAD and MAD trials in healthy volunteers

We conducted a Phase 1 randomized, double-blind, placebo-controlled single ascending dose, or SAD, trial of PRAX-114 in healthy volunteers to evaluate safety and tolerability of PRAX-114. This trial enrolled 36 volunteers who were randomized into cohorts dosed with 1mg, 3mg, 10mg, 30mg or 60mg of PRAX-114 or placebo. PRAX-114 was generally well-tolerated and no serious adverse events, or SAEs, were reported in this trial.

We subsequently conducted a Phase 1 randomized, double-blind, placebo-controlled MAD trial in healthy volunteers in Australia to evaluate the safety, tolerability and pharmacokinetics of PRAX-114 and to assess the effect of food on drug exposure. Thirty-six volunteers were randomized to receive daily doses of 15mg, 30mg or 60mg of PRAX-114 or placebo for 14 days. Ten additional volunteers in a food effect cohort received 30mg doses of PRAX-114 when they were in a fasted state or with a high-fat meal.

As part of our MAD trial, we measured the effect of PRAX-114 on the quantitative EEG, or qEEG, to understand the pharmacodynamic effect of PRAX-114 on GABAA receptor activation. An EEG is a real-time non-invasive measure of electrical activity of neurons in the brain. The frequency and amplitude of the detected electrical signals provide insights into brain function and brain state (e.g., awake, deep sleep, etc). qEEG, also called pharmaco-EEG, is a quantitative measure of the changes in brain activity in specific EEG frequency bands in response to treatment with a brain-active compound. Changes in power in the beta frequency band, specifically, are used as a pharmacodynamic biomarker of GABAA receptor activation in response to a brain active compound.

In both the Phase 1 SAD and MAD trials, we observed fast absorption of PRAX-114 within one to three hours of dosing and approximately dose-proportional increases in peak concentration and total drug exposure. In the MAD trial, the half-life of the drug was between 12.2 and 14.8 hours, consistent with a once-daily dosing paradigm. Little or no accumulation of the drug was observed in the multiple dose trial over the ranges of doses tested.

We believe that the simple nightly administration of PRAX-114 with or without food is key for clinical and commercial success in MDD, as many patients struggle with adherence to medication and forcing a dietary regimen would impose further complications in this vulnerable population. In the food effect cohort of the MAD trial, overall drug exposure as measured by area under the concentration curve, or AUC, of PRAX-114 increased by only 1.17-fold in the fed state versus in the fasted state. The primary effect of food was observed in the Cmax, which was 0.64-fold of that observed under fed conditions. These findings indicate that PRAX-114 does not need to be taken with food to achieve therapeutic exposures. According to results presented in a published patent application, zuranolone, a GABAA PAM neuroactive steroid in development for treatment of MDD, exhibited a food effect that resulted in increases in Cmax of approximately 2.88-fold and in AUC of approximately 1.58-fold in the fed versus the fasted conditions (Table 5). We believe this food effect has led to the development of zuranolone requiring administration with a high-fat meal for the compound reliably achieve target exposures. We believe that the absence of a requirement that PRAX-114 be taken with food creates a potential competitive advantage over drugs that may require administration with food to achieve consistent target exposures, and should allow flexibility to adjust to the comorbid changes in appetite and preferences of MDD patients.

Statistical Analysis of the Effect of High-fat Meal for PRAX-114 suspension (30mg)			Statistical Analysis of the Effect of High-fat Meal for Zuranolone capsules (30mg)		
PK Parameter	**Fed/Fasted Ratio**	**90% Confidence Interval**	**PK Parameter**	**Fed/Fasted Ratio**	**90% Confidence Interval**
Cmax (ng/mL)	0.64	**(0.46, 0.88)**	**Cmax (ng/mL)**	2.879	**(2.56, 3.28)**
AUC0-t (h*ng/mL)	1.17	**(0.91, 1.49)**	**AUC0-t (h*ng/mL)**	1.575	**(1.45, 1.69)**

WO2019/051264 Al Patent

Table 5. Food effect clinical studies of PRAX-114 and Zuranolone (WO2019/051264 A1). Subjects were administered a high-fat meal 30 minutes prior to administration of the compound in both studies.

In the MAD trial, PRAX-114 was generally well-tolerated, with no SAEs reported. The reported treatment-emergent adverse events, or TEAEs, were mild to moderate and were consistent with those expected for the mechanism of action. The most common adverse event was somnolence, which is characterized by sleepiness or drowsiness, and was reported by 78% (7/9) of those subjects receiving the 60mg dose; all events of somnolence were mild in severity. Increases in sleepiness as measured by the Stanford Sleepiness Scale occurred between one- and three-hours post-dosing, consistent with the period of peak drug concentrations; sleepiness ratings at the 60mg dose were similar to placebo within 4 hours post-dose. We did not observe a maximally tolerated dose, or MTD.

In our Phase 1 multiple ascending dose trial of PRAX-114 in healthy volunteers in Australia, we also observed the following TEAEs, all of which were mild to moderate in severity:

- 60mg dose (n=9), we observed nervous system disorder TEAEs, of somnolence (77.8% of subjects), headache (33.3% of subjects), dizziness (55.6% of subjects) and hypoaesthesia, or diminished sense of touch (22.2% of subjects). Other TEAEs observed in more than one subject were euphoric mood (22.2% of subjects), hyperhidrosis, or excessive sweating (22.2% of subjects) and muscle twitching (22.2% of subjects).
- 30mg dose (n=9), we observed nervous system disorder TEAEs of somnolence (44.4% of subjects) and headache (22.2% of subjects). Other TEAEs observed in more than one subject were skin irritation (55.6% of subjects) and euphoric mood (22.2% of subjects).
- 15mg dose (n=9), the only TEAE observed in more than one subject was fatigue (22.2% of subjects).
- Placebo group (n=9), we observed fatigue (22.2% of subjects).

TEAEs appearing to be dose related were somnolence, dizziness, headache, euphoric mood and hypoaesthesia.

We measured changes in qEEG power in our Phase 1 MAD volunteers to assess the effect of PRAX-114 on GABAA receptors in the brain on days 1 and 14 of this trial. PRAX-114 produced marked increases in the power of the alpha and beta-frequency bands. Increases in the beta-frequency band are correlated with GABAergic activation, as previously shown by the marketed $GABA_A$ PAMs, allopregnanolone and lorazepam. PRAX-114 distinctly increases the alpha-frequency band, unlike allopregnanolone and lorazepam, which have shown to decrease the power of the alpha-frequency (Figure 6). We believe this qEEG profile of PRAX-114 is consistent with its extrasynaptic $GABA_A$ receptor preference and differentiated pharmacological profile relative to benzodiazepines and other GABAA PAMs in the class.

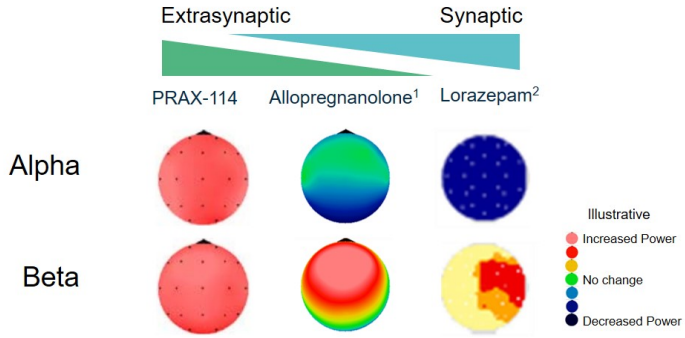
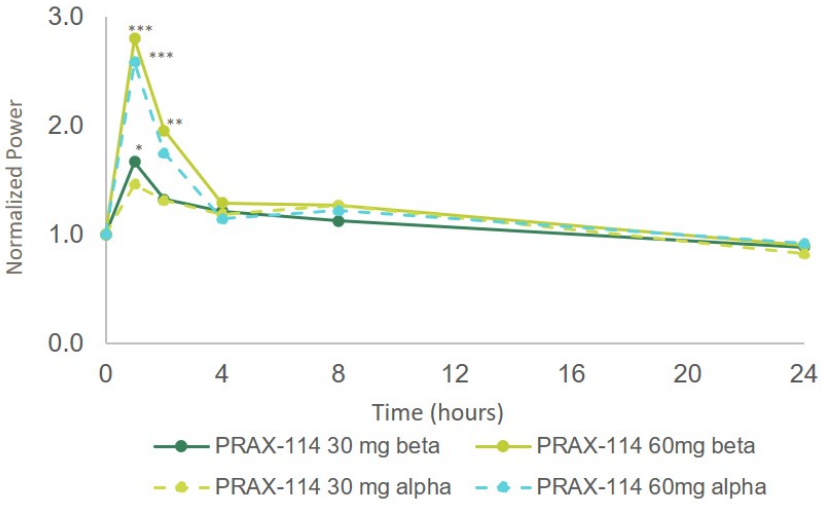


Figure 6. GABAA PAM qEEG signal of PRAX-114, allopregnanolone, and lorazepam. (Adapted from 1. SAGE R&D Day Presentation, 2. Gilles et al. 2002)

Moreover, the PRAX-114 increases in alpha and beta-frequency were strongly correlated with dose and PRAX-114 levels in the blood. In these healthy volunteers at one hour post-dose on Day 1, PRAX-114 30mg resulted in an average increase in qEEG alpha and beta power of approximately 1.5-fold and 1.6-fold compared to baseline, and 60mg resulted in an increase in this measure of 2.6-fold and 2.8-fold compared to baseline, respectively (Figure 7). The effects on the qEEG alpha and beta power were sustained at Day 14. These data show that PRAX-114 engaged GABAA receptors in the brain and produced consistent effects on qEEG within the first hour after dosing with similar effects on Days 1 and 14. This finding also supports comparison and translation of the

pharmacologic activity and qEEG data from the pre-clinical studies, where a 1.6-fold increase in beta power was associated with robust activity in animal models of anxiety and depression and was used to inform dose selection in subsequent clinical trials.



*N= 7-9 human subjects per dose, PRAX-114 only p compared to placebo control, *p < 0.05, ** p < 0.01, *** p < 0.001*

Figure 7. PRAX-114 (30mg and 60mg) showed a robust dose-dependent qEEG signal and target activation that was sustained over 14 days of dosing.

Notably, in the MAD study, PRAX-114 showed increases in beta power up to 2.8-fold without achieving a MTD or demonstrating any SAEs, and a higher dose of 80mg dosed as a single dose in healthy participants for 14 days was also generally well-tolerated in a subsequent clinical trial in MDD, summarized below. In a separate study, another molecule in development in the class resulted in degrees of sedation that were not tolerated at doses that resulted in increases in beta power by approximately 1.7-fold compared to baseline. We believe this highlights the extrasynaptic GABAA receptor preference and unique pharmacological profile of PRAX-114 and its ability to achieve high levels of GABAergic activation with improved tolerability.

This improved tolerability profile of PRAX-114 offers the potential for a wider therapeutic window, increased adherence and a wider dose range for MDD patients.

Phase 2a trial in patients with depression

Based on the observed pharmacology in the Phase 1 trials, we are currently conducting a three-part, open-label, Phase 2a trial in Australia to assess the safety and efficacy of PRAX-114 in patients with moderate to severe MDD or PMD. We have completed Parts A and C of this Phase 2a trial and Part B is ongoing.

Part A results

Part A of the open-label trial included two weeks of treatment and was designed to evaluate the timing and magnitude of the antidepressant effects of PRAX-114 across a range of doses in patients with MDD. Patients were required to be between the ages of 18 and 65 and to have moderate to severe MDD for at least one month as defined by the Hamilton Depression Rating Scale, or HAM-D, score of 22 or higher. The HAM-D, one of the most widely-used clinical rating scales for depression, was the main assessment used to quantify levels of depression in these patients. The 17 items used for scoring this scale cover a wide range of symptoms typically found with depression including mood, suicidal thoughts, insomnia, anxiety, loss of appetite and weight loss. Patients with more severe depression have higher scores. The effect of PRAX-114 was measured by the change in the HAM-D score relative to baseline. Patients who had previously failed to respond to a standard of care antidepressant in their current episode were eligible for inclusion. In addition to HAM-D, other scales used included the Montgomery–Åsberg Depression Rating Scale, or MADRS, the Hamilton Anxiety Rating Scale, or HAM-A, and the Symptoms of

Depression Questionnaire, or SDQ. MADRS is a 10 item rating scale designed to assess the severity of symptoms in a depressive illness. HAM-A is a 14 item scale widely used to measure the severity of anxiety symptoms, including both psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety). SDQ is a 44 item self-reported scale designed to measure the severity of symptoms across several subtypes of depression, including irritability, anger attacks and anxiety.

We selected an initial target dose of 45mg daily of PRAX-114 suspension formulation that was expected to achieve exposures demonstrating full clinical improvement based on the Phase 1 data and qEEG findings. Two additional cohorts were subsequently conducted to assess higher daily doses of 60mg and 80mg PRAX-114 due to the generally well-tolerated profile at 45mg. The first week of treatment was conducted in an inpatient setting to facilitate daily efficacy and safety assessments and then patients were discharged and treated as outpatients for the second week. Patients were instructed to take PRAX-114 at 4:00 PM on Day 1 to support collection of post-dose pharmacokinetics samples and then nightly at 9:30 PM on Days 2-14. Patients were not required to take PRAX-114 with food. Compliance was carefully monitored throughout the duration of the trial, including inpatient and outpatient periods, with the AiCure smartphone adherence monitoring system.

Thirty-three patients were enrolled and completed Part A before the COVID-19 pandemic began impacting clinical trial conduct globally. At baseline, patients had a mean HAM-D total score of 25, ranging from 20 to 33, indicating moderate to severe MDD. Twenty-six of the thirty-three participants had previously received an antidepressant during the current depressive episode but still had moderate to severe MDD. This failure to respond to initial antidepressant treatment has been associated with more severe and refractory depression. The remaining patients were not being treated with any antidepressant for the current episode before enrolling in the trial.

Dosing with PRAX-114 led to a marked improvement in the HAM-D score (Figure 8) within two weeks of treatment. After one week of treatment, least squares, or LS, mean improvements of 15 to 19 points from baseline were noted across the three dose groups. After two weeks of treatment, all 3 dose levels showed improvements from baseline of greater than 13 points with mean improvements from baseline of 14 to 16 points. Across all dose levels, two-thirds of patients were responders (defined as a >=50% reduction in HAM-D) or were clinically in remission (HAM-D<=7) at the end of the 14 day treatment period. Changes in other depression-related scales measured such as MADRS, HAM-A and SDQ were consistent with the changes in HAM-D. While the study was not powered to show differences between dose levels, there was no notable dose response observed, which is common amongst trials of antidepressants.

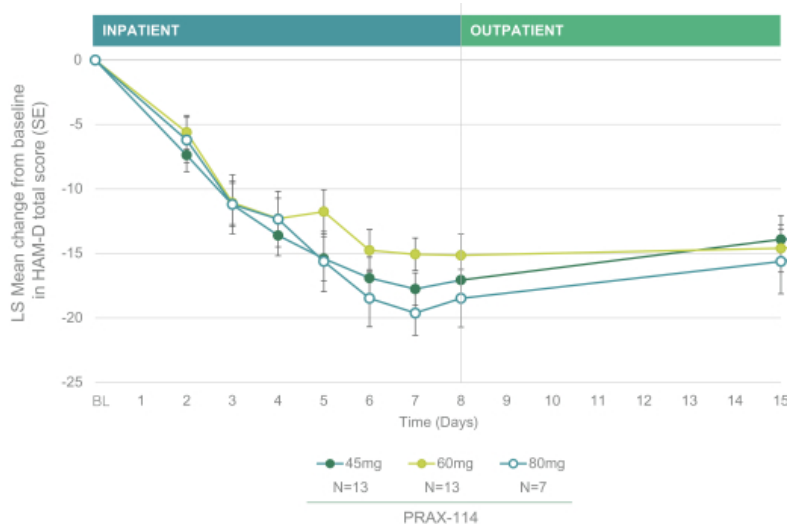


Figure 8. Reduction in HAM-D total score observed in MDD patients treated with PRAX-114.

After 14 days of treatment, patients were monitored for an additional 14 days. During this monitoring period, the core mood symptoms measured by the HAM-D generally remained stable with a slight increase in the insomnia item scores post-treatment.

While our Phase 2a trial is not placebo controlled, prior randomized placebo-controlled MDD trials provide important context for the interpretation of the clinical response. The marked improvements in HAM-D scores seen in MDD patients in Part A within two weeks of treatment compares favorably to published reports on changes in HAM-D scale in clinical trials of approved antidepressants such as vortioxetine and duloxetine, among others, which commonly take approximately six to eight weeks to reach a maximal efficacy and often fail to differentiate from placebo at two weeks. Moreover, mean HAM-D changes from baseline at Day 14 for the placebo group of these randomized controlled antidepressant trials are most often between 4-8 points. Even at the first post-dose assessment on Day 3, patients dosed with PRAX-114 had a mean decrease of over 11 points on the HAM-D scale, which compares favorably with the average changes reported in the placebo groups at Day 14 from randomized studies completed for recently approved antidepressants (Figure 9), and other common antidepressants after several weeks of dosing. The clinical data that we have generated to date, and that we expect to generate in the future, from our clinical studies will constitute the bulk of the data needed to support an application for marketing approval of PRAX-114. Unless we conduct head-to-head studies of PRAX-114 against other molecules as part of our future clinical trials and elect to include the resulting data in an application for regulatory approval, we would not expect to rely upon PRAX-114's potential differentiation from any other molecules in connection with submissions to the FDA or other regulatory agencies, as applicable, for approval or otherwise. As the data presented above is based on a cross-trial comparison and not a head-to-head clinical trial, such data may not be directly comparable due to differences in study protocols, conditions and patient populations. Accordingly, cross-trial comparisons may not be reliable predictors of the relative efficacy or other benefits of PRAX-114 compared to other product candidates that may be approved or that are or were in development for MDD.

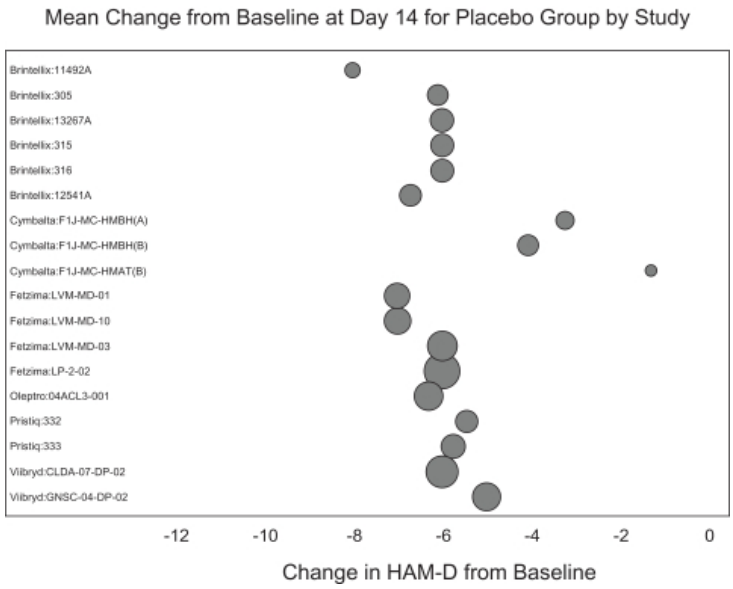


Figure 9. Change from baseline to Day 14 in HAM-D total score for the Placebo arm of selected randomized placebo-controlled studies of recently approved antidepressants. Bubble size is proportional to the sample size of the placebo group in each study. Across studies, the sample size in the placebo group ranged from 89 to 277.

PRAX-114 was generally well-tolerated across the dose range, including at the highest 80mg dose. This is consistent with an expected wider therapeutic window based on the preferential selectivity of PRAX-114 for extrasynaptic GABAA receptors. TEAEs were generally mild to moderate. Rates of somnolence, which is characterized by sleepiness or drowsiness, increased with dose, demonstrating a pharmacological effect which was somewhat mitigated by dosing at night versus the morning. With night-time dosing, 12/33 patients (36%) noted somnolence post-dosing, which was generally time-limited, not experienced during the daytime and substantially lower than the 78% reported in the Phase 1 60mg group with morning dosing. There were no SAEs or discontinuations and study drug cessation at the end of the treatment period was generally well-tolerated.

In this MDD part of the trial, we also observed the following TEAEs in at least 2 subjects per dose level:

- 80mg dose (n=7), headache (42.9% of subjects), somnolence (42.9% of subjects), dizziness (57.1% of subjects), feeling drunk (28.6% of subjects) and diarrhea (28.6% of subjects).
- 60mg dose (n=13), headache (46.2% of subjects), somnolence (53.8% of subjects), dizziness (30.8% of subjects), feeling drunk (23.1% of subjects) and constipation (23.1% of subjects).
- 45mg dose (n=13), headache (53.8% of subjects), somnolence (15.4% of subjects), fatigue (23.1% of subjects), vessel puncture site bruise from blood draws (15.4% of subjects), abdominal distension (15.4% of subjects) and upper respiratory tract infection (15.4% of subjects).

Across all dose levels studied, headache (48.5%), somnolence (36.4%), dizziness (24.2%), fatigue (15.2%), feeling drunk (15.2%), constipation (12.1%) and vessel site puncture bruise (12.1%) were reported in >10% of subjects.

Part B ongoing

We are currently conducting Part B of this trial in order to assess PRAX-114 in PMD patients. We are dosing up to twelve patients with PMD with 60mg of PRAX-114 nightly at 9:30PM for 14 days on an outpatient basis. The dose for this part of the trial was selected based on the data from Part A. Inclusion criteria for Part B are similar to Part A and C, except that it requires participants to be females of 40 years of age or older with irregular menses and hot flushes. Part B will help to determine if PRAX-114 has an effect on broader menopausal symptoms, like hot flushes, in addition to confirming the antidepressant effect. We anticipate topline results in the second half of 2021.

Part C results

Part C of this trial has been completed. The goal of Part C was to evaluate the safety of four-week outpatient dosing with PRAX-114, similar to the study duration of our Phase 2/3 trial, and the treatment effect profile from Day 15 to Day 28.

Inclusion criteria and symptom assessments were the same as Part A. Part C, however, was conducted in Melbourne Australia from June through October 2020, a period of highly restrictive public health lockdown due to the COVID-19 pandemic with closing of non-essential businesses, limited access to healthcare facilities, nightly curfews and restriction of residents to their homes except for essential healthcare or safety reasons. Only one person per household could travel up to 5 km to purchase essential supplies once per day. While the conduct of Part C continued through this period, the public health intervention required an abrupt change to the use of telehealth administered clinical efficacy assessments, mailed self-report assessments, and courier delivery of study drug to participants. These revisions in study conduct successfully supported consistent site and participant adherence to study procedures and study drug administration through completion of Part C. The experience managing these impacts has been integrated into the design and operationalization of the planned Phase 2/3 clinical trials with PRAX-114 in MDD.

A total of thirteen participants were enrolled and completed a nightly 9:30 PM dose of PRAX-114 at 60mg for four weeks. At baseline, patients had a mean HAM-D total score of 25, that ranged from 22 to 30, indicating moderate to severe MDD. Eight of the thirteen participants had previously received an antidepressant during the current depressive episode but still had moderate to severe MDD. This failure to respond to initial antidepressant treatment has been associated with more severe and refractory depression. The remaining patients were not being treated with any antidepressant for the current episode before enrolling in the trial.

PRAX-114 was generally well-tolerated, without a change in safety profile, after four-weeks of 60mg once nightly 9:30 PM outpatient dosing in Part C. We observed no new patterns of AEs in the Day 15 to Day 28 treatment period or post-discontinuation after four-week treatment compared to Part A.

In this part of the MDD trial, we observed the following TEAEs in at least 2 subjects with 60mg PRAX-114:

- Headache (46% of subjects), somnolence (31% of subjects), feeling abnormal (15% of subjects), fatigue (15% of subjects), dry mouth (15% of subjects), nasopharyngitis (15% of subjects), weight decreased (15% of subjects) and nausea (38% of subjects).
- Examination of the nausea AEs, which have been infrequent in prior studies, found patterns inconsistent with direct pharmacological effects in four out of five cases (two cases with onset immediately upon drinking PRAX-114 suspension, one case with 10 min duration in the morning for 7 days, and one case preceding an AE of nasopharyngitis).

Dosing with PRAX-114 for four weeks led to a rapid and marked improvement in the HAM-D score (Figure 10) within two weeks of treatment, with LS Mean improvement of 11 points at Day 15 remained stable through the end of the active treatment period).

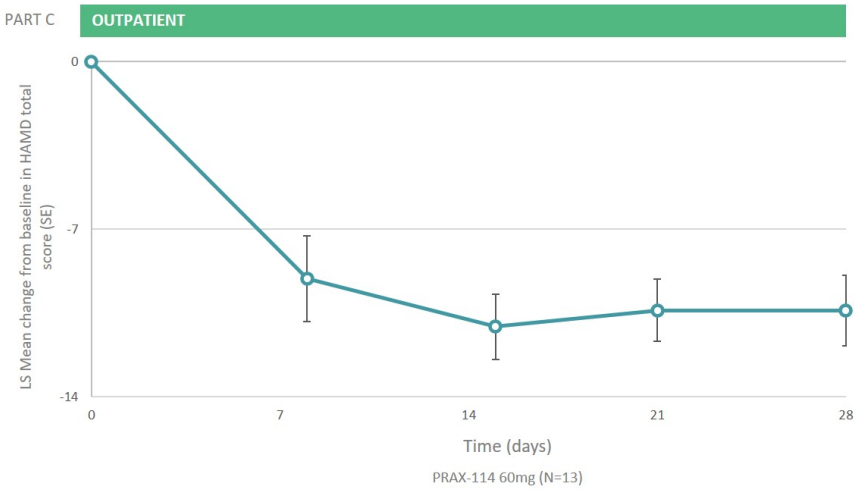


Figure 10. Reduction of HAM-D total score observed in MDD patients treated with PRAX-114 in Part C.

Data from Part B to date shows a safety profile similar to Parts A and C. The preliminary data show that dosing with PRAX-114 led to a marked improvement in the HAM-D score within two weeks of treatment. We expect complete topline data from Part B of the trial in the second half of 2021.

More than 70% of participants from all parts of the study had previously received an antidepressant during the current depressive episode but still had moderate to severe MDD. Preliminary data show greater than 60% of patients were responders or clinically in remission at two weeks. All cohorts demonstrated good tolerability.

Pharmacokinetics bridging study

To date, we have conducted all studies with PRAX-114 using a liquid, suspension formulation. For our registrational studies and subsequent potential commercial use of PRAX-114, we have developed a tablet formulation.

In a clinical PK bridging study, PRAX-114 was administered as a solid dose (i.e., tablet) formulation in single ascending doses of 40mg, 60mg and 80mg and compared to PRAX-114 suspension administered at the 60mg dose. The PK of the tablet formulation was found to be comparable to the suspension formulation at the 60mg dose level (Figure 11). Administration of the 60mg tablet formulation under fasted conditions resulted in a median tmax of ~1.0 hour, Cmax of ~400ng/mL, AUCinf of ~2600 hr*ng/mL and t1/2 of ~11-12 hours, similar to the 60mg oral suspension. Exposure to PRAX-114 increased approximately proportional to dose.

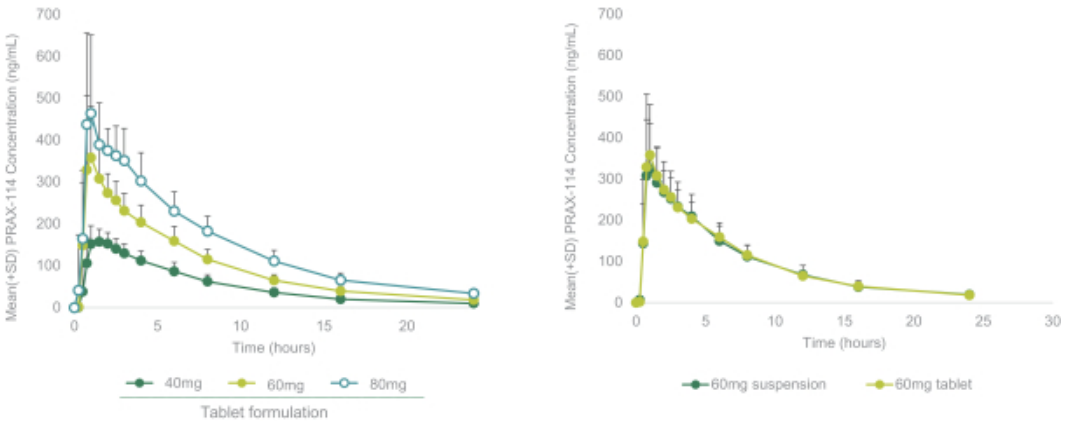


Figure 11. PRAX-114 dose-ranging pharmacokinetic study of tablet formulation and PRAX-114 pharmacokinetic bridging study of suspension and tablet formulations. Arithmetic means are displayed with standard deviations at each collection time point.

When PRAX-114 is administered prior to bedtime on an empty stomach or with a high-fat or high- calorie meal, the rate of absorption is reduced, resulting in a delay in tmax and reduction in Cmax, while AUC is generally unchanged as compared to fasting conditions. Thus, PRAX-114 maintains consistent overall exposure across a wide range of administration conditions within the evaluated dose range, and the reduction in Cmax observed with evening dosing appears to be associated with an improved tolerability profile. Daily administration of 20, 40 and 60mg in the morning under fasted conditions for 14 days resulted in increases in exposure (Cmax and AUC0-24) from Day 1 to Day 7 and was generally comparable between Day 7 and Day 14, with Cmax accumulation ratios of approximately 1.3 consistent with the half-life of PRAX-114 and anticipated achievement of steady-state within two to three days.

Overall, the PK profile of PRAX 114 has demonstrated consistent drug exposure across a wide range of administration conditions, demonstrating a consistent AUC when administered with or without food and at different times of day, and enabling once daily administration at bedtime without the need for additional patient instructions.

Planned PRAX-114 clinical trials

In October 2020, we submitted an IND to support the initiation of a Phase 2/3 clinical trial in the United States and Australia in approximately 200 moderate to severe MDD patients. At the end of the 30-day review period, the FDA notified us that the IND was placed on full clinical hold pending the resolution of certain non-clinical pharmacology and toxicology matters. We subsequently interacted with FDA to gain agreement on a path to initiate the clinical study, which included a proposal to submit available non-clinical data while other GLP reproductive toxicology studies were being completed. Based on this submission the FDA removed the clinical hold in March 2021. We are operationally ready and intend to initiate the Phase 2/3 monotherapy MDD trial by the end of March 2021. If positive, the Phase 2/3 trial is intended to serve as one of two registrational trials required by the FDA to support clinical efficacy for the monotherapy treatment of MDD, and we expect topline data in the first half of 2022. In addition to the Phase 2/3 monotherapy trial, we intend to initiate a Phase 2 dose range finding, or DRF, trial for adjunctive treatment of MDD in the third quarter of 2021 to inform dose selection for Phase 3 and provide controlled data to support advancing a Phase 3 adjunctive MDD trial.

Patients in the Phase 2/3 trial will be randomized 1:1 to receive nightly bedtime doses of PRAX-114 or placebo for 28 days in a fully outpatient setting, with two-weeks of additional follow up after the end of the active treatment period. Patients will be required to be between the ages of 18 and 65, have a diagnosis of MDD with a current episode of at least 8 weeks and not more than 24 months in duration, have a HAM-D total score of 23 or higher consistent with moderate to severe MDD, and have had at least one prior episode of MDD . Participants will be excluded if they are currently being treated with an antidepressant, have demonstrated an inadequate response to antidepressant treatment in the current episode or have treatment resistant depression, or if they have comorbid medical or psychiatric conditions that could interfere with the scientific objectives or safety of the trial. The primary efficacy endpoint will be change in the HAM-D total score from baseline at Day 15. A key secondary endpoint will

be change in the HAM-D score after 28 days of treatment to assess the durability of effect of PRAX-114, and we will also evaluate changes in other depression-related assessments.

As previously described, the initially targeted PRAX-114 oral suspension dose of 45mg was projected to result in the targeted degree of reduction in the HAM-D in patients with MDD. This dose demonstrated rapid and robust improvement in the HAM-D in the Phase 2a MDD trial that was equivalent to the improvement observed in the higher dose groups (60 and 80mg). While all doses were generally well-tolerated and no participants from Part A discontinued from the study due to AEs, the 45 mg dose group demonstrated an optimal benefit/risk profile to guide dose selection for the Phase 2/3 MDD study. These data, in combination with the β-EEG pharmacodynamic biomarker data and the results of the PRAX-114 PK bridging study led to selection of a 40mg PRAX-114 tablet dose for the Phase 2/3 trial. Based on these data, the 40mg PRAX-114 tablet is expected to yield therapeutic exposures that result in effects consistently at or slightly higher than previously seen with the 45mg of the PRAX-114 suspension.

We believe rigor in clinical conduct is essential for a study in MDD to appropriately mitigate historical variability in placebo effect, data reliability and the impact of current social and environmental changes caused by the COVID-19 pandemic. Our operational plan focuses on enrolling the right patients, minimizing placebo response and data variability and ensuring achievement of targeted drug exposure thorough direct verification of study drug adherence. Steps to advance these objectives include:

- Enrollment of patients with moderate to severe MDD and at least one prior episode of MDD (recurrent depression has been associated with a lower placebo response rate).
- A two-level subject and data quality process that includes independent clinical interviews confirming eligibility through the SAFER process and conducting audio confirmation of HAM-D clinical assessments at key timepoints with ongoing rating assessment quality feedback.
- Using sites with a known track-record of high quality data generation and drug-placebo separation in the conduct of MDD trials.
- Integration of a placebo control reminder script at every visit and screening for potential duplicate subjects via a dedicated clinical trial registry.
- Inclusion of the AiCure smartphone-based adherence monitoring system with structured site intervention to address participant adherence issues.

In parallel with the conduct of the Phase 2/3 trial in MDD, an exploratory DRF trial is planned to evaluate additional PRAX-114 doses for inclusion in pivotal Phase 3 studies in MDD. Given that comparable improvement in the HAM-D was observed in all doses (45, 60 & 80mg) examined in the Phase 2a MDD study, this trial will additionally explore the efficacy of lower doses of PRAX-114 to determine the optimal dose range to include in the Phase 3 development program. The planned population for this study is MDD participants who have demonstrated an insufficient response to standard of care antidepressant treatment, based on the following rationale: 1) The preliminary efficacy of PRAX-114 was demonstrated in a MDD population with a majority of participants having demonstrated an insufficient response to standard of care antidepressant treatment, supporting the suitability of this population for efficacy signal detection; 2) to extend these preliminary efficacy findings by generating controlled data for the efficacy of PRAX-114 in the adjunctive MDD population to inform Phase 3 study design in that population; and 3) to support concurrent conduct of the MDD development program studies while realizing data quality and operational efficiency benefits resulting from conducting the DRF study at a subset of the clinical research sites participating in the Phase 2/3 study in MDD.

Patients in this study will be randomized to receive 10, 20, 40, or 60mg adjunctive PRAX-114 or placebo in a 1:1:1:1:1 ratio for 28 days, with 2 weeks of additional follow up after the end of the active treatment period. This trial will enroll approximately 125 patients between the ages of 18 and 65 who are experiencing a current major depressive episode of at least 12 weeks and not more than 24 months in duration, who are being treated with an antidepressant at a stable dose for at least 8 weeks prior to Day 1 and have demonstrated an insufficient clinical response to 1 to 2 adequate trials of antidepressant treatment in the current episode, and who have had at least one prior episode of MDD responsive to antidepressant treatment. Exclusion criteria will be similar to the Phase 2/3 study, with the exception of the insufficient response exclusion. The objective to assess the presence of a dose-response signal for adjunctive PRAX-114 in MDD will use the primary efficacy endpoint of the change from baseline in HAM-D total score at Day 15. Secondary objectives will include evaluating the efficacy for each dose of

adjunctive PRAX-114 in MDD and the effect of adjunctive PRAX-114 on the HAM-D after 28 days of treatment and impact on other depression-related assessments. This trial will employ the full set of clinical trial quality interventions summarized above for the Phase 2/3 study, and the topline data is planned to be delivered in parallel with the Phase 2/3 monotherapy MDD study.

Upon completion of Part B of our Phase 2a trial, we intend to have a meeting with regulators to discuss further development of PRAX-114 in PMD.

PRAX-114 preclinical data

The goal of our preclinical program was to establish the *in-vitro and in-vivo* pharmacological profiles, antidepressant potential and tolerability of PRAX-114. In addition, we evaluated translational pharmacodynamic biomarkers to inform clinical development.

Antidepressant activity

To determine the antidepressant-like activity of PRAX-114, we used the Wistar Kyoto, or WKY, rat model. The WKY rat is an inbred rat strain that has increased sensitivity to stress and displays a depressive-like phenotype that is resistant to SSRI and SNRI treatment. A common way to assess depressive-like symptoms in animals is a test known as the forced swim test, or FST. The FST is based on the natural behavior of an animal when placed in a container filled with water from which it cannot escape. The rat will first make efforts to escape by swimming or climbing, but eventually will exhibit floating behavior, which is an indication of behavioral despair and is seen as a surrogate for depression. WKY rats display longer time inactive (floating) over a given time period than normal rats as an indication of increased behavioral despair.

We administered oral doses of PRAX-114 or a placebo to WKY rats and evaluated performance on the FST. At all doses of PRAX-114 tested, 1mg/kg, 3mg/kg and 10mg/kg, we observed a significant reduction in immobility time compared to rats that received a placebo, which we believe reflects an anti-depressive-like reaction or activity of PRAX-114. Importantly, and as described below, at these doses, PRAX-114 did not impair or enhance overall spontaneous activity of the rats in independent assays in the same animals, which we believe indicates that PRAX-114 was generally well-tolerated at these doses.

Tolerability

A common model to assess sedation in rats is the measure of spontaneous locomotor activity, or sLMA. Dosing rats with sedatives dose-dependently reduces their spontaneous movement in this assay. In this model, doses of PRAX-114 up to 30mg/kg had no significant impact on spontaneous locomotion, while doses as low as 1mg/kg had significant antidepressant-like effects in the WKY rat model, demonstrating a wide therapeutic window in these models with preclinical activity at doses well below sedative doses.

We believe that the therapeutic window observed in our *in-vivo* assays is consistent with the preference of PRAX-114 for extrasynaptic $GABA_A$ potentiation observed *in-vitro*.

EEG as a pharmacodynamic biomarker

In our rat translational biomarker model, we administered PRAX-114 to wild-type rats at doses ranging from 1 to 20mg/kg to assess the impact on power in the beta frequency band. We found that PRAX-114 dose-dependently increased the power in the beta frequency band and these changes correlated with changes in plasma pharmacokinetics. This EEG biomarker was used to inform dose-selection for PRAX-114 clinical studies. In our Phase 1 MAD trial, healthy volunteers administered the 30mg dose of PRAX-114 displayed an approximately 1.6-fold increase in qEEG beta power compared to baseline. In our preclinical studies, doses (and plasma/brain concentrations) that induced a 1.6-fold increase in the beta frequency power in rats were associated with both robust preclinical activity in animal models of depression and anxiety and good tolerability. Specifically, the PRAX-114 dose that is estimated to induce a 1.6-fold increase in EEG beta power activity in rats was efficacious in the rat WKY model of depression and the window between that dose that increased beta power by 1.6-fold increase in EEG and the dose that caused a 50% reduction of spontaneous locomotion in the sLMA sedation assay, or ED_{50}, was ~11-fold, based on brain concentrations. In addition, at this generally well-tolerated brain concentration, PRAX-114 was efficacious in animal models of anxiety including conditional emotional response, or CER, punished drinking, or Vogel, and elevated plus maze, or EPM (Figure 12).

In the figure below, the lower bound of the preclinical activity in animal models and EEG bars are determined by the brain exposure at the lowest dose at which significant activity was observed ($p < 0.05$). The lower bound of the tolerability bar represents the TC_{50} in the brain. The upper bound represents the mean brain concentration at the highest dose tested in a given assay.

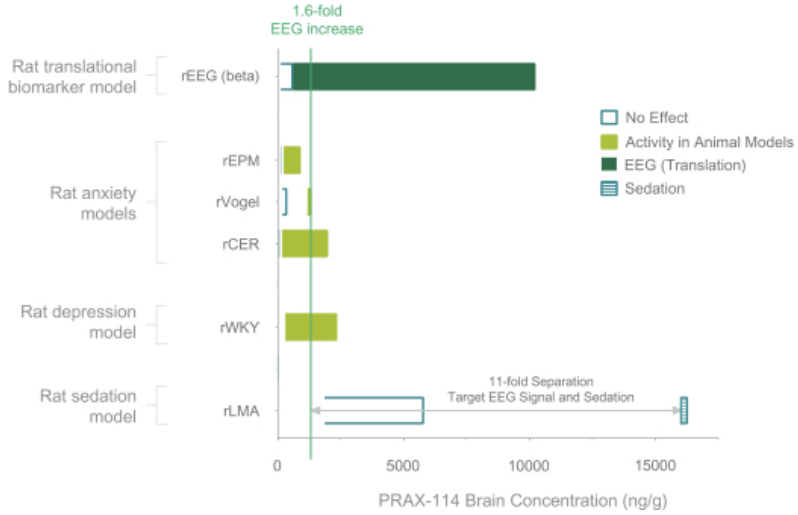


Figure 12. Summary of PRAX-114 preclinical data.

Based on our findings in preclinical models, we believe our initial results in humans are supportive of a wide therapeutic window which, in humans, begins at or below a daily dose of 30mg of PRAX-114 and extends to higher doses prior to the onset of potential dose-limiting somnolence or sedation. Our clinical studies to-date suggest that PRAX-114 doses up to 80mg, the highest we have tested in humans, remain generally well-tolerated. We have yet to identify the MTD.

PRAX-944

We are developing PRAX-944, a potentially differentiated selective small molecule inhibitor of T-type calcium channels, for the treatment of ET. We have evaluated the safety and tolerability of PRAX-944 in over 150 healthy volunteers in five separate clinical trials. In these trials, we have studied the safety of PRAX-944 modified release formulation with titration up to 120mg/day and no MTD has been identified. We are currently conducting a Phase 2a proof-of-concept open-label trial in ET patients. Preliminary site data from six participants of the low dose cohort (maximum dose of 40mg daily) showed tremor reduction, which seems to compare favorably to the standard of care agents. We plan to announce topline open-label safety, tolerability and efficacy data, including a high dose cohort, in mid-year 2021.

There is a large body of clinical, preclinical and genetic evidence that points to the involvement of T-type calcium channels in the cerebello-thalamo-cortical, or CTC, circuit, as a main driver of ET. ET is the most common movement disorder, affecting up to seven million patients in the United States, which is seven times more individuals compared to Parkinson's tremor. ET is a progressive and debilitating movement disorder with action tremors that significantly disrupt daily living. There is a high unmet need for ET patients given the limited treatment options, with only one approved pharmacotherapy that is poorly tolerated, resulting in high discontinuation rates and a small group of patients opting for invasive brain surgeries.

Successful development of T-type calcium channel modulators in ET likely requires a PK profile with a blunted Cmax and thoughtful clinical trial design and endpoint selection. We have designed our development program to include careful selection of clinical endpoints, a modified release formulation and dose titration strategy. We believe the profile of PRAX-944 coupled with its modified release formulation positions it for development as a differentiated therapy in ET.

Because of the gatekeeper role of T-type calcium channels in regulating neuronal firing patterns in multiple neuronal circuits, we believe PRAX-944 is suitable for potential development across a wide-range of indications in psychiatry and neurology, providing sizable expansion opportunities in addition to ET.

Essential Tremor

ET is the most common movement disorder, characterized by involuntary rhythmic movement in the upper limbs, with or without tremor in other body locations such as the head, vocal cords, or legs. ET is a day-time disease associated with debilitating tremors triggered when a patient voluntarily attempts to move. These tremors significantly disrupt daily living and are progressive in nature, with increases in tremor severity and amplitude commonly observed over the course of the disease. The upper-limb tremor can range from barely visible to greater than 20cm in amplitude.

Unlike Parkinson's disease, which is characterized by a rest tremor, the tremor of ET occurs with movement and therefore causes direct disability, as people are unable to perform basic, every-day functions such as writing, typing, drinking or feeding themselves. Given the debilitating physical challenges of the disease, ET has also been associated with high prevalence of comorbidities, including anxiety, depression and social phobia.

ET is a clinically well-recognized indication with defined diagnostic criteria established by The International Parkinson and Movement Disorders Society. ET affects between one and two percent of the worldwide population and approximately five percent of adults over 60 years of age. It is estimated that there are up to seven million individuals with ET in the United States, up to seven times more than the second most common movement disorder, Parkinson's disease.

Despite the prevalence and significant disease burden of ET, only a fraction of patients (an estimated one million based on claims data) are managed with pharmacological therapy, though an estimated 80% of those that are treated discontinue these medications due to limitations in efficacy and tolerability. We believe that the treated population will increase with the availability of new therapies with improved efficacy and tolerability.

Currently, there are only two drugs commonly used in ET. Propranolol, approved by the FDA in 1967, remains the only currently approved therapy for ET in the United States. A non-selective beta blocker, Propranolol is contraindicated for individuals with certain respiratory or cardiac issues, which are common comorbidities in the age group affected by ET. Primidone, an anticonvulsant used off-label, requires slow titration over six to eight weeks and can cause sedation and balance issue while accelerating osteoporosis with long-term use.

As a last line therapy, several thousand ET patients in the United States opt for invasive surgery each year. Interventions include gamma knife and focused ultrasound thalamotomy, where part of the thalamus involved in the CTC circuit is ablated, or deep brain stimulation, or DBS, where an electrode is implanted into the brain. These procedures are generally effective but are associated with significant side effects and risk. Therefore, many patients who are eligible for surgical therapies do not elect to have these procedures.

A significant unmet need remains for the millions of ET patients that are not currently receiving treatment for their ET, or are underserved by existing treatment options. We believe that the relatively concentrated ET treatment setting composed of mainly neurology and movement disorder specialists would allow for the rapid adoption of a new treatment option that offered robust response rates and an improved tolerability profile.

Genetics of Essential Tremor

Our rationale for approaching ET through inhibition of T-type calcium channels is rooted in the genetics of epilepsy. CACNA1G, a gene that encodes for a particular isoform of T-type calcium channels, is one of the most significantly associated genes for generalized genetic epilepsy, or GGE. Some of these epilepsy patients also suffer from comorbid movement disorders such as tremor and ataxia. The odds of observing a T-type calcium channel mutation in the GGE population is 9 times of that of the healthy population. This supports the key role of T-type calcium channels in maintaining excitation and inhibition balance.

Additional human genetic data provide evidence for the role of T-type calcium channels in movement disorders. Whole exome sequencing of early-onset familial ET patients also identified mutations in CACNA1G that segregated with the tremor phenotype in multiple family pedigrees. The importance of T-type Ca++ channels to the function of the CTC circuit is highlighted by variants in the CACNA1G gene which are associated with rare cases of pediatric cerebellar atrophy. Additionally, mutations in the T-type calcium channel have also been reported as

causative of a form of spinocerebellar ataxia. We believe this genetic link, along with the preclinical and clinical evidence, help confirm the role of T-type calcium channels in the pathophysiology of ET.

Role of T-type calcium channels in ET

T-type calcium channels function as the gatekeepers of neuronal firing patterns, controlling the switch between tonic and burst firing in the CTC circuit. The CTC circuit is a series of brain nuclei or neuron clusters, including the inferior olivary nucleus, cerebellar Purkinje cells, deep cerebellar nuclei, ventral motor thalamus and motor cortex, which work together in regulating coordinated movements and when disrupted generate tremor. All nuclei in this circuit contain pacemaker cells with inherent burst firing capability and express T-type calcium channels, which are known drivers of oscillatory burst firing.

T-type calcium channels are low voltage activated channels that respond to weak depolarization of neuronal membranes and are quickly inactivated (a closed state where the channel cannot be reopened for some time). The opening of T-type calcium channels leads to membrane depolarization, which activates voltage-activated sodium channels, leading to the formation of an action potential and neuronal firing. When only a small number of T-type calcium channels are activated, leading to small T-type calcium channel mediated membrane depolarizations, the neuron generally generates unitary action potentials, also called tonic firing. When the activity of T-type calcium channels is increased, either due to genetic mutations or other changes in network activity that recruit more T-type calcium channels, a longer lasting depolarization is generated, resulting in high-frequency clusters of sodium channel driven action potentials, also called burst firing, as illustrated in the figure below.

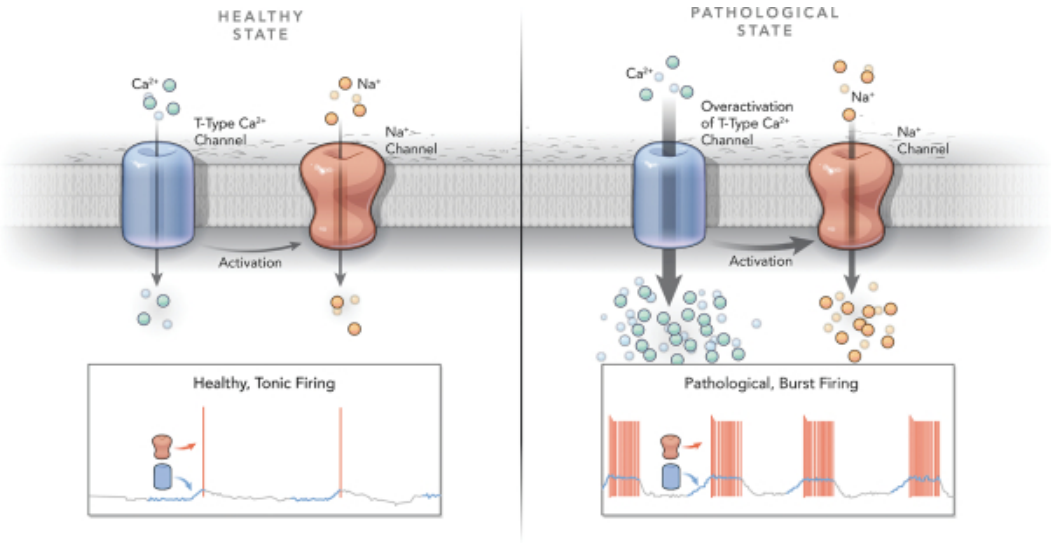


Figure 13. T-Type calcium channels are gatekeepers of neuronal firing patterns.

Neuroimaging and neurophysiology studies in ET patients has consistently demonstrated that individual nuclei along the CTC circuit oscillate at the same frequency as the tremor and with strong coherence amongst the brain regions and movement in the affected muscles. Further, intraoperative real-time single-unit recordings of action potentials of individual neurons in the ventral motor thalamus of severe ET patients receiving DBS implants, in periods with and without tremors, further substantiates the central role of the CTC circuit and T-type calcium channels in ET (Figure 14). When no tremor was observed at rest, tonic firing was recorded in neurons of the ventral motor thalamus. During tremor, the same neurons fire in rhythmic bursts that are highly coherent with tremor activity. Furthermore, the emergence of action tremors coincided with the emergence of burst firing. Lesioning or DBS of the ventral motor thalamus has been shown to silence the oscillatory burst firing activity in the CTC circuit, resulting in significant tremor reduction. The strong temporal coordination between the tremors and burst firing, a neuronal firing pattern frequently gated by T-type calcium channel activity, strongly suggest that pharmacological inhibition of these channels may represent an effective pharmacological approach in ET.

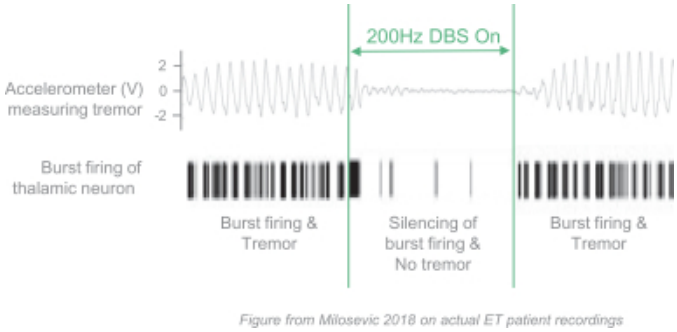


Figure 14. Thalamic neuron burst firing correlated with tremor activity in ET patients.

The role of the CTC circuit and T-type calcium channels has been further confirmed in animal models. A known pharmacological tremor model utilizes administration of harmaline, an alkaloid toxin, to animals. Harmaline, on administration to experimental animals such as rodents, induces an acute action tremor as well as rhythmic burst-firing activity in the CTC circuit similar to that observed in ET patients. We believe this model carries clinically predictive value, as compounds that improve tremor in ET patients clinically (e.g., propranolol, primidone) have also been shown to reduce harmaline-induced tremor preclinically; in contrast compounds that worsen tremor in patients (e.g., caffeine) also worsen tremor in this model. Similar to what's observed in ET patients, normalizing oscillatory activity in the CTC circuit, for example with DBS, reduces harmaline induced tremor in rodents. Pharmacological inhibition or genetic knockout of T-type calcium channels lead to resistance to harmaline-induced tremor.

PRAX-944 in Essential Tremor

We are advancing a modified release formulation of PRAX-944, a potent and selective small molecule inhibitor of T-type calcium channels, for the treatment of ET.

PRAX-944 Clinical Development in ET

We have evaluated the safety and tolerability of PRAX-944 in over 150 healthy volunteers in five separate clinical trials. In these trials, we have studied the safety of PRAX-944 modified release formulation with titration up to 120mg/day and no MTD has been identified. We are currently conducting a Phase 2a proof-of-concept open-label trial in Australia and New Zealand in ET patients. Preliminary site data from six patients of the low dose cohort showed tremor reduction, which seems to compare favorably to the standard of care agents. We plan to announce topline open-label safety, tolerability and efficacy data, including a high dose cohort, in the first half of 2021.

Phase 1 trials in healthy volunteers using previous IR formulation

An immediate release, or IR, formulation of PRAX-944 was used in the initial Phase 1 trials and reached maximal plasma concentrations within one to three hours of dosing. Adverse events like nausea were associated with the high peak levels. This prompted the development of a modified release, or MR, formulation for PRAX-944 that extends the absorption of the drug over a longer period. We have demonstrated that the MR formulation, which releases approximately 80% of the drug product over seven hours in vitro, reduces the maximum plasma concentration and delays the tmax without significantly impacting the overall AUC. We have also observed that this resulted in improved tolerability relative to an immediate release, or IR, formulation and the ability to sustain targeted therapeutic concentrations. The sustained exposure also enables once daily dosing (Figure 15).

Phase 1 trials in healthy volunteers using MR formulation

In our Phase 1 multiple dose trial of the MR formulation of PRAX-944 in England, doses of 20mg and 40mg were generally well-tolerated over 8 days. Adverse events were transient and occurred at a rate similar to placebo. We observed the following TEAEs all of which were mild to moderate:

- 40mg dose (n=6): we observed the nervous system TEAEs of somnolence (33.3%), headache (33.3%) and dizziness (33.3%). The TEAEs also included fatigue (33.3%) and hot flash (33.3%). We observed ECG application site rash, EEG application site skin reaction, nausea, vision blurred, thermal burn (accidental) and euphoric mood in 16.7% of subject each.

- 20mg dose (n=6): we observed the nervous system disorder TEAEs of somnolence (16.7%) and headache (33.3%). We also observed nausea (33.3%), fatigue (16.7%), vomiting (16.7%) and dry throat (16.7%).
- Placebo (n=4): we observed the nervous system TEAEs of headache (25%), somnolence (25%) and dizziness (25%). We also observed fatigue (50%) and nausea (25%).

A single dose of 60mg was not tolerated in the single dose trial due to reports of nausea in five of six subjects and vomiting in three of six subjects. In the multiple dose 20mg and 40mg groups, three subjects reported nausea with one subject also reporting vomiting; these events were mild in severity and resolved on Day 1 of dosing. No subjects reported nausea or vomiting after Day 1 of dosing. While a single dose of 60mg was not well-tolerated, the average peak drug levels (138ng/mL) observed in the 40mg group after eight days of treatment were greater than those seen with the single 60mg dose (130ng/mL) on Day 1. Improved tolerability at higher concentrations following repeated dosing suggests that titration to higher doses might be a viable strategy to further improve the tolerability profile.

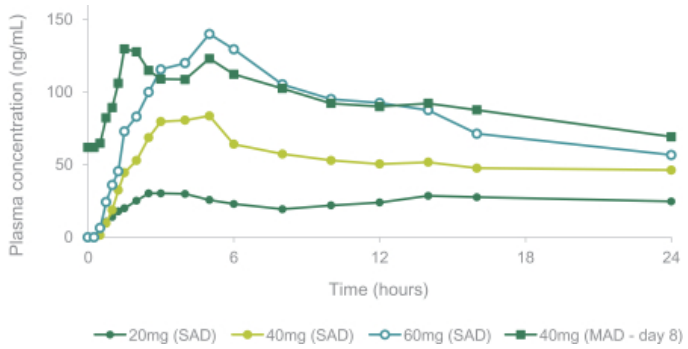


Figure 15. Sustained exposures were observed for the MR formulation of PRAX-944.

Quantitative EEG studies in healthy volunteers were used to assess the pharmacodynamic effect of PRAX-944 on T-type calcium channels in the brain. One frequency band known to be driven by T-type calcium channel activation is the sigma frequency band (11 to 15 Hz) during non-rapid eye movement sleep, or NREM sleep. T-type calcium channels expressed in thalamic neurons are critically involved in the generation and modulation of these rhythmic thalamocortical oscillations during NREM sleep.

In our preclinical studies, dosing of normal rats with PRAX-944 led to robust and dose-dependent changes in EEG activity. Because similarly robust sigma frequency band changes after dosing with PRAX-944 are observed during NREM sleep in rats and humans, our hypothesis is that the inhibition of this EEG signal can be used as a pharmacodynamic biomarker. Because the doses at which EEG changes observed in rats are similar to those that demonstrated activity in a preclinical model of essential tremor, or the harmaline model, we believe that this EEG biomarker can be used to estimate the dose of PRAX-944 that will produce a therapeutic effect in ET.

In our Phase 1 trial, 20mg and 40mg doses of PRAX-944 administered to healthy volunteers produced changes in the qEEG recordings of the sigma frequency band during NREM sleep consistent with those observed in rats (Figure 16). This indicated that PRAX-944 reached target levels in the brain needed to inhibit T-type calcium channels. Based on the overlap of these EEG changes with drug levels showing activity in the preclinical harmaline model, we believe that 20mg and 40mg doses of PRAX-944, which were generally well-tolerated in healthy volunteers without titration, have the potential to reduce tremor in patients with ET.

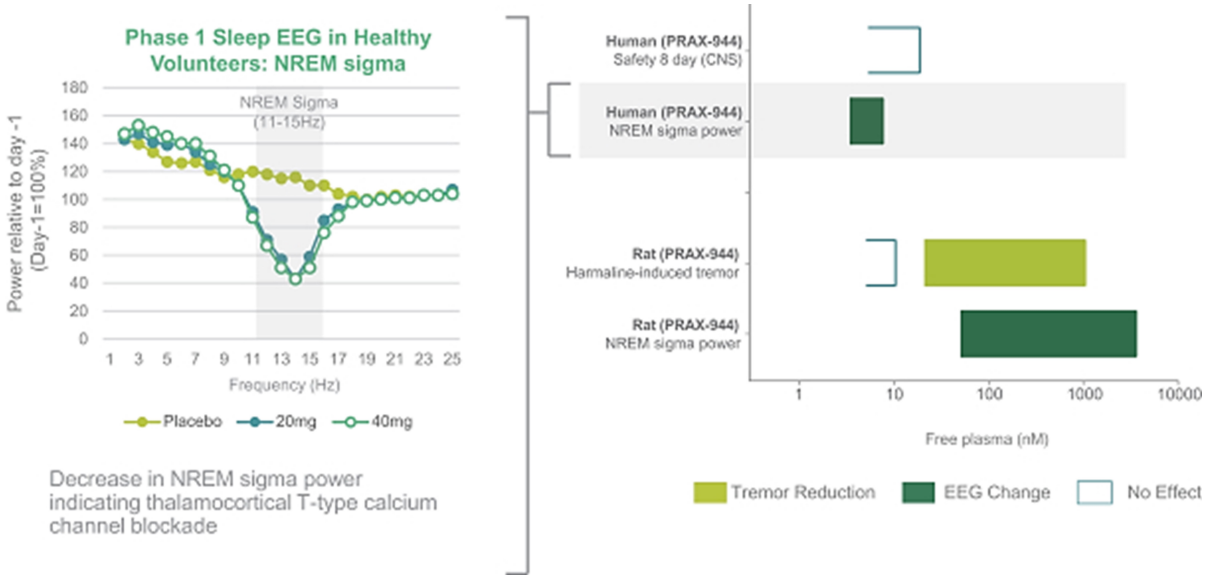


Figure 16. Exposures of PRAX-944 that decreased sigma band activity were generally well-tolerated in healthy volunteers and were associated with harmaline tremor reduction.

Titration trial in healthy volunteers

Considering that improved tolerability is the key unmet need in ET and that existing data suggest that titration is a viable strategy to further improve PRAX-944's tolerability profile, we explored titration in a two-part healthy volunteer study. In Part A, a new 5mg PRAX-944 tablet was assessed for low-dose pharmacodynamic effects at in an open-label titration paradigm from 5mg up to 20mg daily. In Part B, PRAX-944 was titrated from 20mg up to 120mg daily, to assess the safety, tolerability and pharmacodynamic activity of higher doses. Participants were randomized to PRAX-944 or placebo in a 3:1 ratio, starting at 20mg daily in the morning and titrated at 20mg increments up to 120mg daily with up to one week in between each dose increment to achieve steady-state plasma concentrations and for the collection of safety data. The total dosing duration was 31 days.

Dosing has completed in this study. The safety data demonstrated that with titration, PRAX-944 was generally well-tolerated up to 120mg daily. There were no SAEs and no severe AEs. The majority of AEs were mild, transient and resolved without intervention (Figure 17). There were no treatment related ECG or EEG abnormalities. Safety laboratory values have generally been within normal limits and there have been no dose dependent excursion from the normal range. Only 1 of 12 participants randomized to PRAX-944 discontinued for a treatment-related adverse event. This participant dropped out after 1 dose (20mg) due to symptoms the participant described as similar to a prior panic attack (not reported at screening). Vital signs, physical examination, clinical laboratory tests, and ECG parameters were all within normal limits. The symptoms self-resolved.

Importantly, no MTD was identified. We believe this provides an advantage for PRAX-944, as it enables a wide dose range for optimizing efficacy and tolerability profile tailored to the key unmet need in ET as well as individual patient needs. Preliminary analyses confirmed the pharmacodynamic changes seen in the previous Phase 1 trial described above, and we will further assess changes across the dose range up to 120mg/day.

MedDRA Preferred Term	Placebo (N=4) n (%)	PRAX-944 20mg qAM (N=12) n (%)	PRAX-944 40mg qAM (N=11) n (%)	PRAX-944 60mg qAM (N=11) n (%)	PRAX-944 80mg qAM (N=9) n (%)	PRAX-944 100mg qAM (N=8) n (%)	PRAX-944 120mg qAM (N=8) n (%)	PRAX-944 Overall (N=12) n (%)
Participants with at least 1 TEAE	**3 (75.0%)**	**5 (41.7%)**	**3 (27.3%)**	**5 (45.5%)**	**2 (22.2%)**	**6 (75.0%)**	**2 (25.0%)**	**12 (100%)**
Dizziness	0	0	2 (18.2%)	0	1 (11.1%)	0	0	3 (25.0%)
Medical device site dermatitis	2 (50.0%)	1 (8.3%)	0	1 (9.1%)	0	1 (12.5%)	1 (12.5%)	3 (25.0%)
Chest discomfort	0	1 (8.3%)	1 (9.1%)	0	0	0	0	2 (16.7%)
Dry throat	0	0	1 (9.1%)	0	1 (11.1%)	0	0	2 (16.7%)
Feeling drunk	0	2 (16.7%)	0	0	0	0	1 (12.5%)	2 (16.7%)
Headache	2 (50.0%)	1 (8.3%)	0	1 (9.1%)	0	0	0	2 (16.7%)
Palpitations	0	2 (16.7%)	0	0	0	0	0	2 (16.7%)

Source: PRAX-944-105, Draft Table 14.3.1.3.2
Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities; TEAE=treatment emergent adverse events
Note: 4 participants randomized to PRAX-944 group did not complete the planned dosing. Only 1 out of these four dropped out due to a treatment related AE. 1 participant had an unrelated AE and 2 dropped out for non-safety reasons

Figure 17. TEAEs Occurring in at least two participants in a dose group or overall.

Phase 2a trial in patients with ET

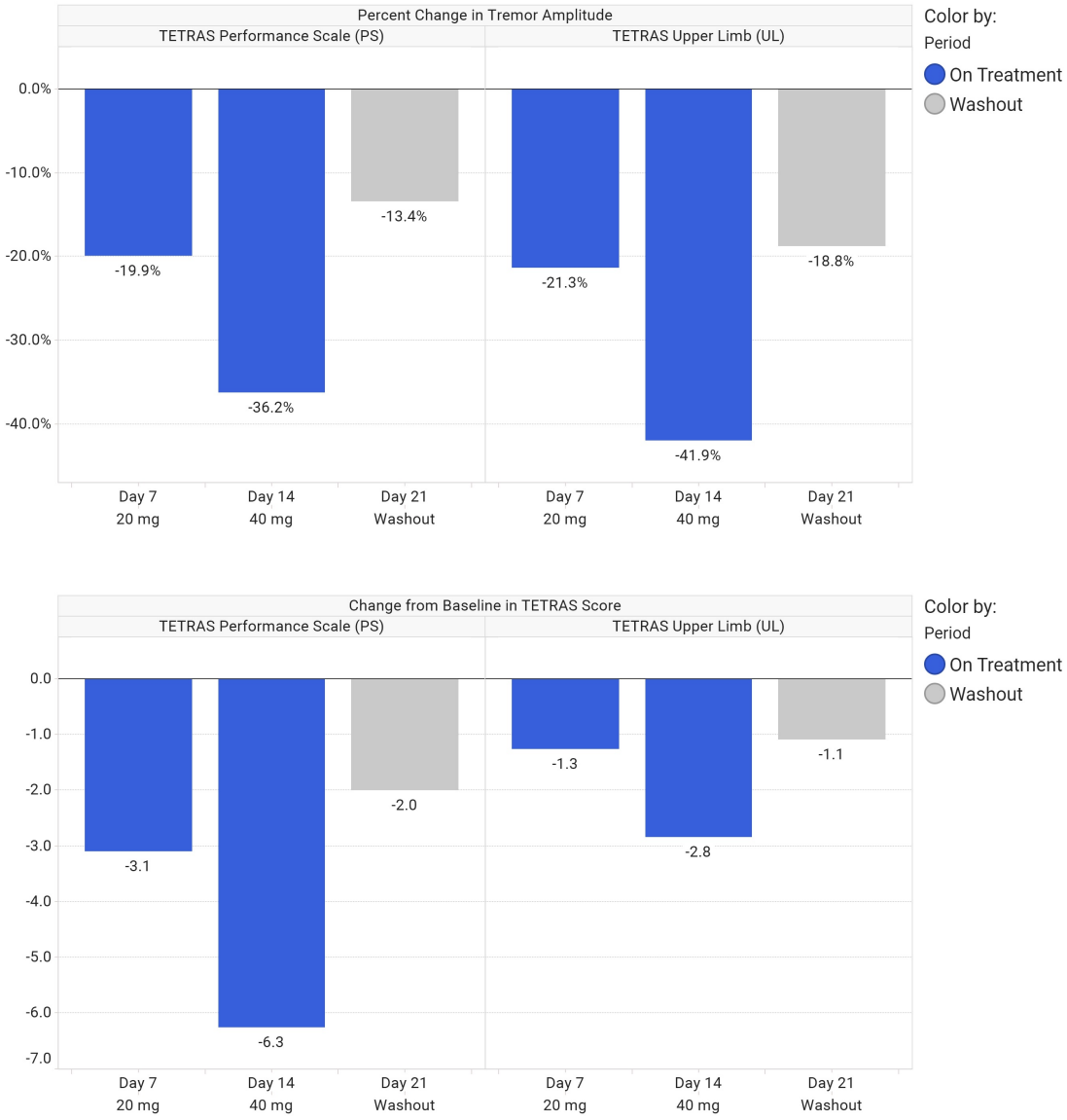
We are currently conducting a Phase 2a proof-of-concept open-label trial in up to 12 patients per cohort with ET in Australia and New Zealand. In the first cohort, participants received 20mg daily dosing of PRAX-944 for one week followed by 40mg daily dosing for the second week, taken in the morning. Based on the data from the titration trial in healthy volunteers, we are enrolling an additional cohort of ET patients dosing up to 120mg.

Studies in movement disorders require careful attention to methods for obtaining and scoring outcome measures. We are measuring changes in tremor with different, complementary approaches including components of the Essential Tremor Rating Scale, or TETRAS, Performance Scale and accelerometry. TETRAS is a widely used clinical rating scale that measures the severity of ET. It was based on similar clinical scales which have been used to support regulatory approval of neurosurgical treatments for severe ET. TETRAS has shown good measurement properties and dynamic range compared to other scales.

We are using change from baseline in the rating of upper limb, or UL, items of the TETRAS as the primary efficacy outcome in this proof-of-concept trial because all ET patients suffer from UL tremor. As the UL items drive most of the score on the overall TETRAS and are more reliably rated than other items on the scale, they are therefore expected to have the best signal to noise ratio. UL items have also been the basis of the most recent regulatory approval of neurosurgical treatments for severe ET. We have established rigorous procedures for training and for blinded scoring of efficacy, including using centralized video assessment as an exploratory endpoint, with randomization of the videos and masking to allow for rating concordance. We have also included the overall TETRAS performance scale, or TETRAS-PS, (both site and central video rating) and Kinesia ONE accelerometer, clinical global impression of severity and improvement, or CGI-S and CGI-I, respectively, and the patient global impression of change, or PGI-C, as secondary endpoints in the current open-label study to assess consistency of response across different endpoints.

In this trial, we are enrolling participants with well-established ET, as defined by the Movement Disorders Society, or MDS, Task Force for Tremor as an isolated tremor syndrome of bilateral UL action tremor with at least 3 years' duration. Patients are required to have a combined bilateral score of ≥10 on the TETRAS UL items as confirmed by site investigator and central video review. This requirement for moderate to severe symptoms at baseline provides a clear and measurable dynamic range for detecting a treatment response. In the first cohort, tremor severity will be evaluated before drug administration, after daily morning dosing of PRAX-944 20mg for 7 days (Day 7), following daily administration of PRAX-944 40mg for seven additional days (Day 14) and one week after administration of PRAX-944 has been stopped (Day 21).

Preliminary data are available from six participants who completed the trial and received PRAX-944 doses of 20mg followed by 40mg, each for seven days (Figure 18). Preliminary site (primary endpoint measure) and central video assessments of participants TETRAS-PS in this cohort showed generally stable tremor severity between screening and baseline visits. The primary endpoint change suggests dose dependent tremor reduction on the TETRAS-UL which compares favorably to the standard of care agents, and the change was consistent with the central video assessment. Placebo effects in tremor trials are typically low. A recent trial in ET demonstrated a 0.1% effect on the clinical rating scale in the control group. Importantly, five of the six participants remained on propranolol in this study, suggesting that PRAX-944 could also be efficacious as an adjunctive treatment. Similar patterns of improvement were also observed in the full TETRAS-PS, and Kinesia ONE accelerometry scores. The site and central ratings were strongly correlated on the TETRAS-UL and TETRAS-PS with r values of 0.8 and 0.83, respectively.



*As TETRAS PS items are rated on a logarithmic scale, the Weber-Fechner law was used to calculate the percent change in tremor amplitude according to the equation presented in Elble (2018).

Figure 18. Change from baseline in TETRAS scores and percent change from baseline in tremor amplitude as measured by site ratings of the TETRAS PS and Upper Limb subscale in Part A of the ET OL study (N=6).

A total of 7 participants have completed Part A of this trial. Participants were administered 20mg PRAX-944 QAM for 7 days followed by 40mg QAM for 7 days. These dose levels have been generally well-tolerated. No SAEs and no severe AEs have been observed. The majority of AEs have been mild, transient and resolved without intervention. Six out of 7 participants completed dosing per protocol. One participant discontinued on Day 8 due to anxiety. This participant was also non-compliant with the protocol, stopping propranolol on Day 3 of dosing without consulting study staff. Due to this protocol deviation which would have impacted this participant's TETRAS scores, this participant is included in safety data but not in efficacy data. No clinically significant ECG or laboratory abnormalities have been reported.

Based on the observed safety profile in the titration healthy volunteer trial and the safety and preliminary activity observed in Part A of the ET trial, we plan to include a high dose cohort (Part B) of up to 12 participants in this on-going ET trial titrating dosing up to 120mg in an open-label fashion. We also are including a randomized, double-blind, placebo-controlled withdrawal phase to the trial, where participants will either be maintained on their final open-label dose or switched to placebo. The goals of the randomized withdrawal are to obtain blinded confirmation of effect from the open-label titration and to assess for durability of effect.

We plan to announce topline open-label safety, tolerability and efficacy data, including the high dose cohort, from this Phase 2a trial in mid-year 2021.

Additional studies planned for the PRAX-944 program

We plan to initiate a Phase 1 study to explore shorter titration schemes in mid-year 2021. In addition, we plan to initiate a Phase 2b randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of PRAX-944 in the treatment of ET patients in the fourth quarter of 2021.

Preclinical support for advancing PRAX-944

PRAX-944 has been shown preclinically to inhibit all three human T-type calcium channel isoforms, CaV3.1, CaV3.2 and CaV3.3, and has demonstrated high selectivity against L and N-type calcium channels, or CaV1.2 and CaV2.2, respectively, and other key ion channels important for normal physiology, such as the cardiac potassium channel human Ether-à-go-go-Related Gene, or hERG, and the voltage gated sodium channel NaV1.5. Robust selectivity and potency have been demonstrated across both exogenously expressed recombinant channels in a human cell line and naïve channels in isolated dorsal root ganglion, or DRG, neurons from rats using electrophysiological techniques.

HEK CELLS		RAT DRG NEURONS	
Channel	**IC50 (nM)**	**Channel**	**IC50 (nM)**
hCaV3.1	**202**	**T-Type**	**50**
hCaV3.2	**240**	N-Type	10,000
hCaV3.3	**188**		
rCaV1.2 (L-Type)	32,000		
rCaV2.2 (N-Type)	11,000		
hNaV1.5	100,000		
hERG	7,800		

Table 19. PRAX-944 is a potent and selective inhibitor of T-type calcium channels.

Consistent with the gatekeeper role of T-type calcium channels in neuronal firing patterns, a gain of function mutation of the T-type calcium channel CaV3.2 leads to pathological burst firing in thalamic neurons in a rat model known as the GAERS model. Administration of PRAX-944 resulted in complete suppression of the pathological burst-firing in thalamic neurons derived from the GAERS model.

We validated the therapeutic potential of PRAX-944 to treat ET using the harmaline-induced tremor model in rats. Administration of harmaline triggers ET-like tremors in experimental animals as well as pathological burst firing throughout the CTC circuit. We observed a large and dose-dependent decrease of harmaline-induced tremor in rats treated with PRAX-944 as compared to vehicle-treated animals, when measured as % increase of tremor from pre-

harmaline baseline. This result served to both demonstrate the potential of PRAX-944 in ET and as independent evidence of the critical role of T-type calcium channels in tremor reduction.

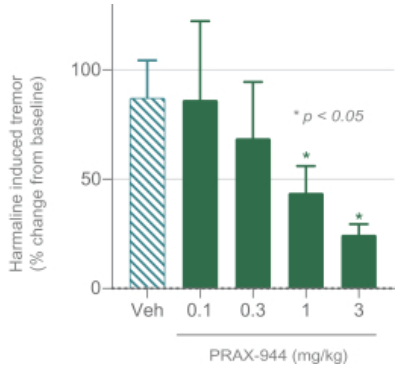


Figure 20. PRAX-944 led to a dose-dependent inhibition of tremors in the rat harmaline model.

EEG as a pharmacodynamic biomarker for dose selection

PRAX-944 robustly and dose-dependently decreased EEG power in the sigma frequency band during NREM sleep in rats. The effect of PRAX-944 on the EEG observed in rats when dosed with PRAX-944 indicates its ability to mediate the blockade of T-type calcium channels in the thalamocortical circuit, suggesting that this effect is a pharmacodynamic biomarker for PRAX-944. Because the doses at which the EEG changes are observed are similar to those that demonstrate tremor reduction in the harmaline model, we believe that this biomarker can be used to estimate the dose that could be effective in treating ET.

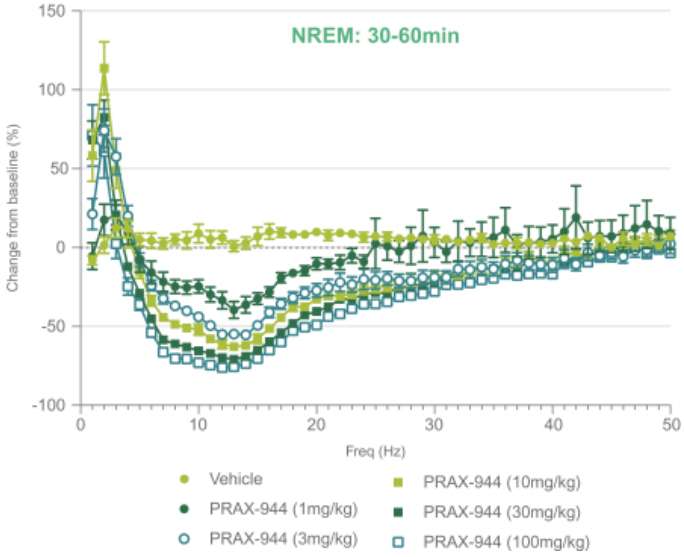


Figure 21. PRAX-944 decreased EEG sigma power during NREM sleep in rats.

RARE DISEASE PORTFOLIO

We are advancing several programs which we believe offer significant therapeutic benefits for rare disease populations over the current standard of care. We believe that all of the programs in our rare disease portfolio have the potential to be differentiated molecules, have foundational underpinnings in human genetics, utilize translational biomarker tools and have the potential for early clinical signal detection.

Our most advanced rare disease candidate is PRAX-562, which is currently in a Phase 1 trial in adult healthy volunteers in Australia. Its mechanism suggests that PRAX-562 has broad potential to treat many diseases of neuronal hyperexcitability. We are pursuing development in a subset of rare devastating diseases, initially rare adult cephalgias and pediatric epilepsies.

The remainder of our current rare disease portfolio consists of precision medicines approaches to address genetically defined populations suffering from Developmental and Epileptic Encephalopathies, or DEEs. DEEs are rare neurologic diseases characterized by early onset (< 2 years of age), frequent seizures, abnormal epileptiform electroencephalographic activity, developmental impairment and resistance to available antiepileptic drugs. Furthermore, DEEs are associated with a high mortality rate and comorbidities such as developmental delay in addition to behavioral disorders, movement disorders, pain and sensory dysfunction and sleep disruptions.

The understanding of the etiology of DEEs has been revolutionized by recent whole-exome sequencing initiatives that showed over 60 genetic causes of epilepsy. An underlying pathologic feature of many DEEs is the dysregulated neuronal activity leading to hyperexcitability, seizures and associated comorbidities. This phenomenon is observed in many pediatric DEEs with an identified genetic cause, such as SCN8A, SCN2A, KCNT1, KCNQ2, KCNQ1, STXBP1 and SYNGAP1 epilepsy, as well as epilepsies in which a genetic cause remains unclear, such as Lennox Gastaut Syndrome, or Doose Syndrome. Up to 40% of DEEs are caused by single gene mutations, enabling precision medicine approaches.

Our lead precision medicine candidate is PRAX-222, an antisense oligonucleotide, or ASO, for lowering the expression levels of the protein encoded by the gene SCN2A, in patients with gain-of-function, or GOF, mutations in SCN2A, the underlying cause of SCN2A GOF DEE. We have also entered into a research collaboration with The Florey Institute of Neuroscience and Mental Health to develop three novel ASO therapies for the treatment of patients with SCN2A loss-of-function mutations and two additional rare epilepsy targets. This partnership positions us at the forefront in rare epilepsy drug development with six distinct programs for the treatment of six different rare epilepsies.

Given the overlapping biology, phenotypic presentation and clinical execution considerations, we believe that developing a portfolio of drugs to treat DEEs will create a distinct body of knowledge and operational synergies across our rare disease portfolio, positioning us as a leader in developing meaningful therapies for this group of patients with devastating unmet clinical needs.

PRAX-562

Standard of care sodium channel blockers, such as Tegretol (carbamazepine), Lamictal (lamotrigine), Dilantin (phenytoin) and many others are an important class of medicines in neurology and psychiatry. All standard of care sodium channel blockers modulate neuronal activity by targeting peak sodium current, which can reverse the pathological neuronal hyperexcitability that underlies many CNS conditions, but simultaneously affects the physiological cellular action potential firing required for a functioning nervous and cardiovascular system. Hence, this class is widely used for the treatment of epilepsy, pain, migraine and bipolar disorder. However, the efficacy of sodium channel blockers is generally limited by side effects, many attributable to on-target toxicological effects.

PRAX-562 is designed as the first selective, persistent sodium current blocker that has the potential of reducing pathological neuronal hyperexcitability with an improved tolerability profile. PRAX-562 is in development for the treatment of a broad range of rare, devastating CNS disorders, such as severe pediatric epilepsies and adult cephalgia. We intend to pursue development in a subset of rare cephalgias, initially Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing, or SUNCT, Short-lasting Unilateral Neuralgiform headache with Autonomic symptoms, or SUNA, and Trigeminal Neuralgia, or TN, along with pediatric epilepsies.

In *in-vitro* studies, PRAX-562 selectively blocks persistent sodium current across all subtypes of sodium channels with minimal effects on the peak sodium current that is critical for the normal physiological function of these channels. In line with this selectivity for persistent current, PRAX-562 has been shown in *ex-vivo* studies to reduce neuronal hyperexcitability without impairing normal neuronal function. This is in contrast to marketed sodium channel blockers which significantly impact normal neuronal function, leading to a narrow therapeutic index.

To date, PRAX-562 has demonstrated robust pharmacological activity in a preclinical *in-vivo* seizure model with significantly improved tolerability compared to other sodium channel blockers, suggesting a potentially improved therapeutic index. The characteristics of PRAX-562 are expected to make it a versatile molecule that we

believe can be broadly applied in diseases of hyperexcitability where sodium channel blockers have demonstrated efficacy but poor tolerability. Recent preclinical studies with PRAX-562 have demonstrated a dose-dependent and complete prevention of spontaneous seizures in a mouse model of SCN2A GOF DEE and evoked seizures in a human knock-in mouse model of SCN8A DEE.

We have initiated a Phase 1 trial of PRAX-562 in Australia to evaluate the safety, tolerability, PK and effects on an exploratory EEG biomarker in up to 129 adult healthy volunteers. This trial has successfully completed the SAD portion up to the maximum planned dose, with no dose limiting toxicities, and has advanced to MAD cohorts. Maximum observed PRAX-562 plasma concentrations observed to date, at Cmax in the SAD study and at trough levels in the MAD study, exceed those at the effective concentration 50, or EC50, in the MES mouse model, a model with good predictive validity, without dose limiting toxicities. We are currently at the highest preplanned dose of PRAX-562 in our MAD trial and intend to escalate further if it continues to be generally well-tolerated. We anticipate the initial proof-of-concept trial in rare adult cephalgia patients to initiate in the second half of 2021.

The clinical development plan for PRAX-562 encompasses exploring the broad potential for the mechanism of action in rare diseases through proof-of-concept trials in rare adult cephalgia patients and then expanding into a range of rare pediatric DEEs. The FDA has granted rare pediatric disease designation for PRAX-562 for the treatment of SCN2A and SCN8A developmental and epileptic encephalopathies, or SCN2A-DEE and SCN8A-DEE, respectively.

Voltage-gated sodium channels, persistent sodium current and neuronal excitability

Voltage-gated sodium channels, or VGSCs, are transmembrane proteins that are required for electrical signaling and therefore communication in neurons. VGSCs respond to changes in the membrane potential and are tightly regulated by their biophysical properties. Upon opening of VGSCs, sodium ions can move into the cell leading to a depolarization and therefore excitation of the neuron. This sodium current is the initiator and driver of neuronal action potentials, or APs, the primary means of electrical signal propagation along the neuron's axon.

The family of VGSCs consists of nine highly related isoforms (NaV1.1 – NaV1.9) with differential tissue distributions and functions. NaV1.1, 1.2 and 1.6 are the major sodium channels expressed in the central nervous system.

Isoform	Gene	Expression
NaV1.1	SCN1A	CNS
NaV1.2	SCN2A	CNS
NaV1.3	SCN3A	CNS/Pancreas
NaV1.4	SCN4A	Muscle
NaV1.5	SCN5A	Heart
NaV1.6	SCN8A	CNS/PNS
NaV1.7	SCN9A	PNS
NaV1.8	SCN10A	PNS
NaV1.9	SCN11A	PNS

CNS: Central Nervous System, PNS: Peripheral Nervous System

Table 22. Sodium Channel Isoforms and tissue distribution.

VGSCs undergo a structural change that alter their ability to conduct sodium ions (Table 22) and are triggered to open upon excitation, or depolarization, of the cell membrane allowing sodium ions to enter the neuron. Sodium influx further excites, or depolarizes, the neuron, leading to the opening of even more sodium channels. This series of events can lead to a large peak sodium current underlying the initiation and propagation of neuronal action potentials, or APs, the primary means by which neurons propagate information in the nervous system. To prevent overexcitation of neurons, or hyperexcitability in the form of excessive high frequency AP firing, the majority of sodium channels only open very briefly after activation (1-2ms), followed by a refractory period of inactivation or non-responsiveness.

However, at membrane potentials below the AP firing threshold, a small subset of sodium channels can remain open for hundreds of milliseconds, carrying the so-called persistent sodium current. Persistent sodium current is present under physiologic conditions where it modulates excitability of neurons and can be significantly increased in pathologic states (Figure 23).

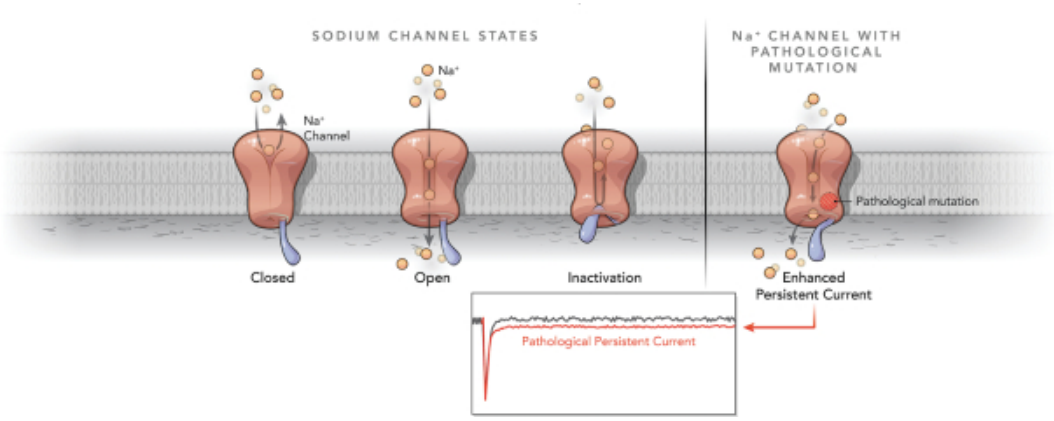


Figure 23. Impact of a pathological mutation on sodium channels.

There are currently more than 15 sodium channel blockers in the market commonly used to treat diseases such as epilepsy, bipolar disorder and pain. While standard of care sodium channel blockers, such as carbamazepine, lamotrigine and phenytoin, inhibit persistent sodium current, they likely also block peak sodium current at therapeutic concentrations, which can cause significant adverse events such as ataxia, drowsiness and dizziness, and therefore have a very narrow Therapeutic Index, or TI.

Genetics of persistent sodium current

In published whole-exome sequencing studies of diverse patient populations, mutations in all voltage gated sodium channel subtypes have been reported as a likely cause of disease. Furthermore, gain-of-function mutations that are associated with disease can cause an increase of persistent sodium current, raising the idea that this might be a critical driver of hyperexcitability in neurologic disorders.

The specific disease that a patient develops depends on both the sodium channel subtype and where the affected sodium channel is expressed. Gain-of-function mutations in SCN2A, or NaV1.2, and SCN8A, or NaV1.6, two of the major sodium channels in the brain, cause early onset epileptic encephalopathies with frequent seizures and developmental delay. Gain-of-function mutations in NaV1.1, NaV1.4, NaV1.5 and NaV1.7 cause familial hemiplegic migraine, myotonia, cardiac arrythmia and severe pain disorders, based on their primary expression in the CNS, muscle, heart and pain pathways, respectively. These channelopathies demonstrate the important role persistent sodium current plays as a modulator of cellular excitability.

Our initial indications for PRAX-562

Developmental and Epileptic Encephalopathy

Approximately 100,000 children suffer from DEEs in the United States alone, with over two hundred thousand children affected world-wide. An underlying pathologic feature of many DEEs with both known and unknown genetic causes, is the dysregulated neuronal activity leading to hyperexcitability and subsequently to seizure.

Sodium channel blockers have been a critical component of the pharmacological management of seizure related conditions, including epilepsy, for decades. However, current standard of care sodium channel blockers are limited by a narrow therapeutic window and inadequate efficacy. We believe these limitations are largely due to blockage of peak sodium current and disruption of normal neuronal function at or near therapeutic doses and significant off-target activity.

Given the role of persistent current in modulating excitability, we believe that PRAX-562 has the potential to be a broadly efficacious and generally well-tolerated antiepileptic drug for the treatment of DEEs of both genetic and unknown etiology.

Cephalgia

SUNCT, SUNA and TN are devastating headache disorders with limited treatment options. SUNCT and SUNA are part of a specific class of cephalgias known as Short Lasting Unilateral Neuralgiform headaches. These headaches are characterized by severe burning, stabbing and electrical unilateral head pain that is typically 9 to 10 in the Visual Analogue Scale, or VAS, for pain. These headache attacks last between one second and ten minutes in duration and can occur up to 600 times per day. SUNCT and SUNA headaches are rare diseases with a prevalence estimated to be 6.6 per 100,000 based on a recent Australian study.

SUNCT and SUNA are often refractory to standard migraine and headache treatments, but are highly responsive to intravenous, or IV, infusion of the sodium channel blocker lidocaine. Response under IV lidocaine requires continuous infusion in an inpatient setting and is associated with side effects such as nausea, vomiting and cardiovascular effects, with headache attacks returning in majority of patients within days of IV lidocaine withdrawal. Preventative treatment of SUNCT and SUNA often includes oral sodium channel blocker lamotrigine, but this is limited by partial efficacy, tolerability concerns and the requirement of several weeks of dose-titration to reach therapeutic doses.

TN, also known as tic douloureux, is characterized by intense, stabbing, electric-shock pain typically in the lower face and jaw, usually on one side of the face. TN is thought to be caused by irritation of the trigeminal nerve. The pain can be triggered by an action as simple as washing or touching the face smiling or talking. These attacks can progressively worsen over time, especially if left untreated. Epidemiologic data are variable across the world and depend on definitions used for diagnosis, with reported annual incidence ranges from 4.3 to 26.8 per 100,000.

Anticonvulsive medications that modulate voltage-gated sodium channels, such as carbamazepine, are considered first line treatment for TN. Additional therapies used to treat TN include other medications (e.g., gabapentin, baclofen, amitriptyline, topiramate), as well as various procedures or surgical interventions (such as vascular decompression or gamma knife). These therapies are reported to all have inconsistent results in controlling the pain, with only about 50% success over time.

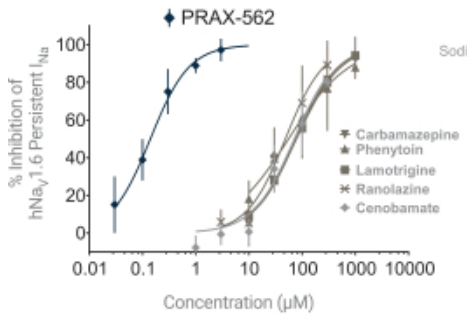
The limited FDA-approved treatments specific to SUNA or TN, or complete absence of FDA-approved treatments specific to SUNCT, combined with high comorbidity and healthcare utilization, substantiates the need for an efficacious, generally well-tolerated and orally bioavailable sodium channel blocker to treat headache attacks in acute and preventative settings.

PRAX-562 preclinical data

PRAX-562 is a highly differentiated, potent and selective inhibitor of persistent sodium current designed to overcome the limitations of currently available sodium channel blockers. PRAX-562 preclinical studies were designed to test our belief that the block of persistent sodium current is sufficient to demonstrate robust activity in animal models of hyperexcitation and that the selective block of persistent sodium current over physiological peak current leads to an improved therapeutic index.

Selective inhibition of persistent sodium channels

In preclinical studies, PRAX-562 is a highly potent inhibitor of persistent sodium current as measured in cell-based assays, in which sodium channel isoforms are heterologously expressed and channel activity is measured via patch clamp electrophysiology. Using electrophysiological voltage protocols, the effect of compounds on a specific channel state (e.g., peak current vs persistent current) can be measured. When compared to other approved sodium channel inhibitors for various neurological indications, PRAX-562 was hundreds of times more potent at inhibiting persistent sodium current. PRAX-562 had an IC50 of 141 nM compared to SOC sodium channel blockers lamotrigine and carbamazepine which had an IC50 of 78,530 nM and 77,520 nM, respectively – a potency difference of over 500-fold. PRAX-562 was ~60 fold selective for inhibiting persistent current over peak current.



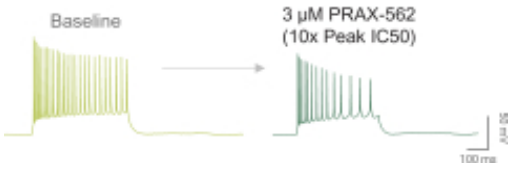
		Persistent INa* IC50 (nM)	Ratio of persistent to peak inhibition (Tonic Block)
Praxis selective INaP blockers	**PRAX-562**	141	60
Sodium Channel Blockers with recent clinical experience	Vixotrigene (BIIB074)	3,676	14
Standard Sodium Channel Blockers	Cenobamate	73,263	23 *Project 1,719,000 uM*
	Carbamazepine	77,520	30
	Ranolazine	48,600	14
	Mexiletine	55,570	7
	Phenytoin	55,770	n/a**
	Lidocaine	68,230	19
	Lamotrigine	78,530	16
	Lacosamide	833,100	n/a**
	Valproic Acid	<10% @ 1 mM	No inhibition

*** solubility concerns*

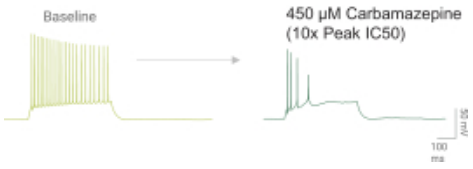
Figure 24. PRAX-562 is approximately 150-fold more potent and two to nine-fold more selective for persistent sodium current than standard sodium channel blockers.

The selective block of persistent sodium current reduces neuronal hyperexcitability without affecting the action potential, or AP, amplitude, which is required for normal neuron function. In mouse brain slice experiments, a hyperexcitable state can be mimicked by artificially depolarizing the neuron using the patch clamp method, which elicits high frequency AP firing. PRAX-562 reduced the neuronal AP firing frequency, an indicator of neuronal excitability, without a significant effect on AP amplitude, an indicator of normal neuronal function, suggesting reduction of hyperexcitability without impacting the ability of the neuron to respond to physiologic stimuli. In comparison, carbamazepine, a SOC sodium channel blocker, at comparable concentrations (relative to the potency in cells heterologously expressing NaV1.6), excessively decreased AP firing almost completely and reduced the amplitude of APs, indicating impairment of normal function.

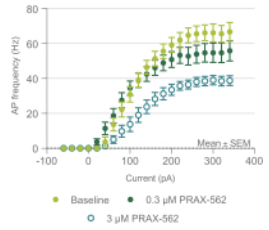
PRAX-562 Representative AP Traces



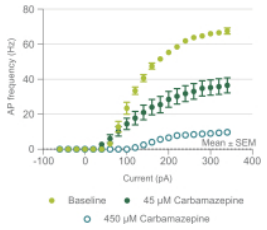
Carbamazepine Representative AP Traces



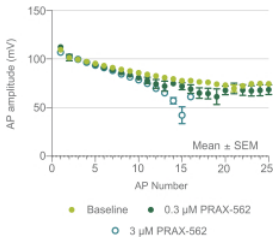
PRAX-562 Average AP Frequency During Increasing Current Steps



Carbamazepine Average AP Frequency During Increase Current Steps



PRAX-562 Average AP Amplitude During Current Step



Carbamazepine Average AP Amplitude During Current Step

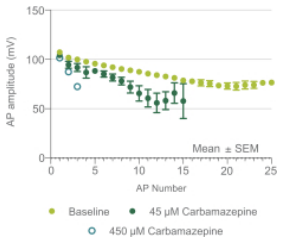


Figure 25. PRAX-562 reduced neuronal hyperexcitability (AP frequency) without impairing normal function (minimal effect on AP amplitude). In contrast, carbamazepine significantly reduced the AP amplitude suggesting impairment of normal function.

Preclinical in vivo pharmacological activity, tolerability and EEG pharmacodynamic biomarker

We investigated the preclinical activity of PRAX-562 in a maximal electroshock model of epilepsy, or MES model, that has shown good predictive validity for clinical anti-convulsant activity, and compared it to the effects of SOC sodium channel blockers carbamazepine and lamotrigine. To determine how well PRAX-562 is tolerated, we compared its effects on spontaneous locomotor activity, or sLMA, to the effects of carbamazepine and lamotrigine.

PRAX-562 was able to block seizures completely in mice at a dose that does not impair locomotor function (10mg/kg). In contrast, carbamazepine and lamotrigine only achieve full block of seizures in this model at doses that also show impairment of locomotion. PRAX-562 at a dose of 2mg/kg, inhibited the epilepsy response to half of its maximum value, or ED_{50}. Inhibition of sLMA required an estimated dose of 44mg/kg to obtain 50 percent inhibition, or TD_{50}.

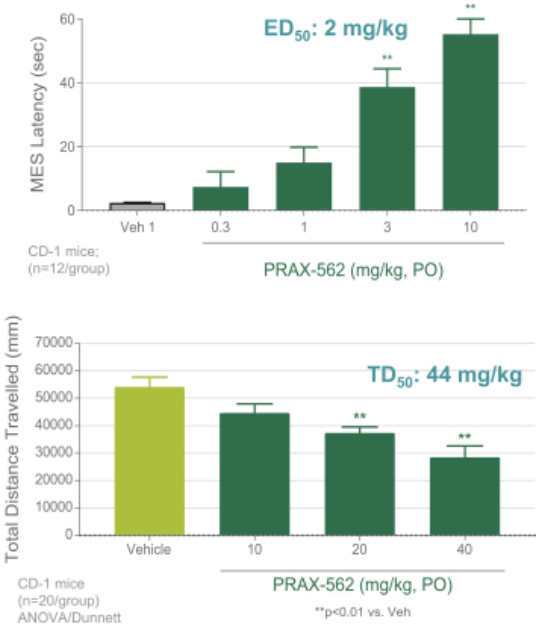


Figure 26. Doses of PRAX-562 resulting in potent anticonvulsant activity were associated with minimal effects on general locomotor activity.

We calculated the therapeutic index, or TI, of each molecule as the preclinical tolerability/pharmacological activity ratio. This ratio is calculated by dividing the plasma and brain concentrations at the dose that reduces locomotion by 50% by the concentrations that reduce seizures by 50%. We found that PRAX-562 had a significantly improved therapeutic index of ~16 fold (based on brain concentrations) and ~17 fold (based on plasma concentrations) compared to the currently prescribed sodium channel blockers carbamazepine and lamotrigine, which had a much lower protective index of three to six-fold. Notably, standard sodium channel blockers, such as carbamazepine and phenytoin, show severe toxicity in humans at exposures that are only about 1.5 to 3 times the target therapeutic exposures, underscoring the need for modulators of sodium channels with an improved tolerability.

Molecule	Plasma Therapeutic Index	Brain Therapeutic Index
PRAX-562	**17.2x**	**16.4x**
Carbamazepine	3.4 x	5.9 x
Lamotrigine	6.4 x	4.6 x

Therapeutic Index (TI) = TC50/ EC50

Table 27. Compared to lamotrigine and carbamazepine, PRAX-562 had an increased ratio between drug levels that demonstrated preclinical pharmacological activity versus those that caused toxicity.

The auditory steady state response, or ASSR, is a non-invasive EEG measure of excitatory/inhibitory balance in the brain. This response is elicited with short lasting (2sec) auditory stimuli that lead to brain activity changes that are measured as a 40Hz EEG signature and depend on network activity between excitatory and inhibitory cortical neurons. We believe that persistent current block has the potential to lead to reduced excitability of the network and will be measurable with this endpoint.

Consistent with this hypothesis, dosing normal mice with PRAX-562 led to a dose-dependent decrease in the ASSR amplitude (40Hz power). This effect was maximal at doses that have robust anticonvulsant effects in the maximal electroshock model.

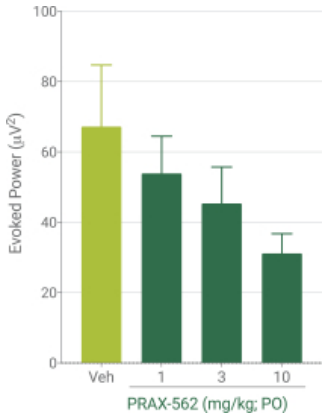


Figure 28. PRAX-562 dose-dependently reduced the 40Hz EEG power of the auditory steady state response in mice.

Together, our data suggest that the selective effects of PRAX-562 on hyperexcitable states without affecting normal neuronal function led to the robust preclinical reduction of seizures and improved tolerability seen in animal models. As shown below, exposures of PRAX-562 that led to biomarker change (ASSR amplitude reduction shown in top row) also demonstrated robust anticonvulsant activity (shown in middle row). Moreover, PRAX-562 has a ~16.4 fold protective index based on the spontaneous locomotor activity (shown in bottom row), which is a significant improvement over reported effects of approved sodium channel blockers. In the figure below, the lower bound of the preclinical pharmacological activity range, EEG and tolerability bars is determined by the brain EC_{50} (preclinical seizure and ASSR assays) or TC_{50} (tolerability assay) in a given assay and the upper bound represents the mean brain concentration at the highest dose tested in a given assay.

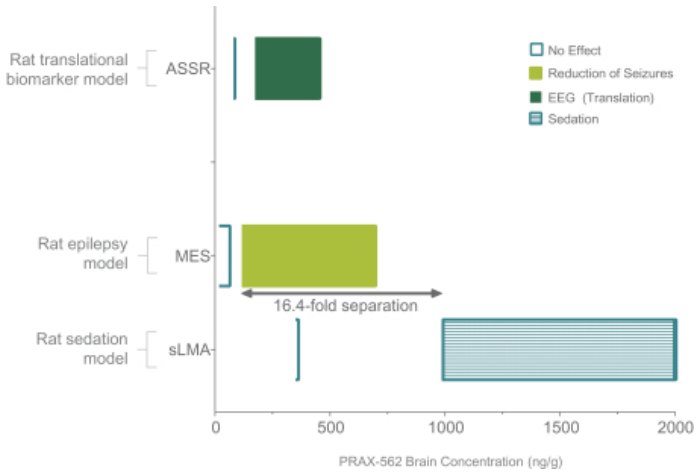


Figure 29. Summary of PRAX-562 preclinical data.

Recent preclinical studies with PRAX-562 have demonstrated a dose-dependent and complete prevention of spontaneous seizures in a mouse model of SCN2A GOF DEE and evoked seizures in a human knock-in mouse model of SCN8A DEE.

We believe that the profile of PRAX-562 may translate into therapies with the potential for clinical efficacy and tolerability across several indications caused by underlying hyperexcitability where standard sodium channel blockers have shown efficacy, albeit with limited tolerability, such as rare pediatric epilepsies and cephalgia like SUNCT/SUNA and TN.

PRAX-562 clinical development in cephalgia and DEEs

We have initiated a randomized, double-blinded Phase 1 trial in Australia to evaluate the safety, tolerability and pharmacokinetics of single and multiple ascending doses of PRAX-562 in up to 129 adult healthy volunteers between the ages of 18 and 55. In addition, we are using ASSR as an exploratory pharmacodynamic biomarker in this trial to determine the doses required to achieve pharmacological blockade of persistent sodium current, which we believe is a potential indicator of efficacy in patients. Preliminary analysis of the completed SAD cohorts indicate that PRAX-562 is generally well-tolerated up to the maximum planned dose. Safety data reviewed included adverse events, vital signs, ECG, C-SSRS, physical examination and safety laboratory data. There have been no reported SAEs, severe AEs or any AEs leading to study withdrawal or discontinuation as of the safety review committee meeting convened on February 18, 2021. The current trial has advanced to MAD evaluations and maximum observed plasma concentrations achieved in healthy normal subjects, at trough levels, exceed those at the effective concentration 50 (EC50), in the MES mouse model. We are currently at the highest preplanned dose of PRAX-562 in our MAD trial and intend to escalate further if it continues to be generally well-tolerated. We anticipate the initial proof-of-concept trial in SUNCT/SUNA and TN patients to initiate in the second half of 2021.

The clinical development plan for PRAX-562 encompasses exploring the broad potential for the mechanism of action in rare diseases through proof-of-concept trials in rare adult cephalgia, then expanding into a range of rare pediatric DEEs. The FDA has granted rare pediatric disease designation for PRAX-562 for the treatment of SCN2A-DEE and SCN8A-DEE.

Along with our PRAX-562 program, we are developing a portfolio of sodium channel blockers that we plan to advance in other rare CNS disorders.

PRAX-222

PRAX-222 is a program for developing an antisense oligonucleotide for patients with gain-of-function SCN2A epilepsy. This program is ongoing under a three-way collaboration with Ionis Pharmaceuticals, Inc., or Ionis, and RogCon Inc., or RogCon. Under the terms of the collaboration agreement, Ionis is responsible for preclinical and IND-enabling toxicology studies and we are responsible for clinical development and commercialization. The FDA has granted both rare pediatric disease and orphan drug designations for PRAX-222 for the treatment of SCN2A-DEE.

SCN2A is the gene that encodes the voltage-gated sodium channel NaV1.2 that is primarily found in excitatory neurons throughout the brain and which plays a critical role in action potential generation and signaling between neurons. Individuals with gain-of-function mutations in SCN2A develop early-onset epileptic encephalopathy with severe seizures that begin within the first month of life that are often refractory to standard of care antiepileptic medications. SCN2A GOF DEE patients also suffer from significant intellectual disability, movement disorders and in some cases early death due to sudden unexpected death in epilepsy, or SUDEP. It is estimated that there are thousands of patients worldwide with gain-of-function changes in SCN2A leading to epileptic encephalopathy.

Candidate ASOs under the PRAX-222 program directly target the cause of disease by down-regulating NaV1.2 expression, an effect that has demonstrated disease-modifying activity in animal models of SCN2A epileptic encephalopathy. In transgenic mice carrying a human SCN2A GOF mutation, we observed a significant, dose-dependent reduction in seizures and increased survival of mice treated with a mouse ASO that down-regulates SCN2A. The survival benefit from the ASO was maintained with repeat dosing. We also observed survival benefits following administration of a mouse ASO to a group of mice after onset of disease and around the time of onset of mortality. This observation suggests that candidate ASOs of the PRAX-222 program may have the potential to provide clinical benefits for children after disease onset. The ASO-treated disease model animals demonstrated similar behavior and locomotor activity as wild type animals, suggesting SCN2A knockdown is generally well-tolerated and that the benefits extend beyond seizure control alone.

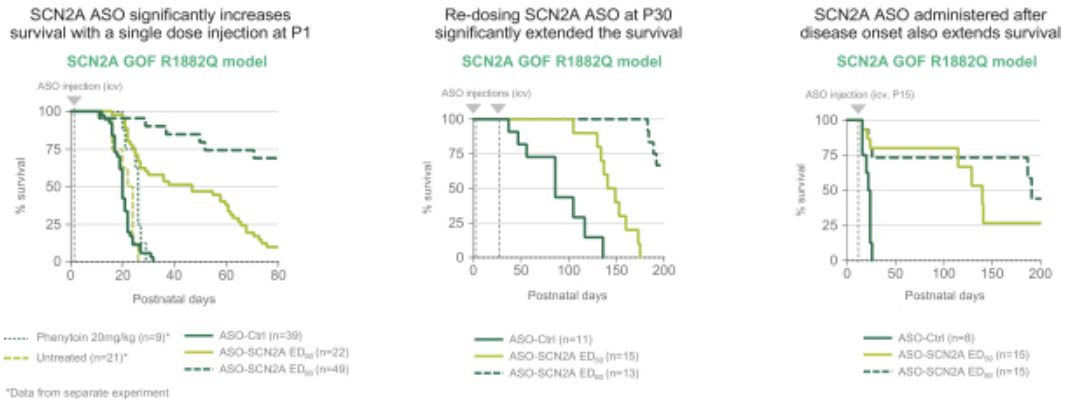


Figure 30. An SCN2A ASO increased survival in a SCN2A gain-of-function mouse model.

Our lead candidate is currently undergoing evaluation in IND-enabling toxicology studies, which are expected to be completed by the end of 2021.

KCNT1 Program

We are currently identifying small molecule inhibitors of the sodium-activated potassium channel encoded by the gene KCNT1 for the treatment of KCNT1 GOF epilepsy. Potassium channels encoded by the KCNT1 gene play a key role in regulating neuronal AP firing. Gain-of-function KCNT1 mutations promote neuronal hyperexcitability, resulting in severe early onset epilepsy with continuous seizures and severe developmental delay, affecting thousands of patients worldwide. KCNT1 GOF epilepsy is often refractory to conventional treatment approaches. Anticonvulsants, such as stiripentol, benzodiazepines, levetiracetam and ketogenic diet, have all demonstrated limited efficacy.

Genetically lowering KCNT1 expression in transgenic mice carrying a KCNT1 human GOF mutation has been reported to result in disease modifying preclinical activity including seizure reduction, improved cognitive function and survival benefit. Through chemical optimization of the potency and pharmacokinetic properties of hits from a high-throughput screen, we have identified novel small molecule inhibitors of KCNT1. These inhibitors restored normal action potential firing *in-vitro* in KCNT1 GOF mutant neurons and reduce seizure and abnormal interictal spikes *in-vivo* in transgenic mice carrying a KCNT1 human GOF mutation, recapitulating the reported disease modifying preclinical activity demonstrated by genetic tools.

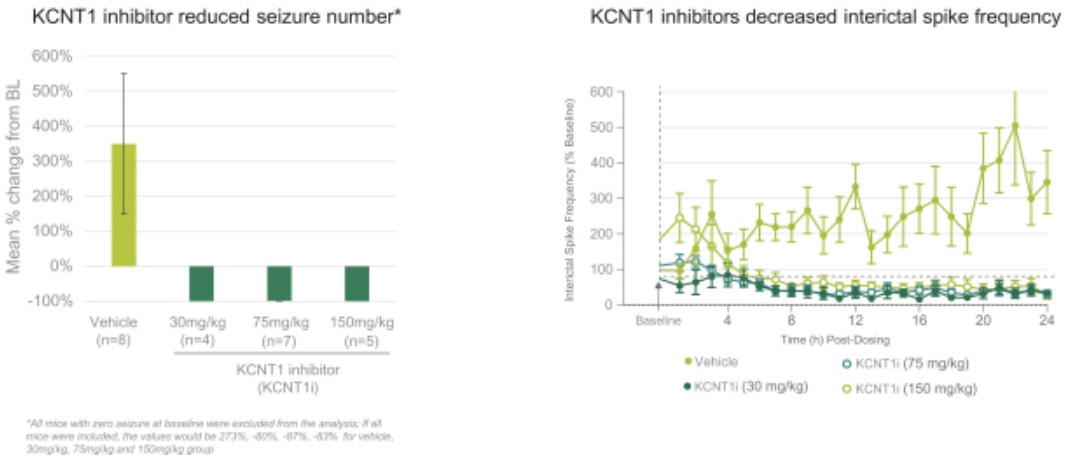


Figure 31. A KCNT1 inhibitor eliminated the occurrence of seizures in a KCNT1 transgenic mouse model and suppressed interictal spikes (or abnormal electrographic discharges observed between seizures) as detected by EEG

We are continuing to optimize the chemical structures of our molecules targeting KCNT1 channels and expect to select a development candidate in 2021.

Novel Collaborations in Rare Epilepsies

We have entered into a research collaboration with The Florey Institute of Neuroscience and Mental Health to develop three novel ASOs for the treatment of SCN2A loss of function mutations and two additional rare epilepsy targets. This partnership expands our rare epilepsy drug development efforts with six distinct programs for the treatment of six different rare epilepsies. This demonstrates our commitment to leading sodium channel research and particularly in the Nav1.2 channel which the SCN2A gene encodes.

Competition

The biopharmaceutical industry is characterized by rapidly advancing technologies, strong competition and an emphasis on proprietary products. While we believe that our technology, knowledge, experience and scientific personnel provide us with competitive advantages, we face substantial competition from many different sources, including large and small pharmaceutical and biotechnology companies, academic research institutions, governmental agencies and public and private institutions.

Any product candidates that we successfully develop and commercialize will compete with currently approved therapies and new therapies that may become available in the future. Key product features that would affect our ability to effectively compete with other therapeutics include the efficacy, safety, convenience, cost, effectiveness of promotional support and intellectual property protection of our products. Our competitors fall primarily into the following groups of treatment:

- GABAA receptor modulator programs in development targeting MDD, including that of SAGE Therapeutics, as well as other programs in clinical development targeting other mechanisms of action and approved therapies such as SSRIs.
- T-type calcium channel inhibitor programs in development targeting ET, including that of Jazz Pharmaceuticals and Neurocrine Biosciences, as well as other programs in clinical development targeting other mechanisms of action and approved therapies, such as propranolol, and off-label therapies, such as primidone.
- Sodium channel blocker programs in development for DEEs, including those of SK-Pharma, Xenon Pharmaceuticals and Neurocrine Biosciences, as well as other programs in clinical development targeting other mechanisms of action and approved therapies including other existing ion channel blockers.
- Treatments for TN include anticonvulsive medications, such as carbamazepine as well as various procedures or surgical interventions (vascular decompression or gamma knife). We are not aware of any

development programs targeting SUNCT and SUNA, but we may face competition from off-label therapies such as intravenous lidocaine.

Many of our competitors have substantially greater financial resources, expertise and capabilities in research and development, the regulatory approval process, manufacturing and marketing than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through M&A activity and sizeable collaborative arrangements with established companies.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to the development of our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets relating to our proprietary technology platform and on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of neuroscience that may be important for the development of our business. We additionally may rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions, where available.

Our commercial success may depend in part on our ability to: obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to limit third parties from making, using, selling, offering to sell, or importing our products may depend on the extent to which we have rights under valid and enforceable licenses, patents, or trade secrets that cover these activities. In some cases, enforcement of these rights may depend on third party licensors. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same.

Patent expiration dates noted in the following paragraphs refer to statutory expiration dates and do not take into account any potential patent term adjustment or extension that may be available.

GABAA receptor positive allosteric modulators

We own eight patent families directed to GABAA receptor positive allosteric modulators. One family discloses and claims salts and polymorphs of PRAX-114, including the lead clinical candidate citrate salt of PRAX-114. Two patents covering the clinical candidate salt have granted in the United States (U.S. 10,562,930 and U.S. 10,927,141) and applications in other potentially commercially relevant jurisdictions are pending, which expire in 2039. A second family covers various methods of use, including treatment of the current lead clinical indication, major depressive disorder, with PRAX-114. This patent family has 2 pending applications, which expire in December 2039. A third family is directed to methods of treating various perimenopausal symptoms with PRAX-114. This family has one pending application and expires in 2040. A fourth family is directed to methods of treating mood disorders (including depression) with combinations of GABA-PAMs (including PRAX-114) with NMDA antagonists, NMDA Negative Allosteric Modulators or NMDA partial agonists. This family has one application and expires in 2040. A fifth family covers deuterated forms of PRAX-114. This has one pending application and expires in February 2041. Five additional U.S. provisional applications have been filed, two covering methods of treating adjustment disorder with PRAX-114; two covering improved methods of treating depression with an evening dose of PRAX-114; and one covering a potential alternative clinical candidate salt of PRAX-114.

T-type Calcium channel blockers

We own five patent families directed to T-type Calcium channel blockers. One family discloses and claims compositions of matter of certain T-type calcium channel modulators, including PRAX-944. This patent family is issued in many major pharmaceutical markets and is pending in others, and expires in 2029. A second family is directed to methods of use of certain T-type calcium channel modulators, including PRAX-944, in treating disease such as epilepsy. This patent family is pending in the United States and expires in December 2037. A third patent family is directed to certain pharmaceutical formulations of PRAX-944 and methods of use in treating disorders such as essential tremor. This patent family is pending in multiple jurisdictions of potential commercial interest. A fourth family is directed to methods of use of PRAX-944. This family is composed of three provisional applications. A fifth

patent family is directed to certain analog compounds of PRAX-944. This patent family is composed of three provisional applications.

Persistent sodium current blockers

We own sixteen patent families directed to persistent sodium current blockers including three patent families that relate to our PRAX-562 program and thirteen families related to other persistent sodium current blockers. Additionally, we have in-licensed one patent family.

Regarding the three families directed to our PRAX-562 program, one family discloses and claims certain persistent sodium current blockers, including PRAX-562, and methods of use in treating diseases such as pediatric epilepsy. This family is pending in multiple jurisdictions, and expires in 2039. A second family discloses other persistent sodium current blockers and generically claims PRAX-562. This family also claims methods of use of the claimed compounds in treating diseases such as pediatric epilepsy. This patent family is pending in multiple jurisdictions, and expires in 2037. A third family is directed to pharmaceutical formulations of PRAX-562, methods of use in treating diseases such as pediatric epilepsy, cephalgia, SUNCT and SUNA and methods of making PRAX-562. This family is pending. A fourth family is directed to methods of use of persistent sodium current blockers, including PRAX-562, in treating diseases such as cephalgia, SUNCT and SUNA. This family is composed of two provisional applications.

The remaining thirteen patent families are directed to a portfolio of sodium channel blockers that we plan to advance in other neuropsychiatric disorders. Eleven patent families disclose and claim persistent sodium current blockers of various core structures and methods of use in treating diseases such as pediatric epilepsy, which include nine families pending in the United States, expiring between 2037 and 2040, and two families pending, expiring between 2039 and 2040. Two families are directed to methods of use of certain persistent sodium current blockers in treating diseases such as cephalgia, SUNCT and SUNA. The two families are composed of four provisional applications.

We have exclusively in-licensed one patent family directed to additional persistent sodium current blockers. This family is owned by Gilead. This family has claims directed to certain persistent sodium current blockers and methods of use. This patent family is issued in multiple jurisdictions of potential commercial interest and is pending in other jurisdictions of interest, and expires in 2030.

KCNT1 blockers

We own ten patent families directed to KCNT1 blockers including nine families related to our KCNT1 program and one family related to antisense oligonucleotides.

Nine patent families are directed to our KCNT1 program and disclose and claim small molecule KCNT1 blockers and methods of use in treating diseases such as epilepsy, including epilepsy having certain KCNT1 mutations. Three families are pending as PCTs, and expire in 2040 or 2041. Six families are provisional applications.

One family is directed to certain antisense oligonucleotides and methods of use in treating diseases such as epilepsy, including epilepsy having certain KCNT1 mutations. This family is pending and expires in December 2039.

SCN2A downregulation

We have exclusively in-licensed two patent families directed to our SCN2A program. These patent families are owned by RogCon. These families disclose and claim certain antisense oligonucleotides targeting SCN2A and methods of use in treating diseases such as epilepsy, including epilepsy having certain SCN2A mutations. One family is pending in the United States and expires in August 2039. A second family is pending as a PCT in which the claims are directed to methods of treating an SCN1A encephalopathy.

We own one patent family directed to our PRAX-222 program and a method of treating SCN2A gain of function neurological diseases using certain antisense oligonucelotides. This patent family is pending as a provisional application.

We have an exclusive option to in-license one patent family directed to compositions of matter of PRAX-222. This patent family is owned by Ionis and pending as a provisional application.

License Agreements

License Agreement with RogCon

In September 2019, we and RogCon entered into a Cooperation and License Agreement, or the RogCon Agreement, to collaborate to develop antisense oligonucleotides for the treatment of epilepsy caused by mutations of the SCN2A gene. RogCon had an existing collaboration arrangement with Ionis and as a result, we and Ionis negotiated a Research Collaboration, Option and License Agreement, or the Ionis Agreement, (described below) in order to complete the license agreement with RogCon. In December 2018, we entered into an agreement with RogCon to advance to them a fully refundable deposit of up to $1.0 million while the RogCon Agreement was being negotiated. Under the RogCon Agreement, RogCon granted us, subject to a concurrent license grant of certain rights to Ionis, an exclusive, worldwide license under RogCon's intellectual property to research, develop and commercialize products for the treatment of all forms of epilepsy and/or neurodevelopmental disorders in each case caused by any mutation of the SCN2A gene. Under the RogCon Agreement, we will conduct, at our own cost and expense, the research and development activities assigned to us under the research plan set out in the Research Collaboration, Option and License Agreement with Ionis. Under the terms of the RogCon Agreement, RogCon is eligible to receive a one-time milestone payment of $3.0 million as well as profit share payments as a percentage of net profits in the mid-teens. Profit share payments will be calculated and due quarterly on any net profits generated from a product commercialized under the RogCon Agreement. The $3.0 million milestone payment will become due when (i) the first profit share payment has become due and payable and (ii) the Additional Milestone, the Initial Interest Amount and the Second Interest Amount (each as defined within the Ionis Agreement as described below) have all become due and payable to Ionis under our collaboration agreement with Ionis. As part of the RogCon Agreement, we agreed to provide up-front consideration of $2.1 million, consisting of a $1.0 million deposit, $0.7 million in cash reimbursements for certain historical costs previously incurred by RogCon and $0.4 million for the retirement of existing loan balances as of September 11, 2019.

Subsequent to September 11, 2019, we will reimburse RogCon for its out-of-pocket costs incurred for activities performed under the RogCon Agreement. We expense these costs as incurred as research and development. Since the acquisition date, we expensed $0.2 million and $0.1 million related to the reimbursement of RogCon's out-of-pocket costs in the years ended December 31, 2020 and 2019, respectively.

Additionally, RogCon has agreed to certain defined exclusivity obligations. The RogCon Agreement, unless earlier terminated, will continue until the latest of: (i) the expiration of all patent rights within RogCon patents, (ii) we certify we have abandoned the research, development and commercialization of product with no intention to re-establish such activities and (iii) no third party is obligated to pay any amounts that comprise net sublicense revenue. Either party may terminate the RogCon Agreement for material breach or insolvency of the other party. Additionally, we may terminate for convenience with prior written notice to RogCon. Upon termination by either party, all rights and licenses granted by RogCon to us will revert back to RogCon.

Ionis Collaboration Agreement

In September 2019, we and Ionis entered into the Ionis Agreement to discover and develop antisense oligonucleotides to treat forms of epilepsy caused by mutations of the SCN2A gene. Pursuant to the Ionis Agreement, we and Ionis will each conduct certain research activities and Ionis will be responsible for identifying a development candidate and conducting an IND-enabling toxicology study. The design of the IND-enabling toxicology study will be prepared and mutually agreed to by us and Ionis. We are obligated to reimburse any out-of-pocket costs incurred by Ionis related to research activities, identification of a development candidate and conducting IND-enabling studies. We hold an exclusive option, which we may exercise following the results of the IND-enabling toxicology study, to obtain the rights and license to further develop and commercialize a development candidate in the field of epilepsy and neurodevelopmental disorders, other than Dravet Syndrome. Upon the exercise of such option, we will be required to pay Ionis a $2.0 million license fee. In addition, after option exercise, Ionis is eligible to receive certain contingent payments from us relating to development and other milestones, interest payments, royalties as a percentage of net product sales worldwide in the low-20s and any potential sublicense fees calculated as a percentage of sublicense revenue using a rate in the low-to-mid double digits.

Development milestones of $5.0 million for each product developed under the agreement are due upon the completion of the first clinical trial for each product, or the Development Milestone. Ionis will be entitled to receive an additional one-time milestone payment of $5.0 million, or the Additional Milestone, upon the earliest to occur of the

following (each, a Payment Trigger): (i) the first acceptance of an NDA filing for a product by the regulatory authority in a major market, (ii) we have both (a) received, in the aggregate, $300.0 million in cash since September 11, 2019 and (b) initiated the first clinical study with respect to a product or (iii) the closing of a change of control event affecting Praxis. In addition, upon the occurrence of a Payment Trigger, Ionis is also entitled to certain interest payments equal to (i) 10% simple interest per annum calculated from the effective date of the agreement on the Additional Milestone, or the Initial Interest Amount, plus (ii) 10% simple interest per annum calculated from the date the Additional Milestone is paid on the initial Interest Amount, or the Second Interest Amount, until the earliest to occur of the following: (i) aggregate net sales of $100.0 million has been received, (ii) a change in control event affecting Praxis occurs or (iii) the Ionis Agreement has been terminated. Upon the occurrence of one of these three payment triggers, both the Initial Interest Amount and Second Interest Amount are due and payable to Ionis.

The Ionis Agreement will continue in full force and effect until the expiration of all payment obligations to Ionis, unless terminated earlier by either party. Either party may terminate the agreement upon material breach or insolvency of the other party or if Ionis is unable to identify a development candidate. Praxis is able to terminate the Ionis Agreement for convenience with prior written notice. Ionis may terminate if we fail to achieve certain performance milestones or Ionis' failure to identify a development candidate. Upon termination by us for convenience, we will stop selling all products, subject to certain wind-down provisions and all products will revert back to Ionis.

License Agreement with Purdue

In December 2017, we and Purdue Neuroscience Company, or Purdue, entered into a license agreement, or the Purdue Agreement, pursuant to which we were granted exclusive rights under certain Purdue know-how to research, develop and commercialize pharmaceutical products concerning a GABAA positive allosteric modulator. We are obligated to make future milestone payments based on the achievement of specified development and sales milestones up to $33.0 million. Additionally, under the Purdue Agreement, we were obligated to sell to Purdue $0.6 million of our Series B Preferred Stock in connection with our Series B financing. In addition, as consideration for the license obtained, we issued Purdue the anti-dilution obligation to ensure Purdue's ownership remained at a specified percentage throughout the Series B financing. Further, we are obligated to pay to Purdue a royalty percentage in the low single-digits of net sales of each licensed product for 12 years from the date of the first commercial sale of such product.

The Purdue Agreement will remain in effect until the expiration of our royalty obligation for all licensed products. Either us or Purdue may terminate the agreement in the event of a material breach by the other party and such party fails to cure such breach within a certain period of time. Either party may voluntarily terminate the agreement with prior notice. If the agreement is voluntarily terminated by Purdue, our license rights will survive such termination and such rights will become fully paid, perpetual and irrevocable. Purdue may also terminate in the event of our insolvency.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently source all of our non-clinical and clinical compound supply through third-party contract development and manufacturing organizations, or CDMOs.

For clinical supply, we use CDMOs who act in accordance with the FDA's current Good Manufacturing Practices, cGMP, for the manufacture of drug substance and product. We expect to rely on third parties for our manufacturing processes and the production of all clinical supply drug substance and drug product and currently expect to continue to do so for commercial supplies of our product candidates, if approved. We use additional contract manufacturers to fill, label, package, store and distribute our investigational drug products and currently expect to continue to do so for commercial supplies of our product candidates, if approved. It is our intent to identify and qualify additional manufacturers to provide active pharmaceutical ingredient and fill-and-finish services prior to submission of an NDA to the FDA for any product candidates that complete clinical development.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of prescription drugs, such as those we are developing. These agencies regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting,

sampling and export and import of drug products and product candidates. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

U.S. government regulation of drug products

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The FDA also regulates biological products under the FDCA and the Public Health Service Act, or PHSA. If we advance clinical development of a biologic candidate in the future, these development activities will be subject to additional regulatory requirements specific to biologics. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties brought by the FDA and the Department of Justice, or DOJ, or other governmental entities.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- Completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- Submission to the FDA of an IND which must become effective before human clinical trials may begin;
- Approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug product for each indication;
- Submission to the FDA of an NDA or BLA;
- Satisfactory completion of an FDA advisory committee review, if applicable;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- Satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- Payment of user, product and establishment fees and securing FDA approval of the NDA, including agreement to compliance with any post-approval requirements; and
- Compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical studies

Before testing any drug or biological product candidate, including our product candidates, in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies generally include laboratory evaluation of product chemistry, formulation and stability, as well as animal studies to assess potential toxicity, which support subsequent clinical testing. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature and a proposed clinical protocol, among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before human clinical trials may begin.

Clinical trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all

research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it initiates at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their www.clinicaltrials.gov website. Information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in some cases for up to two years after the date of completion of the trial.

An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to be initiated. Additionally, FDA will review any data from clinical trials conducted outside the United States when determining whether to allow an IND to proceed in the U.S. Specifically, FDA's acceptance of data from trials conducted outside of the U.S. is subject to certain conditions, including that the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with GCPs; the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful; and that the trials are conducted in compliance with all applicable U.S. laws and regulations. Clinical holds also may be imposed by the FDA at any time before or during studies due to safety concerns or non-compliance.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution for a variety of reasons, including if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow up. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the drug or biologic as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidates do not undergo unacceptable deterioration over their shelf life.

Marketing application submission and FDA review and approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has ten months from the date of "filing" of a standard NDA for a new molecular entity in which to complete its initial review and respond to the applicant, and six months from the filing date for priority applications. The FDA does not always meet its PDUFA goal dates, and the review process can be extended by FDA requests for additional information or clarification and a sponsor's process to respond to such inquiries. This FDA review typically takes twelve months from the date the NDA is submitted to FDA (for a standard review) or eight months (for a priority review) because the FDA has approximately two months, or 60 days, after submission to make a "filing" decision on whether to accept an NDA for review.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review and informs the sponsor by the 74th day after the FDA's receipt of the submission whether an application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

Additionally, the FDA may refer any application to an advisory committee, including applications for novel drug candidates that present difficult questions of safety or efficacy. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan, if it determines that a REMS is necessary to ensure that the benefits of the drug outweigh its risks and to assure the safe use of the drug product. The REMS plan could include medication guides, physician communication plans, assessment plans and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS plan is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without a REMS, if required.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue either an approval letter or a complete response letter, or CRL. An approval letter authorizes commercial marketing of the drug with specific prescribing information and for specific indications. A CRL generally outlines the deficiencies in the submission and contains a statement of specific conditions that must be met in order to secure final approval of the NDA; it may require additional clinical or preclinical testing and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing in order for FDA to reconsider the application. If a CRL is issued, the applicant may choose to either resubmit the NDA, addressing all of the

deficiencies identified in the letter, or withdraw the application. If and when those deficiencies have been addressed to the FDA's satisfaction, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan drug designation and exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Further, the FDA may approve more than one product for the same orphan indication or disease as long as the products contain different active ingredients. Moreover, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity.

Rare pediatric disease designation and priority review vouchers

Under the FDCA, the FDA incentivizes the development of drugs products that meet the definition of a "rare pediatric disease," defined to mean a serious or life-threatening disease in which the serious of life-threatening manifestations primarily affect individuals aged from birth to 18 years and the disease affects fewer than 200,000 individuals in the United States or affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making in the United States a drug product for such disease or condition will be received from sales in the United States of such drug product. The sponsor of a product candidate for a rare pediatric disease may be eligible for a voucher that can be used to obtain a priority review for a subsequent human drug product application after the date of approval of the rare pediatric disease drug product, referred to as a priority review voucher, or PRV. A sponsor may request rare pediatric disease designation from the FDA prior to the submission of its NDA. A rare pediatric disease designation does not guarantee that a sponsor will receive a PRV upon approval of its NDA. Moreover, a sponsor who chooses not to submit a rare pediatric disease designation request may nonetheless receive a PRV upon approval of their marketing application if they request such a voucher in their original marketing application and meet all of the eligibility criteria. If a PRV is received, it may be sold or transferred an unlimited number of times. Congress has extended the PRV program through September 30, 2024, with the potential for PRVs to be granted through September 30, 2026.

Fast track, breakthrough therapy and priority review designations

The FDA is authorized to designate certain products for expedited development or review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include fast track designation, breakthrough therapy designation and priority review designation.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address unmet medical needs for the condition. Fast track designation provides opportunities for more frequent interactions with the FDA review team to expedite development and review of the product. The FDA may also review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable and the sponsor pays any required user fees upon submission of the first section of the application. The sponsor can request the FDA to designate the product for fast track status any time before receiving NDA approval, but ideally no later than the pre-NDA meeting. Fast track designation may be withdrawn by the sponsor or rescinded by the FDA if the designation is no longer supported by data emerging in the clinical trial process.

In addition, with the enactment of FDASIA in 2012, Congress created a new regulatory program for product candidates designated by FDA as “breakthrough therapies” upon a request made by IND sponsors. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. If the FDA designates a breakthrough therapy, it may take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout the development of the therapy; providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the non-clinical and clinical data necessary for approval is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and considering alternative clinical trial designs when scientifically appropriate, which may result in smaller trials or more efficient trials that require less time to complete and may minimize the number of patients exposed to a potentially less efficacious treatment. Breakthrough therapy designation comes with all of the benefits of fast track designation, which means that the sponsor may file sections of the NDA for review on a rolling basis if certain conditions are satisfied, including an agreement with the FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review. Finally, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines at the time that the marketing application is submitted, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications and to shorten the FDA’s goal for taking action on a marketing application from ten months to six months for an NDA for a new molecular entity from the date of filing. If criteria are not met for priority review, the application for a new molecular entity is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, fast track designation, priority review and breakthrough therapy designation do not change the standards for approval and may not ultimately expedite the development or approval process.

Accelerated approval pathway

A drug product may also be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition and provides a meaningful therapeutic benefit over existing treatments. Such products can be approved on the basis of adequate and well-controlled clinical trials establishing an effect on either

a surrogate endpoint that is reasonably likely to predict clinical benefit or on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the disease or condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials to verify and describe the predicted effect on IMM or other clinical endpoint. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

In addition, all promotional materials for products approved under the accelerated approval program are subject to prior review by the FDA, a requirement that could adversely impact the timing of the commercial launch of the product. FDA may withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product.

U.S. marketing and data exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain follow-on drug applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an Abbreviated New Drug Application, or ANDA, or a 505(b)(2) NDA submitted by another company for a generic or follow-on version of the protected drug product, respectively, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement.

The FDCA also provides three years of data exclusivity when an NDA or a supplement to an existing NDA, includes new clinical investigations, other than bioavailability studies, conducted or sponsored by the applicant that are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs or follow-on 505(b)(2) NDAs if the protected clinical data are not referenced. Five-year and three-year exclusivity will not delay the submission or approval of a stand-alone NDA submitted under section 505(b)(1) of the FDCA. However, an applicant submitting a stand-alone NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness, if applicable.

Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing regulatory exclusivity periods. This six-month exclusivity may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued “Written Request” for such a trial.

Patent term restoration

Depending upon the timing, duration and specifics of FDA approval of our drug product candidates, some of our U.S. patents may be eligible for limited patent term extension. These patent term extensions permit a patent restoration term of up to five years as compensation for any patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the drug product’s approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a New Drug Application, or NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the extension must be applied for prior to expiration of the patent. The United States Patent and Trademark Office, or the USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Post-approval requirements

Following approval of a new prescription drug product, the manufacturer and the approved drug are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to monitoring and recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs must be promoted by a manufacturer and any third parties acting on behalf of a manufacturer only for the approved indications and in a manner consistent with the approved label for the product. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-

label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability. After approval, most changes to the approved product, such as adding new indications or other labeling claims or changes to the manufacturing processes or facilities, are subject to prior FDA review and approval. There are continuing, annual user fee requirements for any marketed products and the establishments where such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval of a drug is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- Restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- Fines, warning letters or other enforcement-related letters or clinical holds on post-approval clinical trials;
- Refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or suspension or revocation of product approvals;
- Product seizure or detention, or refusal to permit the import or export of products; and
- Injunctions or the imposition of civil or criminal penalties.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. From time to time, new legislation and regulations may be implemented that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. It is impossible to predict whether further legislative or regulatory changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Other healthcare laws and regulations

Healthcare providers, physicians and third party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any drug products for which we obtain marketing approval. Our current and future arrangements with third party payors, customers, healthcare providers, physicians and others, in connection with the clinical research, sales, marketing and promotion of products, once approved, and related activities, may expose a pharmaceutical manufacturer to broadly applicable fraud and abuse and other healthcare laws and regulations. In particular, the research of our product candidates, as well as the promotion, sales and marketing of healthcare items and services and certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business or financial arrangements.

The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include, but are not limited to:

- the U.S. federal Anti-Kickback Statute, which makes it illegal for any person or entity, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement, or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. The term remuneration has been interpreted broadly to include anything of value. Further, courts have found that if "one purpose" of renumeration is to induce referrals, the federal Anti-Kickback Statute is violated. Violations are subject to significant civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment and exclusion from government healthcare programs. In addition, a claim submitted for payment to any federal healthcare program that includes items or services that were made as a result of a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or FCA. The Anti-Kickback Statute has been interpreted to apply to arrangements between biopharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers, among others, on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution;

- the U.S. federal civil and criminal false claims laws, including the FCA, which can be enforced through "qui tam" or "whistleblower" actions, and civil monetary penalty laws, which impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal health care programs that are false, fictitious or fraudulent; knowingly making, using, or causing to be made or used, a false record or statement material to a false, fictitious or fraudulent claim or an obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing or concealing such an obligation. to pay money to the federal government. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation. A claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim under the FCA. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. When an entity is determined to have violated the FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;

- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false fictitious or fraudulent statement or entry in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA fraud provisions without actual knowledge of the statute or specific intent to violate it;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements relating to the privacy, security and transmission of individually identifiable health information on certain covered healthcare providers, health plans and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the creation, use, receipt, maintenance or disclosure of individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil

actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;

- the U.S. federal Physician Payments Sunshine Act, created under Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, and its implementing regulations, which require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the Centers for Medicare and Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS, under the Open Payments Program, information related to direct or indirect payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made during the previous year to certain non-physician providers such as physician assistants and nurse practitioners;

- U.S. federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and

- analogous U.S. state, local and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and other relevant compliance guidance promulgated by the federal government that otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information, some of which may be more stringent than those in the United States (such as the European Union, which adopted the General Data Protection Regulation, which became effective in May 2018) in certain circumstances, and may differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Additionally, on November 20, 2020, HHS finalized a regulation that, among other things, (i) removed safe harbor protection for price reductions from pharmaceutical manufacturers, and (ii) created new safe harbor for certain fixed fees. It is not clear at this time what effect, if any, these and other changes to the Anti-Kickback Safe Harbors, in effect as of January 19, 2021, will have on our business.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Efforts to ensure that business arrangements comply with applicable healthcare laws involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting its rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, imprisonment, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, reporting obligations and oversight if we become subject to integrity and oversight agreements to resolve allegations of non-compliance, contractual damages, reputational harm, diminished profits and future earnings and curtailment of operations, any of which could adversely affect our ability to operate our business and the results of operations. In addition, commercialization of any drug product outside the United States will also likely be subject to foreign equivalents of the healthcare laws mentioned above, among other foreign laws. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business with are found to be not in compliance with applicable laws, they may be subject to similar penalties.

Other data privacy and security laws

In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use, disclosure and protection of health-related and other personal information outside of HIPAA and its implementing regulations. For example, in June 2018, the State of California enacted the California Consumer Privacy Act of 2018, or the CCPA, which came into effect on January 1, 2020 and provides new data privacy rights for consumers and new operational requirements for companies, which may increase our compliance costs and potential liability. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact certain of our business activities. The CCPA could mark the beginning of a trend toward more stringent state privacy legislation in the United States, which could increase our potential liability and adversely affect our business.

In the event we decide to conduct clinical trials or continue to enroll subjects in our ongoing or future clinical trials, we may be subject to additional privacy restrictions imposed by other countries and jurisdictions. The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the European Economic Area, or EEA, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. Further, the United Kingdom's decision to leave the EU, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated now that the United Kingdom has left the EU.

Current and future healthcare reform legislation

In both the United States and certain foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes regarding the health care system directed at broadening the availability of healthcare, improving the quality of healthcare and containing or lowering the cost of healthcare. For example, in March 2010 the ACA was enacted, which substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower-cost biosimilars, expands the types of entities eligible for the 340B drug discount program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations; established annual fees and taxes on manufacturers of certain branded prescription drugs; and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, or BBA, effective as of January 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there remain judicial, administrative, executive and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future.

Various portions of the ACA are currently undergoing legal and constitutional challenges in the United States Supreme Court; the Trump Administration has issued various Executive Orders which eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices; and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. Also, in December 2018, CMS issued a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program. Since then, the ACA risk adjustment program payment parameters have been updated annually. It is unclear whether the ACA will be overturned, repealed, replaced, or further amended.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs, including aggregate reductions of Medicare payments to providers of up to 2% per fiscal year. These reductions went into effect on April 1, 2013, and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act and subsequent legislation, these Medicare sequester reductions under the Budget Control Act of 2011 will be suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. Proposed legislation, if passed, would extend this suspension until the end of the COVID-19 pandemic. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additionally, the BBA, among other things, also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount (from 50% under the ACA to 70%) that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole".

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. There also has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. For example, at the federal level, the U.S. government's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses and place limits on pharmaceutical price increases. Moreover, the U.S. Presidential administration previously released a "Blueprint" to lower drug prices and reduce out-of-pocket costs of drugs that contained proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. HHS has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule that would allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. In addition, there have been several changes to the 340B drug pricing program, which imposes ceilings on prices that drug manufacturers can charge for medications sold to certain health care facilities. It is unclear how these developments could affect covered hospitals who might purchase our future products and affect the rates we may charge such facilities for our approved products in the future, if any.

Additionally, on July 24, 2020 and September 13, 2020, former President Trump signed a series of Executive Orders aimed at lowering drug prices and at implementing several of the administration's proposals. In response, the FDA released a final rule on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada, as further discussed below. Further, on November 20 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN,

Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and will apply in all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. The Interim Final Rule has not been finalized and is subject to revision and challenge. Additionally, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Although a number of these and other measures may require additional authorization to become effective, and the Biden administration may reverse or otherwise change these measures, Congress has indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors.

At the state level, legislatures in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs.

In the European Union and in other foreign jurisdictions, similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or EU member state level may result in significant additional requirements or obstacles that may increase our operating costs.

Legislative and regulatory proposals, and enactment of laws, at the foreign, federal and state levels, directed at containing or lowering the cost of healthcare, will likely continue into the future.

Rest of world regulation

For other countries outside of the European Union and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing product development, the conduct of clinical trials, manufacturing, distribution, marketing approval, advertising and promotion, product licensing, pricing and reimbursement vary from country to country. Additionally, clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Additionally, to the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

Additional laws and regulations governing international operations

If we further expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered by U.S. authorities that enforce the FCPA, including the Department of Justice, to be foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

Coverage, pricing and reimbursement

Significant uncertainty exists as to the coverage, pricing and reimbursement status of any products seeking regulatory approval. Successful commercialization of new drug products depends in part on the extent to which coverage and reimbursement for those drug products will be available from government health administration authorities, private health insurers and other organizations. The availability and extent of reimbursement depend substantially, both domestically and abroad, on the extent to which the costs of drugs products are paid for by third-party payors, such as government health care programs (e.g., Medicare, Medicaid), health maintenance organizations, managed care providers, pharmacy benefit and similar healthcare management organizations, private health coverage insurers and other third-party payors. These third-party payors decide which medications they will pay for and will establish reimbursement levels.

In the United States, the principal decisions about reimbursement for new drug products are typically made by CMS. CMS decides whether and to what extent a new drug product will be covered and reimbursed under Medicare, and private payors tend to follow CMS to a substantial degree. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

In the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors and coverage and reimbursement levels for drug products can differ significantly from payor to payor. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. One payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product. Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication.

Various federal laws may impact the extent of coverage and reimbursement status provided by government health care programs. For instance, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each Part D prescription drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each

therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for drugs for which we obtain marketing approval. Any negotiated prices for any of our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the average manufacturer price, or AMP, and Medicaid rebate amounts reported by the manufacturer. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although under the current state of the law these newly eligible entities (with the exception of children's hospitals) will not be eligible to receive discounted 340B pricing on orphan drugs. As 340B drug pricing is determined based on average manufacturer price, or AMP, and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase. The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by HHS, the Agency for Healthcare Research and Quality and the National Institutes for Health and periodic reports on the status of the research and related expenditures are made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our product candidates, if any such drug or the condition that they are intended to treat are the subject of a trial.

It is also possible that comparative effectiveness research, whether conducted by government or private entities, demonstrating benefits in a competitor's drug could adversely affect the sales of our product candidate. If third party payors do not consider our drugs to be cost-effective compared to other available therapies, they may not cover our drugs after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our drugs on a profitable basis.

In addition to the above-mentioned laws, increasing efforts by third party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates, if approved, may nonetheless not be considered medically necessary or cost-effective. If third party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. We expect to experience pricing pressures from third party payors in connection with the potential sale of any of our product candidates

Outside of the United States, the pricing of pharmaceutical products and medical devices is subject to governmental control in many countries. For example, in the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost effectiveness of a particular therapy to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. Other countries may allow companies to fix their own prices for products, but monitor and control product volumes and issue guidance to physicians to limit prescriptions. Efforts to control prices and utilization of pharmaceutical products and medical devices will likely continue as countries attempt to manage healthcare expenditures. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

Human Capital

At Praxis, we are fiercely dedicated to our mission to translate genetic insights into the development of therapies for CNS disorders characterized by neuronal imbalance. While we strive each day to innovate and adapt

to deliver treatments that could potentially change the course of CNS disorders, we are also committed to developing our culture and our employees through our company core values – ***Trust***, ***Ownership***, ***Curiosity*** and ***Results***.

High talent density is our ultimate goal. Our culture is how we attract talent to join Praxis, which is how we were able to grow from 29 employees in three states at the end of 2019 to 67 in 12 states as of January 31, 2021.

We ***Trust*** each other's judgement, which is why we do not implement excessive policies, and we value transparency among team members that leads to direct, clear, and timely feedback so we can all improve together. We commit to be one another's checks and balances. We respect all opinions and encourage diversity. Discrimination is never tolerated. Because we trust employees to have good judgment, there is a lot of freedom built into the way we operate. As an example, we do not have prescriptive policies on vacation, sick or personal time – we encourage employees to take that time as they need it and simply align with their manager about their plans.

Companies have learned to adapt on the fly during a global pandemic, and ***Ownership*** is something we have been sure to emphasize during this time. We want employees to own projects and stay engaged through communication, but we also make sure employees know that Praxis is not a nine-to-five culture. We are a culture where employees have real accountability as we all work towards a greater goal. We understand the adjustment of working from home, connecting virtually instead of in person, and, for some, serving as teacher for children in virtual school. We also acknowledge the stresses of living through a pandemic. Being able to own projects, while expressing when you need a break, is something we value. Allowing employees to best structure their days to their needs is one of the most important foundations we believe is necessary for having a sturdy organization.

Curiosity is at the center of innovation and we are always asking how we can better help our patients. We love to learn. Every first Monday of the month, we commit to what we call "Curiosity Day." We ask our employees to step away from the computer for a day to learn more about something that interests them. Whether it is diving deeper into a rare disease we do not currently support, revisiting a historical moment in time, perfecting a new skill, or even taking a day to safely enjoy the outdoors, these opportunities have made a positive impact for our employees, and they bring the new knowledge back to deliver on our mission.

As we pursue objectives to achieve the ultimate ***Results***, we challenge ourselves daily. Through trust, ownership and curiosity, our employees are positioned to leave lasting results that reach the communities we serve. At the end of the day, the magic we witness when employees put their minds together is what our company is most proud of.

To hold ourselves accountable for fulfilling our core values, we have abandoned traditional performance management systems. With our work being done by agile, self-managed teams, we have developed a unique social feedback system in which, each employee chooses approximately 10 reviewers to give feedback on the employee's performance and Praxis values, on a regular basis. Reviewers are instructed to be candid but with positive intent, so that the feedback receiver has the opportunity to learn valuable lessons and identify development opportunities, which are crucial for our collective and individual growth. To promote a culture of openness and transparency, the feedback is not given anonymously, and each employee sees the reviewer's ratings and comments. We feel the breadth of feedback helps ensure employees best understand what they do well, what they have improved on, where improvement is still needed and ultimately results in a high-performance culture.

In line with our core values, we are committed to providing a competitive total rewards package. Our compensation is a mix of salary, bonus, long-term equity and health and welfare benefits.

Available Information

Our Internet address is http://praxismedicines.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act are available through the "Investors + Media" portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information on our website is not part of this Annual Report on Form 10-K or any of our other securities filings unless specifically incorporated herein by reference. In addition, our filings with the SEC may be accessed through the SEC's Interactive Data Electronic Applications system at http://www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or

information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K and in our other filings with the Securities and Exchange Commission, or SEC, before deciding to invest in our common stock. The risks described below are not the only risks facing our company. The occurrence of any of the following risks, or of additional risks and uncertainties not presently known to us or that we currently believe to be immaterial, could cause our business, prospects, operating results and financial condition to suffer materially. In such event, the trading price of our common stock could decline, and you might lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

Risks Related to Past Financial Condition

We are a clinical-stage biopharmaceutical company and we have incurred significant losses since our inception. We anticipate that we will continue to incur significant losses for the foreseeable future.

Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any revenue to date, and we will continue to incur significant research and development and other expenses related to our clinical development and ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception. Since our inception, we have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and our clinical trials. Our financial condition and operating results, including net losses, may fluctuate significantly from quarter to quarter and year to year. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance. Additionally, net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' (deficit) equity and working capital. Our net losses were $61.8 million and $35.5 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $149.6 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for our product candidates in our initial and potential additional indications as well as for other product candidates.

We anticipate that our expenses will increase substantially if and as we:

- continue to develop and conduct clinical trials, including in expanded geographies such as the United States or Europe, for PRAX-114, PRAX-944 and PRAX-562 for our initial and potential additional indications;
- initiate and continue research and development, including preclinical, clinical, and discovery efforts for any future product candidates;
- seek to identify additional product candidates;
- seek regulatory approvals for PRAX-114, PRAX-944 and PRAX-562, or any other product candidates that successfully complete clinical development;
- add operational, financial and management information systems and personnel, including personnel to support our product candidate development and help us comply with our obligations as a public company;
- hire and retain additional personnel, such as clinical, quality control, scientific, commercial and administrative personnel;
- maintain, expand and protect our intellectual property portfolio;
- establish sales, marketing, distribution, manufacturing, supply chain and other commercial infrastructure in the future to commercialize various products for which we may obtain regulatory approval;
- add equipment and physical infrastructure to support our research and development;

- acquire or in-license other product candidates and technologies; and
- incur increased costs as a result of operating as a public company.

Our expenses could increase beyond our expectations if we are required by the U.S. Food and Drug Administration, or the FDA, or other regulatory authorities to perform clinical trials in addition to those that we currently expect, or if there are any delays in establishing appropriate manufacturing arrangements for or in completing our clinical trials or the development of any of our product candidates.

Risks Related to Future Financial Condition

We will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product discovery and development programs or commercialization efforts.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to continue the preclinical and clinical development of our current and future programs. If we are able to gain marketing approval for product candidates that we develop, including any indication for which we are developing or may develop PRAX-114, PRAX-944 and PRAX-562, we will require significant additional amounts of cash in order to launch and commercialize such product candidates to the extent that such launch and commercialization are not the responsibility of a future collaborator that we may contract with in the future. In addition, other unanticipated costs may arise in the course of our development efforts. Because the design and outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of any product candidates we develop.

Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of researching and developing PRAX-114, PRAX-944 and PRAX-562 for our initial and potential additional indications, as well as other product candidates we may develop;
- the timing and uncertainty of, and the costs involved in, obtaining marketing approvals for PRAX-114, PRAX-944 and PRAX-562 for our initial and potential additional indications, and other product candidates we may develop and pursue;
- the number of future product candidates that we may pursue and their development requirements;
- the number of jurisdictions in which we plan to seek regulatory approvals;
- if approved, the costs of commercialization activities for PRAX-114, PRAX-944 and PRAX-562 for any approved indications, or any other product candidate that receives regulatory approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of regulatory approval, revenue, if any, received from commercial sales of PRAX-114, PRAX-944 and PRAX-562 for any approved indications or any other product candidates;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies;
- our headcount growth and associated costs as we expand our research and development, increase our office space, and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights, including enforcing and defending intellectual property related claims; and
- the ongoing costs of operating as a public company.

We cannot be certain that additional funding will be available on acceptable terms, or at all. We have no committed source of additional capital and if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Any of our current or future license agreements may also be terminated if we are unable to meet the payment or other obligations under the agreements.

We believe that our cash and cash equivalents as of December 31, 2020 will enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2022. Our estimate may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing

circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We expect our expenses to increase in connection with our planned operations. Unless and until we can generate a substantial amount of revenue from our product candidates, we expect to finance our future cash needs through public or private equity offerings, debt financings, collaborations, licensing arrangements or other sources, or any combination of the foregoing. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, your ownership interest may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder. In addition, debt financing, if available, may result in fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise additional funds through collaborations or marketing, distribution, licensing and royalty arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We are in the early stages of clinical drug development and have a very limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.

We are a clinical-stage biopharmaceutical company with a very limited operating history, focused on translating genetic insights into the development of high-impact therapies for people with prevalent, as well as rare, CNS disorders characterized by neuronal imbalance. We commenced operations in 2016, have no products approved for commercial sale and have not generated any revenue from product sales. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We are conducting Phase 1 or Phase 2a clinical trials for our PRAX-114, PRAX-944 and PRAX-562 programs, and have not initiated clinical trials for any of our other current product candidates. To date, our clinical trials have been conducted only in Australia, New Zealand and England, and we have not initiated or completed a pivotal clinical trial, obtained marketing approval for any product candidates, manufactured a commercial scale product or arranged for a third party to do so on our behalf, or conducted sales and marketing activities necessary for successful product commercialization. Our short operating history as a company makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will suffer.

Drug development is a highly uncertain undertaking and involves a substantial degree of risk.

We have no products approved for commercial sale. To obtain revenues from the sales of our product candidates that are significant or large enough to achieve profitability, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing, and marketing therapies with significant commercial success. Our ability to generate revenue and achieve profitability depends on many factors, including:

- initiating and successfully completing research and preclinical and clinical development of our product candidates;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development and clinical trials;
- developing a sustainable and scalable manufacturing process for our product candidates, as well as establishing and maintaining commercially viable supply relationships with third parties that can provide

adequate products and services to support clinical activities and commercial demand of our product candidates;

- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- launching and successfully commercializing product candidates for which we obtain regulatory and marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;
- obtaining and maintaining an adequate price for our product candidates in the countries where our products are commercialized;
- obtaining adequate reimbursement for our product candidates from payors;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- receiving milestone and other payments under any future collaboration arrangements;
- maintaining, protecting, expanding and enforcing our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the FDA or foreign regulatory agencies to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our or our future collaborators' clinical trials or the development of any of our product candidates. Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with launching and commercializing any approved product candidate and ongoing compliance efforts.

Due to the significant resources required for the development of our programs, and depending on our ability to access capital, we must prioritize development of certain product candidates. Moreover, we may expend our limited resources on programs that do not yield a successful product candidate or fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We currently have three product candidates in clinical trials. Together, the development of these programs and product candidates require significant capital investment. Due to the significant resources required for the development of our programs and product candidates, we must focus our programs and product candidates on specific diseases and disease pathways and decide which product candidates to pursue and advance and the amount of resources to allocate to each. Our drug development strategy is to clinically test and seek regulatory approval for our product candidates in indications in which we believe there is the most evidence that we will be able to efficiently generate proof-of-concept data. We then intend to expand to clinical testing and seek regulatory approvals in other neurological and psychiatric disease indications based on genetic and mechanistic overlap with the primary indication. However, even if our product candidates are able to gain regulatory approval in one indication, there is no guarantee that we will be able to expand to other indications, and we may expend significant resources in seeking such approvals.

In addition, we may focus resources on pursuing indications outside of neurology based on the same strategic approach (e.g., human genetics, mechanistic rationale, the availability of translational tools, clinical development path, commercial opportunity) we utilize in determining on which of our discovery programs to focus. Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Additionally, we may reprioritize product candidate development plans and activities at any time and delay or terminate development of any product candidates we identify. For example, we have prioritized developing PRAX-144 for major depressive disorder, or MDD, ahead of perimenopausal depression, or PMD. Similarly, our potential decisions to delay, terminate, or collaborate with third parties in respect of certain programs may subsequently also prove to be suboptimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the biopharmaceutical industry, in particular for neurological

and psychiatric diseases, our business, financial condition, and results of operations could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

Risks Related to Research and Development and the Biopharmaceutical Industry

Risks Related to Preclinical and Clinical Development

Our business substantially depends upon the successful development of PRAX-114, PRAX-944 and PRAX-562. If we are unable to obtain regulatory approval for, and successfully commercialize, PRAX-114, PRAX-944 or PRAX-562, our business may be materially harmed.

We currently have no products approved for sale and are investing the majority of our efforts and financial resources in the development of our lead product candidates, PRAX-114 for the treatment of MDD and PMD and PRAX-944 for the treatment of essential tremor, or ET. We have also commenced a first-in-human trial of PRAX-562 in healthy volunteers. We plan to initiate a Phase 2 trial in patients with rare adult cephalgias, including Short-lasting Unilateral Neuralgiform headache with Conjunctival injection and Tearing, or SUNCT, Short-lasting Unilateral Neuralgiform headache attacks with Autonomic symptoms, or SUNA, and Trigeminal Neuralgia, or TN, to demonstrate clinical proof-of-concept and then subsequently expand into severe pediatric epilepsies. Successful continued development and ultimate regulatory approval of PRAX-114, PRAX-944 and PRAX-562 for our initial and potential additional indications is critical to the future success of our business. We will need to raise sufficient funds for, and successfully enroll and complete, our clinical development programs of PRAX-114 for the treatment of MDD and PMD, PRAX-944 for the treatment of ET, and possibly other diseases, and PRAX-562 for the treatment of a broad range of rare, devastating central nervous system, or CNS, disorders, such as severe pediatric epilepsies and rare adult cephalgias.

Before we can generate any revenue from sales of PRAX-114, PRAX-944, PRAX-562 or any of our other product candidates, we must undergo additional preclinical and clinical development, regulatory review and approval in one or more jurisdictions. To date, our clinical trials have been conducted exclusively in Australia and, for PRAX-944, in New Zealand as well. We are planning to pursue clinical trials in the United States for all of our clinical programs. In October 2020, we submitted an Investigational New Drug Application, or IND, for PRAX-114 with the FDA to support the initiation of a Phase 2/3 clinical trial in the United States and Australia. At the end of the 30-day review period, the FDA notified us that the IND was placed on full clinical hold pending the resolution of certain non-clinical pharmacology and toxicology matters. We subsequently interacted with the FDA to gain agreement on a path to initiate the clinical study, which included a proposal to submit available non-clinical data while other GLP reproductive toxicology studies were being completed. Based on this submission, the FDA removed the clinical hold in March 2021. In addition, if one or more of our product candidates are approved, we must ensure access to sufficient commercial manufacturing capacity and conduct significant marketing efforts in connection with any commercial launch. These efforts will require substantial investment, and we may not have the financial resources to continue development of our product candidates or commercialization of any products.

We may experience setbacks that could delay or prevent regulatory approval of our product candidates or our ability to commercialize any products, including:

- negative or inconclusive results from our preclinical studies or clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- product-related side effects experienced by subjects in our clinical trials or by individuals using drugs or therapeutics similar to our product candidates;
- delays in submitting INDs in the United States or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators or institutional review boards to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- if the FDA or comparable foreign authorities do not accept the earlier preclinical and clinical trial work, then we may need to conduct additional preclinical or clinical trials beyond that which we currently have planned and significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our drug candidates or allow our competitors to bring products to

market before we do and impair our ability to successfully commercialize our drug candidates and may harm our business and results of operations;

- conditions imposed by the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- delays in contracting with clinical sites or enrolling subjects in clinical trials, including due to the COVID-19 pandemic;
- delays or interruptions in the supply of materials necessary for the conduct of our clinical trials;
- regulators or institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- the FDA or other comparable regulatory authorities may disagree with our clinical trial design, including with respect to dosing levels administered in our planned clinical trials, which may delay or prevent us from initiating our clinical trials with our originally intended trial design;
- delays in reaching, or failure to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- the number of subjects required for clinical trials of any product candidates may be larger than we anticipate or subjects may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors for preclinical studies or clinical trials may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or take actions that could cause clinical sites or clinical investigators to drop out of the trial, which may require that we add new clinical trial sites or investigators;
- due to the impact of the COVID-19 pandemic, we may experience some delays and interruptions to our preclinical studies and clinical trials, we may experience delays or interruptions to our manufacturing supply chain, or we could suffer delays in reaching, or we may fail to reach, agreement on acceptable terms with third-party service providers on whom we rely;
- greater than anticipated clinical trial costs, including as a result of delays or interruptions that could increase the overall costs to finish our clinical trials as our fixed costs are not substantially reduced during delays;
- we may elect to, or regulators, IRBs, Data Safety Monitoring Boards, or DSMBs, or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- we may not have the financial resources available to begin and complete the planned trials, or the cost of clinical trials of any product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate to initiate or complete a given clinical trial;
- the FDA or other comparable foreign regulatory authorities may require us to submit additional data such as long-term toxicology studies, or impose other requirements before permitting us to initiate a clinical trial, including because the FDA has not reviewed our preclinical or clinical data, to date, having been developed outside the United States in Australia and New Zealand;
- inability to compete with other therapies;
- poor efficacy of our product candidates during clinical trials;
- unfavorable FDA or other regulatory agency inspection and review of clinical trial sites or manufacturing facilities;
- unfavorable product labeling associated with any product approvals and any requirements for a Risk Evaluation and Mitigation Strategy, or REMS, that may be required by the FDA or comparable requirements in other jurisdictions to ensure the benefits of an individual product outweigh its risks;
- unfavorable acceptance of our clinical trial data by the patient or medical communities or third-party payors;

- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays related to the impact or the spread of COVID-19 or other pandemics, including the impact of COVID-19 on the FDA's, or similar foreign regulatory agencies, ability to continue its normal operations;
- delays and changes in regulatory requirements, policy and guidelines, including the FDA's evolving recommendations for developers of antisense oligonucleotide drug products with single participant trials and the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or
- varying interpretations of data by the FDA and similar foreign regulatory agencies.

We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and our manufacturing, marketing, distribution and sales efforts or that of any future collaborator.

In addition, of the large number of drugs in development in the biopharmaceutical industry, only a small percentage result in the submission of a marketing application, such as a new drug application, or NDA, to the FDA, and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval for PRAX-144, PRAX-944 or PRAX-562 for any indication, any such approval may be subject to limitations on the indications or uses or patient populations for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we cannot assure that we will successfully develop or commercialize PRAX-114, PRAX-944 or PRAX-562 for any indication. If we or any of our future collaborators are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize PRAX-114, PRAX-944 or PRAX-562 for our initial or potential additional indications, we may not be able to generate sufficient revenue to continue our business. In addition, our failure to demonstrate positive results in our clinical trials in any indication for which we are developing PRAX-114, PRAX-944 and PRAX-562 could adversely affect our development efforts for PRAX-114, PRAX-944 and PRAX-562 in other indications.

Clinical development involves a lengthy, complex and expensive process, with an uncertain outcome. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials, which to date have primarily been conducted in Australia and New Zealand, may not satisfy the requirements of the FDA or comparable foreign regulatory authorities.

To obtain the requisite regulatory approvals to commercialize any product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. In particular, in the United States where we hope to advance our product development efforts in the future, the general approach for FDA approval of a new drug is dispositive data from two well-controlled, Phase 3 clinical trials of the relevant drug in the relevant patient population. Phase 3 clinical trials typically involve hundreds of patients, have significant costs and take years to complete. A product candidate can fail at any stage of testing, even after observing promising signs of activity in earlier preclinical studies or clinical trials. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or emergence of unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence clinical trials are never approved as products and there can be no assurance that any of our future clinical trials will ultimately be successful or support further clinical development of PRAX-114, PRAX-944, PRAX-562 or any of our other product candidates. Product candidates that appear promising in the early phases of development may fail to reach the market for several reasons, including:

- preclinical studies or clinical trials may show the product candidates to be less effective than expected (e.g., a clinical trial could fail to meet its primary endpoint(s)) or to have unacceptable side effects or toxicities;
- failure to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful;
- failure to receive the necessary regulatory approvals;

- manufacturing issues, formulation issues, pricing or reimbursement issues or other factors that make a product candidate uneconomical; and
- the proprietary rights of others and their competing products and technologies that may prevent one of our product candidates from being commercialized.

In addition, differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products.

Additionally, some of our trials may be open-label studies, where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. For example, prior MDD studies have exhibited a high placebo effect. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Therefore, it is possible that positive results observed in open-label trials will not be replicated in later placebo-controlled trials. To date, we have conducted some trials as open-label trials, including with PRAX-114 and PRAX-944. Additionally, the trial design differences and placebo effects that may be possible in clinical research for the indications we are studying may make it difficult to extrapolate the results of earlier clinical trials to later clinical trials or to interpret the clinical data in any of our trials.

The standards that foreign regulatory authorities and the FDA use when regulating us require judgment and can change, which makes it difficult to predict with certainty how they will be applied. Although we are initially focusing our efforts on development of small molecule drug products, we intend to develop a potential antisense oligonucleotide candidate for genetic epilepsies and may in the future pursue development of biological products, each of which could make us subject to additional regulatory requirements. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. Our clinical trials have primarily been conducted in Australia and New Zealand. The FDA’s acceptance of data from clinical trials outside of the United States is subject to certain conditions, including that the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with good clinical practice, that the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful, and that the trials are conducted in compliance with all applicable U.S. laws and regulations. If the FDA or comparable foreign regulatory authorities do not accept earlier preclinical or clinical data, we may need to conduct additional preclinical studies or clinical trials.

We may also encounter unexpected delays or increased costs due to new government regulations. Examples of such regulations include future legislation or administrative action, or changes in foreign regulatory authority or FDA policy during the period of product development and regulatory review. It is impossible to predict whether legislative changes will be enacted, or whether foreign or FDA regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be. In the United States, where we plan to develop our candidates in the future, the FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding on the FDA, may have a significant impact on our ability to obtain approval of any product candidates that we develop.

If we seek to continue conducting clinical trials in foreign countries or pursue marketing approvals in foreign jurisdictions, we must comply with numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries and jurisdictions and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ jurisdiction-to-jurisdiction from that required to obtain FDA approval. Approval by foreign regulatory authorities does not ensure approval by the FDA and, similarly, approval by the FDA does not ensure approval by regulatory authorities outside the United States.

Successful completion of clinical trials is a prerequisite to submitting a marketing application to foreign regulatory authorities or the FDA, for each product candidate and, consequently, the ultimate approval and commercial marketing of any product candidates. We may experience negative or inconclusive results, or regulators

may be unwilling to accept preclinical or clinical data obtained in foreign jurisdictions, which may result in our deciding, or our being required by regulators, to conduct additional clinical studies or trials or abandon some or all of our product development programs, which could have a material adverse effect on our business.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following regulatory approval, if obtained.

Undesirable side effects caused by PRAX-114, PRAX-944, PRAX-562 or any future product candidate could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. In addition, many compounds that have initially showed promise in clinical or earlier stage testing are later found to cause undesirable or unexpected side effects that prevented further development of the compound. Additionally, the composition of our product candidates or learnings in preclinical studies or clinical trials may result in contraindications for any product candidates for which we may obtain regulatory approval.

If unacceptable side effects arise in the development of our product candidates, we, foreign regulatory authorities, or, in the future, the FDA, the IRBs, DSMBs or independent ethics committees at the institutions in which our trials are conducted could suspend or terminate our preclinical studies or clinical trials or foreign regulatory authorities or the FDA could order us to cease preclinical studies or clinical trials or deny approval of our product candidates for any or all targeted indications.

Treatment-emergent side effects that are deemed to be drug-related could also affect subject recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Undesirable side effects in one of our clinical trials for our product candidates in one indication could adversely affect enrollment in clinical trials, regulatory approval and commercialization of our product candidates in other indications. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. Any of these occurrences may harm our business, financial condition and prospects significantly.

Moreover, clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. Clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. If our product candidates receive marketing approval and we or others identify undesirable side effects caused by such product candidates (or any other similar products) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such product candidates;
- regulatory authorities may require the addition of labeling statements, such as a Boxed Warning or contraindications;
- we may be required to change the way such product candidates are distributed or administered, or change the labeling of the product candidates;
- FDA may require a REMS plan to mitigate risks, which could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools, and regulatory authorities in other jurisdictions may require comparable risk mitigation plans;
- we may be subject to regulatory investigations and government enforcement actions;
- the FDA or a comparable foreign regulatory authority may require us to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety and efficacy of the product;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and
- our reputation may suffer.

For example, we are developing PRAX-114, an extrasynaptic-preferring GABAA receptor positive allosteric modulator, or PAM, for the treatment of patients suffering from MDD and PMD. There have been documented cases of approved GABAA receptor modulators leading to addiction and having the potential for abuse. To date, there has

been no indication of this side effect for PRAX-114 in our clinical trials; however, in any such instance, we would be subject to the risks outlined above, which would impact our ability to achieve or maintain market acceptance.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates and could substantially increase the costs of commercializing our product candidates, if approved, and significantly impact our ability to successfully commercialize our product candidates and generate revenues.

If we encounter difficulties enrolling patients in our future clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion.

Patient enrollment is affected by many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- in the case clinical trials focused on rare disease, the small size of the patient population and the potential of a patient being undiagnosed or misdiagnosed;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications that we are investigating;
- the impacts of the COVID-19 pandemic on clinical trial sites, personnel and patient travel;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or might require us to abandon one or more clinical trials altogether. Delays in patient enrollment may result in increased costs, affect the timing or outcome of the planned clinical trials, product candidate development and approval process and jeopardize our ability to seek and obtain the regulatory approval required to commence product sales and generate revenue, which could prevent completion of these trials, adversely affect our ability to advance the development of our product candidates, cause the value of our company to decline and limit our ability to obtain additional financing if needed.

We are also required to register certain clinical trials and post the results of completed clinical trials on a government-sponsored database, such as www.ClinicalTrials.gov in the United States, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available, and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary, interim or topline data from our clinical trials. These interim updates are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations

may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously reported. As a result, topline data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse changes between interim data and final data could significantly harm our business and prospects. Some of our trials may be open- label studies, where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. For example, prior MDD studies have exhibited a high placebo effect. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Therefore, it is possible that positive results observed in open-label trials will not be replicated in later placebo-controlled trials. Additionally, the trial design differences and placebo effects that may be possible in clinical research for the indications we are studying may make it difficult to extrapolate the results of earlier clinical trials to later clinical trials or to interpret the clinical data in any of our trials. Further, additional disclosure of interim data by us or by our competitors in the future could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the preliminary or topline data that we report differ from late, final or actual results, or if others, including the FDA and comparable foreign regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize our product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

The markets for PRAX-114 for MDD and PMD, PRAX-944 for ET, PRAX-562 for multiple rare neurological conditions and any other product candidates we may develop may be smaller than we expect.

Our estimates of the potential market opportunity for PRAX-114 for the treatment of MDD and PMD, PRAX-944 for the treatment of ET, PRAX-562 for the treatment of multiple rare neurological conditions, including severe pediatric epilepsies and rare adult cephalgias, as well as any other product candidates, include several key assumptions based on our industry knowledge, industry publications and third-party research reports. There can be no assurance that any of these assumptions are, or will remain, accurate. If the actual market for PRAX-114, PRAX-944 and PRAX-562 for these or other indications, or for any other product candidate we may develop, is smaller than we expect, our revenues, if any, may be limited and it may be more difficult for us to achieve or maintain profitability.

We may not be successful in our efforts to identify or discover additional product candidates in the future.

Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development or commercialization for a number of reasons, including:

- our inability to design such product candidates with the pharmacological or pharmacokinetic properties that we desire; or
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be medicines that will receive marketing approval and achieve market acceptance.

Research programs to identify new product candidates require substantial technical, financial and human resources. If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

We may in the future conduct clinical trials for our product candidates in the United States, Europe or other jurisdictions, and the FDA, the European Medicines Agency, or EMA, and applicable foreign regulatory authorities may not accept data from trials conducted outside those respective jurisdictions.

We may in the future choose to conduct one or more of our clinical trials in the United States, Europe or in other foreign jurisdictions outside of Australia and New Zealand where our trials currently are being conducted for PRAX-114, PRAX-944 and PRAX-562. The acceptance of study data from preclinical studies and clinical trials conducted outside those jurisdictions may be subject to certain conditions for acceptance. For example, in cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to Good Clinical Practices, or GCP, regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies, such as the EMA, have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA or any applicable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, EMA or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

We have obtained orphan drug designation for PRAX-222 and plan to seek orphan drug designation for additional product candidates, but we may be unable to obtain or maintain such a designation or the benefits associated with orphan drug status, including marketing exclusivity, which may cause our revenue, if any, to be reduced.

In the United States, under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested and granted by the FDA before a new NDA is submitted. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. After the FDA grants orphan drug designation, it will disclose publicly the generic identity of the drug and its potential orphan use. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Such a designation may also be revoked by the FDA in certain circumstances, such as if the agency finds that the applicant's request for designation request omitted material information required under the Orphan Drug Act and its implementing regulations. In January 2021, the FDA granted orphan drug designation to PRAX-222 for the treatment of SCN2A developmental and epileptic encephalopathy, or SCN2A-DEE.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity. This means that the FDA may not approve any other marketing applications for the same drug and the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan exclusivity or if FDA finds that the holder of the orphan exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan product to meet the needs of patients with the disease or condition for which the drug was designated. Furthermore, the FDA can waive orphan exclusivity if the applicant is unable to manufacture sufficient supply of the product subject to a period of orphan drug marketing exclusivity. Because we are developing PRAX-562 and PRAX-222 for indications we believe to be rare, we are pursuing orphan designations for our candidates as applicable in the jurisdictions where development activities are planned.

We have received rare pediatric disease designation for PRAX-562 and PRAX-222. However, a marketing application for these product candidates, if approved, may not meet the eligibility criteria for a rare pediatric disease priority review voucher.

We have received rare pediatric disease designation for PRAX-562 for the treatment of SCN2A-DEE and for the treatment of SCN8A developmental and epileptic encephalopathy, or SCN8A-DEE, and for PRAX-222 for the treatment of SCN2A-DEE. Designation of a drug product as a product for a rare pediatric disease does not guarantee that a NDA for such drug product will meet the eligibility criteria for a rare pediatric disease priority review voucher at the time the application is approved. Under the Federal Food, Drug, and Cosmetic Act, or FDCA, we will need to request a rare pediatric disease priority review voucher in our original NDA for our product candidates for

which we have received rare pediatric disease designation. The FDA may determine that a NDA for any such product candidates, if approved, do not meet the eligibility criteria for a priority review voucher.

The authority for the FDA to award rare pediatric disease priority review vouchers for drug products after September 30, 2024 is currently limited to products that receive rare pediatric disease designation on or prior to September 30, 2024, and FDA may only award rare pediatric disease priority review vouchers through September 30, 2026. However, it is possible the authority for FDA to award rare pediatric disease priority review vouchers will be further extended by Congress.

A Breakthrough Therapy Designation by the FDA may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

We do not currently have Breakthrough Therapy Designation for any of our product candidates, but we may seek Breakthrough Therapy Designation for any product candidate that we plan to develop in the United States if we believe the qualifying criteria for such a designation can be met. A Breakthrough Therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as Breakthrough Therapies by the FDA are also eligible for accelerated approval and priority review.

The FDA has discretion to determine whether the criteria for a Breakthrough Therapy has been met and whether to grant a Breakthrough Therapy Designation to an investigational product. Accordingly, even if we believe a product candidate we develop meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even after granting Breakthrough Therapy Designation to our product candidates, the FDA may later decide that the drugs no longer meet the conditions for qualification and withdraw the designation.

A Fast Track Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval.

We do not currently have Fast Track Designation for any of our product candidates, but we may seek such a designation for the product candidates we plan to develop in the United States if we believe the qualifying criteria for such a designation have been met. If a product is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address an unmet medical need for this condition, the product sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw the Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many drugs that have received Fast Track Designation have failed to obtain regulatory approval.

Risks Related to Regulatory Approval

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants approval of a product candidate, comparable regulatory authorities in other jurisdictions, including Australia and Europe, must also approve the manufacturing, marketing and sale of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must also be

approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to governmental approval. Additionally, as of June 23, 2020, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals; however, FDA may not be able to continue its current pace and approval timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the COVID-19 pandemic and travel restrictions FDA is unable to complete such required inspections during the review period. In 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any partner we work with fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Any of our current and future product candidates for which we, or any future collaborators, obtain regulatory approval in the future will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. If approved, our product candidates could be subject to post-marketing restrictions or withdrawal from the market and we, or any future collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our products following approval.

Any of our product candidates for which we, or any future collaborators, obtain regulatory approval, as well as the manufacturing processes, post- approval studies, labeling, advertising and promotional activities for such product, among other things, will be subject to ongoing requirements of and review by the FDA, if approved in the United States, and other regulatory authorities. These requirements include submissions of safety and other post- marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. We and our contract manufacturers will also be subject to user fees and periodic inspection by the FDA in the United States and other regulatory authorities, including similar regulatory authorities in foreign jurisdictions, to monitor compliance with these requirements and the terms of any product approval we may obtain. Even if regulatory approval of a product candidate is granted, the approval may be subject to limitations on the indications or uses for which the product may be marketed or to the conditions of approval, including the potential requirement in the United States to implement a REMS.

Regulatory authorities may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. In the United States, the FDA and other agencies, including the Department of Justice, closely regulate and monitor the post- approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use of approved drug products. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. If we, or any future collaborators, do not market any of our product candidates for which we, or they, receive regulatory approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing if it is alleged that we are doing so. In the United States, violation of the Federal Food, Drug and Cosmetic Act and other statutes relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws, including the federal False Claims Act, or the FCA.

In addition, later discovery of previously unknown adverse events or other problems with our products or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on the manufacturing of such products;
- restrictions on the labeling or marketing of such products;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;

- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenues;
- exclusion from U.S. federal health care programs such as Medicare and Medicaid;
- suspension or withdrawal of regulatory approvals;
- refusal to permit the import or export of products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Even if we, or any future collaborators, obtain regulatory approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products, which could impair our ability to generate revenue.

Once regulatory approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any future collaborators, must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain regulatory approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we and any future collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive regulatory requirements, including under FDA authorities ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practices, or cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, any future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by regulatory authorities to monitor and ensure compliance with cGMPs. Despite our efforts to inspect and verify regulatory compliance, one or more of our third-party manufacturing vendors may be found on regulatory inspection to be not in compliance with cGMP requirements, which may result in shutdown of the third-party vendor or invalidation of drug product lots or processes. In some cases, a product recall may be warranted or required, which would materially affect our ability to supply and market our drug products.

Accordingly, assuming we, or any future collaborators, receive regulatory approval for one or more of our product candidates, we, and any future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, or any future collaborators, are not able to comply with post-approval regulatory requirements, we, or any future collaborators, could have the regulatory approvals for our products withdrawn by regulatory authorities and our, or any future collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Changes in regulatory requirements or regulatory guidance or unanticipated events during our non-clinical studies and clinical trials of our product candidates may occur, which may result in changes to non-clinical studies and clinical trial protocols or the need for additional non-clinical studies and clinical trials, which could result in increased costs to us and could delay our development timelines.

Changes in regulatory requirements or regulatory guidance or unanticipated events during our non-clinical studies and clinical trials may force us to amend non-clinical studies and clinical trial protocols or the applicable regulatory authority may impose additional non-clinical studies and clinical trial requirements. Amendments or changes to our clinical trial protocols would generally require resubmission to the applicable regulatory authority and IRBs for review and approval, which may adversely impact the cost, timing or successful completion of clinical trials. These decisions may increase costs, and cause us not to meet expected timelines and, correspondingly, our business and financial prospects could be adversely affected. Similarly, amendments to our non-clinical studies may adversely impact the cost, timing or successful completion of those non-clinical studies. If we experience delays

completing, or if we terminate, any of our non-clinical studies or clinical trials, or if we are required to conduct additional non-clinical studies or clinical trials, the development pathway, and ultimately the commercial prospects, for our product candidates may be harmed and our ability to generate product revenue from resulting products, if any, will be delayed.

We could be subject to product liability lawsuits based on the use of our product candidates in clinical testing or, if obtained, following our products' marketing approval and commercialization. Product liability lawsuits brought against us or any of our future collaborators could divert our resources and attention, require us to cease clinical testing, cause us to incur substantial liabilities or limit commercialization of our product candidates.

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of biopharmaceutical products. Currently, we have no products that have been approved for commercial sale; however, the use of our product candidates by us and any collaborators in clinical trials may expose us to liability claims. We will face an even greater risk if product candidates are approved by regulatory authorities and introduced commercially. Product liability claims may be brought against us or our partners if any product candidate we develop allegedly causes injury or is found to be otherwise unsuitable for human use during product testing, manufacturing, marketing or sale. Any such product liability claim may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. Such claims could be made by participants enrolled in our clinical trials, patients, health care providers, biopharmaceutical companies, our collaborators or others using, administering or selling any of our future approved products. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources.

Regardless of the merits or eventual outcome, product liability claims may result in:

- decreased demand for any of our future approved products;
- injury to our reputation;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- significant litigation costs;
- substantial monetary awards to, or costly settlements with, patients or other claimants;
- product recalls or a change in the indications for which any approved drug products may be used;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize our product candidates.

Although the clinical trial process is designed to identify and assess potential side effects, clinical development does not always fully characterize the safety and efficacy profile of a new medicine, and it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If our product candidates were to cause adverse side effects during clinical trials or after approval, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates. If any of our product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of us and the safety and quality of our products. We could be adversely affected if we are subject to negative publicity associated with illness or other adverse effects resulting from physicians' or patients' use or misuse of our products or any similar products distributed by other companies.

Although we maintain product liability insurance coverage including clinical trial liability, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if we commercialize any product that receives regulatory approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could harm our business, financial condition, results of operations and prospects.

We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours, which may negatively impact our ability to successfully market or commercialize any product candidates we may develop and ultimately harm our financial condition.

The development and commercialization of new drug products is highly competitive. We may face competition with respect to any product candidates that we seek to develop or commercialize in the future from biopharmaceutical companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing and commercialization.

Specifically, we face competition with GABAA receptor modulator programs in development targeting MDD, including that of SAGE Therapeutics, as well as other programs in clinical development targeting other mechanisms of action and approved therapies such as selective serotonin reuptake inhibitors, or SSRIs; T-type calcium channel inhibitor programs in development targeting ET, including that of Jazz Pharmaceuticals and Neurocrine Biosciences, as well as other programs in clinical development targeting other mechanisms of action, and approved therapies, such as propranolol, and off-label therapies, such as primidone; and sodium channel blocker programs in development for DEE, including those of SK-Pharma, Xenon Pharmaceuticals and Neurocrine Biosciences, as well as other programs in clinical development targeting other mechanisms of action, and approved therapies including other existing ion channel blockers.

If any of these competitors or competitors for our other product candidates receive FDA approval before we do, our product candidates would not be the first treatment on the market, and our market share may be limited. In addition to competition from other companies targeting our target indications, any products we may develop may also face competition from other types of therapies.

Many of our current or potential competitors, either alone or with their strategic partners, have:

- greater financial, technical and human resources than we have at every stage of the discovery, development, manufacture and commercialization of products;
- more extensive experience in preclinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing, marketing and selling drug products;
- products that have been approved or are in late stages of development; and
- collaborative arrangements in our target markets with leading companies and research institutions.

Mergers and acquisitions in the biopharmaceutical industry may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of our targeted disease indications or similar indications, which could give such products significant regulatory and market timing advantages over our product candidates. Our competitors also may obtain FDA, EMA or other comparable foreign regulatory approval for their products more rapidly than we may obtain approval for ours and may obtain orphan product exclusivity from the FDA for indications that we are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity and/or enforceability of our patents relating to our competitors' products and our competitors may allege that our products infringe, misappropriate or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

Risks Related to the Commercialization of our Product Candidates

Risks Related to Post-Marketing Regulatory Requirements

Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Even if the FDA or a comparable foreign regulatory authority approves any of our product candidates, we will be subject to ongoing regulatory requirements in the applicable jurisdictions for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-market information. In addition, we will be subject to continued compliance with cGMP and GCP requirements for any clinical trials that we conduct post-approval.

Manufacturers and their facilities are required to comply with extensive regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any marketing application, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. In the United States, the FDA may also require a REMS program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration.

In the United States, the FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information or other restrictions; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the manufacturing of our products, the approved manufacturers or the manufacturing process;
- withdrawal of the product from the market or voluntary product recalls;
- requirements to conduct post-marketing studies or clinical trials;
- fines, restitution or disgorgement of profits or revenues;
- warning or untitled letters from the FDA or comparable notice of violations from foreign regulatory authorities;
- suspensions of any of our ongoing clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or withdrawal of marketing approvals;
- product seizure or detention or refusal to permit the import or export of products; and
- consent decrees, injunctions or the imposition of civil or criminal penalties.

Regulatory authorities strictly regulate marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. However, in the United States, companies may share truthful and not misleading information that is not inconsistent with the labeling. The FDA and other regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may also lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws. Accordingly, to the extent we receive marketing approval for one or more of our product candidates, we and our third-party partners will continue

to expend time, money and effort in all areas of regulatory compliance, including promotional and labeling compliance, manufacturing, production, product surveillance and quality control.

The policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow to, or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

Risks Related to Sales, Marketing and Competition

Our commercial success depends upon attaining significant market acceptance of our drug product candidates, if approved, among physicians, patients, third-party payors and other members of the medical community.

Even if any of the product candidates we develop receives marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, such as Medicare and Medicaid programs and managed care organizations in the United States, and others in the medical community. In addition, the availability of coverage by third-party payors may be affected by existing and future health care reform measures designed to reduce the cost of health care. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable.

The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our products, if approved, for sale at competitive prices;
- relative convenience and ease of administration compared to alternative treatments;
- perceptions by the medical community, physicians, and patients, regarding the safety and effectiveness of our products and the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the size of the market for such product candidate, based on the size of the patient subsets that we are targeting, in the territories for which we gain regulatory approval;
- the recommendations with respect to our product candidates in guidelines published by various scientific organizations applicable to us and our product candidates;
- the strength of sales, marketing and distribution support;
- the timing of any such marketing approval in relation to other product approvals;
- any restrictions on concomitant use of other medications;
- support from patient advocacy groups;
- the ability to obtain sufficient third-party coverage and adequate reimbursement; and
- the prevalence and severity of any side effects.

If government and other third-party payors do not provide coverage and adequate reimbursement levels for any products we commercialize, market acceptance and commercial success would be reduced.

The successful commercialization of our product candidates in the United States will depend in part on the extent to which third-party payors, including governmental authorities and private health insurers, provide coverage and adequate reimbursement levels, as well as implement pricing policies favorable for our product candidates. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States and in other countries, patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their

treatment. The availability of coverage and adequacy of reimbursement for our products by third-party payors, including government health care programs (e.g., Medicare, Medicaid, TRICARE), managed care providers, private health insurers, health maintenance organizations and other organizations is essential for most patients to be able to afford medical services and biopharmaceutical products such as our product candidates. Third-party payors decide which medications they will pay for and establish reimbursement levels.

In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent our products will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for our products and related treatments will be available from third-party payors. Moreover, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

In the United States, no uniform policy for coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for our products can differ significantly from payor to payor. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. One payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product. Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates.

A decision by a third-party payor not to cover or not to separately reimburse for our medical products or therapies using our products could reduce physician utilization of our products once approved. Assuming there is coverage for our product candidates, or therapies using our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States will be available for our current or future product candidates, or for any procedures using such product candidates, and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future.

Further, increasing efforts by third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates may nonetheless not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. We expect to experience pricing pressures from third-party payors in connection with the potential sale of any of our product candidates.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, in the

European Union, Member States can restrict the range of medicinal products for which their national health insurance systems provide reimbursement and they can control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Approaches between Member States are diverging. For example, in France, effective market access will be supported by agreements with hospitals and products may be reimbursed by the Social Security Fund. The price of medicines is negotiated with the Economic Committee for Health Products, or CEPS. There can be no assurance that any country that has price controls or reimbursement limitations for biopharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

Even if we obtain approval of any of our product candidates in the United States or Europe, we may never obtain approval or commercialize such products in other countries, which would limit our ability to realize their full market potential.

In order to market any products in the United States or European Union, we must establish and comply with numerous and varying regulatory requirements regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals outside of where our clinical trials currently have been conducted could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed.

We currently have no marketing and sales organization and have no experience as a company in commercializing products, and we may have to invest significant resources to develop these capabilities. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if approved, we may not be able to generate product revenue.

We have no internal sales, marketing or distribution capabilities, nor have we commercialized a product. If any of our product candidates ultimately receives regulatory approval, we expect to establish a marketing and sales organization with technical expertise and supporting distribution capabilities to commercialize each such product in major markets, which will be expensive and time consuming. We have no prior experience as a company in the marketing, sale and distribution of biopharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may also choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenues and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we are not successful in commercializing our products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

Risks Related to Ongoing Regulatory and Legal Compliance

Risks Related to Healthcare and Related Laws

Our relationships with healthcare providers and physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Although we do not currently have any products on the market, upon commercialization of our product candidates, if approved, we will be subject to additional health care statutory and regulatory requirements and oversight by federal and state governments in the United States as well as foreign governments in the jurisdictions in which we conduct our business. Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare providers, third-party payors, customers and others may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. In particular, the research of our product candidates, as well as the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business or financial arrangements.

The applicable federal, state and foreign healthcare laws and regulations laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity can be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. The term remuneration has been interpreted broadly to include anything of value. Further, courts have found that if “one purpose” of renumeration is to induce referrals, the federal Anti-Kickback statute is violated. Violations are subject to significant civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment and exclusion from government healthcare programs. In addition, a claim submitted for payment to any federal healthcare program that includes items or services that were made as a result of a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. The Anti-Kickback Statute has been interpreted to apply to arrangements between biopharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers, among others, on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution;
- the federal civil and criminal false claims laws, including the FCA, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false, fictitious or fraudulent claims for payment to, or approval by Medicare, Medicaid, or other federal healthcare programs; knowingly making, using or causing to be made or used, a false record or statement material to a false, fictitious or fraudulent claim or an obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. A claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim under the FCA. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The FCA also permits a private individual acting as a “whistleblower” to bring qui tam actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery or settlement. When an entity is determined to have violated the FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private), and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making

any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false fictitious or fraudulent statement or entry in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA fraud provisions without actual knowledge of the statute or specific intent to violate it;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose, among other things, certain requirements relating to the privacy, security and transmission of individually identifiable health information on certain covered healthcare providers, health plans and healthcare clearinghouses, known as covered entities, as well as their respective "business associates," those independent contractors or agents of covered entities that create, receive, maintain, transmit or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- the federal Physician Payments Sunshine Act, created under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the ACA, and its implementing regulations, which require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to direct or indirect payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made in the previous year to certain non-physician providers such as physician assistants and nurse practitioners;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous U.S. state, local and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers, and may be broader in scope than their federal equivalents; state and foreign laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and other relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing; state and local laws that require the registration of biopharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information, some of which may be more stringent than those in the United States (such as the European Union, which adopted the General Data Protection Regulation, which became effective in May 2018) in certain circumstances, and may differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Additionally, as further discussed below, on November 20, 2020, HHS finalized a regulation that, among other things, (i) removed safe harbor protection for price reductions from pharmaceutical manufacturers, and (ii) created new safe harbor for certain fixed fees. It is not clear at this time what effect, if any, these and other changes to the Anti-Kickback Safe Harbors, in effect as of January 19, 2021, will have on our business. Furthermore, the distribution of biopharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of biopharmaceutical products.

If the FDA or a comparable foreign regulatory authority approves any of our product candidates, we will be subject to an expanded number of these laws and regulations and will need to expend resources to develop and implement policies and processes to promote ongoing compliance. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Ensuring business arrangements comply with applicable

healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business.

It is possible that governmental and enforcement authorities will conclude that our business practices, including our arrangements with physicians and other healthcare providers, some of whom may receive stock options as compensation for services provided, may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to significant sanctions, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, reputational harm, exclusion from participation in federal and state funded healthcare programs, contractual damages and the curtailment or restricting of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws.

Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to similar penalties. Any action for violation of these laws, even if successfully defended, could cause us to incur significant legal expenses and divert management's attention from the operation of the business. In addition, the approval and commercialization of any product candidate we develop outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws. All of these could harm our ability to operate our business and our financial results.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

We may be subject to, or may in the future become subject to, U.S. federal and state, and foreign laws and regulations imposing obligations on how we collect, use, disclose, store and process personal information. Our actual or perceived failure to comply with such obligations could result in liability or reputational harm and could harm our business. Ensuring compliance with such laws could also impair our efforts to maintain and expand our customer base, and thereby decrease our revenue.

In many activities, including the conduct of clinical trials, we may be subject to laws and regulations governing data privacy and the protection of health-related and other personal information. These laws and regulations govern our processing of personal data, including the collection, access, use, analysis, modification, storage, transfer, security breach notification, destruction and disposal of personal data.

The privacy and security of personally identifiable information stored, maintained, received or transmitted, including electronically, is subject to significant regulation in the United States and abroad. While we strive to comply with all applicable privacy and security laws and regulations, legal standards for privacy continue to evolve and any failure or perceived failure to comply may result in proceedings or actions against us by government entities or others, or could cause reputational harm, which could have a material adverse effect on our business.

Numerous foreign, federal and state laws and regulations govern collection, dissemination, use and confidentiality of personally identifiable health information, including state privacy and confidentiality laws (including state laws requiring disclosure of breaches), federal and state consumer protection and employment laws; HIPAA and European and other foreign data protection laws. These laws and regulations are increasing in complexity and number, and may change frequently and sometimes conflict. The European Union's omnibus data protection law, the General Data Protection Regulation, or GDPR, took effect in May 2018. The GDPR imposes numerous requirements on entities that process personal data in the context of an establishment in the European Economic Area, or EEA, or that process the personal data of data subjects who are located in the EEA. These requirements include, for example, establishing a basis for processing, providing notice to data subjects, developing procedures to vindicate expanded data subject rights, implementing appropriate technical and organizational measures to safeguard personal data and complying with restrictions on the cross-border transfer of personal data from the EEA to countries that the European Union does not consider to have in place adequate data protection legislation, such as the United States. The GDPR additionally establishes heightened obligations for entities that process "special categories" of personal data, such as health data. Nearly all clinical trials involve the processing of these "special categories" of personal data, and thus processing of personal data collected during the course of clinical trials is

subject to heightened protections under the GDPR. Violations of the GDPR can lead to penalties of up to $20 million or 4% of an entity's annual turnover.

As a means to transfer personal data from the EEA to the U.S., U.S.-based companies may certify compliance with the privacy principles of the EU-U.S. Privacy Shield, or the Privacy Shield. Certification to the Privacy Shield, however, is not mandatory. If a U.S.-based company does not certify compliance with the Privacy Shield, it may rely on other authorized mechanisms to transfer personal data. Notably, the Privacy Shield is currently subject to challenge in the EU courts, and it is possible that it will be invalidated, which was the fate of its predecessor, the EU-U.S. Safe Harbor. In the event of invalidation of the Privacy Shield, U.S. companies that currently rely on the Privacy Shield as the basis for cross-border transfer of personal data will need to establish another basis for cross-border transfer of personal data.

HIPAA establishes a set of national privacy and security standards for the protection of individually identifiable health information, including protected health information, or PHI, by health plans, certain health care clearinghouses and health care providers that submit certain covered transactions electronically, or covered entities, and their "business associates," which are persons or entities that perform certain services for, or on behalf of, a covered entity that involve creating, receiving, maintaining or transmitting PHI. While we are not currently a covered entity or business associate under HIPAA, we may receive identifiable information from these entities. Failure to receive this information properly could subject us to HIPAA's criminal penalties, which may include fines up to $250,000 per violation and/or imprisonment. In addition, responding to government investigations regarding alleged violations of these and other laws and regulations, even if ultimately concluded with no findings of violations or no penalties imposed, can consume company resources and impact our business and, if public, harm our reputation.

In addition, various states, such as California and Massachusetts, have implemented similar privacy laws and regulations, such as the California Confidentiality of Medical Information Act, that impose restrictive requirements regulating the use and disclosure of health information and other personally identifiable information. In addition to fines and penalties imposed upon violators, some of these state laws also afford private rights of action to individuals who believe their personal information has been misused. California's patient privacy laws, for example, provide for penalties of up to $250,000 and permit injured parties to sue for damages. In addition to the California Confidentiality of Medical Information Act, California also recently enacted the California Consumer Privacy Act of 2018, or CCPA, which was effective January 1, 2020. The CCPA has been characterized as the first "GDPR-like" privacy statute to be enacted in the United States because it mirrors a number of the key provisions of the EU General Data Protection Regulation. The CCPA establishes a new privacy framework for covered businesses in the State of California, by creating an expanded definition of personal information, establishing new data privacy rights for consumers imposing special rules on the collection of consumer data from minors and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches.

The interplay of federal and state laws may be subject to varying interpretations by courts and government agencies, creating complex compliance issues for us and potentially exposing us to additional expense, adverse publicity and liability. Further, as regulatory focus on privacy issues continues to increase and laws and regulations concerning the protection of personal information expand and become more complex, these potential risks to our business could intensify. The legislative and regulatory landscape for privacy and data security continues to evolve, and there has been an increasing focus on privacy and data security issues which may affect our business. Failure to comply with current and future laws and regulations could result in government enforcement actions (including the imposition of significant penalties), criminal and/or civil liability for us and our officers and directors, private litigation and/or adverse publicity that negatively affects our business.

Ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.

Changes in U.S. and foreign regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the U.S. and in some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative initiatives and regulatory changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare. For example, in March 2010, the ACA was enacted, which substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. biopharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower-cost biosimilars, expands the types of

entities eligible for the 340B drug discount program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations; established annual fees and taxes on manufacturers of certain branded prescription drugs; and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, or BBA, effective as of January 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been numerous judicial, administrative, executive and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Various portions of the ACA are currently undergoing legal and constitutional challenges in the United States Supreme Court; the Trump Administration has issued various Executive Orders which eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers or manufacturers of pharmaceuticals or medical devices; and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. Also, in December 2018, CMS issued a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program. Since then, the ACA risk adjustment program payment parameters have been updated annually. It is unclear whether the ACA will be overturned, repealed, replaced or further amended. We cannot predict what affect further changes to the ACA would have on our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, on August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs, including aggregate reductions of Medicare payments to providers of up to 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, unless additional Congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, and subsequent legislation, these Medicare sequester reductions will be suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. Proposed legislation, if passed, would extend this suspension until the end of the COVID-19 pandemic. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additionally, the BBA, among other things, amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount (from 50% under the ACA to 70%) that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole".

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. Recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their products. Such scrutiny has resulted in several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, at the federal level, the U.S. government's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Additionally, the Trump administration previously released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contained proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. HHS has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule that would allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning

January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. In addition, there have been several changes to the 340B drug pricing program, which imposes ceilings on prices that drug manufacturers can charge for medications sold to certain health care facilities. Some of these changes are undergoing legal challenges, and their status is currently in question. It is unclear how these developments could affect covered hospitals who might purchase our future products and affect the rates we may charge such facilities for our approved products in the future, if any.

Additionally, on July 24, 2020 and September 13, 2020, former President Trump signed a series of Executive Orders aimed at lowering drug prices and at implementing several of the administration's proposals. In response, the FDA released a final rule on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada, as further discussed below. Further, on November 20 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and will apply in all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. The Interim Final Rule has not been finalized and is subject to revision and challenge. Additionally, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Although a number of these and other measures may require additional authorization to become effective, and the Biden administration may reverse or otherwise change these measures, Congress has indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

At the state level in the United States, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biologic product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions on coverage or access could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates that we successfully commercialize or put pressure on our product pricing.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or in any other jurisdictions. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Recent federal legislation and actions by federal, state and local governments may permit reimportation of drugs from foreign countries into the United States, including foreign countries where the drugs are sold at lower prices than in the United States, which could materially adversely affect our operating results.

We may face competition in the United States for our product candidates and investigational medicines, if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. In the United States, the Medicare Modernization Act, or MMA, contains provisions that call for the promulgation of regulations that expand pharmacists' and wholesalers' ability to import cheaper versions of an approved drug and competing products from Canada, where there are government price controls. Further, the MMA provides that these changes to U.S. importation laws will not take effect, unless and until the Secretary of the U.S. Department of Health & Human Services, or HHS, certifies that the changes will pose no additional risk to the public's health and safety and will result in a significant reduction in the cost of products to consumers. On September 23, 2020, the Secretary of the HHS made such certification to Congress, and on October 1, 2020, FDA published a final rule that allows for the importation of certain prescription drugs from Canada. Under the final rule, states and Indian Tribes, and in certain future circumstances pharmacists and wholesalers, may submit importation program proposals to the FDA for review and authorization. Since the issuance of the final rule, several industry groups have filed federal lawsuits challenging multiple aspects of the final rule, and authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. On September 25, 2020, CMS

stated drugs imported by States under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for “best price” or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. Separately, the FDA also issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code, or NDC, for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. The market implications of the final rule and guidance are unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability.

In the United States, inadequate funding for the FDA, the SEC, and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical employees and stop critical activities. Separately, in response to the COVID-19 pandemic. Since March 2020, foreign and domestic inspections by FDA have largely been on hold with FDA announcing plans in July 2020 to resume prioritized domestic inspections. Should FDA determine that an inspection is necessary for approval of a marketing application and an inspection cannot be completed during the review cycle due to restrictions on travel, FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, FDA may defer action on the application until an inspection can be completed. In 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Risks Related to International Regulations

EU drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for our products in the European member states.

We ultimately intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU, the pricing of drugs is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future health care reform measures.

Much like the federal Anti-Kickback Statute prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU Member States, and in respect of the U.K. (which is

longer a member of the EU), the U.K. Bribery Act of 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

In addition, in most foreign countries, including the EEA, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In some countries, we may be required to conduct a clinical study or other studies that compare the cost-effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for biopharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales and the potential profitability of any of our product candidates in those countries would be negatively affected.

Legal, political and economic uncertainty surrounding the exit of the U.K. from the EU may be a source of instability in international markets, create significant currency fluctuations, adversely affect our operations in the U.K. and pose additional risks to our business, revenue, financial condition and results of operations.

On June 23, 2016, the U.K. held a referendum in which a majority of the eligible members of the electorate voted to leave the EU, commonly referred to as Brexit. Pursuant to Article 50 of the Treaty on EU, the U.K. ceased being a Member State of the EU on January 31, 2020. However, the terms of the withdrawal have yet to be fully negotiated. The implementation period began February 1, 2020 and will continue until December 31, 2020. During this 11-month period, the U.K. will continue to follow all of the EU's rules, the EU's pharmaceutical law remains applicable to the U.K. and the U.K.'s trading relationship will remain the same. However, regulations (including financial laws and regulations, tax and free trade agreements, intellectual property rights, data protection laws, supply chain logistics, environmental, health and safety laws and regulations, medicine licensing and regulations, immigration laws and employment laws), have yet to be addressed. This lack of clarity on future U.K. laws and regulations and their interaction with the EU laws and regulations may negatively impact foreign direct investment in the U.K., increase costs, depress economic activity and restrict access to capital.

The uncertainty concerning the U.K.'s legal, political and economic relationship with the EU after Brexit may be a source of instability in the international markets, create significant currency fluctuations and/or otherwise adversely affect trading agreements or similar cross-border co-operation arrangements (whether economic, tax, fiscal, legal, regulatory or otherwise) beyond the date of Brexit.

These developments, or the perception that any of them could occur, may have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and limit the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the U.K. financial and banking markets, as well as on the regulatory process in Europe. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility.

If the U.K. and the EU are unable to negotiate acceptable agreements or if other EU member states pursue withdrawal, barrier-free access between the U.K. and other EU member states or among the European Economic Area overall could be diminished or eliminated. The long-term effects of Brexit will depend on any agreements (or lack thereof) between the U.K. and the EU and, in particular, any arrangements for the U.K. to retain access to EU markets either during a transitional period from January 1, 2021 or more permanently.

Such a withdrawal from the EU is unprecedented, and it is unclear how the U.K.'s access to the European single market for goods, capital, services and labor within the EU, or single market, and the wider commercial, legal and regulatory environment, will impact our current and future operations (including business activities conducted by third parties and contract manufacturers on our behalf) and clinical activities in the U.K. In addition to the foregoing, our U.K. operations support our current and future operations and clinical activities in the EU and European Economic Area, or EEA, and these operations and clinical activities could be disrupted by Brexit.

We may also face new regulatory costs and challenges that could have an adverse effect on our operations. Depending on the terms of the U.K.'s withdrawal from the EU, the U.K. could lose the benefits of global trade agreements negotiated by the EU on behalf of its members, which may result in increased trade barriers that could make our doing business in the EU and the EEA more difficult. Since the regulatory framework in the U.K. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime with respect to the approval of our product candidates in the U.K. For instance, in November 2017, EU member states voted to move the EMA, the EU's regulatory body, from London to Amsterdam. Operations in Amsterdam commenced in March 2019, and the move itself may cause significant disruption to the regulatory approval process in Europe. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the U.K. Any delay in obtaining, or an inability to obtain, any regulatory approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the U.K. and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the U.K. and/or EU for our product candidates, which could significantly and materially harm our business. Even prior to any change to the U.K.'s relationship with the EU, the announcement of Brexit has created economic uncertainty surrounding the terms of Brexit and its consequences could adversely impact customer confidence resulting in customers reducing their spending budgets on our product candidates, if approved, which could adversely affect our business, financial condition, results of operations and could adversely affect the market price of our common stock.

Additional laws and regulations governing international operations could negatively impact or restrict our operations.

For our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The U.S. Foreign Corrupt Practices Act, or the FCPA, prohibits any U.S. individual or business entity from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the biopharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals and healthcare providers in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions. Recently the SEC and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents or contractors, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information products classified for national security purposes, as well as certain products, technology and technical data relating

to those products. If we continue and expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers or our employees, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs and prohibitions on the conduct of our business.

Any such violations could include prohibitions on our ability to offer our products, if approved, in one or more countries and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees and our business, prospects, operating results and financial condition. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Risks Related to Our Intellectual Property

Risks Related to Licensed Intellectual Property

Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.

Our business will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates, their respective components, synthetic intermediates, formulations, combination therapies and methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents that cover these activities and whether a court would issue an injunctive remedy. If we are unable to secure and maintain patent protection for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any product candidates we may develop may be adversely affected.

The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue, obtain, or maintain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors or licensees.

The strength of patents in the biotechnology and biopharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our technology, including our product candidates, or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates.

Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced.

We cannot be certain that we were the first to file any patent application related to our technology, including our product candidates, and, if we were not, we may be precluded from obtaining patent protection for our technology, including our product candidates.

We cannot be certain that we are the first to invent the inventions covered by pending patent applications and, if we are not, we may be subject to priority disputes. Furthermore, for United States applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the United States Patent and Trademark Office, or USPTO, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Similarly, for United States applications in which at least one claim is not entitled to a priority date before March 16, 2013, derivation proceedings can be instituted to determine whether the subject matter of a patent claim was derived from a prior inventor's disclosure.

We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent or patent application claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, would adequately protect our product candidates, or would be found by a court to be infringed by a competitor's technology or product. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities, and consider that we are free to operate in relation to our product candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our product candidates or our activities infringing such claims. The possibility exists that others will develop products which have the same effect as our products on an independent basis which do not infringe our patents or other intellectual property rights, or will design around the claims of patents that may issue that cover our products.

Recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Under the enacted Leahy-Smith America Invents Act, or America Invents Act, enacted in 2013, the United States moved from a "first to invent" to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear as the USPTO only recently developed new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the "first-to-file" provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds that are similar to the compositions of our product candidates but that are not covered by the claims of our patents or those of our licensors;
- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regards to any in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies;
- it is possible that our pending patent applications will not result in issued patents;

- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents or become hostile to us or the patents or patent applications on which they are named as inventors;
- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- we have engaged in scientific collaborations in the past, and will continue to do so in the future. Such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- it is possible that product candidates or diagnostic tests we develop may be covered by third parties' patents or other exclusive rights; or
- the patents of others may have an adverse effect on our business.

Risks Related to License and Collaboration Agreements

We have entered into, and may enter into, license or other collaboration agreements that impose certain obligations on us. If we fail to comply with our obligations under such agreements with third parties, we could lose license rights that may be important to our business.

In connection with our efforts to expand our pipeline of product candidates, we have entered into and may further enter into certain licenses or other collaboration agreements in the future pertaining to the in-license of rights to additional candidates. Such agreements may impose various diligence, milestone payment, royalty, insurance or other obligations on us. If we fail to comply with these obligations, our licensor or collaboration partners may have the right to terminate the relevant agreement, in which event we would not be able to develop or market the products covered by such licensed intellectual property.

Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our product candidates, technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property

that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

In addition, we may have limited control over the maintenance and prosecution of these in-licensed patents and patent applications, or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by any future licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to patent protection, we rely heavily upon know-how and trade secret protection, as well as non-disclosure agreements and invention assignment agreements with our employees, consultants and third parties, to protect our confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not, for example, in the case of misappropriation of a trade secret by an employee or third-party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, trade secrets may be independently developed by others in a manner that could prevent legal recourse by us. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed.

In addition, courts outside the United States are sometimes less willing to protect trade secrets. If we choose to go to court to stop a third-party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology.

Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties. We have also adopted policies and conduct training that provides guidance on our expectations, and our advice for best practices, in protecting our trade secrets.

Risks Related to Potential Third-Party Claims

Third-party claims of intellectual property infringement may prevent or delay our product discovery and development efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and biopharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future

litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and biopharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

We also may be subject to other third party claims relating to alleged infringement of intellectual property or other proprietary rights, including breach of nondisclosure, nonuse, noncompetition and non-solicitation provisions, intellectual property assignment and ownership, and misuse or misappropriation of intellectual property, trade secrets and other confidential information, among others. If a court of competent jurisdiction finds us liable for any such claims, we may be prohibited from using certain intellectual property, trade secrets and confidential information, effectively blocking our ability to seek patent protection for our inventions and halting the progress of our clinical development and commercialization efforts. For example, on May 20, 2020, we received a cease and desist letter from Sage Therapeutics, Inc., or Sage, in which Sage alleges a claim that we improperly accessed and benefited from Sage confidential information in connection with the in-license of our PRAX-114 development program as a result of our employment or engagement of former Sage employees and consultants. We believe that there is no merit to these claims and intend to defend our position. However, an adverse result could harm our business and result of operations.

If a third-party claims that we infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;
- substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third-party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third-party licenses its product rights to us, which it is not required to do;
- if a license is available from a third-party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products and any license that is available may be non-exclusive, which could result in our competitors gaining access to the same intellectual property; and
- redesigning our product candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure.

Our collaborators may assert ownership or commercial rights to inventions they develop from research we support or that we develop or otherwise arising from the collaboration.

We collaborate with several institutions, universities, medical centers, physicians and researchers in scientific matters and expect to continue to enter into additional collaboration agreements. In certain cases, we do not have written agreements with these collaborators, or the written agreements we have do not cover intellectual property rights. Also, we rely on numerous third parties to provide us with materials that we use to conduct our research activities and develop our product candidates. If we cannot successfully negotiate sufficient ownership and commercial rights to any inventions that result from our use of a third-party collaborator's materials, or if disputes arise with respect to the intellectual property developed with the use of a collaborator's samples, or data developed

in a collaborator's study, we may be limited in our ability to capitalize on the market potential of these inventions or developments.

Third parties may assert that we are employing their proprietary technology without authorization.

There may be third-party patents of which we are currently unaware with claims to compositions of matter, materials, formulations, methods of manufacture or methods for treatment that encompass the composition, use or manufacture of our product candidates. There may be currently pending patent applications of which we are currently unaware which may later result in issued patents that our product candidates or their use or manufacture may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third- party patent were held by a court of competent jurisdiction to cover our product candidates, intermediates used in the manufacture of our product candidates or our materials generally, aspects of our formulations or methods of use, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible, or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly.

Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.

As is common in the biotechnology and biopharmaceutical industries, we employ individuals who were previously employed at universities or other biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

We may not be successful in obtaining or maintaining necessary rights to develop any future product candidates on acceptable terms.

Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights.

Our product candidates may also require specific formulations to work effectively and efficiently and these rights may be held by others. We may develop products containing our compounds and pre-existing biopharmaceutical compounds. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

Additionally, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents or the patents of our current or future licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question or for other reasons. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly, and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

We may choose to challenge the patentability of claims in a third-party's U.S. patent by requesting that the USPTO review the patent claims in an *ex-parte* re-examination, *inter partes* review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third-party's patent in patent opposition proceedings in the European Patent Office, or EPO, or other foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third-party alleging that the patent may be infringed by our product candidates or proprietary technologies.

In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our owned and in-licensed issued patents or our pending applications, or that we or, if applicable, a licensor were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our owned and in-licensed patent

applications or patents, which could require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to those owned by or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference or derivation proceeding declared by the USPTO to determine priority of invention in the United States. If we or one of our licensors is a party to an interference or derivation proceeding involving a U.S. patent application on inventions owned by or in-licensed to us, we may incur substantial costs, divert management's time and expend other resources, even if we are successful.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Litigation or interference proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Risks Related to Patent Laws and Protection

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application process and following the issuance of a patent. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In certain circumstances, even inadvertent noncompliance events may permanently and irrevocably jeopardize patent rights. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Any patents, if issued, covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO.

If we or one of our licensors initiate legal proceedings against a third-party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third-party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, inter partes review, post grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

Likewise, our current licensed or owned patents are expected to expire between 2029 and 2041, without taking into account any possible patent term adjustments or extensions. Our earliest patents may expire before, or soon after, our first product achieves marketing approval in the United States or foreign jurisdictions. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a similar material adverse effect on our business, results of operations, financial condition and prospects. Our current licensed or owned pending patent applications covering our proprietary technologies or our product candidates that if issued as patents are expected to expire from 2029 through 2041, without taking into account any possible patent term adjustments or extensions. However, we cannot be assured that the USPTO or relevant foreign patent offices will grant any of these patent applications.

Changes in patent law in the United States and in foreign jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 16, 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. On March 16, 2013, under the America Invents Act, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO on or after March 16, 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, inter-parties review and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biopharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world.

We have limited intellectual property rights outside the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong

as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of, and may require a compulsory license to, patents, trade secrets and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally.

The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions such as patent term adjustments and/or extensions, may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Our Dependence on Third Parties

Risks Related to Third Parties Generally

We rely on third parties to assist in conducting our preclinical studies and clinical trials. If they do not perform satisfactorily, we may not be able to obtain regulatory approval or commercialize our product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed.

We have relied upon and plan to continue to rely on third parties, such as laboratories, CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our preclinical studies and clinical trials and expect to rely on these third parties to conduct preclinical studies and clinical trials of any other product candidate that we develop. Any of these third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which could negatively impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

Although our reliance on these third parties for preclinical and clinical development activities limits our control over these activities, we remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. Moreover, human clinical research must comply with GCPs for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and IRBs. If we or our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the regulatory authorities may require us to perform additional clinical trials before approving our product candidates, which would delay the regulatory approval process. We cannot be certain that, upon inspection, a regulatory authority will determine that any of our clinical trials comply with GCPs.

The third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. These outside contractors may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties, including clinical investigators, do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In such an event, our financial results and the commercial prospects for any product candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

If our relationships with any third parties conducting our studies are terminated, we may be unable to enter into arrangements with alternative third parties on commercially reasonable terms, or at all. Switching or adding third parties to conduct our studies involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired preclinical and clinical development timelines. Although we carefully manage our relationships with third parties conducting our studies, we cannot assure that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material and adverse effect on our business, financial condition and results of operations.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or regulatory approval of our product candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

Furthermore, we may also engage third parties to develop companion or complementary diagnostics for use in our clinical trials, as applicable, but such third parties may not be successful in developing such companion or complementary diagnostics, furthering the difficulty in identifying patients with the targeted eligibility criteria for our clinical trials. If we are required to develop companion or complementary diagnostics and are unable to do so or unable to obtain any required regulatory clearance or approval of those diagnostics, this could compromise our ability to seek participation in the U.S. in certain of the FDA's expedited review and development programs, including those that may accelerate clinical development and regulatory timelines, and could limit our ability to seek regulatory approval for our product candidates.

Risks Related to Third-Party Manufacturers

The manufacture of our product candidates is complex, and we may encounter difficulties in production. We currently rely completely on third parties to formulate and manufacture our preclinical, clinical trial and commercial drug supplies. The development and commercialization of any of our product candidates could be stopped, delayed or made less profitable if those third parties fail to provide us with sufficient quantities of such drug supplies or fail to do so at acceptable quality levels, including in accordance with rigorously enforced regulatory requirements or contractual obligations, and our operations could be harmed as a result.

The processes involved in manufacturing our drug product candidates are complex, expensive, highly-regulated and subject to multiple risks. Further, as product candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could require the conduct of bridging studies and could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials. We have limited experience in drug formulation or manufacturing. Currently, we rely on an extensive network of contract manufacturers, and in some cases sole source suppliers, for the production of our product candidates for current and planned clinical trials.

In order to conduct clinical trials of our product candidates, or supply commercial products, if approved, we will need to manufacture them in large quantities. Our contract development and manufacturing organizations, or CDMOs, may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If our CDMOs are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. The same risk would apply to our internal manufacturing facilities, should we in the future decide to build internal manufacturing capacity. In addition, building internal manufacturing capacity would carry significant risks in terms of being able to plan, design and execute on a complex project to build manufacturing facilities in a timely and cost-efficient manner, and the resources associated with ensuring the ongoing regulatory compliance of such manufacturing facilities would be significant.

In addition, the manufacturing process for any products that we may develop is subject to FDA, EMA, and foreign regulatory authority approval processes and continuous oversight, and we will need to contract with manufacturers who can meet all applicable FDA, EMA and foreign regulatory authority requirements, including complying with current good manufacturing practices, or cGMPs, on an ongoing basis. Although our agreements with our CDMOs require them to perform according to certain cGMP requirements such as those relating to quality control, quality assurance and qualified personnel, we cannot control the ability of our CDMOs to implement and maintain these standards. If we or our third-party manufacturers are unable to reliably produce products to specifications acceptable to the FDA, EMA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CDMOs will be able to manufacture the approved product to specifications acceptable to the FDA, EMA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates, impair commercialization efforts, increase our cost of goods and have an adverse effect on our business, financial condition, results of operations and growth prospects.

If any third-party manufacturer of our product candidates is unable to increase the scale of its production of our product candidates, and/or increase the product yield of its manufacturing, then our costs to manufacture the product may increase and commercialization may be delayed.

In order to produce sufficient quantities to meet the demand for clinical trials and, if approved, subsequent commercialization of our product candidates that we may develop, our third-party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of the product. The transition to larger scale production could prove difficult. In addition, if our third party manufacturers are not able to optimize their manufacturing processes to increase the product yield for our product candidates, or if they are unable to produce increased amounts of our product candidates while maintaining the quality of the product, then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate profits and have a material adverse impact on our business and results of operation.

Risks Related to Third-Party Suppliers

We depend on third-party suppliers for key raw materials used in our manufacturing processes, some of which are our sole source of supply, and the loss of these third-party suppliers or their inability to supply us with adequate raw materials could harm our business.

We rely on our CDMOs to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical trials. We do not have, nor do we expect to enter into, any agreements for the commercial production of these raw materials, and we do not expect to have any control over the process or timing of our CDMOs' acquisition of raw materials needed to produce our product candidates. Any significant delay in the supply of a product candidate or the raw material components thereof for an ongoing clinical trial due to a manufacturer's need to replace a third-party supplier of raw materials could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates. Additionally, if our future manufacturers or we are unable to purchase these raw materials to commercially produce any of our product candidates that gains regulatory approvals, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates.

Furthermore, for those third-party suppliers who may be our sole source of supply of certain materials, we may not have arrangements in place for a redundant or second-source supply of any such materials in the event any of our current suppliers cease their operations for any reason. Establishing additional or replacement suppliers for the raw materials used in our product candidates, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory inspection or approval, which could result in further delay.

We expect to depend on collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.

We may seek third-party collaborators for the research, development and commercialization of certain of the product candidates we may develop. For example, we have a collaboration with Ionis Pharmaceuticals, Inc. to further our development of product candidates and to enhance our research efforts directed to developing a product candidate for the treatment of epilepsy. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies and academic institutions. If we enter into any such arrangements with any third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs, or any product candidates we may develop, pose the following risks to us:

- collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not properly obtain, maintain, enforce or defend intellectual property or proprietary rights relating to our product candidates or research programs, or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property related proceedings, including proceedings challenging the scope, ownership, validity and enforceability of our intellectual property;
- collaborators may own or co-own intellectual property covering our product candidates or research programs that results from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates or research programs;
- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- collaborators may control certain interactions with regulatory authorities, which may impact our ability to obtain and maintain regulatory approval of our products candidates;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or research programs or that result in costly litigation or arbitration that diverts management attention and resources;

- collaborators may decide to not pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates or research programs if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators may restrict us from researching, developing or commercializing certain products or technologies without their involvement;
- collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may grant sublicenses to our technology or product candidates or undergo a change of control and the sublicensees or new owners may decide to take the collaboration in a direction which is not in our best interest;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, know-how or intellectual property of the collaborator relating to our products, product candidates or research programs;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short and long-term expenditures, issue securities that dilute our stockholders or disrupt our management and business;
- if our collaborators do not satisfy their obligations under our agreements with them, or if they terminate our collaborations with them, we may not be able to develop or commercialize product candidates as planned;
- collaborations may require us to share in development and commercialization costs pursuant to budgets that we do not fully control and our failure to share in such costs could have a detrimental impact on the collaboration or our ability to share in revenue generated under the collaboration;
- collaborations may be terminated in their entirety or with respect to certain product candidates or technologies and, if so terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates or technologies; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our development or commercialization program under such collaboration could be delayed, diminished or terminated.

We may face significant competition in seeking appropriate collaborations. Recent business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elects not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. The failure to develop and commercialize a product candidate pursuant to our agreements with our current or future collaborators could prevent us from receiving future payments under such agreements, which could negatively impact our revenues. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section also apply to the activities of our collaborators and any negative impact on our collaborators may adversely affect us.

We may acquire businesses or products, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions or alliances.

We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

Risks Related to Employee Matters, Managing Our Business and Operations

Risks Related to Business Operations

Business interruptions resulting from COVID-19 or a similar pandemic, epidemic or outbreak of an infectious disease in the United States or worldwide may adversely affect our business.

If a pandemic, epidemic or outbreak of an infectious disease occurs in the United States or worldwide our business may be adversely affected. In December 2019, a novel strain of coronavirus named SARS-CoV-2 was identified in Wuhan, China. This virus continues to spread globally, including in the United States and the disease it causes, COVID-19, has been declared a pandemic by the World Health Organization. The COVID-19 pandemic has impacted the global economy and may impact our operations, including the potential interruption of our clinical trial activities, regulatory reviews and our supply chain. For example, the COVID-19 pandemic may delay enrollment in our clinical trials due to prioritization of hospital resources toward the outbreak or other factors, and some patients may be unwilling to enroll in our trials or be unable to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services, which would delay our ability to conduct clinical trials or release clinical trial results and could delay our ability to obtain regulatory approval and commercialize our product candidates. Furthermore, the spread of the virus may affect the operations of key governmental agencies, such as the FDA, which may delay the development or approval process for our product candidates.

The spread of COVID-19 may also result in the inability of our suppliers to deliver components or raw materials on a timely basis or at all. Three vaccines for COVID-19 were granted Emergency Use Authorization by the FDA in late 2020 and early 2021, and more are likely to be authorized in the coming months. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. In addition, hospitals may reduce staffing and reduce or postpone certain treatments in response to the spread of an infectious disease. Such events may result in a period of business disruption, and in reduced operations, or doctors and medical providers may be unwilling to participate in our clinical trials, any of which could materially affect our business, financial condition and results of operations. We continue to closely monitor the COVID-19 pandemic as we evolve our business continuity plans, clinical development plans and response strategy. The extent to which the COVID-19 pandemic impacts our business will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity of the novel coronavirus and the actions to contain the coronavirus or treat its impact, among others. At present, we are not experiencing significant impact or delays from the COVID-19 pandemic on our business, operations and, if approved, commercialization plans. In addition, we have taken steps to mitigate against COVID-19 pandemic-related delays, and may take additional measures, intended to help minimize the risk of the virus to our employees, including

temporarily requiring all employees to work remotely, suspending all non-essential travel worldwide for our employees, and discouraging employee attendance at industry events and in-person work-related meetings, which could negatively affect our business.

While we have taken and are continuing to take steps to mitigate against possible delays, our planned clinical trials may be affected by the COVID-19 pandemic, including (i) delays or difficulties in enrolling and retaining patients in our planned clinical trials, including patients that may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services; (ii) delays or difficulties in clinical site initiation, including difficulties in recruiting and retaining clinical site investigators and clinical site staff; (iii) diversion or prioritization of healthcare resources away from the conduct of clinical trials and towards the COVID-19 pandemic, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials, and because, who, as healthcare providers, may have heightened exposure to COVID-19 and adversely impact our clinical trial operations; (iv) interruption of our future clinical supply chain or key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal, state/provincial or municipal governments, employers and others; and (v) limitations in outsourced third-party resources that would otherwise be focused on the conduct of our planned clinical trials, including because of sickness of third-party personnel or their families, or the desire of third-party personnel to avoid contact with large groups of people. A significant outbreak of other infectious diseases in the future also could result in a widespread health crisis that could adversely affect the economies and financial markets worldwide, resulting in an economic downturn that could impact our business, financial condition and results of operations.

Our business is subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. Some of our suppliers and collaborative relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing and changing regulatory requirements in non-U.S. countries;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations
- potential liability under the FCPA, U.K. Bribery Act of 2010 or comparable foreign laws;
- business interruptions resulting from geo-political actions, including war and terrorism, natural disasters including earthquakes, typhoons, floods and fires, or health epidemics such as COVID-19; and
- cyberattacks, which are growing in frequency, sophistication and intensity, and are becoming increasingly difficult to detect.

These and other risks associated with our planned international operations may materially adversely affect our ability to attain profitable operations.

Risks Related to Employees

We depend heavily on our executive officers, principal consultants and others, and the loss of their services would materially harm our business.

Our success depends, and will likely continue to depend, upon our ability to hire, retain the services of our current executive officers, principal consultants and others, including Marcio Souza, our President and Chief Executive Officer, and Bernard Ravina, our Chief Medical Officer. We have entered into employment agreements with Mr. Souza and Dr. Ravina, but they may terminate their employment with us at any time. The loss of their services might impede the achievement of our research, development and commercialization objectives. We do not maintain “key person” insurance for any of our executives or other employees.

Our ability to compete in the biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. Our industry has experienced a high rate of turnover of management personnel in recent years. Replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully.

Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize our product candidates will be limited.

We only have a limited number of employees to manage and operate our business. If we are unable to hire to retain adequate personnel, then we may not be able to meet our operational goals.

As of January 31, 2021, we had 67 full-time employees. Our focus on the clinical development of PRAX-114, PRAX-944 and PRAX-562 requires us to optimize cash utilization and to manage and operate our business in a highly efficient manner. We cannot ensure that we will be able to hire and/or retain adequate staffing levels to develop PRAX-114, PRAX-944 and PRAX-562 or to run our operations and/or to accomplish all of the objectives that we otherwise would seek to accomplish.

Our employees, independent contractors, consultants, collaborators and contract research organizations may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors, consultants, collaborators and contract research organizations may engage in fraudulent conduct or other illegal activity. Misconduct by those parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates:

- regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities;
- manufacturing standards;
- federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities; and
- laws that require the accurate reporting of financial information or data.

Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of product materials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this kind of activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, integrity oversight and reporting obligations, possible exclusion from participation in the United States in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm,

diminished profits and future earnings and curtailment of our operations, any of which could have a material adverse effect on our ability to operate our business and our results of operations.

We expect to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of regulatory affairs and sales, marketing and distribution, as well as to support our public company operations. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Our management may need to devote a significant amount of its attention to managing these growth activities. Moreover, our expected growth could require us to relocate to a different geographic area of the country. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion or relocation of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion or relocation of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates.

Risks Related to Data Privacy

Cyber-attacks or other failures in our telecommunications or information technology systems, or those of our collaborators, contract research organizations, third-party logistics providers, distributors or other contractors or consultants, could result in information theft, data corruption and significant disruption of our business operations.

We, our collaborators, our CROs, third-party logistics providers, distributors and other contractors and consultants utilize information technology, or IT, systems and networks to process, transmit and store electronic information in connection with our business activities. As use of digital technologies has increased, cyber incidents, including third parties gaining access to employee accounts using stolen or inferred credentials, computer malware, viruses, spamming, phishing attacks or other means, and deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. These threats pose a risk to the security of our, our collaborators', our CROs', third-party logistics providers', distributors' and other contractors' and consultants' systems and networks, and the confidentiality, availability and integrity of our data. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. Similarly, there can be no assurance that our collaborators, CROs, third-party logistics providers, distributors and other contractors and consultants will be successful in protecting our clinical and other data that is stored on their systems. Any cyber-attack, data breach or destruction or loss of data could result in a violation of applicable U.S. and international privacy, data protection and other laws, and subject us to litigation and governmental investigations and proceedings by federal, state and local regulatory entities in the United States and by international regulatory entities, resulting in exposure to material civil and/or criminal liability. Further, our general liability insurance and corporate risk program may not cover all potential claims to which we are exposed and may not be adequate to indemnify us for all liability that may be imposed; and could have a material adverse effect on our business and prospects. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials for any of our product candidates could result in delays in our development and regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to implement further data protection measures.

We rely on a set of cloud-based software services and access these services via the Internet for the vast majority of our computing, storage, bandwidth and other services. Any disruption of or interference with our use of our cloud-based services would negatively affect our operations and could seriously harm our business.

We use several distributed computing infrastructure platforms for business operations, or what is commonly referred to as "cloud" computing services and we access these services via the Internet. Any transition of the cloud

services currently provided by an existing vendor to another cloud provider would be difficult to implement and will cause us to incur significant time and expense. Given this, any significant disruption of or interference with our use of these cloud computing services would negatively impact our operations and our business would be seriously harmed. If our employees or partners are not able to access our cloud computing services or encounter difficulties in doing so, we may experience business disruption. The level of service provided by our cloud computing vendors, including the ability to secure our confidential information and the confidential information of third parties that is shared with us, may also impact the perception of our company and could seriously harm our business and reputation and create liability for us. If a cloud computing service that we use experiences interruptions in service regularly or for a prolonged basis, or other similar issues, our business could be seriously harmed.

In addition, a cloud computing service may take actions beyond our control that could seriously harm our business, including:

- discontinuing or limiting our access to its platform;
- increasing pricing terms;
- terminating or seeking to terminate our contractual relationship altogether; or
- modifying or interpreting its terms of service or other policies in a manner that impacts our ability to run our business and operations.

Our cloud computing services have broad discretion to change and interpret its terms of service and other policies with respect to us, and those actions may be unfavorable to us. Our cloud computing services may also alter how we are able to process data on the platform. If a cloud computing services makes changes or interpretations that are unfavorable to us, our business could be seriously harmed.

Our efforts to protect the information shared with us may be unsuccessful due to the actions of third parties, software bugs or other technical malfunctions, employee error or malfeasance or other factors. In addition, third parties may attempt to fraudulently induce employees or users to disclose information to gain access to our data or third-party data entrusted to us. If any of these events occur, our or third-party information could be accessed or disclosed improperly. Some partners or collaborators may store information that we share with them on their own computing system. If these third parties fail to implement adequate data-security practices or fail to comply with our policies, our data may be improperly accessed or disclosed. And even if these third parties take all of these steps, their networks may still suffer a breach, which could compromise our data.

Any incidents where our information is accessed without authorization, or is improperly used, or incidents that violate our policies, could damage our reputation and our brand and diminish our competitive position. In addition, affected parties or government authorities could initiate legal or regulatory action against us over those incidents, which could cause us to incur significant expense and liability or result in orders or consent decrees forcing us to modify our business practices. Concerns over our privacy practices, whether actual or unfounded, could damage our reputation and brand and deter users, advertisers and partners from using our products and services. Any of these occurrences could seriously harm our business.

We are also subject to many federal, state and foreign laws and regulations, including those related to privacy, rights of publicity, data protection, content regulation, intellectual property, health and safety, competition, protection of minors, consumer protection, employment and taxation. These laws and regulations are constantly evolving and may be interpreted, applied, created or amended in a manner that could seriously harm our business.

Risks Related to Tax Laws

Legislation or other changes in U.S. tax law could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many changes have been made to applicable tax laws and changes are likely to continue to occur in the future.

For example, the Tax Cuts and Jobs Act, or the TCJA, was enacted in 2017 and made significant changes to corporate taxation, including the reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for net operating losses from taxable years beginning after December 31, 2017 to 80% of current year taxable income and the elimination of net operating loss carrybacks generated in taxable years ending after December 31, 2017 (though any such net operating losses may be carried

forward indefinitely) and the modification or repeal of many business deductions and credits. In addition, on March 27, 2020, President Trump signed into law the "Coronavirus Aid, Relief, and Economic Security Act" or the CARES Act, which included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 public health emergency, including temporary beneficial changes to the treatment of net operating losses, interest deductibility limitations and payroll tax matters.

It cannot be predicted whether, when, in what form or with what effective dates new tax laws may be enacted, or regulations and rulings may be enacted, promulgated or issued under existing or new tax laws, which could result in an increase in our or our shareholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof.

Our ability to use our U.S. net operating loss carryforwards and certain other U.S. tax attributes may be limited.

Our ability to use our U.S. federal and state net operating losses to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income to use all of our net operating losses.

Unused losses for the tax year beginning before January 1, 2018 and prior tax years will carry forward to offset future taxable income, if any, until such unused losses expire. Unused losses generated for the tax year beginning after December 31, 2017, under new tax legislation will not expire and may be carried forward indefinitely, and generally may not be carried back to prior taxable years, except that, under the CARES Act, net operating losses generated in 2018, 2019 and 2020 may be carried back five taxable years. Additionally, for taxable years beginning after December 31, 2020, the deductibility of such U.S. federal net operating losses is limited to 80% of our taxable income in any future taxable year. In addition, both our current and our future unused losses may be subject to limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, if we undergo an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside our control.

Risks Related to Our Common Stock

Risks Related to Investment in Securities

An active trading market for our common stock may not be sustained.

In October 2020, we closed our initial public offering, or IPO. Prior to our IPO, there was no public market for our common stock. Although we have completed our IPO and shares of our common stock are listed and trading on the Nasdaq Global Select Market, an active trading market for our shares may not be sustained. If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at or above the prices at which they acquired their shares or sell their shares at the time they would like to sell. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

The price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this "Risk Factors" section, these factors include:

- the commencement, enrollment, completion or results of our current Phase 2a clinical trials of PRAX-114 and PRAX-944 and current Phase 1 trial of PRAX-562;
- any delay in identifying and advancing a clinical candidate for our other programs;
- any delay in our regulatory filings for PRAX-114, PRAX-944, PRAX-562 or our future product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- adverse results or delays, suspensions or terminations in future preclinical studies or clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;

- adverse regulatory decisions, including failure to receive regulatory approval of PRAX-114, PRAX-944, PRAX-562 or any other product candidate or the failure of a regulatory authority to accept data from preclinical studies or clinical trials conducted in other countries;
- changes in laws or regulations applicable to PRAX-114, PRAX-944, PRAX-562 or any other product candidate, including but not limited to clinical trial requirements for approvals;
- adverse developments concerning our manufacturers;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- our inability to establish collaborations, if needed;
- our failure to commercialize our product candidates, if approved;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of PRAX-114, PRAX-944, PRAX-562 or any other product candidate;
- introduction of new products or services offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or product candidates in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- changes in the structure of the healthcare payment systems;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the market for biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies, including as a result of the COVID-19 pandemic. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources.

A significant portion of our total outstanding shares are eligible to be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Following the closing of our IPO, we had outstanding 36,749,675 shares of common stock, of which 26,737,873 shares were subject to restrictions on transfer under 180-day lock-up arrangements with the underwriters of our IPO. These restrictions are due to expire in April 2021, resulting in the majority of these shares then being eligible for public sale if they are registered under the Securities Act of 1933, as amended (the "Securities Act"), or if they qualify for an exemption from registration under the Securities Act including under Rules 144 or 701.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. We may never obtain research coverage by industry or financial analysts. If no securities or industry analysts commence coverage of our company, the trading price for our stock would likely be negatively impacted. In the event securities or industry analysts initiate coverage, if one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Furthermore, future debt or other financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock.

Our issuance of additional capital stock in connection with financings, acquisitions, investments, our stock incentive plans or otherwise will dilute all other stockholders.

We expect to issue additional capital stock in the future that will result in dilution to all other stockholders. We expect to grant equity awards to employees, directors and consultants under our stock incentive plans. We may also raise capital through equity financings in the future. As part of our business strategy, we may acquire or make investments in complementary companies, products or technologies and issue equity securities to pay for any such acquisition or investment. Any such issuances of additional capital stock may cause stockholders to experience significant dilution of their ownership interests and the per share value of our common stock to decline.

Our executive officers, directors and their affiliates and our principal stockholders own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Based on shares outstanding as of October 20, 2020, our executive officers, directors and their affiliates and our principal stockholders beneficially hold, in the aggregate, approximately 47.5% of our outstanding voting stock. These stockholders, acting together, would be able to significantly influence all matters requiring stockholder approval. The concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. This concentration of ownership control may adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change in control;
- entrenching our management and the board of directors;
- impeding a merger, consolidation, takeover or other business combination involving us that other stockholders may desire; and/or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

Risks Related to Our Controls and Reporting Requirements

We will continue to incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and The Nasdaq Global Select Market to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial reporting controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd- Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as “say on pay” and proxy access. Recent legislation permits EGCs to implement many of these requirements over a longer period and up to five years from the IPO. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

The rules and regulations applicable to public companies substantially increase our legal and financial compliance costs and make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have an adverse effect on our business. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

We are an emerging growth company and a smaller reporting company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors.

We are an emerging growth company, or EGC, as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012. For as long as we continue to be an EGC, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not EGCs, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an EGC for up to five years following the year in which we completed our IPO, although circumstances could cause us to lose that status earlier. We will remain an EGC until the earlier of (i) the last day of the fiscal year (a) following the fifth anniversary of the completion of our IPO, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed $700.0 million as of the prior June 30th, and (ii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three- year period.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting burdens. In particular, we have not included all of the executive compensation information that would be required if we were not an EGC. We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, EGCs can also delay adopting new or revised accounting standards until such time as those standards apply to private companies, which may make our financial statements less comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

Even after we no longer qualify as an emerging growth company, we may still qualify as a “smaller reporting company,” which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely

on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an EGC, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an EGC for up to five years. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to restatements of our financial statements and require us to incur the expense of remediation.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

We have broad discretion over the use of our cash and cash equivalents and may not use them effectively.

Our management has broad discretion to use our cash and cash equivalents to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending our use to fund operations, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

Risks Related to Charter and Bylaws

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;

- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue convertible preferred stock on terms determined by the board of directors without stockholder approval and which convertible preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

Our amended and restated bylaws designate certain courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our amended and restated bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our bylaws (in each case, as they may be amended from time to time) or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein; provided, however, that this exclusive forum provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our bylaws further provide that, unless we consent in writing to an alternative forum, the United States District Court for the District of Massachusetts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. We have chosen the United States District Court for the District of Massachusetts as the exclusive forum for such Securities Act causes of action because our principal executive offices are located in Cambridge, Massachusetts. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions. We recognize that the forum selection clause in our bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts, as applicable. Additionally, the forum selection clause in our bylaws may limit our stockholders' ability to bring a claim in a forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. The Court of Chancery of the State of Delaware or the United States District Court for the District of Massachusetts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Facilities

We sublease a facility containing 6,374 square feet of office space, which is located at One Broadway, Cambridge, Massachusetts 02142. Our sublease expires on December 30, 2021. We believe that our current facilities are sufficient to meet our current and near-term needs and that, should it be needed, suitable additional space will be available.

Item 3. Legal Proceedings

We are not currently a party to any material legal matters or claims. We may become party to legal matters and claims arising in the ordinary course of business. We cannot predict the outcome of any such legal matters or claims, and despite the potential outcomes, the existence thereof may have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Certain Information Regarding the Trading of Our Common Stock

Our common stock trades under the symbol “PRAX” on the Nasdaq Global Select Market and has been publicly traded since October 16, 2020. Prior to this time, there was no public market for our common stock.

Holders of Our Common Stock

As of March 1, 2021, there were approximately 41 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in “nominee” or “street” name.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain any future earnings to fund the development and expansion of our business, and therefore we do not anticipate paying cash dividends on our common stock in the foreseeable future.

Recent Sales of Unregistered Securities

Set forth below is information regarding shares of our common stock, shares of our preferred stock issued, and stock options granted by us during the period covered by this Annual Report on Form 10-K that were not registered under the Securities Act. Included is the consideration, if any, we received for such shares and options and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

Issuances of Capital Stock

On April 15, 2020 and May 8, 2020, we completed closings for the sale and issuance of 4,563,108 shares of Series C redeemable convertible preferred stock at $5.15 per share for aggregate cash proceeds of $23.5 million, net of issuance costs.

No underwriters were involved in the foregoing sales of securities. The sales of securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act, including Regulation D and Rule 506 promulgated thereunder, as transactions by an issuer not involving a public offering. All of the purchasers in these transactions represented to us in connection with their purchase that they were acquiring the securities for investment and not distribution, that they could bear the risks of the investment and could hold the securities for an indefinite period of time. Such purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration. All of the foregoing securities are deemed restricted securities for the purposes of the Securities Act.

Option Issuances

On October 15, 2020, and prior to our Registration Statement on Form S-8 going effective on October 16, 2020, we granted to employees options to purchase an aggregate of 37,615 shares of our common stock, with an exercise price of $19.00 per share, pursuant to our 2020 Stock Option and Incentive Plan.

Shares Authorized for Issuance Under Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Use of Proceeds from Initial Public Offering

In October 2020, we completed the initial public offering of our common stock, or IPO, pursuant to which we issued and sold 11,500,000 shares of our common stock at a price to the public of $19.00 per share.

All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-249074), which was declared effective by the Securities and Exchange Commission, or the SEC, on October 15, 2020. Following the sale of all shares, including shares sold pursuant to the underwriters' option to purchase an additional 1,500,000 shares exercised in October 2020, the offering terminated. Cowen and Company, LLC, Evercore Group L.L.C. and Piper Sandler & Co. acted as joint book-running managers, Wedbush Securities Inc. acted as lead manager and Blackstone Securities Partners L.P. acted as co-manager of the IPO.

We received aggregate gross proceeds from our IPO of approximately $218.5 million, or aggregate net cash proceeds of approximately $200.3 million after deducting underwriting discounts and commissions and offering expenses. None of the underwriting discounts and commissions or offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10% or more of our common stock or to any of our affiliates.

Information related to use of proceeds from registered securities is incorporated herein by reference to the “Use of Proceeds” section of our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on October 16, 2020. There has been no material change in the planned use of proceeds from our IPO as described in our final prospectus.

Issuer Purchases of Equity Securities

None.

Item 6. Selected Financial Data

Reserved.

Item 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the "Selected Consolidated Financial Data" section of this Annual Report on Form 10-K and our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for central nervous system, or CNS, disorders characterized by neuronal imbalance. Normal brain function requires a delicate balance of excitation and inhibition in neuronal circuits, which, when dysregulated, leads to abnormal function and disease. We are applying insights from genetic epilepsies to broader neurological and psychiatric disorders, using our understanding of shared biological targets and circuits in the brain. We apply a deliberate and pragmatic precision approach, leveraging a suite of translational tools including novel transgenic and predictive translational animal models and electrophysiology markers, to enable an efficient path to proof-of-concept in patients. Through this approach, we have established a broad portfolio, including multiple disclosed programs across CNS disorders, including depression, epilepsy, movement disorders and pain syndromes, with three clinical-stage product candidates. We intend to develop differentiated therapies that can deliver long-term benefits to human health by meaningfully impacting patients and society. We expect multiple topline clinical trial readouts from all three programs in the next year and anticipate the launch of a new clinical development program in 2021. We intend to develop differentiated therapies that can deliver long-term benefits to human health by meaningfully impacting patients and society.

Our most advanced programs, PRAX-114 and PRAX-944, are currently in Phase 2 development. PRAX-114 is being developed for the treatment of major depressive disorder and perimenopausal depression. Together, these conditions affect more than 22 million patients in the United States. PRAX-944 is a selective small molecule inhibitor of T-type calcium channels for the treatment of essential tremor, a progressive and debilitating movement disorder affecting up to seven million people in the United States. In addition, we initiated a Phase 1 trial of PRAX-562, a persistent sodium current blocker, for the treatment of a broad range of rare, devastating CNS disorders, such as severe pediatric epilepsies and rare adult cephalgias. In addition to our clinical programs, we have multiple disclosed preclinical product candidates in development for severe genetic epilepsies.

We were incorporated in 2015 and commenced operations in 2016. Since inception, we have devoted substantially all of our resources to developing our preclinical and clinical product candidates, building our intellectual property portfolio, business planning, raising capital and providing general and administrative support for these operations. We employ a "virtual" research and development model, relying heavily upon external consultants, collaborators and contract research organizations to conduct our preclinical and clinical activities. Since inception, we have financed our operations primarily with proceeds from the issuance of convertible debt and sales of our Series A redeemable convertible preferred stock, Series B redeemable convertible preferred stock, Series B-1 redeemable convertible preferred stock, Series C redeemable convertible preferred stock and Series C-1 redeemable convertible preferred stock and the closing of our initial public offering, or IPO.

On October 20, 2020, we completed our IPO in which we issued and sold 11,500,000 shares of our common stock at a public offering price of $19.00 per share, including 1,500,000 shares of common stock sold pursuant to the underwriters' exercise of their option to purchase additional shares of common stock, for aggregate gross proceeds of $218.5 million. We raised approximately $200.3 million in net proceeds after deducting underwriting discounts and commissions and offering expenses payable by us. Upon the closing of the IPO, all of the outstanding shares of our Series A redeemable convertible preferred stock, Series B redeemable convertible preferred stock, Series B-1 redeemable convertible preferred stock, Series C redeemable convertible preferred stock and Series C-1 redeemable convertible preferred stock automatically converted into 25,067,977 shares of common stock. Subsequent to the closing of the IPO, there were no shares of redeemable convertible preferred stock outstanding. In connection with the closing of the IPO, we filed an Amended and Restated Certificate of Incorporation to change the authorized capital stock to 150,000,000 shares of common stock and 10,000,000 shares of undesignated preferred stock.

We are a development stage company and we have not generated any revenue from product sales, and do not expect to do so for several years, if at all. All of our programs are still in preclinical and clinical development. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates, if approved. We have incurred recurring operating losses since inception, including net losses of $61.8 million and $35.5 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $149.6 million. We expect to incur significant expenses and operating losses for the foreseeable future as we expand our research and development activities. In addition, our losses from operations may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenditures on other research and development activities. We anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- advance our lead product candidates, PRAX-114 and PRAX-944, to late stage clinical trials;
- advance our PRAX-562 product candidate to Phase 2 clinical trials;
- advance our discovery-stage programs to clinical trials;
- further invest in our pipeline;
- further invest in our manufacturing capabilities;
- seek regulatory approval for our investigational medicines;
- maintain, expand, protect and defend our intellectual property portfolio;
- acquire or in-license technology;
- secure facilities to support continued growth in our research, development and commercialization efforts;
- take temporary precautionary measures to help minimize the risk of COVID-19 to our employees;
- increase our headcount to support our development efforts and to expand our clinical development team; and
- incur additional costs and headcount associated with operating as a public company.

In addition, as we progress toward marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2020, we had cash and cash equivalents of $296.6 million. We believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditures into the fourth quarter of 2022. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See “—Liquidity and Capital Resources.”

COVID-19 Business Update

With the global spread of the ongoing COVID-19 pandemic in 2020, we have implemented business continuity plans designed to address and mitigate the impact of the COVID-19 pandemic on our employees and our business, including our preclinical studies and clinical trials. Our operations are considered an essential business and we are

continuing to operate during this period. We have taken measures to secure our research and development activities. While we are experiencing limited financial impacts at this time, given the global economic slowdown, the overall disruption of global healthcare systems and the other risks and uncertainties associated with the pandemic, our business, financial condition and results of operations could be materially adversely affected. We continue to closely monitor the COVID-19 pandemic as we evolve our business continuity plans, clinical development plans and response strategy.

In addition, while we have taken and are continuing to take steps to mitigate against COVID-19 pandemic-related delays, our planned clinical trials may be affected by the COVID-19 pandemic, including (i) delays or difficulties in enrolling and retaining patients in our planned clinical trials, including patients that may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services; (ii) delays or difficulties in clinical site initiation, including difficulties in recruiting and retaining clinical site investigators and clinical site staff; (iii) diversion or prioritization of healthcare resources away from the conduct of clinical trials and towards the COVID-19 pandemic, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials, and because, who, as healthcare providers, may have heightened exposure to COVID-19 and adversely impact our clinical trial operations; (iv) interruption of our future clinical supply chain or key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal, state/provincial or municipal governments, employers and others; and (v) limitations in outsourced third-party resources that would otherwise be focused on the conduct of our planned clinical trials, including because of sickness of third-party personnel or their families, or the desire of third-party personnel to avoid contact with large groups of people.

Financial Operations Overview

Revenue

We have not generated any revenue since inception and do not expect to generate any revenue from the sale of products for several years, if at all. If our development efforts for our current or future product candidates are successful and result in marketing approval or collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from collaboration or license agreements that we may enter into with third parties.

Operating Expenses

Research and Development Expense

The nature of our business and primary focus of our activities generate a significant amount of research and development costs. Research and development expenses represent costs incurred by us for the following:

- costs to develop our portfolio;
- discovery efforts leading to development candidates;
- clinical development costs for our programs; and
- costs to develop our manufacturing technology and infrastructure.

The costs above comprise the following categories:

- personnel-related expenses, including salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with third parties, such as consultants, investigative sites and contract research organizations, or CROs, that conduct our preclinical and clinical studies and in-licensing arrangements;
- costs incurred to maintain compliance with regulatory requirements;
- costs incurred with third-party contract development and manufacturing organizations, or CDMOs, to acquire, develop and manufacture materials for preclinical and clinical studies; and
- depreciation, amortization and other direct and allocated expenses, including rent, insurance and other operating costs, incurred as a result of our research and development activities.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors and

our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our consolidated balance sheets as prepaid expenses or accrued research and development expenses. Non-refundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized, even when there is no alternative future use for the research and development. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

A significant portion of our research and development costs have been external costs. We track direct external research and development expenses to specific programs upon commencement. Due to the number of ongoing programs and our ability to use resources across several projects, indirect or shared operating costs incurred for our research and development programs, such as personnel, facility costs and certain consulting costs, are not recorded or maintained on a program-specific basis.

Our major programs, PRAX-114, PRAX-944 and PRAX-562, are those for which we have initiated clinical activities. Our discovery-stage programs are those which are at an earlier point in the development process. The following table reflects our research and development expenses, including direct program-specific expenses summarized by major program, discovery-stage program costs and indirect or shared operating costs recognized as research and development expenses during each period presented (in thousands):

	Year Ended December 31,	
	2020	2019
PRAX-114	$ 13,071	$ 7,192
PRAX-944	4,158	4,035
PRAX-562	4,566	4,276
Discovery-stage programs	6,093	5,909
Personnel-related (including stock-based compensation)	13,483	5,398
Other indirect research and development expenses	3,605	2,747
Total research and development expenses	$ 44,976	$ 29,557

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase in the foreseeable future as we advance our product candidates through the development phase, and as we continue to discover and develop additional product candidates, build manufacturing capabilities and expand into additional therapeutic areas.

At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from sales or licensing of our product candidates. This is due to the numerous risks and uncertainties associated with drug development, including the uncertainty of:

- our ability to add and retain key research and development personnel;
- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- our ability to successfully complete clinical trials with safety, tolerability and efficacy profiles that are satisfactory to U.S. Food and Drug Administration, or the FDA, or any comparable foreign regulatory authority;
- our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize, our product candidates;
- our successful enrollment in and completion of clinical trials;

- the costs associated with the development of any additional product candidates we identify in-house or acquire through collaborations;
- our ability to discover, develop and utilize biomarkers to demonstrate target engagement, pathway engagement and the impact on disease progression of our product candidates;
- our ability to establish and maintain agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if our product candidates are approved;
- the terms and timing of any collaboration, license or other arrangement, including the terms and timing of any milestone payments thereunder;
- our ability to obtain and maintain patent, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates if and when approved;
- our receipt of marketing approvals from applicable regulatory authorities;
- our ability to commercialize products, if and when approved, whether alone or in collaboration with others; and
- the continued acceptable safety profiles of the product candidates following approval.

A change in any of these variables with respect to the development of any of our product candidates would significantly change the costs, timing and viability associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time to complete our clinical development activities. We may never obtain regulatory approval for any of our product candidates. Drug commercialization will take several years and millions of dollars in development costs.

General and Administrative Expense

General and administrative expenses consist primarily of personnel-related costs, including salaries, benefits and stock-based compensation, for personnel in our executive, finance, legal, business development and administrative functions. General and administrative expenses also include legal fees relating to corporate matters; professional fees for accounting, auditing, tax and administrative consulting services; insurance costs; administrative travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for office rent and other operating costs. These costs relate to the operation of the business, unrelated to the research and development function, or any individual program. Costs to secure and defend our intellectual property, or IP, are expensed as incurred and are classified as general and administrative expenses.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support the expected growth in our research and development activities and the potential commercialization of our product candidates. We also expect to incur increased expenses associated with being a public company, including increased costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance costs and investor and public relations costs. We also expect to incur additional IP-related expenses as we file patent applications to protect innovations arising from our research and development activities.

Total Other Income

Interest Income

Interest income consists of interest earned on our cash and cash equivalents.

Income Taxes

Since our inception, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in each year or for our earned research and development tax credits, due to our uncertainty of realizing a benefit from those items. As of December 31, 2020 and 2019, we had U.S. federal and state net operating loss carryforwards which may be available to offset future taxable income and which would begin to expire in 2035. As of December 31, 2020 and 2019, we also had federal and state research and development tax credit carryforwards which may be available to offset future income tax liabilities and which would begin to expire in 2031.

Income taxes are determined at the applicable tax rates adjusted for non-deductible expenses, research and development tax credits and other permanent differences. Our income tax provision may be significantly affected by changes to our estimates. The income tax benefit recognized for the years ended December 31, 2020 and 2019 related to income tax benefits associated with our operations in Australia.

Results of Operations

Comparison of the Years Ended December 31, 2020 and 2019

The following table summarizes our consolidated statements of operations for each period presented (in thousands):

	Year Ended December 31,		Change
	2020	2019	
Operating expenses:			
Research and development	$ 44,976	$ 29,557	$ 15,419
General and administrative	16,992	6,232	10,760
Total operating expenses	61,968	35,789	26,179
Loss from operations	(61,968)	(35,789)	(26,179)
Total other income:			
Interest income	140	193	(53)
Total other income, net	140	193	(53)
Loss before benefit from income taxes	(61,828)	(35,596)	(26,232)
Benefit from income taxes	(8)	(84)	76
Net loss	$ (61,820)	$ (35,512)	$ (26,308)

Research and Development Expense

The following table summarizes our research and development expenses for each period presented, along with the changes in those items (in thousands):

	Year Ended December 31,		Change
	2020	2019	
PRAX-114	$ 13,071	$ 7,192	$ 5,879
PRAX-944	4,158	4,035	123
PRAX-562	4,566	4,276	290
Discovery-stage programs	6,093	5,909	184
Personnel-related (including stock-based compensation)	13,483	5,398	8,085
Other indirect research and development expenses	3,605	2,747	858
Total research and development expenses	$ 44,976	$ 29,557	$ 15,419

Research and development expenses increased $15.4 million from $29.6 million for the year ended December 31, 2019 to $45.0 million for the year ended December 31, 2020. The increase in research and development expenses was primarily attributable to the following:

- $8.1 million increase in personnel-related costs primarily due to increased headcount, including an increase of $0.9 million in stock-based compensation expense;
- $5.9 million increase in expense related to our PRAX-114 program, primarily driven by a $6.4 million increase in clinical-related spend for our ongoing Phase 2a clinical trial for this program, partially offset by a $0.5 million decrease in preclinical spend;

- $0.9 million increase in other indirect research and development expenses, primarily driven by an increase in facility, office, software and other overhead costs due to increased research and development headcount; and
- $0.3 million increase in expense related to our PRAX-562 program, primarily driven by a $2.0 million increase in clinical and manufacturing spend related to our Phase 1 clinical trial for this program, partially offset by a $1.7 million decrease in preclinical spend due to prior year work to nominate our clinical candidate.

General and Administrative Expense

General and administrative expenses increased $10.8 million from $6.2 million for the year ended December 31, 2019 to $17.0 million for the year ended December 31, 2020. The increase in general and administrative expenses was primarily attributable to the following:

- $7.0 million increase in personnel-related costs, primarily driven by increased headcount, including an increase of $3.6 million in stock-based compensation expense, of which $2.1 million related to a stock option modification in the fourth quarter of 2020;
- $2.5 million increase in professional fees including legal and consulting services, driven by a $2.1 million increase in consulting costs, including $1.0 million in the accounting function in support of our IPO and $0.9 million of increased corporate development spend, primarily to support commercial assessments of our clinical-stage programs, and a $0.4 million increase in legal fees, primarily related to intellectual property filing and defense matters as we expand our research and development activities and develop our patent portfolio; and
- $1.3 million increase in other general and administrative expenses expenses, including a $1.1 million increase in insurance and related costs, primarily due to becoming a public company and a $0.2 million increase in other expenses to support our growing organization.

Total other income

Total other income for the years ended December 31, 2020 and 2019, was comprised of interest income on our cash and cash equivalents.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have incurred significant losses in each period. We have not yet commercialized any of our product candidates, which are in various phases of preclinical and clinical development, and we do not expect to generate revenue from sales of any products for several years, if at all.

Since our inception, we have funded our operations with proceeds from the sales of our redeemable convertible preferred stock, the issuance of convertible promissory notes and proceeds from our IPO. We raised an aggregate of $206.7 million in proceeds from the sale of our redeemable convertible preferred stock, $4.0 million in proceeds from the issuance of convertible promissory notes, and $200.3 million in net proceeds from our IPO, after deducting underwriting discounts and commissions and offering expenses payable by us. As of December 31, 2020, we had cash and cash equivalents of $296.6 million.

Historical Cash Flows

The following table provides information regarding our cash flows for each period presented (in thousands):

	Year Ended December 31,	
	2020	2019
Net cash provided by (used in):		
Operating activities	$ (52,623)	$ (33,420)
Investing activities	—	(103)
Financing activities	304,416	60,388
Net increase in cash, cash equivalents and restricted cash	$ 251,793	$ 26,865

Operating Activities

Our cash flows from operating activities are greatly influenced by our use of cash for operating expenses and working capital requirements to support the business. We have historically experienced negative cash flows from operating activities as we invested in developing our portfolio, drug discovery efforts and related infrastructure. The cash used in operating activities resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital, which are primarily the result of increased expenses and timing of vendor payments.

During the year ended December 31, 2020, net cash used in operating activities of $52.6 million was primarily due to our $61.8 million net loss, partially offset by $6.0 million of non-cash charges and $3.2 million in changes in operating assets and liabilities.

During the year ended December 31, 2019, net cash used in operating activities of $33.4 million was primarily due to our $35.5 million net loss, partially offset by $1.3 million of non-cash charges and $0.7 million in changes in operating assets and liabilities.

Investing Activities

There were no cash flows from investing activities during the year ended December 31, 2020. During the year ended December 31, 2019, net cash used in investing activities related to the purchase of property and equipment.

Financing Activities

During the year ended December 31, 2020, net cash provided by financing activities of $304.4 million primarily consisted of net proceeds from our IPO and from the issuance of our Series C and Series C-1 redeemable convertible preferred stock, partially offset by our repurchase of Series C redeemable convertible preferred stock.

During the year ended December 31, 2019, net cash provided by financing activities of $60.4 million was primarily from net proceeds from the issuance of our Series B-1 redeemable convertible preferred stock and from the issuance of our Series C redeemable convertible preferred stock.

Plan of Operation and Future Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing research and development activities, particularly as we advance the preclinical activities and clinical trials of our product candidates. We also expect to continue to incur additional costs associated with operating as a public company. As a result, we expect to incur substantial operating losses and negative operating cash flows for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- advance the clinical development of our PRAX-114, PRAX-944 and PRAX-562 product candidates;
- advance the development of any additional product candidates;
- conduct research and continue preclinical development of potential product candidates;
- make strategic investments in manufacturing capabilities;
- maintain our current intellectual property portfolio and opportunistically acquire complementary intellectual property;
- seek to obtain regulatory approvals for our product candidates;

- potentially establish a sales, marketing and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts and to support our transition to a public company; and
- experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues or other regulatory challenges.

We are unable to estimate the exact amount of our working capital requirements, but based on our available cash resources, we expect to have sufficient cash and cash equivalents on hand to support current operations into the fourth quarter of 2022.

Because of the numerous risks and uncertainties associated with product development, and because the extent to which we may enter into collaborations with third parties for the development of our product candidates is unknown, we may incorrectly estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our funding requirements and timing and amount of our operating expenditures will depend on many factors, including, but not limited to:

- the scope, progress, results and costs of preclinical studies and clinical trials for our programs and product candidates;
- the number and characteristics of programs and technologies that we develop or may in-license;
- the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the costs necessary to obtain regulatory approvals, if any, for products in the United States and other jurisdictions, and the costs of post-marketing studies that could be required by regulatory authorities in jurisdictions where approval is obtained;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the continuation of our existing licensing arrangements and entry into new collaborations and licensing arrangements;
- the costs we incur in maintaining business operations;
- the costs associated with being a public company;
- the revenue, if any, received from commercial sales of any product candidates for which we receive marketing approval;
- the effect of competing technological and market developments;
- the impact of any business interruptions to our operations or to those of our manufacturers, suppliers or other vendors resulting from the COVID-19 pandemic or similar public health crisis; and
- the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates, although we currently have no commitments or agreements to complete any such acquisitions or investments in businesses.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if ever. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives.

Adequate additional funds may not be available to us on acceptable terms, or at all. We do not currently have any committed external source of funds. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms

of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Additional debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute your ownership interest.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit or terminate our product development programs or any future commercialization efforts or grant rights to develop and market product candidates to third parties that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2020 and the effects that such obligations are expected to have on our liquidity and cash flows in future periods (in thousands):

	Payments Due by Period				
	Total	Less Than 1 Year	1 to 3 Years	3 to 5 Years	More Than 5 Years
Operating lease commitments(1)	$ 791	$ 791	$ —	$ —	$ —
Total	$ 791	$ 791	$ —	$ —	$ —

(1) We sublease building space in Cambridge, Massachusetts. Our sublease will expire on December 30, 2021. The amounts in the table above represent the fixed contractual lease obligations.

We have collaboration and license agreements with Purdue Neuroscience Company, or Purdue, RogCon Inc., or RogCon, and Ionis Pharmaceuticals, Inc., or Ionis, under which we could be obligated to pay certain fees, milestone payments and cost reimbursements.

Under our license agreement with Purdue, we are obligated to make future milestone payments of up to $33.0 million based on the achievement of specified development and sales milestones. Furthermore, we will pay Purdue royalties of a low-single-digit percentage of annual net sales of licensed products. Either party may terminate the license agreement for convenience or in the event of a material breach by the other party and failure to cure such breach within a certain period of time. If the agreement is voluntarily terminated by Purdue, our license rights will survive such termination and such rights will become fully paid, perpetual and irrevocable. As the agreement may be terminated for convenience, the payments are not included in the table above. See “Business—License Agreements—License Agreement with Purdue.”

Under our license agreement with RogCon, we will reimburse RogCon for its out-of-pocket costs incurred for activities performed under the license agreement. Additionally, we may pay RogCon a milestone payment of $3.0 million and profit share payments. The $3.0 million milestone payment will become due when the first profit share payment has become due and payable and certain contingent payments have become due and payable to Ionis under our collaboration agreement with Ionis. The profit share payments will be based on a low-double-digit percentage of net profits, depending on sales volume. Either party may terminate the license agreement for material breach or insolvency of the other party. Additionally, we may terminate for convenience with prior notice to RogCon. As such, we do not include variable and contingent payments under our agreement with RogCon in the table above as they are not fixed and estimable. See “Business—License Agreements—License Agreement with RogCon.”

Under our collaboration agreement with Ionis, we are obligated to reimburse any out-of-pocket costs incurred by Ionis related to research activities, identification of a development candidate and conducting an IND-enabling toxicology study. We also have an exclusive option to obtain the rights and license related to the development candidate following the completion of the IND-enabling toxicology study. If we exercise our development candidate option, we may be required to make additional payments to Ionis including a license fee, development milestone payments, additional milestone payments and sales royalties or sublicense fees. However, we are not obligated to

exercise our development candidate option and are able to terminate our collaboration agreement with Ionis for convenience. Either party may terminate the collaboration agreement upon material breach or insolvency of the other party or if Ionis is unable to identify a development candidate. Ionis may terminate if we fail to achieve a performance milestone. As such, payments due pursuant to the exercise of our development candidate option are contingent and therefore excluded from the table above as they are not fixed and estimable. See “Business—License Agreements—Ionis Collaboration Agreement.”

We have agreements with certain vendors for various services, including services related to clinical operations and support, for which we are not contractually able to terminate for convenience and avoid any and all future obligations to the vendors. Under such agreements, we are contractually obligated to make certain payments to vendors to reimburse them for their unrecoverable outlays incurred prior to cancellation. The exact amounts of such obligations are dependent on the timing of termination and the exact terms of the relevant agreement and cannot be reasonably estimated. We do not include these payments in the table above as they are not fixed and estimable.

In addition, we enter into indemnification agreements and agreements containing indemnification provisions in the ordinary course of business. Pursuant to these agreements, we agree to indemnify, hold harmless and reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally our business partners, in connection with any U.S. patent or any copyright or other intellectual property infringement claim by any third party with respect to our products. The term of these indemnification agreements is generally perpetual upon execution of the agreement. The maximum potential amount of future payments we could be required to make under these indemnification agreements cannot be reasonably estimated and therefore is not included in the table above.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Critical Accounting Policies and Significant Judgments and Estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies used in the preparation of our consolidated financial statements require the most significant judgments and estimates.

Research and Development Expenses and Related Accruals

Research and development expenses include costs directly attributable to the conduct of research and development programs, including personnel-related expenses such as salaries, benefits and stock-based compensation expense; materials; supplies; manufacturing and external costs related to outside vendors engaged to conduct both preclinical studies and clinical trials; and the allocable portions of facility costs, such as rent, utilities, depreciation and general support services. All costs associated with research and development activities are expensed as incurred.

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf, and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in our financial

statements based on facts and circumstances known to us at that time. When evaluating the adequacy of the accrued liabilities, we analyze progress of the studies or trials, including the phase or completion of events, invoices received and contracted costs. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with performing research services and preclinical and clinical studies;
- investigative sites or other providers in connection with preclinical and clinical studies;
- vendors in connection with preclinical and clinical development activities; and
- vendors related to product manufacturing, development and distribution of preclinical and clinical supplies.

The financial terms of our agreements with CROs are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and the level of effort expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period.

Stock-Based Compensation

We issue stock-based awards to employees and non-employees, generally in the form of stock options, restricted stock awards and restricted stock units. We measure all stock-based awards granted to employees and non-employees as stock-based compensation expense at fair value in accordance with FASB ASC Topic 718, Compensation—Stock Compensation, or ASC 718.

For stock-based awards issued to employees, non-employees and members of the board of directors, or the Board, for their services on the Board, we measure the estimated fair value of the stock-based award on the date of the grant. We recognize compensation expense for those awards granted to employees and members of the Board over the requisite service period, which is generally the vesting period of the respective award. For non-employee awards, compensation expense is recognized as the services are provided, which is generally ratably over the vesting period. We issue stock-based awards with service-based vesting conditions and record the expense for these awards on a straight-line basis over the vesting period. To date, we have not issued any stock-based awards with performance or market-based vesting conditions. We account for forfeitures as they occur.

We classify stock-based compensation expense in our consolidated statements of operations and comprehensive loss in the same manner in which the award recipient’s salary or service payments are classified.

Fair Value of Stock-Based Awards

We determine the fair value of restricted stock based on the fair value of our common stock less purchase price.

We estimate the fair value of our stock options using the Black-Scholes option pricing model, which requires inputs of subjective assumptions, including: (i) the expected volatility of our stock; (ii) the expected term of the award; (iii) the risk-free interest rate; (iv) expected dividends; and (v) the fair value of common stock. Due to the lack of company-specific historical and implied volatility data for our common stock, we determine the volatility for awards granted based on an analysis of reported data for a group of guideline publicly-traded companies that issued options with substantially similar terms. For this analysis, we select companies with comparable characteristics to ours including enterprise value, risk profiles and with historical share price information sufficient to meet the expected life of the stock-based awards. We determine expected volatility using a weighted average of the historical volatilities of the guideline group of companies. We will continue to apply this process until such a time as we have adequate historical data regarding the volatility of our own traded stock price. As permitted under ASC 718, we have elected to use the contractual term as the expected term for certain non-employee awards, on an award-by-award basis. For all other awards, we determined the expected term utilizing the “simplified” method whereby the

expected term equals the average of the vesting term and the original contractual term of the option, on a weighted basis based on the vesting of each tranche. We utilize this method as we have insufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. For the determination of the risk-free interest rate, we utilize the U.S. Treasury yield curve for instruments in effect at the time of measurement with a term commensurate with the expected term assumption. The expected dividend yield is assumed to be zero as we have never paid dividends, and do not have current plans to pay any dividends on our common stock.

Determination of Fair Value of Common Stock

Prior to our IPO, we determined the estimated fair value of our common stock based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector. We utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants' Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of our common stock. Each valuation methodology included estimates and assumptions that required our judgment. These estimates and assumptions included a number of objective and subjective factors in determining the value of our common stock at each grant date, such as the following: (i) prices paid for our redeemable convertible preferred stock, and the rights, preferences, and privileges of our redeemable convertible preferred stock and common stock; (ii) our stage of development; (iii) the fact that the grants of stock-based awards related to illiquid securities in a private company; and (iv) the likelihood of achieving a liquidity event for the common stock underlying the stock-based awards, such as an IPO or sale of the company, given prevailing market conditions. Prior to the IPO, the methodologies utilized to estimate the fair value of our common stock were the option-pricing method ("OPM") and, beginning in the year ended December 31, 2020, the hybrid probability-weighted expected return method ("PWERM"). The OPM was used to back-solve the estimated value of our equity and corresponding value of our common stock. The hybrid PWERM determined the fair value of our common stock using a probability-weighted present value of expected future investment returns considering various outcomes, as well as the rights of each class of stock, with one of the outcomes calculated using an OPM. The hybrid PWERM considered three scenarios: an "early" IPO completed in 2020, a "late" IPO completed in 2021, and a "remain private" scenario in which value was allocated using the OPM. An incremental discount for lack of marketability ("DLOM") was applied to the values of the common stock. The DLOM was estimated using a put option model which considered the expected time to liquidity and the volatility of the common shares. The hybrid PWERM used a risk-adjusted discount rate. The fair value of our common stock was calibrated to contemporaneous transactions in our redeemable convertible preferred stock.

Subsequent to the IPO, the fair value of the common stock underlying our stock-based awards is the closing price of our common stock on the date of grant.

JOBS Act and Emerging Growth Company Status

In April 2012, the JOBS Act was enacted. As an emerging growth company, or EGC, under the JOBS Act, we may delay the adoption of certain accounting standards until such time as those standards apply to private companies. Other exemptions and reduced reporting requirements under the JOBS Act for EGCs include presentation of only two years of audited financial statements in a registration statement for an initial public offering, an exemption from the requirement to provide an auditor's report on internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, an exemption from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation and less extensive disclosure about our executive compensation arrangements. Additionally, the JOBS Act provides that an EGC can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an EGC to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of the extended transition period and, therefore, while we are an EGC we will not be subject to new or revised accounting standards at the same time that they become applicable to other public companies that are not EGCs, unless we choose to early adopt a new or revised accounting standard.

We will remain classified as an EGC until the earlier of: (i) the last day of our first fiscal year in which we have total annual gross revenues of $1.07 billion or more, (ii) the last day of the fiscal year following the fifth anniversary of completion of our initial public offering, (iii) the date on which we have issued more than $1.0 billion of non-convertible debt instruments during the previous three fiscal years or (iv) the date on which we are deemed a "large accelerated filer" under the rules of the SEC.

Recently Issued Accounting Pronouncements

We have reviewed all recently issued standards and have determined that, other than as disclosed in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, such standards will not have a material impact on our financial statements or do not otherwise apply to our current operations.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Fluctuation Risk

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our cash equivalents are invested in short-term U.S. Treasury obligations. However, because of the short-term nature of the instruments in our portfolio, an immediate change in market interest rates of 100 basis points would not have a material impact on the fair market value of our investment portfolio or on our financial position or results of operations.

Foreign Currency Fluctuation Risk

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we have contracted with and may continue to contract with foreign vendors. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Inflation Fluctuation Risk

Inflation generally affects us by increasing our cost of labor. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2020 and 2019.

Item 8. Financial Statements and Supplementary Data

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Praxis Precision Medicines, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Praxis Precision Medicines, Inc. (the Company) as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' (deficit) equity, and cash flows for each of the two years in the period ended December 31, 2020, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2019.
Boston, Massachusetts
March 17, 2021

PRAXIS PRECISION MEDICINES, INC.

CONSOLIDATED BALANCE SHEETS

(Amounts in thousands, except share and per share data)

	December 31,	
	2020	2019
Assets		
Current assets:		
Cash and cash equivalents	$ 296,608	$ 44,815
Prepaid expenses and other current assets	5,718	681
Total current assets	302,326	45,496
Property and equipment, net	82	128
Operating lease right-of-use assets	754	1,450
Other non-current assets	15	620
Total assets	$ 303,177	$ 47,694
Liabilities, redeemable convertible preferred stock and stockholders' (deficit) equity		
Current liabilities:		
Accounts payable	$ 4,088	$ 2,667
Accrued expenses	10,869	3,455
Operating lease liabilities	763	696
Total current liabilities	15,720	6,818
Long-term liabilities:		
Non-current portion of operating lease liabilities	—	763
Total liabilities	15,720	7,581
Commitments and contingencies (Note 7)		
Series A redeemable convertible preferred stock, $0.0001 par value; 8,075,799 shares authorized and 8,075,799 shares issued and outstanding as of December 31, 2019; liquidation value of $9,932 as of December 31, 2019	—	9,932
Series B redeemable convertible preferred stock, $0.0001 par value; 14,913,704 shares authorized and 14,913,704 shares issued and outstanding as of December 31, 2019; liquidation value of $49,969 as of December 31, 2019	—	49,969
Series B-1 redeemable convertible preferred stock, $0.0001 par value; 2,666,666 shares authorized and 2,666,666 shares issued and outstanding as of December 31, 2019; liquidation value of $10,431 as of December 31, 2019	—	10,431
Series C redeemable convertible preferred stock, $0.0001 par value; 11,067,963 shares authorized and 9,805,827 shares issued and outstanding as of December 31, 2019; liquidation value of $50,789 as of December 31, 2019	—	50,789
Stockholders' equity (deficit):		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized and no shares issued or outstanding as of December 31, 2020	—	—
Common stock, $0.0001 par value; 150,000,000 shares and 46,000,000 shares authorized as of December 31, 2020 and 2019, respectively; 38,268,543 shares issued and outstanding as of December 31, 2020, and 1,670,070 shares issued and 1,621,880 shares outstanding as of December 31, 2019	4	1
Additional paid-in capital	437,007	—
Accumulated deficit	(149,554)	(81,009)
Total stockholders' equity (deficit)	287,457	(81,008)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 303,177	$ 47,694

The accompanying notes are an integral part of these consolidated financial statements.

PRAXIS PRECISION MEDICINES, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(Amounts in thousands, except share and per share data)

	Year Ended December 31,	
	2020	**2019**
Operating expenses:		
Research and development	$ 44,976	$ 29,557
General and administrative	16,992	6,232
Total operating expenses	61,968	35,789
Loss from operations	(61,968)	(35,789)
Total other income:		
Interest income	140	193
Total other income	140	193
Loss before benefit from income taxes	(61,828)	(35,596)
Benefit from income taxes	(8)	(84)
Net loss and comprehensive loss	$ (61,820)	$ (35,512)
Accretion and cumulative dividends on redeemable convertible preferred stock	(8,996)	(5,170)
Gain on repurchase of redeemable convertible preferred stock	493	—
Net loss attributable to common stockholders	$ (70,323)	$ (40,682)
Net loss per share attributable to common stockholders, basic and diluted	$ (7.86)	$ (26.60)
Weighted average common shares outstanding, basic and diluted	8,950,152	1,529,629

The accompanying notes are an integral part of these consolidated financial statements.

PRAXIS PRECISION MEDICINES, INC.

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' (DEFICIT) EQUITY

(Amounts in thousands, except share data)

	Series A Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Series B-1 Redeemable Convertible Preferred Stock		Series C Redeemable Convertible Preferred Stock		Series C-1 Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at December 31, 2018	8,075,799	$ 9,284	14,913,704	$ 46,436	—	$ —	—	$ —	$ —	—	1,408,677	$ 1	$ 326	$ (41,365)	$ (41,038)
Issuance of Series B-1 redeemable convertible preferred stock, net of issuance costs of $61	—	—	—	—	2,666,666	9,939	—	—	—	—	—	—	—	—	—
Issuance of Series C redeemable convertible preferred stock, net of issuance costs of $165	—	—	—	—	—	—	9,805,827	50,336	—	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	668	—	668
Accretion of redeemable convertible preferred stock to redemption value	—	648	—	3,533	—	492	—	453	—	—	—	—	(994)	(4,132)	(5,126)
Vesting of restricted stock awards	—	—	—	—	—	—	—	—	—	—	213,203	—	—	—	—
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	(35,512)	(35,512)
Balance at December 31, 2019	8,075,799	$ 9,932	14,913,704	$ 49,969	2,666,666	$ 10,431	9,805,827	$ 50,789	$ —	—	1,621,880	$ 1	$ —	$ (81,009)	$ (81,008)
Repurchase of Series C redeemable convertible preferred stock	—	—	—	—	—		(5,825,243)	(30,493)	—	—	—	—	—	493	493
Issuance of Series C redeemable convertible preferred stock, net of issuance costs of $41	—	—	—	—	—		4,563,108	23,459	—	—	—	—	—	—	—
Issuance of Series C-1 redeemable convertible preferred stock, net of issuance costs of $154	—	—	—	—	—		—	—	19,444,453	110,096	—	—	—	—	—
Accretion of redeemable convertible preferred stock to redemption value	—	519	—	2,875	—	642	—	2,682	—	2,278	—	—	(1,778)	(7,218)	(8,996)
Conversion of redeemable convertible preferred stock to common stock	(8,075,799)	(10,451)	(14,913,704)	(52,844)	(2,666,666)	(11,073)	(8,543,692)	(46,437)	(19,444,453)	(112,374)	25,067,977	2	233,176	—	233,178
Issuance of common stock upon initial public offering, net of underwriting discounts, commissions and offering costs	—	—	—	—	—		—	—	—	—	11,500,000	1	200,310	—	200,311
Vesting of restricted common stock awards	—	—	—	—	—		—	—	—	—	48,190	—	—	—	—
Exercise of stock options	—	—	—	—	—		—	—	—	—	30,496	—	88	—	88
Stock-based compensation expense	—	—	—	—	—		—	—	—	—	—	—	5,211	—	5,211
Net loss	—	—	—	—	—		—	—	—	—	—	—	—	(61,820)	(61,820)
Balance at December 31, 2020	—	$ —	—	$ —	—	$ —	—	$ —	$ —	$ —	38,268,543	$ 4	$ 437,007	$ (149,554)	$ 287,457

The accompanying notes are an integral part of these consolidated financial statements.

PRAXIS PRECISION MEDICINES, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(Amounts in thousands)

	Year Ended December 31,	
	2020	**2019**
Cash flows from operating activities:		
Net loss	$ (61,820)	$ (35,512)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	50	37
Stock-based compensation expense	5,211	668
Non-cash operating lease expense	696	642
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(4,437)	495
Other non-current assets	5	—
Accounts payable	960	(837)
Accrued expenses	7,408	1,742
Operating lease liabilities	(696)	(633)
Other	—	(22)
Net cash used in operating activities	(52,623)	(33,420)
Cash flows from investing activities:		
Purchases of property and equipment	—	(103)
Net cash used in investing activities	—	(103)
Cash flows from financing activities:		
Proceeds from initial public offering of common stock, net of issuance costs	200,886	—
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	133,442	60,388
Repurchase of Series C redeemable convertible preferred stock	(30,000)	—
Proceeds from exercise of options to purchase common stock	88	—
Net cash provided by financing activities	304,416	60,388
Increase in cash, cash equivalents and restricted cash	251,793	26,865
Cash, cash equivalents and restricted cash, beginning of period	45,415	18,550
Cash, cash equivalents and restricted cash, end of period	$ 297,208	$ 45,415
Supplemental disclosures of non-cash activities:		
Accretion of redeemable convertible preferred stock to redemption value	$ 8,996	$ 5,126
Operating lease liabilities recorded upon adoption of ASC 842	$ —	$ 2,092
Purchases of property and equipment included in accounts payable	$ 4	$ —
Deferred offering costs included in accounts payable and accrued expenses	$ 575	$ —
Redeemable convertible preferred stock issuance costs included in accounts payable	$ —	$ 113

The accompanying notes are an integral part of these consolidated financial statements.

1. Nature of the Business

Praxis Precision Medicines, Inc. (“Praxis” or the “Company”) is a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for central nervous system (“CNS”) disorders characterized by neuronal imbalance. The Company has established a broad portfolio, including multiple disclosed programs across CNS disorders, including depression, epilepsy, movement disorders and pain syndromes, with three clinical-stage product candidates. We intend to develop differentiated therapies that can deliver long-term benefits to human health by meaningfully impacting patients and society. The Company’s most advanced programs, PRAX-114 and PRAX-944, are currently in Phase 2 development. PRAX-114 is being developed for the treatment of major depressive disorder and perimenopausal depression, and PRAX-944 is a selective small molecule inhibitor of T-type calcium channels for the treatment of essential tremor.

Praxis was incorporated in 2015 and commenced operations in 2016. The Company has funded its operations primarily with proceeds from the issuance of convertible debt, Series A redeemable convertible preferred stock (the “Series A Preferred Stock”), Series B redeemable convertible preferred stock (the “Series B Preferred Stock”), Series B-1 redeemable convertible preferred stock (the “Series B-1 Preferred Stock”), Series C redeemable convertible preferred stock (the “Series C Preferred Stock”) and Series C-1 redeemable convertible preferred stock (the Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series C-1 Preferred Stock are collectively referred to as the “Redeemable Convertible Preferred Stock”), and from proceeds from its initial public offering ("IPO"). From inception through December 31, 2020, the Company raised $411.0 million in aggregate cash proceeds from these transactions, net of issuance costs.

On October 8, 2020, the board of directors and the Company’s stockholders approved a one-for-2.14 reverse stock split. Effective on October 8, 2020, the reverse stock split impacted the Company’s issued and outstanding shares of common stock. Stockholders entitled to fractional shares as a result of the reverse stock split are entitled to receive a cash payment in lieu of receiving fractional shares. All shares of common stock, per share amounts, aggregate par value and additional paid-in capital amounts for all periods presented in the accompanying consolidated financial statements and related notes have been retroactively adjusted, where applicable, to reflect the reverse stock split. Shares of common stock underlying outstanding stock options and other equity instruments were proportionately reduced and the respective exercise prices were proportionately increased, as applicable, in accordance with the terms of the agreements governing such securities. The respective conversion prices of the Redeemable Convertible Preferred Stock were proportionately increased. The number of shares of common stock authorized for issuance and the per share par value of common stock were not adjusted as a result of the reverse stock split.

On October 20, 2020, the Company completed its IPO, in which the Company issued and sold 11,500,000 shares of its common stock at a public offering price of $19.00 per share, including 1,500,000 shares of common stock sold pursuant to the underwriters’ exercise of their option to purchase additional shares of common stock, for aggregate gross proceeds of $218.5 million. The Company raised approximately $200.3 million in net proceeds after deducting underwriting discounts and commissions and offering expenses payable by the Company. Upon the closing of the IPO, all of the outstanding shares of the Company’s Redeemable Convertible Preferred Stock automatically converted into 25,067,977 shares of common stock. On October 20, 2020, in connection with the closing of the IPO, the Company filed its Amended and Restated Certificate of Incorporation which provides that the authorized capital stock of the Company consists of 150,000,000 shares of common stock and 10,000,000 shares of undesignated preferred stock, both with a par value of $0.0001 per share.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including but not limited to, risks associated with completing preclinical studies and clinical trials, receiving regulatory approvals for product candidates, development by competitors of new biopharmaceutical products, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Programs currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate

personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize revenue from product sales.

Liquidity

In accordance with the Financial Accounting Standards Board ("FASB") Accounting Standards Update ("ASU") 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued.

The Company has incurred recurring losses since its inception, including net losses of $61.8 million and $35.5 million for the years ended December 31, 2020 and 2019, respectively. In addition, as of December 31, 2020, the Company had an accumulated deficit of $149.6 million. The Company expects to continue to generate operating losses for the foreseeable future.

As a result of proceeds raised from its IPO and issuance of its Series C Preferred Stock and Series C-1 Preferred Stock, the Company expects that its cash and cash equivalents as of December 31, 2020 of $296.6 million will be sufficient to fund the operating expenditures and capital expenditure requirements necessary to advance its research efforts and clinical trials for at least one year from the date of issuance of these consolidated financial statements. The future viability of the Company beyond one year from the date of issuance of these consolidated financial statements is dependent on its ability to raise additional capital to finance its operations. The Company's inability to raise capital as and when needed could have a negative impact on its financial condition and ability to pursue its business strategies. There can be no assurance that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and ASUs of the FASB.

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries, Praxis Security Corporation and Praxis Precision Medicines Australia Pty Ltd. All intercompany transactions have been eliminated in consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual for research and development expenses, stock-based compensation expense, the valuation of equity awards and the recoverability of the Company's net deferred tax assets and related valuation allowance. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ materially from those estimates.

Segments

The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purposes of assessing performance and allocating resources. The majority of the Company's long-lived assets are held in the United States.

Cash, Cash Equivalents and Restricted Cash

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. Cash and cash equivalents include cash held in banks and amounts held in interest-bearing money market funds. Cash equivalents are carried at cost, which approximates their fair market value.

Restricted cash comprises a letter of credit for the benefit of the landlord in connection with the Company's lease facility. Restricted cash is classified as either current or non-current based on the terms of the underlying lease arrangement.

The following table presents cash, cash equivalents and restricted cash as reported on the consolidated balance sheets that equal the total amounts on the consolidated statements of cash flows (in thousands):

	December 31,	
	2020	2019
Cash and cash equivalents	$ 296,608	$ 44,815
Restricted cash	600	600
Total cash, cash equivalents and restricted cash as shown on the consolidated statements of cash flows	$ 297,208	$ 45,415

Concentrations of Credit Risk and Significant Suppliers and License Agreements

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and restricted cash. The Company maintains deposits in accredited financial institutions in excess of federally insured limits. Bank accounts in the United States are insured by the Federal Deposit Insurance Corporation (the "FDIC") up to $250,000. As of December 31, 2020 and 2019, the Company's primary operating accounts significantly exceeded the FDIC limits. The Company deposits its cash in financial institutions that it believes have high credit quality, and has not experienced any losses on such accounts and does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on third-party manufacturers to supply materials for research and development activities of its programs, including preclinical and clinical testing. In particular, the Company relies, and expects to continue to rely, on a small number of third-party manufacturers to produce and process its current and potential product candidates and to manufacture supply of its current and potential product candidates for preclinical and clinical activities. These programs could be adversely affected by a significant interruption in the supply of the necessary materials. The Company is also dependent on third parties who provide license rights used in the development of certain programs. The Company could experience delays in the development of its programs if any of these license agreements are terminated, if the Company fails to meet the obligations required under its arrangements, or if the Company is unable to successfully secure new strategic alliances or licensing agreements.

Off-Balance Sheet Risk

As of December 31, 2020 and 2019, the Company had no off-balance sheet risk such as foreign exchange contracts, option contracts or other hedging arrangements.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value under GAAP. The fair values of the Company's financial assets and liabilities reflects the Company's estimate of the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of

unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

An entity may choose to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings.

The carrying amounts reflected in the consolidated balance sheets for cash, cash equivalents, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to the short-term nature of these assets and liabilities.

Property and Equipment

Property and equipment are recorded at cost. Depreciation is calculated using the straight-line method over the following estimated useful lives of the assets:

	Estimated Useful Life
Office furniture and equipment	5 years
Laboratory equipment	3 years
Computer equipment	3 years

Upon disposal, retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in the results of operations. Expenditures for repairs and maintenance that do not improve or extend the lives of the respective assets are charged to expense as incurred.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows. The Company did not record any impairment losses on long-lived assets in either year ended December 31, 2020 or December 31, 2019.

Leases

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. This standard established a right-of-use model that requires all lessees to recognize right-of-use assets and lease liabilities on their balance sheet that arise from leases as well as provide disclosures with respect to certain qualitative and quantitative information related to a company's leasing arrangements to meet the objective of allowing users of financial statements to assess the amount, timing and uncertainty of cash flows arising from leases. The FASB subsequently issued the following amendments to ASU 2016-02 that have the same effective date and transition date: ASU No. 2018-01, *Leases (Topic 842): Land Easement Practical Expedient for Transition to Topic 842*, ASU No. 2018-10, *Codification Improvements to Topic 842, Leases*, ASU No. 2018-11, *Leases (Topic 842): Targeted Improvements*, ASU No. 2018-20, *Narrow-Scope Improvement for Lessors*, and ASU No. 2019-01, *Leases (Topic 842): Codification Improvements*. The Company adopted these amendments with ASU 2016-02 (collectively, the "new leasing standards"), effective January 1, 2019.

The Company adopted the new leasing standards using the modified retrospective transition approach, with no restatement of prior periods and there was no cumulative adjustment to retained earnings. Upon adoption, the Company elected the package of transition practical expedients, which allowed the Company to not reassess the following: (i) whether any expired or existing contracts are or contain leases, (ii) the lease classification for any expired or existing leases and (iii) the treatment of initial direct costs for existing leases. The Company made an accounting policy election to not recognize short-term leases with an initial term of twelve months or less within its consolidated balance sheets and to recognize those lease payments on a straight-line basis in its consolidated statements of operations and comprehensive loss over the lease term. Upon adopting the new leasing standards, the Company recognized an operating lease right-of-use asset of $2.1 million and a corresponding operating lease liability of $2.1 million, which are included in its consolidated balance sheets. The adoption of the new leasing standards did not have a material impact on the Company's consolidated statements of operations and comprehensive loss.

The Company determines if an arrangement is a lease at contract inception. Operating lease right-of-use assets represent the Company's right to use an underlying asset for the lease term and operating lease liabilities represent its obligation to make lease payments arising from the lease. Operating right-of-use assets and liabilities are recognized at the commencement date of the lease based upon the present value of lease payments over the lease term. When determining the lease term, the Company includes options to extend or terminate the lease when it is reasonably certain that the option will be exercised.

The Company uses the implicit rate when readily determinable and uses its incremental borrowing rate when the implicit rate is not readily determinable, based upon the information available at the commencement date in determining the present value of the lease payments. The incremental borrowing rate is determined using a secured borrowing rate for the same currency and term as the associated lease.

The lease payments used to determine operating lease right-of-use assets may include lease incentives and stated rent increases. The Company's lease agreements may include both lease and non-lease components, which the Company accounts for as a single lease component when the payments are fixed, for all classes of underlying assets. Variable payments included in the lease agreement are expensed as incurred.

The Company's operating leases are reflected in operating lease right-of-use assets and in current operating lease liabilities and long-term operating lease liabilities in its consolidated balance sheets. The Company's operating lease right-of-use asset as of December 31, 2020 and 2019 did not include any lease incentives. Lease expense for future lease payments is recognized on a straight-line basis over the lease term. There were no new leases entered into during the year ended December 31, 2020.

Deferred Offering Costs

The Company capitalizes certain legal, accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After the consummation of the equity financing, these costs are recorded in stockholders' (deficit) equity as a reduction of additional paid-in capital or the associated preferred stock account, as applicable. In the event the offering is

terminated, all capitalized deferred offering costs are expensed. Upon the closing of the IPO on October 20, 2020, deferred offering costs of $2.9 million were recognized through additional paid-in capital as a reduction of the gross proceeds received from the offering. No deferred offering costs were capitalized as of December 31, 2020 or December 31, 2019.

Redeemable Convertible Preferred Stock

Prior to the automatic conversion of all outstanding shares of the Redeemable Convertible Preferred Stock upon the closing of the IPO, the Company recorded all Redeemable Convertible Preferred Stock upon issuance at its respective fair value or original issuance price, less issuance costs and any associated discounts. The Company classified its Redeemable Convertible Preferred Stock outside of stockholders' (deficit) equity as the redemption of such shares was outside the Company's control. The Company adjusted the carrying values of the Redeemable Convertible Preferred Stock to redemption value when the redemption value exceeded the carrying value. Upon the closing of the IPO, all of the outstanding shares of Redeemable Convertible Preferred Stock automatically converted into 25,067,977 shares of common stock.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries, stock-based compensation and benefits, facilities costs, depreciation, third-party license fees, and external costs of outside vendors engaged to conduct preclinical development activities and clinical trials as well as to manufacture research and development materials. Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are recognized as an expense as the goods are delivered or the related services are performed or until it is no longer expected that the goods will be delivered or the services rendered. Costs incurred to obtain licenses are recognized as research and development expense as incurred if the technology licensed has no alternative future uses.

The Company has entered into various research and development related contracts with parties both inside and outside of the United States. These agreements are cancellable, and related fees are recorded as research and development expenses as incurred. The Company records accrued liabilities for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies or clinical trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent-Related Costs

Patent-related costs incurred in connection with patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses in the accompanying consolidated statement of operations and comprehensive loss.

Stock-Based Compensation

The Company accounts for all stock-based awards granted to employees and non-employees as stock-based compensation expense at fair value in accordance with FASB ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). For stock-based awards issued to employees, non-employees and members of the Company's board of directors (the "Board") for their services on the Board, the Company measures the estimated fair value of the stock-based award on the date of the grant. The Company recognizes compensation expense for those awards granted to employees and members of the Board over the requisite service period, which is generally the vesting period of the respective award. For non-employee awards, compensation expense is recognized as the services are provided, which is generally ratably over the vesting period. The Company determines the fair value of restricted stock awards in reference to the fair value of its common stock less any applicable purchase price. The Company issues stock-based awards with service-based vesting conditions and records the expense for these awards on a straight-line basis over the vesting period. To date, the Company has not issued any stock-based awards with performance or market-based vesting conditions. The Company accounts for forfeitures as they occur.

The Company classifies stock-based compensation expense in its consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's salary or service payments are classified.

The fair value of each stock option award is estimated on the date of grant using the Black-Scholes option pricing model, which requires inputs of subjective assumptions, including: (i) the expected volatility of the Company's stock; (ii) the expected term of the award; (iii) the risk-free interest rate; (iv) expected dividends; and (v) the fair value of common stock. Due to the lack of Company-specific historical and implied volatility data, the Company determines the volatility for awards granted based on an analysis of reported data for a group of guideline publicly-traded companies that issued options with substantially similar terms. For this analysis, the Company selects companies with comparable characteristics including enterprise value, risk profiles, and with historical share price information sufficient to meet the expected life of the stock-based awards. The Company determines expected volatility using a weighted average of the historical volatilities of the guideline group of companies. The Company expects to continue to apply this process until such time as it has adequate historical data regarding the volatility of its own traded stock price. As permitted under ASC 718, the Company has elected to use the contractual term as the expected term for certain non-employee awards, on an award-by-award basis. For all other awards, the expected term of the Company's stock options has been determined utilizing the "simplified" method whereby the expected term equals the average of the vesting term and the original contractual term of the option, on a weighted basis based on the vesting of each tranche. The Company utilizes this method as it has insufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for instruments with a term commensurate with the expected term assumption. The expected dividend yield is assumed to be zero as the Company has never paid dividends, and does not have current plans to pay any dividends on its common stock.

For periods prior to the IPO, the fair value of shares of common stock underlying the Company's stock-based awards was determined on each grant date due to the absence of an active market for the Company's common stock. The Company determined the estimated fair value of its equity instruments based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector. The Company utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants' Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its common stock. Each valuation methodology included estimates and assumptions that required the Company's judgment. These estimates and assumptions included a number of objective and subjective factors in determining the value of the Company's common stock at each grant date, such as the following: (i) prices paid for the Company's redeemable convertible preferred stock, and the rights, preferences, and privileges of the Company's redeemable convertible preferred stock and common stock; (ii) the Company's stage of development; (iii) the fact that the grants of stock-based awards related to illiquid securities in a private company; and (iv) the likelihood of achieving a liquidity event for the common stock underlying the stock-based awards, such as an IPO or sale of the Company, given prevailing market conditions. Prior to the IPO, the methodologies utilized to estimate the fair value of the Company's common stock were the option-pricing method ("OPM") and, beginning in the year ended December 31, 2020, the hybrid probability-weighted expected return method ("PWERM"). The OPM was used to back-solve the estimated value of the Company's equity and corresponding value of the Company's common stock. The hybrid PWERM determined the fair value of the Company's common stock using a probability-weighted present value of expected future investment returns considering various outcomes, as well as the rights of each class of stock, with one of the outcomes calculated using an OPM. The hybrid PWERM considered three scenarios: an "early" IPO completed in 2020, a "late" IPO completed in 2021, and a "remain private" scenario in which value was allocated using the OPM. An incremental discount for lack of marketability ("DLOM") was applied to the values of the common stock. The DLOM was estimated using a put option model which considered the expected time to liquidity and the volatility of the common shares. The hybrid PWERM used a risk-adjusted discount rate. The fair value of the Company's common stock was calibrated to contemporaneous transactions in the Series C Preferred Stock and Series C-1 Preferred Stock.

Subsequent to the IPO, the fair value of the common stock underlying the Company's stock-based awards is the closing price of the Company's common stock on the date of grant.

Foreign Currency

The functional currency of the Company's wholly owned foreign subsidiary in Australia is the U.S. dollar. Monetary assets and liabilities resulting from transactions denominated in currencies other than the functional currency are remeasured into the functional currency at exchange rates prevailing at the balance sheet date. Non-monetary assets and liabilities denominated in foreign currencies are measured using historical exchange rates prevailing at the date of the transaction and are not subsequently remeasured. Exchange gains or losses arising from foreign currency transactions are included in the determination of net loss. There were no material foreign currency gains or losses for the years ended December 31, 2020 and 2019.

Income Taxes

Deferred tax assets and liabilities are determined on the basis of the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent that it believes based upon the weight of available evidence it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established.

The Company accounts for uncertain tax positions recognized in the consolidated financial statements by prescribing a more-likely-than-not threshold for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' (deficit) equity that are excluded from net loss. The Company's comprehensive loss was equal to net loss for the years ended December 31, 2020 and 2019.

Net Loss per Share

The Company follows the two-class method to compute net loss per share attributable to common stockholders as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income (losses) for the period to be allocated between common and participating securities based upon their respective rights to share in the earnings as if all income (losses) for the period had been distributed. During periods of loss, there is no allocation required under the two-class method since the participating securities do not have a contractual obligation to fund the losses of the Company.

Net loss attributable to common stockholders is equal to the net loss for the period, as adjusted for: (i) cumulative dividends accrued for redeemable convertible preferred stock, whether or not declared, (ii) increases in carrying value recorded for redeemable convertible preferred stock, including accretion on redeemable convertible preferred stock to redemption value for amounts other than cumulative dividends and (iii) gains on the redemptions of redeemable convertible preferred stock.

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, which excludes shares of restricted common stock that are not vested. Diluted net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, after giving consideration to the dilutive effect of potentially dilutive common shares. For purposes of this calculation, outstanding options to purchase shares of common stock, unvested shares of restricted common stock and shares of redeemable convertible preferred stock are considered potentially dilutive common shares. The Company has generated a net loss in all periods presented so the basic and diluted net loss per share attributable to common stockholders are the same as the inclusion of the potentially dilutive securities would be anti-dilutive.

Emerging Growth Company Status

The Company is an "emerging growth company" ("EGC"), as defined in the Jumpstart Our Business Startups Act ("JOBS Act"), and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not EGCs. The Company may take advantage of these exemptions until it is no longer an EGC under Section 107 of the JOBS Act, which provides that an EGC can take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. The Company has elected to avail itself of the extended transition period and, therefore, while the Company is an EGC it will not be subject to new or revised accounting standards the same time that they become applicable to other public companies that are not EGCs, unless it chooses to early adopt a new or revised accounting standard.

Recent Accounting Pronouncements

Recently Adopted Accounting Pronouncements

In January 2016, the FASB issued ASU No. 2016-01*, Financial Instruments—Overall (Subtopic 825-10)—Recognition and Measurement of Financial Assets and Financial Liabilities,* which has been subsequently amended by ASU No. 2018-03, ASU No. 2019-04, ASU No. 2020-01 and ASU No. 2020-03 ("ASU 2016-01"). The provisions of ASU 2016-01 make targeted improvements to enhance the reporting model for financial instruments to provide users of financial statements with more decision-useful information, including certain aspects of recognition, measurement, presentation, and disclosure of financial instruments. The Company early adopted ASU 2016-01 effective January 1, 2019. The implementation of this standard had no impact on the Company's financial position or results of operations.

In February 2016, the FASB issued the new leasing standards to increase transparency and comparability among organizations related to their leasing activities. The Company early adopted the new leasing standards effective January 1, 2019. For additional information on the adoption of the new leasing standards, please read the Company's policy above entitled Leases, and Note 7, Commitments and Contingencies, to these consolidated financial statements.

In July 2017, the FASB issued ASU No. 2017-11, *Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480), Derivatives and Hedging (Topic 815) I. Accounting for Certain Financial Instruments with Down Round Features II*. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception ("ASU 2017-11"). Part I applies to entities that issue financial instruments such as warrants, convertible debt or convertible preferred stock that contain down-round features. Part II replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within ASC Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. The Company early adopted ASU 2017-11 effective January 1, 2019. The adoption of ASU 2017-11 had no impact on the Company's financial position or results of operations.

Recently Issued Accounting Pronouncements

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326)—Measurement of Credit Losses on Financial Instruments,* which has been subsequently amended by ASU No. 2018-19, ASU No. 2019-04, ASU No. 2019-05, ASU No. 2019-10, ASU No. 2019-11 and ASU No. 2020-03 ("ASU 2016-13"). The provisions of ASU 2016-13 modify the impairment model to utilize an expected loss methodology in place of the currently used incurred loss methodology and require a consideration of a broader range of reasonable and supportable information to inform credit loss estimates. ASU 2016-13 is effective for the Company on January 1, 2023, with early adoption permitted. The Company is currently evaluating the potential impact that this standard may have on its financial position and results of operations, as well as the timing of its adoption of this standard.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740)—Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), as part of its initiative to reduce complexity in the accounting standards. The amendments in ASU 2019-12 eliminate certain exceptions related to the approach for intraperiod tax

allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. ASU 2019-12 also clarifies and simplifies other aspects of the accounting for income taxes. ASU 2019-12 is effective for the Company on January 1, 2022, with early adoption permitted. The Company is currently evaluating the potential impact that this standard may have on its financial position and results of operations, as well as the timing of its adoption of this standard.

3. Restricted Cash

As of December 31, 2020 and 2019, the Company had restricted cash of $0.6 million, held as a letter of credit for the benefit of the landlord in connection with the Company's lease in Cambridge, Massachusetts. The lease term expires on December 30, 2021. Restricted cash was classified within prepaid expenses and other current assets on the consolidated balance sheet as of December 31, 2020 as the lease term expires less than twelve months from the consolidated balance sheet date. Restricted cash was classified within other non-current assets on the consolidated balance sheet as of December 31, 2019.

4. Fair Value of Financial Assets and Liabilities

The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicates the level of the fair value hierarchy utilized to determine such fair values (in thousands):

	As of December 31, 2020			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 290,931	$ —	$ —	$ 290,931
	$ 290,931	—	—	$ 290,931

	As of December 31, 2019			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 44,429	$ —	$ —	$ 44,429
	$ 44,429	$ —	$ —	$ 44,429

5. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2020	2019
Office furniture and equipment	$ 113	$ 113
Laboratory equipment	48	48
Computer equipment	9	5
Total property and equipment	170	166
Less: Accumulated depreciation	(88)	(38)
Property and equipment, net	$ 82	$ 128

Depreciation expense was not significant for the years ended December 31, 2020 and 2019.

6. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2020	2019
Accrued personnel-related expenses	$ 5,516	$ 1,059
Accrued external research and development expenses	4,206	1,552
Accrued license fees	—	363
Accrued other	1,147	481
Total accrued expenses	$ 10,869	$ 3,455

7. Commitments and Contingencies

Leases

In October 2018, the Company entered into a sublease agreement for office space located in Cambridge, Massachusetts which expires on December 30, 2021, with no option to renew or terminate early. The base rent increases by approximately 1% annually. The Company issued a letter of credit to the landlord related to the security deposit, secured by restricted cash (Note 3). This lease qualifies as an operating lease.

In January 2019, the Company entered into an arrangement with a third party to sublease a portion of its Cambridge, Massachusetts office space. This sublease was terminated in November 2019.

The following table summarizes the presentation of the operating lease in the Company's consolidated balance sheets (in thousands):

	As of December 31,	
	2020	2019
Assets:		
Operating lease right-of-use assets	$ 754	$ 1,450
Liabilities:		
Current operating lease liabilities	$ 763	$ 696
Non-current portion of operating lease liabilities	—	763
Total lease liabilities	$ 763	$ 1,459

The following table summarizes total lease costs recognized in the Company's consolidated statements of operations and comprehensive loss (in thousands):

	For the year ended	
	2020	2019
Operating lease cost	$ 782	$ 782
Variable lease costs	14	3
Sublease income	—	(31)
Total lease costs	$ 796	$ 754

Variable lease costs were primarily related to operating expenses, taxes and insurance associated with the operating lease, which were assessed based on the Company's proportionate share of such costs for the leased premises. As these costs are generally variable in nature, they are not included in the measurement of the operating lease right-of-use asset and related lease liability. Total lease costs are included as operating expenses in the Company's consolidated statements of operations and comprehensive loss.

Future lease payments under non-cancelable lease agreements as of December 31, 2020 were as follows (in thousands):

Year Ended December 31,	Future Lease Payments
2021	$ 791
Total future lease payments	$ 791
Less: interest	(28)
Present value of operating lease liabilities	$ 763

The weighted average remaining lease term and weighted average incremental borrowing rate of the Company's operating lease were as follows:

	As of December 31,	
	2020	2019
Weighted average remaining lease term (in years)	1.0	2.0
Weighted average incremental borrowing rate	8.0 %	8.0 %

Legal Proceedings

The Company, from time to time, may be party to litigation arising in the ordinary course of business. The Company was not subject to any legal proceedings during the years ended December 31, 2020 and 2019, and no material legal proceedings are currently pending or threatened.

Purchase Orders

The Company has agreements with third parties for various services, including services related to research, preclinical and clinical operations and support, for which the Company is not contractually able to terminate for convenience to avoid future obligations to the vendors. Certain agreements provide for termination rights subject to termination fees or wind down costs. Under such agreements, the Company is contractually obligated to make certain payments to vendors, primarily to reimburse them for their unrecoverable outlays incurred prior to cancellation. The actual amounts the Company could pay in the future to the vendors under such agreements may differ from the purchase order amounts due to cancellation provisions.

Indemnification Agreements

The Company enters into indemnification agreements and agreements containing indemnification provisions in the ordinary course of business. Pursuant to these agreements, the Company agrees to indemnify, hold harmless, and to reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally the Company's business partners, in connection with any U.S. patent or any copyright or other intellectual property infringement claim by any third party with respect to the Company's products. The term of these indemnification agreements is generally perpetual upon execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements.

8. Redeemable Convertible Preferred Stock

On October, 20 2020, upon the closing of the IPO, all 53,644,314 outstanding shares of the Redeemable Convertible Preferred Stock were converted into 25,067,977 shares of common stock. Pursuant to the terms of the Company's Amended and Restated Certificate of Incorporation, all series of the Redeemable Convertible Preferred Stock outstanding automatically converted into shares of common stock based on each series' respective then-current conversion ratio.

As of December 31, 2020, the Company did not have any shares of redeemable convertible preferred stock authorized, issued or outstanding.

The redeemable convertible preferred stock on December 31, 2019 consisted of the following (in thousands, except share amounts):

	As of December 31, 2019					
	Shares Authorized	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation Preference	Redemption Value	Common Stock Issuable Upon Conversion
Series A Preferred Stock	8,075,799	8,075,799	$ 9,932	$ 9,932	$ 9,932	3,773,820
Series B Preferred Stock	14,913,704	14,913,704	49,969	49,969	49,969	6,969,173
Series B-1 Preferred Stock	2,666,666	2,666,666	10,431	10,431	10,431	1,246,133
Series C Preferred Stock	11,067,963	9,805,827	50,789	50,789	50,789	4,582,257
	36,724,132	35,461,996	$ 121,121	$ 121,121	$ 121,121	16,571,383

Common stock issuable upon conversion in the table above represents shares of common stock issuable upon an automatic conversion in the event of a qualified public offering, pursuant to the Company’s then-current Amended and Restated Certificate of Incorporation, effective prior to the completion of the IPO.

On June 18, 2019, the Company entered into the Series B-1 Preferred Stock Purchase Agreement which authorized the sale and issuance of up to 2,666,666 shares of its Series B-1 Preferred Stock at a purchase price of $3.75 per share. During the year ended December 31, 2019, the Company issued all 2,666,666 shares of Series B-1 Preferred Stock for gross cash proceeds of $10.0 million, and incurred an immaterial amount of issuance costs. The issuance of the Series B-1 Preferred Stock resulted in changes to certain rights, preferences and privileges of the Series A Preferred Stock and the Series B Preferred Stock. The Company concluded that such changes were not significant and resulted in a modification, rather than an extinguishment, of the Series A Preferred Stock and the Series B Preferred Stock. The changes to the terms of the Series A Preferred Stock and the Series B Preferred Stock did not result in incremental value to the shareholders, and therefore there was no impact to the accounting for the Series A Preferred Stock and the Series B Preferred Stock.

On November 18, 2019, the Company entered into the Series C Preferred Stock Purchase Agreement which authorized the sale and issuance of up to 5,825,243 shares at $5.15 per share. On December 10, 2019, the Company executed Amendment No. 1 and Joinder to the Series C Preferred Stock Purchase Agreement which authorized the sale and issuance of an additional 5,242,720 shares at $5.15 per share. During the year ended December 31, 2019, the Company issued 9,805,827 shares of Series C Preferred Stock for gross cash proceeds of $50.5 million, and incurred issuance costs of $0.2 million. Although there were multiple closings of the Series C Preferred Stock, there was no obligation under the initial closing for investors to purchase, or for the Company to sell to such investors, additional shares of Series C Preferred Stock. The issuance of the Series C Preferred Stock resulted in changes to certain rights, preferences and privileges of the Series A Preferred Stock, the Series B Preferred Stock and the Series B-1 Preferred Stock. The Company concluded that such changes were not significant and resulted in a modification, rather than an extinguishment, of the Series A Preferred Stock, the Series B Preferred Stock and the Series B-1 Preferred Stock. The changes to the terms of the Series A Preferred Stock, the Series B Preferred Stock and the Series B-1 Preferred Stock did not result in incremental value to the shareholders, and therefore there was no impact to the accounting for the Series A Preferred Stock, the Series B Preferred Stock and the Series B-1 Preferred Stock.

On January 20, 2020, the Company granted two investors holding 5,825,243 shares of Series C Preferred Stock that were purchased in December 2019 the option to put their shares back to the Company at the original issuance price. On February 19, 2020 and March 3, 2020, the investors exercised their put option in full via the execution of Stock Redemption and Release Agreements in order to effect the repurchase. Pursuant to the Stock Redemption and Release Agreements, the Company agreed to repurchase a total of 5,825,243 shares of Series C Preferred Stock at the original issuance price of $5.15 per share, for an aggregate cash repurchase price of 30.0 million. Under the terms of the Stock Redemption and Release Agreements, the investors waived their right to cumulative dividends that had accumulated from the original issuance date through the date of repurchase. The 5,825,243 shares of Series C Preferred Stock were retired upon repurchase, and subsequently authorized for reissuance pursuant to a waiver to the Company's Amended and Restated Certificate of Incorporation entered into by the Company and the holders of the Redeemable Convertible Preferred Stock.

The Company determined that the additional put right that was granted to the investors represented a modification of the affected shares of Series C Preferred Stock, but that it did not result in incremental value to the shareholders. As there was no incremental value associated with the modification, there was no impact to the accounting for the Series C Preferred Stock. The Company also determined that the put right did not require bifurcation, as it does not contain the characteristics of a derivative instrument. Further, the Company determined that the shares of Series C Preferred Stock that were subject to repurchase did not become mandatorily redeemable until the execution of the Stock Redemption and Release Agreements because the parties did not have an unconditional legal obligation to complete the redemptions until the associated agreements were finalized. Such determination was made in consultation with legal counsel. Accordingly, the Company recorded each of the redemptions on the respective date of repurchase and recognized a gain on repurchase equal to the difference between the repurchase price and the carrying value of the Series C Preferred Stock on the respective date of repurchase. The aggregate gain of $0.5 million was recorded upon repurchase as an adjustment to accumulated deficit in the statement of redeemable convertible preferred stock and stockholders' deficit. The gain relates exclusively to the dividends accrued on the repurchased shares, which were waived by the investors as part of the Stock Redemption and Release Agreements.

On April 15, 2020 and May 8, 2020, the Company completed additional closings for the sale and issuance of its Series C Preferred Stock for a total of 4,563,108 shares at $5.15 per share for aggregate cash proceeds of $23.5 million, less an immaterial amount of issuance costs.

On July 24, 2020, the Company entered into the Series C-1 Preferred Stock Purchase Agreement, which authorized the sale and issuance of up to 19,444,453 shares of its Series C-1 Preferred Stock at a purchase price of $5.67 per share. During the year ended December 31, 2020, the Company issued all 19,444,453 shares of Series C-1 Preferred Stock for gross cash proceeds of $110.3 million, and incurred issuance costs of approximately $0.2 million. Although there were multiple closings of the Series C-1 Preferred Stock, there was no obligation under the initial closing for investors to purchase, or for the Company to sell to such investors, additional shares of Series C-1 Preferred Stock. The issuance of the Series C-1 Preferred Stock resulted in changes to certain rights, preferences and privileges of the Series A Preferred Stock, the Series B Preferred Stock, the Series B-1 Preferred Stock and the Series C Preferred Stock. The Company concluded that such changes were not significant and resulted in a modification, rather than an extinguishment, of the previously outstanding Redeemable Convertible Preferred Stock. The changes to the terms of the Series A Preferred Stock, the Series B Preferred Stock, the Series B-1 Preferred Stock and the Series C Preferred Stock did not result in incremental value to the shareholders, and therefore there was no impact to the accounting for the previously outstanding Redeemable Convertible Preferred Stock.

Rights, Preferences and Privileges

Prior to the conversion of the Redeemable Convertible Preferred Stock into shares of common stock upon the completion of the IPO on October 20, 2020, the holders of the Redeemable Convertible Preferred Stock had the following rights, preferences and privileges:

Voting Rights

The holders of outstanding shares of the Redeemable Convertible Preferred Stock were entitled to vote, together with the holders of common stock, on all matters submitted to the stockholders for a vote, and were entitled

to the number of votes equal to the number of whole shares of common stock into which such holders of the Redeemable Convertible Preferred Stock could convert on the record date for determining stockholders entitled to vote. Except for the actions requiring the approval or consent of the majority of the holders of the Redeemable Convertible Preferred Stock, the holders of the Redeemable Convertible Preferred Stock would vote together with the holders of common stock and vote as a single class. The holders of the Series A Preferred Stock, exclusively and as a separate class, were entitled to elect two directors of the Company. The holders of the Series B Preferred Stock and Series B-1 Preferred Stock, exclusively and together as a separate class, were entitled to elect two directors of the Company. The holders of common stock and of any other class or series of voting stock (including the Redeemable Convertible Preferred Stock), exclusively and voting as a single class, were entitled to elect the balance of total number of directors of the Company.

Dividends

The holders of the Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series C-1 Preferred Stock were entitled to accrue cumulative dividends at an annual rate of $0.08, $0.24, $0.30, $0.412 and $0.4536 per share, respectively, subject to adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Redeemable Convertible Preferred Stock. Dividends accrued from day to day whether or not declared by the Board, and were payable only when, as, and if declared by the Board. No dividends were declared or paid by the Company on the Redeemable Convertible Preferred Stock.

The Company's cumulative dividends on its Redeemable Convertible Preferred Stock as of December 31, 2019 were as follows (in thousands):

Series A Preferred Stock	$	1,857
Series B Preferred Stock		5,228
Series B-1 Preferred Stock		431
Series C Preferred Stock		289
	$	7,805

No dividends could be declared, paid or set aside to any other class or series of capital stock (other than dividends on shares of common stock payable in common stock) unless, in addition to obtaining any consents otherwise required in the Company's Amended and Restated Certificate of Incorporation, the holders of the Redeemable Convertible Preferred Stock first received a dividend on each outstanding share in an amount at least equal to the greater of: (i) all accrued and unpaid dividends and (ii) in the case of a dividend being distributed to common stock or any class or series of capital stock that is convertible into common stock, the equivalent dividend on an as-converted basis or (iii) in the case of a dividend being distributed on a series or class not convertible into common stock, an additional dividend equal to a dividend rate calculated based on the respective original issue price of the Preferred Stock. The original issue price per share was equal to $1.00 for the Series A Preferred Stock, $3.00 for the Series B Preferred Stock, $3.75 for the Series B-1 Preferred Stock and $5.15 for the Series C Preferred Stock. The holders of the Series C Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock were entitled to receive dividends prior to any dividends on the Series A Preferred Stock.

Liquidation Rights

In the event of any voluntary or involuntary liquidation event, dissolution, winding up of the Company or upon the occurrence of certain events designated by a majority of the holders of the Redeemable Convertible Preferred Stock, and at least two out of three specific holders, to be a deemed liquidation event, each holder of the then outstanding Series C-1 Preferred Stock, Series C Preferred Stock, Series B-1 Preferred Stock and Series B Preferred Stock was entitled to receive, prior and in preference to any distributions to the holders of Series A Preferred Stock and common stock, an amount equal to the greater of (i) original issuance price (adjusted in the event of any stock dividend, stock split, combination or other similar activity) plus any cumulative accrued dividends, whether or not declared, with any other dividends declared but unpaid thereon, or (ii) the amount such holder would have received if such holder had converted its shares into common stock immediately prior to such liquidation event.

After the payment of all preferential amounts to the holders of the Series C-1 Preferred Stock, Series C Preferred Stock, Series B-1 Preferred Stock and Series B Preferred Stock, each holder of the then outstanding Series A Preferred Stock was entitled to receive, prior and in preference to any distributions to the holders of common stock, an amount equal to the greater of (i) original issuance price (adjusted in the event of any stock dividend, stock split, combination or other similar activity) plus any cumulative accrued dividends, whether or not declared, with any other dividends declared but unpaid thereon, or (ii) the amount such holder would have received if such holder had converted its shares into common stock immediately prior to such liquidation event.

After payments have been made in full to the holders of the Redeemable Convertible Preferred Stock, then, to the extent available, the remaining amounts would be distributed among the holders of the shares of common stock, pro rata based on the number of shares held by each holder.

Conversion

Each share of the Redeemable Convertible Preferred Stock was convertible, at any time, at the option of the holder, and without the payment of additional consideration, into such shares of non-assessable shares of common stock as is determined by dividing the original issue price by the applicable conversion price in effect at the time of conversion. The applicable conversion price for the Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series C-1 Preferred Stock was initially equal to $2.14, $6.42, $8.03, $11.02 and $12.13, respectively, as adjusted for the Company's reverse stock split. Each share of the Redeemable Convertible Preferred Stock would automatically convert into common stock at the applicable conversion ratio then in effect for each series of the Redeemable Convertible Preferred Stock upon either (i) the closing of the sale of shares of common stock at a price of at least $10.30 per share in a firm-commitment underwritten public offering pursuant to an effective registration statement resulting in at least $75.0 million of gross proceeds and the listing of the Company’s common stock on the New York Stock Exchange, The Nasdaq Global Select Market, or The Nasdaq Global Market or (ii) the date and time, or the occurrence of an event, specified by vote or written consent of the holders of a majority of the outstanding Redeemable Convertible Preferred Stock, voting together as a single class and at least two of three specific holders. As of December 31, 2019, each share of the Redeemable Convertible Preferred Stock was convertible into 0.4673 shares of common stock, as adjusted for the Company's reverse stock split. Upon conversion pursuant to the completion of the IPO, the applicable conversion price for the Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series C-1 Preferred Stock was equal to $2.14, $6.42, $8.03, $11.02 and $12.13, respectively, as adjusted for the Company’s reverse stock split. Accordingly, each share of the Redeemable Convertible Preferred Stock converted into approximately 0.4673 shares of common stock.

Redemption

Each series of the Redeemable Convertible Preferred Stock was redeemable at a price equal to the applicable original issuance price per share (adjusted in the event of any stock dividend, stock split, combination or other similar activity), plus any cumulative accrued dividends, whether or not declared together with any other dividends declared but unpaid, in three annual installments commencing not more than 60 days on or after July 24, 2025 at the written election of at least a majority of the holders of the Redeemable Convertible Preferred Stock voting together as a single class and at least two out of three specific parties.

9. Common Stock and Preferred Stock

Common Stock

On October 20, 2020, the Company completed its IPO, pursuant to which it issued and sold 11,500,000 shares of its common stock at a public offering price of $19.00 per share, including 1,500,000 shares of common stock issued and sold pursuant to the underwriters’ exercise of their option to purchase additional shares of common stock. The IPO resulted in net proceeds of $200.3 million, after deducting underwriting discounts and commissions and other offering expenses. Upon the closing of the IPO, all 53,644,314 outstanding shares of the Redeemable Convertible Preferred Stock automatically converted into 25,067,977 shares of common stock pursuant to the terms of the Company's Amended and Restated Certificate of Incorporation at the then-current conversion ratio for each series, as adjusted for the Company's reverse stock split.

As of December 31, 2020, the authorized capital stock of the Company included 150,000,000 shares of common stock, $0.0001 par value, pursuant to the Amended and Restated Certificate of Incorporation effective upon the completion of the IPO. Holders of such shares of common stock have the exclusive right to vote for the election of the Company's directors and are entitled to one vote per share. In the event of the voluntary or involuntary liquidation, dissolution or winding up of the Company, the holders of common stock are entitled to a pro rata distribution of the Company's net assets. Dividends may be declared and paid to such holders only when, as, and if declared by the Board or an authorized committee thereof.

As of December 31, 2019, the authorized capital stock of the Company included 46,000,000 shares of common stock, $0.0001 par value. Such holders had rights, preferences and privileges subject to and qualified by the rights, preferences and privileges of the Redeemable Convertible Preferred Stock. Such holders of common stock were entitled to one vote per share, together with the holders of the Redeemable Convertible Preferred Stock, on all matters submitted to the stockholders for a vote, and were not entitled to receive dividends. In the event of a voluntary or involuntary liquidation, dissolution or winding up of the Company, after the payment of preferential amounts required to be paid to the holders of the Redeemable Convertible Preferred Stock, the holders of common stock were entitled to a pro rata distribution of the Company's remaining assets based on the number of shares held by each such holder.

As of December 31, 2020, the Company did not hold any treasury shares.

Shares Reserved for Future Issuance

The Company had reserved the following shares of common stock for future issuance:

	December 31,	
	2020	2019
Shares reserved for exercise of outstanding stock options	5,944,546	1,634,686
Shares reserved for future awards under the 2020 Stock Option and Incentive Plan	3,036,776	—
Shares reserved for future awards under the 2020 Employee Stock Purchase Plan	327,102	—
Shares reserved for future awards under the 2017 Stock Incentive Plan	—	617,101
Series A Preferred Stock	—	3,773,820
Series B Preferred Stock	—	6,969,173
Series B-1 Preferred Stock	—	1,246,133
Series C Preferred Stock	—	4,582,257
Shares reserved for vesting of restricted stock	—	48,190
Total shares of authorized common stock reserved for future issuance	9,308,424	18,871,360

Preferred Stock

As of December 31, 2020, the Company was authorized to issue 10,000,000 shares of undesignated preferred stock, $0.0001 par value, in one or more series, and is authorized to fix the powers, designations, preferences and relative participating option or other rights thereof, including dividend rights, conversion rights, voting rights, redemption rights, liquidation preferences and the number of shares constituting any series, without any further vote or action by the Company's shareholders. The Company was not authorized to issue any such shares as of December 31, 2019. As of December 31, 2020, the Company had no shares of undesignated preferred stock issued or outstanding.

10. Stock-Based Compensation

2020 Stock Option and Incentive Plan

On September 9, 2020, the Board approved the 2020 Stock Option and Incentive Plan (the "2020 Plan"), which was subsequently approved by its stockholders and became effective on October 15, 2020. The 2020 Plan replaced the 2017 Stock Incentive Plan (the "2017 Plan") and no additional awards will be granted under the 2017 Plan following the closing of the IPO. The 2017 Plan will continue to govern outstanding equity awards granted thereunder. The 2020 Plan allows the Company to grant stock options, restricted stock, restricted stock units and other stock-based awards to officers, employees, directors and consultants. The 2020 Plan is administered by the Compensation Committee of the Board, which has the authority to grant awards, to accelerate at any time the exercisability or vesting of any award and to determine the specific terms and conditions of each award, subject to the provisions of the 2020 Plan.

The total number of shares of common stock authorized for issuance under the 2020 Plan as of December 31, 2020 was 3,271,028 shares. There were no shares of common stock authorized for issuance under the 2020 Plan as of December 31, 2019.

As of December 31, 2020, the Company had issued only stock options under the 2020 Plan. Stock options issued comprise service-based awards granted to employees. Stock options issued under the 2020 Plan typically have vesting conditions in which 25% vests upon the first anniversary of a specified vesting commencement date, and the remaining 75% vests in 36 monthly installments over the remaining three years. Vesting of stock options is subject to the recipient’s continued employment or service. Stock options issued under the 2020 Plan expire 10 years from the date of grant.

Shares that expire, are terminated, surrendered or canceled under the 2020 Plan without having been fully exercised will be available for future awards. In addition, shares of common stock that are tendered to the Company by a participant to exercise an award are added to the number of shares of common stock available for future awards. Upon stock option exercise, the Company issues new shares and delivers them to the participant.

2017 Stock Incentive Plan

On May 9, 2017, the Board adopted the 2017 Plan. The 2017 Plan allows the Company to grant stock options, restricted stock, restricted stock units and other stock-based awards to employees, officers, directors, consultants and advisors of the Company. The 2017 Plan is administered by the Board, which has the authority to grant awards and determine the terms of awards under the 2017 Plan, provided that generally the exercise price per share of stock options granted may not be less than 100% of the fair market value of a share of the Company’s common stock on the date of grant, and the term of stock options granted may not exceed ten years.

The total number of shares of common stock authorized for issuance under the 2017 Plan as of December 31, 2020 and 2019 was 5,937,763 shares and 2,356,927 shares, respectively. Any authorization to issue new options under the 2017 Plan was cancelled upon the effectiveness of the 2020 Plan and no further awards will be granted under the 2017 Plan.

As of December 31, 2020 and 2019, the Company had issued only stock options and restricted stock under the 2017 Plan. Stock options issued comprise service-based awards granted to employees, directors and non-employee consultants. Stock options and restricted stock issued under the 2017 Plan typically have vesting conditions in which 25% vests upon the first anniversary of a specified vesting commencement date, and the remaining 75% vests in 36 monthly installments over the remaining three years. Vesting of stock options is subject to the recipient’s continued employment or service. The Company has the right to repurchase any unvested shares of restricted stock held by a recipient during the vesting period if the relationship between the recipient and the Company has terminated. Stock options issued under the 2017 Plan expire ten years from the date of grant.

Shares that expire, are terminated, surrendered or canceled under the 2017 Plan without having been fully exercised will be available for future awards under the 2020 Plan. In addition, shares of common stock that are tendered to the Company by a participant to exercise an award are added to the number of shares of common stock

available for future awards. Upon stock option exercise, the Company issues new shares and delivers them to the participant.

2020 Employee Stock Purchase Plan

On September 9, 2020, the Board approved the 2020 Employee Stock Purchase Plan (the "2020 ESPP"), which was subsequently approved by its stockholders and became effective on October 15, 2020. The 2020 ESPP permits employees whose customary employment is for more than 20 hours per week to purchase common stock through payroll deductions (which cannot exceed 15 percent of each employee's compensation) at the lower of 85 percent of fair market value at the beginning of the purchase period or the end of each purchase period. The Company may make one or more offerings each year to its employees to purchase shares under the 2020 ESPP. Offerings will usually begin on or around each May 1 and November 1 and will continue for six-month periods, referred to as offering periods. During the year ended December 31, 2020, there were no shares purchased under the 2020 ESPP as the first offering period had not opened as of December 31, 2020. The total shares authorized for issuance under the 2020 ESPP were 327,102 shares as of December 31, 2020. There were no shares authorized for issuance under the 2020 ESPP as of December 31, 2019.

Restricted Common Stock

Prior to the adoption of the 2017 Plan, the Company granted restricted common stock in 2016 with time-based vesting conditions to certain employees and non-employee founders of the Company pursuant to individual award agreements. The restricted common stock granted pursuant to these agreements vests either: (i) 25% upon vesting commencement or the first anniversary of a specified vesting commencement date, and the remaining 75% monthly over 36 months thereafter, (ii) monthly over 48 months after a specified vesting commencement date, or (iii) monthly over 12 months from a specified vesting commencement date. The Company had the right to repurchase the unvested shares held by a recipient during the vesting period if the relationship between the recipient and the Company has terminated. Shares of restricted common stock are not accounted for as outstanding common stock until they have vested. Unvested shares of restricted common stock may not be sold or transferred by the holder. All granted restricted common stock had vested as of December 31, 2020. The Company did not grant any restricted common stock during the years ended December 31, 2020 and 2019.

The following table summarizes all of the Company's restricted common stock activity, including restricted common stock issued under the 2017 Plan and under individual award agreements prior to the adoption of the 2017 Plan:

	Shares	Weighted Average Grant Date Fair Value
Unvested as of December 31, 2019	48,190	$ 0.06
Issued	—	—
Vested	(48,190)	0.06
Repurchased	—	—
Unvested as of December 31, 2020	—	$ —

The total fair value of restricted common stock that vested during the years ended December 31, 2020 and 2019 was $0.5 million and $0.6 million, respectively.

Stock Options

The following table summarizes the Company's stock option activity:

	Number of Shares	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
			(In years)	(In thousands)
Outstanding as of December 31, 2019	1,634,686	$ 2.46		
Granted	4,529,870	9.10		
Exercised	(30,496)	2.87		$ 696
Cancelled or Forfeited	(189,514)	4.00		
Outstanding as of December 31, 2020	5,944,546	$ 7.47	9.19	$ 282,686
Exercisable as of December 31, 2020	1,017,306	$ 2.31	7.85	$ 53,624
Vested and expected to vest as of December 31, 2020	5,794,877	$ 7.47	9.19	$ 275,562

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the underlying stock options and the estimated fair value of the Company's common stock for those stock options that had exercise prices lower than the estimated fair value of the Company's common stock at December 31, 2020.

Stock Option Valuation

The weighted-average assumptions that the Company used in the Black-Scholes option pricing model to determine the grant-date fair value of stock options granted to employees, members of the Board and non-employees on the date of grant were as follows:

	Year Ended December 31,	
	2020	2019
Risk-free interest rate	0.47 %	1.55 %
Expected term (in years)	6.20	6.00
Expected volatility	85.94 %	79.09 %
Expected dividend yield	— %	— %

The weighted-average grant-date fair value of the Company's stock options granted during the years ended December 31, 2020 and 2019 was $6.51 and $2.25, respectively.

In December 2020, the Company recognized approximately $2.1 million of stock-based compensation expense, recorded within general and administrative expense, related to the modification of option awards granted to former employee in conjunction with their termination of employment. The former employee will continue to vest in 53,319 option awards through September 2021.

Stock-Based Compensation

Stock-based compensation expense was allocated as follows (in thousands):

	Year Ended December 31,	
	2020	2019
Research and development	$ 1,357	$ 430
General and administrative	3,854	238
Total stock-based compensation expense	$ 5,211	$ 668

As of December 31, 2020, total unrecognized compensation cost related to unvested stock-based awards was $26.7 million, which is expected to be recognized over a weighted-average period of 3.58 years.

11. Significant Agreements

Purdue License Agreement

On December 31, 2017, the Company entered into a License Agreement with Purdue (the "Purdue License Agreement"), pursuant to which Purdue granted the Company exclusive rights under certain Purdue know-how to research, develop and commercialize pharmaceutical products concerning a GABAA positive allosteric modulator. The Company is obligated to make future milestone payments based on the achievement of specified development and sales milestones up to $33.0 million. Furthermore, the Company is required to pay Purdue royalties of a low-single-digit percentage of annual net sales of licensed products.

The Purdue License Agreement will remain in effect until the expiration of the Company's royalty obligation for all licensed products. Either the Company or Purdue may terminate the agreement in the event of a material breach by the other party and fails to cure such breach within a certain period of time. Either party may voluntarily terminate the agreement with prior notice. If the agreement is voluntarily terminated by Purdue, the Company's license rights will survive such termination and such rights will become fully paid, perpetual and irrevocable.

As of December 31, 2020, none of the developmental or sales milestones under the Purdue License Agreement were achieved.

RogCon and Ionis Agreements

During 2018, the Company began negotiating a license agreement with RogCon Inc. ("RogCon") for intellectual property related to treating SCN2A mutations in epilepsy, which is recognized as the second most common genetic cause of epilepsy. RogCon had an existing collaboration with Ionis Pharmaceuticals, Inc. ("Ionis") and as a result the Company needed to negotiate an agreement with Ionis in order to complete the license agreement with RogCon. On December 21, 2018, the Company entered into an agreement with RogCon to advance RogCon a deposit of up to $1.0 million on the pending license agreement while the agreement with Ionis was being negotiated. The deposit was fully refundable to the Company. On September 11, 2019, the Company entered into both a Cooperation and License Agreement (the "License Agreement") with RogCon, and a Research, Collaboration, Option and License Agreement (the "Collaboration Agreement") with Ionis. The agreements were entered into contemporaneously to enable the parties to advance their collective efforts related to SCN2A. Upon execution of the License Agreement, the $1.0 million outstanding balance of the deposit was applied toward the purchase price of the License Agreement.

RogCon Agreement

Under the License Agreement, RogCon granted to the Company an exclusive, worldwide license under RogCon's intellectual property to research, develop and commercialize products for the treatment of all forms of epilepsy and/or neurodevelopmental disorders in each case caused by any mutation of the SCN2A gene. Under the License Agreement, the Company will conduct, at its own cost and expense, the research and development activities assigned to it under the research plan. In addition, the Company is responsible for reimbursing RogCon for any costs associated with research and development activities RogCon performs at the request of the Company. As part of the agreement, the Company agreed to provide up-front consideration of $2.1 million, consisting of the $1.0 million deposit, $0.7 million in cash reimbursements for certain historical costs previously incurred by RogCon, and $0.4 million for the retirement of existing loan balances as of September 11, 2019.

The Company concluded that the License Agreement represented the acquisition of in-process research and development assets with no alternative future use. Therefore, the aggregate acquisition cost of $2.2 million, consisting of the $2.1 million of up-front consideration and $0.1 million of acquisition costs, was expensed as research and development on September 11, 2019.

Subsequent to September 11, 2019, the Company will reimburse RogCon for its out-of-pocket costs incurred for activities performed under the License Agreement. The Company expenses these costs as incurred as research

and development. The Company expensed $0.2 million and $0.1 million for the reimbursement of RogCon's out-of-pocket costs in the years ended December 31, 2020 and 2019, respectively.

Additionally, the Company may pay RogCon a milestone payment of $3.0 million and profit share payments. The $3.0 million milestone payment will become due when the first profit share payment has become due and certain contingent payments have become payable to Ionis under the Collaboration Agreement, which are subject to the Company exercising its option to obtain license rights to a development candidate, as well as other contingent events. The profit share payments will be based on a low-double-digit percentage of net profits, depending on sales volume.

The License Agreement, unless earlier terminated, will continue until the latest of: (i) expiration of all patent rights within RogCon patents, (ii) the Company and its affiliates certify they have abandoned the research, development and commercialization of product with no intention to re-establish such activities, and (iii) no third party is obligated to pay the Company or its affiliates any amounts that comprise net sublicense revenue. Either party may terminate the License Agreement for material breach or insolvency of the other party. Additionally, the Company may terminate for convenience with prior written notice to RogCon. Upon termination by either party, all rights and licenses granted by RogCon to the Company will revert back to RogCon.

Ionis Collaboration Agreement

Under the Collaboration Agreement, both parties will participate in research activities related to the downregulation of SCN2A gene products associated with the treatment of any and all forms of epilepsy and/or neurodevelopmental disorders in each case caused by any mutation of the SCN2A gene, other than one severe type of epilepsy. Ionis will also be responsible for identifying a development candidate and conducting an IND-enabling toxicology study. The Company will reimburse Ionis for any out-of-pocket costs incurred related to the research activities, identification of a development candidate and conducting an IND-enabling toxicology study. Additionally, the Company agreed to reimburse $0.3 million of costs incurred by Ionis for the performance of research activities prior to the execution of the Collaboration Agreement, which the Company recognized as research and development expense. The reimbursement of out-of-pocket costs is recognized as research and development expense as incurred. The Company expensed a total of $1.7 million and $0.6 million, inclusive of the upfront payment of $0.3 million, as research and development expense under the Collaboration Agreement for the years ended December 31, 2020 and 2019, respectively.

Ionis granted the Company an exclusive option to obtain the rights and license related to the development candidate, which the Company may exercise following completion of the IND-enabling toxicology study. Upon option exercise, the Company will pay Ionis a $2.0 million license fee. After option exercise, the Company is responsible for clinical development and commercialization of the development candidate. If the option is not exercised, the Collaboration Agreement will expire, and the Company will have no further rights to the development candidate. Additionally, if the option is not exercised, at the request of Ionis, the Company will assign the RogCon License Agreement to Ionis. The Company concluded that there is no accounting recognition for the exclusive option unless and until such option is exercised because it is a unilateral right of the Company that is priced at an amount that approximates fair value.

If the Company exercises its exclusive option, Ionis may be entitled to development milestone payments, additional milestone payments, and sales royalties or sublicense fees.

The Collaboration Agreement will continue until the expiration of all payment obligations to Ionis, unless earlier terminated. Either party may terminate the Collaboration Agreement upon material breach or insolvency of the other party or if Ionis is unable to identify a development candidate. Ionis may terminate if the Company fails to achieve a performance milestone. The Company may terminate for convenience with prior written notice to Ionis. Upon termination by the Company for convenience, the Company will stop selling all products, subject to certain wind-down provisions, and all products will revert back to Ionis.

12. Net Loss per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows (in thousands, except share and per share data):

	Years Ended December 31,	
	2020	2019
Numerator:		
Net loss	$ (61,820)	$ (35,512)
Accretion and cumulative dividends on redeemable convertible preferred stock	(8,996)	(5,170)
Gain on repurchase of redeemable convertible preferred stock	493	—
Net loss attributable to common stockholders	$ (70,323)	$ (40,682)
Denominator:		
Weighted average common shares outstanding, basic and diluted	8,950,152	1,529,629
Net loss per share attributable to common stockholders, basic and diluted	$ (7.86)	$ (26.60)

The following potential common shares, presented based on amounts outstanding at each period end, were excluded from the calculation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have been anti-dilutive:

	Year Ended December 31,	
	2020	2019
Outstanding stock options	5,944,546	1,634,686
Series A Preferred Stock	—	3,773,820
Series B Preferred Stock	—	6,969,173
Series B-1 Preferred Stock	—	1,246,133
Series C Preferred Stock	—	4,582,257
Unvested restricted common stock	—	48,190
	5,944,546	18,254,259

The shares of common stock issuable upon conversion of the Redeemable Convertible Preferred Stock for the year ended December 31, 2019 assumed automatic conversion in the event of a qualified public offering.

13. Income Taxes

The Company maintains a full valuation allowance on its U.S. net deferred tax assets due to the uncertainty of future taxable income. The Company did not recognize an income tax benefit in the years ended December 31, 2020 or 2019 related to its U.S. operations due to the uncertainty regarding future taxable income. In the years ended December 31, 2020 and 2019, the difference between the statutory tax rate in the U.S. and the Company's effective tax rate was due primarily to the valuation allowance recorded to offset any potential tax benefit. The income tax benefit recognized for the years ended December 31, 2020 and 2019 related to income tax associated with the Company's operations in Australia.

The reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate is as follows:

	Year Ended December 31,	
	2020	2019
Federal statutory income tax rate	21.0 %	21.0 %
State taxes, net of federal benefit	5.6 %	6.0 %
Federal and state research and development credits	2.9 %	2.9 %
Non-deductible items	(1.8)%	(0.4)%
Foreign	0.2 %	0.2 %
Change in valuation allowance	(27.9)%	(29.6)%
Other	— %	0.1 %
Effective income tax rate	— %	0.2 %

Net deferred tax assets consisted of the following (in thousands):

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 26,441	$ 14,502
Amortization	5,774	3,512
Research and development credits	3,053	1,230
Accrued expenses	1,433	340
Leases	207	396
Stock-based compensation	170	60
Total gross deferred tax assets	$ 37,078	$ 20,040
Less: Valuation allowance	(36,873)	(19,647)
Net deferred tax assets	$ 205	$ 393
Deferred tax liabilities:		
Operating lease right-of-use asset	(205)	(393)
Total gross deferred tax liabilities	(205)	(393)
Net deferred tax assets	$ —	$ —

As of December 31, 2020 and 2019, the Company had U.S. federal net operating loss carryforwards which may be able to offset future income tax liabilities of approximately $97.1 million and $53.4 million, respectively. Federal net operating loss carryforwards of $7.7 million will expire at various dates through 2037 and approximately $89.4 million may be carried forward indefinitely. As of December 31, 2020 and 2019, the Company also had state net operating loss carryforwards of approximately $94.5 million and $52.0 million, respectively, which may be available to offset future income tax liabilities and expire at various dates through 2040.

As of December 31, 2020 and 2019, the Company had federal research and development tax credit carryforwards of approximately $2.4 million and $0.9 million, respectively, available to reduce future tax liabilities which expire at various dates through 2040. As of December 31, 2020 and 2019, the Company had state research and development tax credit carryforwards of approximately $0.9 million and $0.4 million, respectively, available to reduce future tax liabilities which expire at various dates through 2035. The Company has generated research credits but has not conducted a study to document the qualified activity. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed, and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has

been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. Further, until a study is completed by the Company and any limitation is known, no amounts are being presented as an uncertain tax position.

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of the evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all of the evidence, both positive and negative, the Company has recorded a valuation allowance against its deferred tax assets at December 31, 2020 and 2019 because management has determined that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets, primarily due to its history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception. As a result, a valuation allowance of $36.9 million and $19.6 million has been established at December 31, 2020 and 2019, respectively. Management reevaluates the positive and negative evidence at each reporting period. The valuation allowance increased by approximately $17.3 million and $10.5 million during the years ended December 31, 2020 and 2019, respectively, due primarily to the generation of net operating losses.

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2020 and 2019. The Company's policy is to record interest and penalties related to uncertain tax positions as part of its income tax provision. As of December 31, 2020 and 2019, the Company had no accrued interest or penalties related to uncertain tax positions and no such amounts have been recognized in the Company's consolidated statement of operations and comprehensive loss for either year ended December 31, 2020 or 2019. The statute of limitations for federal and state tax authorities is open for tax years ended December 31, 2017 through December 31, 2020. Since the Company is in a net loss carryforward position, the Company is generally subject to examination by the U.S. federal, state and local income tax authorities for all tax years in which a loss carryforward is available.

14. Related Party Transactions

One of the founders of RogCon became the Company's General Counsel in June 2020. During the years ended December 31, 2020 and 2019, the Company reimbursed RogCon for its out-of-pocket costs incurred for activities performed under the License Agreement (Note 11).

A former member of the Board was affiliated with Purdue through September 2020. During the years ended December 31, 2020 and 2019, the Company performed certain research and development activities pursuant to the Purdue License Agreement (Note 11).

During the years ended December 31, 2020 and 2019, related parties participated in each of the

Company's offerings of the Redeemable Convertible Preferred Stock (Note 8).

During the year ended December 31, 2019, the Company reimbursed $0.2 million of third-party recruiting costs incurred by a significant shareholder on behalf of the Company. These amounts were recorded in general and administrative expenses during the year ended December 31, 2019 and were within accrued expenses as of December 31, 2019.

15. Employee Benefit Plan

The Company has a defined contribution savings plan under Section 401(k) of the Internal Revenue Code for eligible employees. The plan covers substantially all employees who meet a minimum age requirement and allows participants to defer a portion of their annual compensation on a pre-tax basis. Under the plan, the Company is not obligated to match any participant contributions. The Company made contributions of $0.5 million during the year ended December 31, 2020 and did not make any contributions to the plan during the year ended December 31, 2019.

16. Subsequent Events

The Company has completed an evaluation of subsequent events after the consolidated balance sheet date of December 31, 2020 through the date these consolidated financial statements were issued. The Company has concluded that no subsequent events have occurred that require disclosure.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosures

None.

Item 9A. Controls and Procedures

Disclosure Controls and Procedures

We maintain “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Our management, with the participation of our Chief Executive Officer (our principal executive officer) and Vice President of Finance (our principal accounting officer and interim principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2020. Based on the evaluation of our disclosure controls and procedures as of December 31, 2020, our Chief Executive Officer and Vice President of Finance concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the the three months ended December 31, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Annual Report on Internal Control over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The following table sets forth the name, age, and position of each of our current executive officers and directors as of March 1, 2021:

Name	Age	Position
Executive Officers:		
Marcio Souza	41	President, Chief Executive Officer, Director
Bernard Ravina, M.D.	53	Chief Medical Officer
Alex Nemiroff, J.D.	41	General Counsel, Secretary
Nicole Sweeny	46	Chief Commercial Officer
Non-Employee Directors:		
Dean Mitchell(2)	65	Chairman, Director
Nicholas Galakatos, Ph.D.(2)(3)	63	Director
Gregory Norden(1)	63	Director
Kiran Reddy, M.D.	44	Director
Stefan Vitorovic(1)(3)	36	Director
William Young(1)(2)(3)	76	Director

(1) Member of the audit committee.

(2) Member of the compensation committee.

(3) Member of the nominating and corporate governance committee.

Executive Officers

Marcio Souza has served as a director and our President and Chief Executive Officer since April 2020. Prior to joining us, Mr. Souza was at PTC Therapeutics, Inc., or PTC, where he served as its Chief Operating Officer from May 2017 to April 2020 and its Senior Vice President and Head of Product Strategy from July 2016 to May 2017. Prior to joining PTC, Mr. Souza served in positions of increasing responsibility at NPS Pharmaceuticals, Inc., Shire Human Genetic Therapies Inc. and Sanofi Genzyme Corporation. From May 2019 to May 2020, Mr. Souza also served on the board of directors of Clearpoint Neuro, Inc. (NASDAQ: CLPT) (previously MRI Interventions, Inc.). Mr. Souza received a degree in pharmacy and biochemistry with a specialization in toxicology and clinical analysis from the University of São Paulo and an M.B.A. from Fundação Dom Cabral. We believe Mr. Souza is qualified to serve on our board of directors because of his business and leadership experience in the life sciences industry and his scientific background.

Bernard Ravina, M.D., has served as our Chief Medical Officer since August 2018. Prior to joining us, Dr. Ravina was at Voyager Therapeutics, Inc. (NASDAQ: VYGR), where he served as Chief Medical Officer from February 2017 to August 2018 and as Vice President of Clinical Development from March 2014 to January 2017. Dr. Ravina was also Medical Director in Clinical Development at Biogen Inc. (NASDAQ: BIIB), or Biogen, from 2010 to 2014, where he worked on both small molecule drugs and biologics for the treatment of neurological disorders. From 2005 to 2010, Dr. Ravina was an Associate Professor of Neurology, Director of the Movement and Inherited Neurological Disorders Unit, Associate Director of Clinical Trials Coordination Center and Vice Chair of Neurology at the University of Rochester School of Medicine. Dr. Ravina received a B.A. in psychology from Columbia University, an M.D. from Johns Hopkins University School of Medicine and an M.S.C.E. in clinical epidemiology from the University of Pennsylvania where he completed his residency and fellowship training in Neurology.

Alex Nemiroff, J.D., has served as our General Counsel since June 2020. Prior to his role as General Counsel, Mr. Nemiroff served as our VP of Legal from January 2020 to June 2020. Mr. Nemiroff was also a co-founder of RogCon, Inc. and RogCon U.R., Inc., and he has served as both entities' Chief Executive Officer since inception in November 2015. Mr. Nemiroff has experience working in commercial and securities litigation while at Greenberg Traurig LLP, and served as law clerk to the Honorable Paul C. Huck of the United States District Court

for the Southern District of Florida. Mr. Nemiroff received a B.B.A from the University of Michigan's Ross School of Business, and a J.D. from Northwestern University School of Law.

Nicole Sweeny has served as our Chief Commercial Officer since August 2020. Prior to joining us, Ms. Sweeny was at Takeda Pharmaceuticals (NYSE: TAK) where she served as a Vice President, Franchise Head, Rare Diseases from February 2019 to July 2020. Prior to Takeda, Ms. Sweeny served in several roles at Shire Pharmaceuticals plc (later acquired by Takeda Pharmaceuticals Company Limited) from August 2010 to January 2019, including Vice President, Head of US Marketing from September 2017 to January 2019 and Vice President, Global Product Strategy Lead from December 2016 to August 2017. Prior to joining Shire, Ms. Sweeny served in commercial positions of increasing responsibility at AMAG Pharmaceuticals and Sanofi Genzyme Corporation. Ms. Sweeny received her B.S. from Boston College.

Non-Employee Directors

Dean Mitchell has served as chairman of our board of directors since September 2020. He served as executive chairman of the board of directors of Covis Pharma Holdings, a specialty pharmaceutical company, from August 2013 until its sale in March 2020 and was chairman of PaxVax Corporation from January 2016 until its sale in October 2018. Mr. Mitchell served as President and Chief Executive Officer of Lux Biosciences, Inc., a biotechnology company focusing on the treatment of ophthalmic diseases, from July 2010 to August 2013. Prior to Lux Biosciences, he served as President and Chief Executive Officer of both Alpharma, Inc., a publicly traded specialty pharmaceutical company, from 2006 until its acquisition by King Pharmaceuticals, Inc. in 2008, and Guilford Pharmaceuticals, Inc., a publicly traded pharmaceutical company focused in oncology and acute care, from 2004 until its acquisition by MGI Pharma Inc. in 2005. From 2001 to 2004, he served in various senior executive capacities in the worldwide medicines group of Bristol-Myers Squibb Company, a pharmaceutical company. Prior to the Bristol-Myers Squibb Company, he spent 14 years at GlaxoSmithKline plc, in assignments of increasing responsibility spanning sales, marketing, general management, commercial strategy and clinical development and product strategy. Mr. Mitchell currently serves on the board of directors of Theravance Biopharma, Inc. (NASDAQ: TBPH), ImmunoGen Inc. (NASDAQ: IMGN), Precigen Inc. (formerly Intrexon Inc.) (NASDAQ: PGEN) and Kinnate Biopharma Inc. (NASDAQ: KNTE). Mr. Mitchell holds an M.B.A. from City University London and a B.Sc. in biology from Coventry University. We believe Mr. Mitchell is qualified to serve on our board of directors because of his management experience in the pharmaceutical and biotherapeutics industries and his experience as a President, Chief Executive Officer and board member of multiple biotechnology companies.

Nicholas Galakatos, Ph.D., has served as a member our board of directors since September 2015. Dr. Galakatos is the Global Head of Life Sciences of The Blackstone Group Inc., or Blackstone. Prior to joining Blackstone, Dr. Galakatos was a co-Founder and Managing Director of Clarus Ventures, LLC (acquired by Blackstone in 2018), or Clarus, since the firm's inception in 2005. Dr. Galakatos is currently the chairman of the board of directors of Anthos Therapeutics, Inc., or Anthos, a private, clinical-stage cardiovascular biotech founded in 2019, and a member of the board of directors of Talaris, Inc. He is a member of the Director's Council of the Koch Institute at MIT and a member of the Board of Trustees at Reed College. Dr. Galakatos received a B.A. in chemistry from Reed College and a Ph.D. in organic chemistry from the Massachusetts Institute of Technology. We believe Dr. Galakatos is qualified to serve on our board of directors because of his business and leadership experience in the life sciences industry and his scientific background.

Gregory Norden is the former Chief Financial Officer of Wyeth and has served as a member of our board of directors since March 2019. Mr. Norden currently serves as the Managing Director of G9 Capital Group LLC, which invests in early stage ventures and provides corporate finance advisory services, since 2010. Mr. Norden currently serves on the boards of directors of Zoetis (NYSE: ZTS), the leading animal health company, NanoString Technologies (NASDAQ: NSTG), a leading provider of life science tools for translational research, Royalty Pharma (NASDAQ: RPRX), a leading funder of innovation across the biopharmaceutical industry. Mr. Norden is a former director of Human Genome Sciences, Welch Allyn, Univision Communications and Entasis Therapeutics. Mr. Norden received a B.S. in management and economics from the State University of New York at Plattsburgh and an M.S. in accounting from Long Island University—C.W. Post. We believe Mr. Norden is qualified to serve on our board of directors because of his background in finance and experience as a senior executive in the global healthcare and pharmaceutical industries, as well as his public company board experience.

Kiran Reddy, M.D., has served as a member of our board of directors since September 2015. Prior to his role as our director, Dr. Reddy served as our President and Chief Executive Officer from November 2015 to April 2020. Dr. Reddy is also currently a Managing Director at Blackstone, a position he has served in since May 2020.

Dr. Reddy was a venture partner at Clarus from November 2015 to November 2019 prior to its acquisition by Blackstone. From 2014 to 2015, Dr. Reddy served as part of Biogen's Corporate Strategy leadership team, where he focused on sourcing new technologies and product opportunities to support the Company's growth. Dr. Reddy was previously a Howard Hughes science fellow and has authored several peer-reviewed scientific papers in the field of epilepsy, neuroimmunology and neurodegenerative diseases. Dr. Reddy received a B.S. in economics, an M.D. and an M.B.A. from Georgetown University. We believe Dr. Reddy is qualified to serve on our board of directors because of his corporate leadership experience, business background, and perspective and experience as one of Praxis' former executive officers.

Stefan Vitorovic has served as a member of our board of directors since March 2018 . Mr. Vitorovic is the co-founder and Managing Director of Vida Ventures, LLC, or Vida Ventures, a role he has served in since January 2017. Prior to Vida Ventures, Mr. Vitorovic was a Principal at Third Rock Ventures, where he was employed from July 2014 to January 2017. Prior to Third Rock Ventures, Mr. Vitorovic was a healthcare private equity investor at TPG Capital from August 2012 to June 2014. Mr. Vitorovic received a B.S. with honors in molecular & cellular biology and an M.S. in molecular & cellular biology from Stanford University as well as an M.B.A from Harvard University. We believe Mr. Vitorovic is qualified to serve on our board of directors because of his scientific background and business experience.

William Young has served as a member of our board of directors since December 2016. Mr. Young is a Senior Advisor with Blackstone. Prior to its acquisition by Blackstone, Mr. Young joined Clarus in March 2010 and held various roles, including Venture Partner, Senior Advisor and portfolio company board member. Mr. Young currently serves as the chairman of the board of directors of Annexon, Inc. (NASDAQ: ANNX) and NanoString, and as a member of the board of directors of Theravance BioPharma Inc. (NASDAQ: TBPH). Mr. Young also served on the boards of directors of Vertex Pharmaceuticals Inc. (NASDAQ: VRTX) from May 2015 to June 2020 and BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) from September 2010 to November 2015. Mr. Young was elected to the National Academy of Engineering in 1993 for his contributions to biotechnology. Mr. Young received a B.S. in chemical engineering from Purdue University and an M.B.A. from Indiana University in marketing and finance and holds an honorary doctorate in engineering from Purdue University. We believe Mr. Young is qualified to serve on our board of directors because of his scientific background, business experience and his service on the board of directors of other life sciences companies.

Family Relationships

There are no family relationships among any of our executive officers or directors.

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires our directors, executive officers, and persons holding more than 10% of our common stock to report their initial ownership of the common stock and other equity securities and any changes in that ownership in reports that must be filed with the SEC. The SEC has designated specific deadlines for these reports, and we must identify in this Annual Report those persons who did not file these reports when due.

Based solely on a review of reports furnished to us, and written representations from our directors and officers, we believe all directors, executive officers, and 10% owners timely filed all reports regarding transactions in our securities required to be filed for 2020 by Section 16(a) under the Exchange Act, with the exception of a Form 4/A filed by Stefan Vitorovic on February 16, 2021 to report a purchase of common stock in our initial public offering.

Code of Business Conduct and Ethics

Our board of directors has adopted a written code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. Our code of business conduct and ethics is available on the Corporate Governance section of our website at https://praxismedicines.com. We intend to disclose any amendments to the code, or any waivers of its requirements, on our website or in a Current Report on Form 8-K as may be required by SEC or Nasdaq rules. We do not incorporate the information on or accessible through our website into this Annual Report, and you should not consider any information on, or that can be accessed through, our website as part of this Annual Report.

Recommendation of Director Nominees by Stockholders

There have been no material changes to the procedures by which our stockholders may recommend nominees to the board of directors.

Composition of Our Board of Directors

Our board of directors currently consists of nine members, each of whom are members pursuant to the board composition provisions of our amended and restated certificate of incorporation and agreements with our stockholders, which agreements are described under "Item 13. Certain Relationships and Related Party Transactions, and Director Independence." Our nominating and corporate governance committee and our board of directors may therefore consider a broad range of factors relating to the qualifications and background of nominees, which may include diversity, which is not only limited to race, gender or national origin. Our nominating and corporate governance committee's and our board of directors' priority in selecting board members is identification of persons who will further the interests of our stockholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape and professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal. Our amended and restated certificate of incorporation and amended and restated bylaws also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 66.67% of the votes that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Staggered Board

In accordance with the terms of our amended and restated certificate of incorporation and amended and restated bylaws, our board of directors are divided into three staggered classes of directors and each director is assigned to one of the three classes. At each annual meeting of the stockholders, a class of directors is elected for a three-year term to succeed the directors of the same class whose terms are then expiring. The terms of the directors expire upon the election and qualification of successor directors at the annual meeting of stockholders to be held during the years 2021 for Class I directors, 2022 for Class II directors and 2023 for Class III directors.

- Our Class I director is Dean Mitchell;
- Our Class II directors are Nicholas Galakatos, Ph.D., Kiran Reddy, M.D., and Stefan Vitorovic; and
- Our Class III directors are Gregory Norden, Marcio Souza and William Young.

Board Leadership Structure and the Role of the Board in Risk Oversight

Board Leadership Structure

The positions of our chairman of the board and chief executive officer are separated, with Mr. Souza serving as our Chief Executive Officer and Mr. Mitchell serving as the chairman of our board of directors. Separating these positions allows Mr. Souza, as our Chief Executive Officer, to focus on our day-to-day business, while allowing the chairman of the board to lead the board of directors in its fundamental role of providing advice to and independent oversight of management. Our board of directors recognizes the time, effort and energy that Mr. Souza, as our Chief Executive Officer, must devote to his position in the current business environment, as well as the commitment required to serve as our chairman, particularly as the board of directors' oversight responsibilities continue to grow. Our board of directors also believes that this structure ensures a greater role for the independent directors in the oversight of our company and active participation of the independent directors in setting agendas and establishing priorities and procedures for the work of our board of directors. Our board of directors believes its administration of its risk oversight function has not affected its leadership structure. Our board of directors believes that having separate positions is the appropriate leadership structure for us at this time and demonstrates our commitment to good corporate governance.

Role of the Board in Risk Oversight

Risk is inherent with every business, and how well a business manages risk can ultimately determine its success. We face a number of risks, including those described under the section titled "Risk Factors" in this prospectus. Our board of directors is actively involved in oversight of risks that could affect us. This oversight is conducted primarily by our full board of directors, which has responsibility for general oversight of risks.

Our board of directors satisfies this responsibility through full reports by each committee chair regarding the committee's considerations and actions, as well as through regular reports directly from officers responsible for oversight of particular risks within our company. Our board of directors believes that full and open communication between management and the board of directors is essential for effective risk management and oversight.

Committees of Our Board of Directors

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which operates pursuant to a charter adopted by our board of directors. Our board of directors may establish other committees to facilitate the management of our business. The composition and functioning of all of our committees comply with all applicable requirements of the Sarbanes-Oxley Act of 2002, Nasdaq and U.S. Securities and Exchange Commission rules and regulations. Members will serve on these committees until their resignation or until otherwise determined by our board of directors. In addition, from time to time, special committees may be established under the direction of our board of directors when necessary to address specific issues.

Audit Committee

Gregory Norden, Stefan Vitorovic and William Young serve on the audit committee, which is chaired by Gregory Norden. Our board of directors has determined that Gregory Norden, Stefan Vitorovic and William Young are "independent" for audit committee purposes as that term is defined in the rules of the SEC and the applicable Nasdaq rules, and each has sufficient knowledge in financial and auditing matters to serve on the audit committee. Our board of directors has designated Gregory Norden as an "audit committee financial expert," as defined under the applicable rules of the SEC. The audit committee's responsibilities include:

- appointing, approving the compensation of and assessing the independence of our independent registered public accounting firm;
- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending based upon the audit committee's review and discussions with management and our independent registered public accounting firm whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related person transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing quarterly earnings releases.

Compensation Committee

Nicholas Galakatos, Dean Mitchell and William Young serve on the compensation committee, which is chaired by William Young. Our board of directors has determined that Nicholas Galakatos, Dean Mitchell and William Young are independent" as defined in the applicable Nasdaq rules. The compensation committee's responsibilities:

- annually reviewing and approving corporate goals and objectives relevant to the compensation of our chief executive officer;
- evaluating the performance of our chief executive officer in light of such corporate goals and objectives and determining the compensation of our chief executive officer;

- reviewing and approving the compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- evaluating and assessing potential and current compensation advisors in accordance with the independence standards identified in the applicable Nasdaq rules;
- retaining and approving the compensation of any compensation advisors;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- evaluating director compensation and making recommendations on director compensation to the Board;
- preparing the compensation committee report required by SEC rules to be included in our annual proxy statement; and
- reviewing and approving the retention or termination of any consulting firm or outside advisor to assist in the evaluation of compensation matters.

Nominating and Corporate Governance Committee

Nicholas Galakatos, Stefan Vitorovic and William Young serve on the nominating and corporate governance committee, which is chaired by Nicholas Galakatos. Our board of directors has determined that Nicholas Galakatos, Stefan Vitorovic and William Young are "independent" as defined in the applicable Nasdaq rules. The nominating and corporate governance committee's responsibilities include:

- developing and recommending to the board of directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- reviewing the size and composition of the board of directors to ensure that it is composed of members containing the appropriate skills and expertise to advise us;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board's committees;
- developing and recommending to the board of directors a code of business conduct and ethics and a set of corporate governance guidelines; and
- overseeing the evaluation of our board of directors and management.

Our board of directors may from time to time establish other committees.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee. For a description of transactions between us and members of our compensation committee and affiliates of such members, please see "Item 13. Certain Relationships and Related Party Transactions, and Director Independence."

Item 11. Executive Compensation

Executive Compensation Overview

Our compensation programs are designed to:

- attract, motivate, incentivize and retain key management personnel who contribute to our long-term success;
- emphasize performance-based compensation that rewards the achievement of our business objectives; and
- effectively align the interests of our executives with those of our stockholders by focusing on long-term equity incentives that correlate with the growth of sustainable long-term value for our stockholders.

The compensation committee of our board of directors, or the compensation committee, which is comprised entirely of independent directors, is responsible for discharging our board of directors' responsibilities relating to compensation of our executive officers, overseeing our overall compensation structure, policies and programs, and reviewing our processes and procedures for the consideration and determination of executive compensation. Our Chief Executive Officer makes recommendations for the respective executive officers that report to him to our compensation committee and typically attends compensation committee meetings. Our Chief Executive Officer makes such recommendations (other than with respect to himself) regarding base salary, and short-term and long-term compensation, including equity incentives, for our executive officers based on our results, an executive officer's individual contribution toward these results, the executive officer's role and performance of his or her duties and his or her achievement of individual goals. Our compensation committee then reviews the recommendations and other data, including various compensation survey data and publicly-available data of our peers, and makes decisions as to the target total direct compensation for each executive officer, including our Chief Executive Officer, as well as each individual compensation element. While our Chief Executive Officer typically attends meetings of the compensation committee, the compensation committee meets outside the presence of our Chief Executive Officer when discussing his compensation and when discussing certain other matters.

Our compensation committee is authorized to retain the services of one or more executive compensation advisors, as it sees fit, in connection with the establishment of our executive compensation programs and related policies. In 2020, our compensation committee engaged FW Cook, an independent executive compensation consultant, to provide guidance with respect to the development and implementation of our compensation programs. During 2020, FW Cook did not provide services to us other than the services to our compensation committee described herein. Our compensation committee performs an annual assessment of its compensation consultants' independence to determine whether the consultants are independent. Based on its evaluation, the compensation committee has determined that FW Cook is independent and that its work has not raised any conflicts of interest.

The compensation provided to our named executive officers for the fiscal year ended December 31, 2020 is detailed in the 2020 Summary Compensation Table and accompanying footnotes and narrative that follow. Our named executive officers for the fiscal year ended December 31, 2020 were:

- Marcio Souza, our President Chief Executive Officer;
- Bernard Ravina, M.D., our Chief Medical Officer;
- Nicole Sweeny, our Chief Commercial Officer;
- Kiran Reddy, M.D., our former President and Chief Executive Officer; and
- Stuart Chaffee, Ph.D., our former Chief Financial Officer.

In April 2020, Dr. Reddy resigned as our President and Chief Executive Officer and Marcio Souza became our President and Chief Executive Officer. In August 2020, Ms. Sweeny joined us as our Chief Commercial Officer and, in December 2020, Dr. Chaffee resigned as our Chief Financial Officer.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to our named executive officers for services rendered to us in all capacities during the fiscal years indicated.

Name and Principal Position	Year	Salary ($)	Bonus ($)(1)	Stock Awards ($)	Option Awards ($)(2)	Non-Equity Incentive Plan Compensation ($)(3)	All Other Compensation ($)(4)	Total ($)
Marcio Souza *President and Chief Executive Officer (5)*	2020	385,417	24,000	—	10,301,160	1,001,000	30,382	11,741,959
Bernard Ravina, M.D. *Chief Medical Officer*	2020	425,000	—	—	911,197	357,000	17,813	1,711,010
	2019	350,000	75,000	—	—	126,000	271	551,271
Nicole Sweeny *Chief Commercial Officer (6)*	2020	142,500	60,000	—	1,343,151	99,750	8,651	1,654,052
Kiran Reddy, M.D. *Former President and Chief Executive Officer(7)*	2020	132,998	—	—	—	—	16,244	149,242
	2019	385,500	—	—	—	190,823	269	576,592
Stuart Chaffee, Ph.D. *Former Chief Financial Officer (8)*	2020	341,114	—	—	852,959	—	453,610	1,647,683
	2019	308,250	—	—	—	83,228	297	391,775

(1) The amounts reported for 2020 represent a one-time $24,000 sign-on bonus paid to Mr. Souza under the terms of his employment agreement and a one-time $60,000 sign-on bonus paid to Ms. Sweeny under the terms of her offer letter. The amount for 2019 represents a $75,000 bonus paid to Dr. Ravina pursuant to the terms of his offer letter.

(2) The amounts reported represent the aggregate grant date fair value of the stock options awarded to the named executive officers during 2020 and 2019, calculated in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, ASC, Topic 718. Such grant date fair values do not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in this column are set forth in Note 10 to our consolidated financial statements for the year ended December 31, 2020 included in this Annual Report on Form 10-K. The amounts reported in this column reflect the accounting cost for these stock options and do not correspond to the actual economic value that may be received by the named executive officers upon the exercise of the stock options or any sale of the underlying shares of common stock.

(3) Amounts represent annual cash bonuses paid based on achievement of corporate performance metrics and individual performance in 2020 and 2019, as applicable, which were paid in February 2021 and March 2020, respectively. The corporate performance metrics for 2020 and 2019 were achieved at 200% and 90% of target, respectively. Individual performance achievement levels varied.

(4) Amounts reported include tax gross-ups on taxable long-term disability, commuter benefits, gym reimbursement, reimbursement for social distancing activities, disability insurance, and life insurance in the following amounts for 2020: Mr. Souza—$204 for long-term disability benefits, $3,569 for disability insurance, and $965 for life insurance; Dr. Ravina—$227 for long-term disability benefits, $411 for commuter benefits, and $75 for reimbursement for social distancing activities; Ms. Sweeny—$101 for long-term disability benefits; Dr. Reddy—$81 for long-term disability benefits and $248 for commuter benefits; and Dr. Chaffee—$225 for long-term disability benefits, $578 for commuter benefits and $374 for gym reimbursement. Amounts also include discretionary company contributions under our 401(k) plan, in the following amounts for 2020: $17,100 for Mr. Souza, Dr. Ravina and Dr. Chaffee; $8,550 for Ms. Sweeny; and $7,980 for Dr. Reddy. For Mr. Souza, the amount reported for 2020 also includes $6,726 for reimbursement for premiums on a supplemental long-term disability policy owned by him and $1,818 for reimbursement for premiums on a term life insurance policy owned by him. For Dr. Reddy, the amount reported for 2020 also includes $7,935 in fees for his services as a non-employee member of the board of directors in 2020 following his resignation as President and Chief Executive Officer. For Dr. Chaffee, the amount reported for 2020 also includes $435,333 in cash severance

payable to Dr. Chaffee pursuant to the terms of his separation and transition agreement with us, which is described below under the heading "Employment Arrangements with our Named Executive Officers".

(5) Mr. Souza was appointed President and Chief Executive Officer effective April 20, 2020.
(6) Ms. Sweeny was appointed Chief Commercial Officer effective August 10, 2020.
(7) Dr. Reddy resigned as our President and Chief Executive Officer effective April 20, 2020.
(8) Dr. Chaffee resigned as our Chief Financial Officer effective December 2, 2020.

Narrative to the 2020 Summary Compensation Table

Base Salaries

Each named executive officer's base salary is a fixed component of annual compensation for performing specific duties and functions, and has been established by our board of directors or compensation committee taking into account each individual's role, responsibilities, skills and expertise. Base salaries are reviewed annually, typically in connection with our annual performance review process, approved by our compensation committee or our board of directors and adjusted from time to time to realign salaries with market levels after taking into account individual responsibilities, performance and experience. During 2020, the annual base salaries for Mr. Souza, Dr. Ravina, Ms. Sweeny, Dr. Reddy, and Dr. Chaffee were $550,000, $425,000 and $360,000, $398,993, and $330,000 (which was increased to $400,000 effective as of May 28, 2020), respectively.

Annual Bonus

For the fiscal year ended December 31, 2020, each of our named executive officers was eligible to earn an annual bonus based on the achievement of certain pre-determined corporate performance objectives and individual performance. During 2020, the target annual bonuses for Mr. Souza, Dr. Ravina, Ms. Sweeny, Dr. Reddy, and Dr. Chaffee were 70%, 40%, 35%, 55%, and 30% (which was increased to 40% effective May 28, 2020) of their base salary, respectively. The annual bonus earned by each named executive officer with respect to the fiscal year ended December 31, 2020 is reported under the "Non-Equity Incentive Plan Compensation" column in the "2020 Summary Compensation Table" above and was determined based upon achievement of the corporate performance objectives at 200% of target and achievement of individual performance objective at varied levels.

Equity Compensation

We believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants promote executive retention because they incentivize our executive officers to remain in our employment during the vesting period. Accordingly, our compensation committee or board of directors periodically reviews the equity incentive compensation of our named executive officers and may grant equity incentive awards to them from time to time. Our named executive officers have been granted certain options to purchase shares of our common stock, as described in more detail in the "Outstanding Equity Awards at 2020 Fiscal Year-End" table below.

Employment Arrangements with our Named Executive Officers

We initially entered into an offer letter or employment agreement with each of the named executive officers in connection with his or her employment with us, which set forth the terms and conditions of his or her employment, including base salary, target annual bonus opportunity and initial equity awards. In April 2020, we entered into employment agreements with Dr. Ravina and Dr. Chaffee that replaced the offer letters or prior employment agreements and provided for specified payments and benefits in connection with a termination of employment in certain circumstances.

We entered into amended and restated employment agreements with Mr. Souza, Dr. Ravina, Ms. Sweeny and Dr. Chaffee effective as of the closing of our initial public offering in October 2020, or the New Employment Agreements.

The New Employment Agreements provide for specified payments and benefits in connection with a termination of employment in certain circumstances. The material terms of the New Employment agreements with Mr. Souza, Dr. Ravina, Ms. Sweeny and Dr. Chaffee and the offer letter with Dr. Reddy are summarized below.

In connection with the termination of his employment, we entered into a separation and transition agreement with Dr. Chaffee, which provided for certain payments and benefits. The material terms of the separation and transition agreement with Dr. Chaffee are summarized below.

Marcio Souza. Under the New Employment Agreement with Mr. Souza, Mr. Souza has continued to serve as our President and Chief Executive Officer on an at-will basis. Mr. Souza's current annual base salary is $575,000, which is subject to annual review, and he is eligible to earn an annual bonus with a target amount equal to 75% of

his base salary. Mr. Souza is also eligible to participate in the employee benefit plans available to our employees, subject to the terms of those plans.

Bernard Ravina, M.D. Under the New Employment Agreement with Dr. Ravina, Dr. Ravina has continued to serve as our Chief Medical Officer on an at-will basis. Dr. Ravina's current annual base salary is $475,000, which is subject to annual review, and he is eligible to earn an annual bonus with a target amount equal to 40% of his base salary. Dr. Ravina is also eligible to participate in the employee benefit plans available to our employees, subject to the terms of those plans.

Nicole Sweeny. Under the New Employment Agreement with Ms. Sweeny, Ms. Sweeny has continued to serve as our Chief Commercial Officer on an at-will basis. Ms. Sweeny's current annual base salary is $400,000, which is subject to annual review, and she is eligible to earn an annual bonus with a target amount equal to 40% of her base salary. Ms. Sweeny is also eligible to participate in the employee benefit plans available to our employees, subject to the terms of those plans.

Pursuant to the New Employment Agreements, in the event that Mr. Souza's, Dr. Ravina's, or Ms. Sweeny's employment is terminated by us without "cause" or Mr. Souza, Dr. Ravina, or Ms. Sweeny resigns for "good reason" (as defined in the New Employment Agreements), subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, Mr. Souza, Dr. Ravina, or Ms. Sweeny, as applicable, (i) will be entitled to receive base salary continuation for nine months (12 months for Mr. Souza) following termination, and (ii) subject to the executive's co-payment of premium amounts at the applicable active employees' rate and proper election to continue COBRA health coverage, we will cover the portion of the premium amount equal to the amount that we would have paid to provide health insurance to the executive had such executive remained employed with us until the earliest of (A) nine months (12 months for Mr. Souza) following termination, (B) the executive's eligibility for group medical plan benefits under any other employer's group medical plan or (C) the end of the executive's COBRA health continuation period.

In lieu of the payments and benefits described in the preceding sentence, in the event Mr. Souza's, Dr. Ravina's or Ms. Sweeny's employment is terminated by us without cause or Mr. Souza, Dr. Ravina, or Ms. Sweeny resigns for good reason, in either case on or within 12 months following a "change of control" (as defined in the New Employment Agreements), subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, (i) the executive will be entitled to receive a lump sum in cash equal to one times (1.5 times for Mr. Souza) the sum of (A) the executive's then-current annual base salary (or the executive's annual base salary in effect immediately prior to the change of control, if higher) plus (B) the executive's target annual cash incentive compensation for the year of termination (or the executive's target annual cash incentive compensation in effect immediately prior to the change of control, if higher), (ii) subject to the executive's co-payment of premium amounts at the applicable active employees' rate and proper election to continue COBRA health coverage, we will cover the portion of the premium amount equal to the amount that we would have paid to provide health insurance to the executive had such executive remained employed with us until the earliest of (A) 12 months (18 months for Mr. Souza) following termination, (B) the executive's eligibility for group medical plan benefits under any other employer's group medical plan or (C) the end of the executive's COBRA health continuation period, and (iii) the vesting of 100% of all stock options and other stock-based awards subject solely to time-based vesting held by the executive shall be accelerated.

The payments and benefits provided to each of the executives in connection with a change of control may not be eligible for a federal income tax deduction for the company pursuant to Section 280G of the Code and may subject the executive to an excise tax under Section 4999 of the Code. If the payments or benefits payable to the executive in connection with a change of control would be subject to the excise tax on golden parachutes imposed under Section 4999 of the Code, then those payments or benefits will be reduced if such reduction would result in a higher net after-tax benefit to the executive.

Kiran Reddy, M.D. Dr. Reddy resigned as our President and Chief Executive Officer effective April 20, 2020. In connection with the commencement of his employment with us, Clarus Ventures entered into an offer letter with Dr. Reddy to serve as Chief Executive Officer of our company, which set forth his initial annual base salary, target bonus and initial equity award. In addition, the offer letter provided that, if he transitioned from the position of Chief Executive Officer of our company for good reason, he would have the opportunity to join Clarus Ventures as a venture partner at his current compensation for a period of one year.

Stuart Chaffee, Ph.D. Under the New Employment Agreement with Dr. Chaffee, Dr. Chaffee continued to serve as our Chief Financial Officer on an at-will basis until his resignation. Prior to his resignation, Dr. Chafee was entitled to the same severance and change of control benefits as Dr. Ravina and Ms. Sweeny under his New Employment Agreement. Dr. Chaffee resigned as our Chief Financial Officer effective December 2, 2020 and transitioned to a role as strategic advisor. In connection with his resignation, and subject to the Company's receipt of a general release of claims and pursuant to the terms of a separation and transition agreement, Dr. Chaffee is entitled to receive (i) continuation of his current base salary for nine months following his separation from the Company, (ii) his

target cash bonus amount for fiscal year 2020, payable in nine equal monthly installments following his separation, and (iii) continued time-based vesting of the unvested portions of Dr. Chaffee's outstanding equity awards during the period in which Dr. Chaffee provides advisory services to us.

Outstanding Equity Awards at 2020 Fiscal Year-End

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2020. Each of the awards set forth in the table below was granted under our 2017 Stock Incentive Plan, or the 2017 Plan, or our 2020 Stock Option and Incentive Plan, or the 2020 Plan.

			Option Awards			
Name	Grant Date	Vesting Commencement Date	Number of Securities Underlying Unexercised Options (#) Exercisable (1)	Number of Securities Underlying Unexercised Options (#) Unexercisable (1)	Option Exercise Price ($)	Option Expiration Date
Marcio Souza	06/05/2020	04/20/2020	—	955,349	5.59	06/03/2030
	09/14/2020	09/08/2020	—	1,028,037	8.91	09/12/2030
Bernard Ravina, M.D.	10/19/2018	08/21/2018	103,020	81,459	2.27	10/16/2028
	06/05/2020	05/28/2020	—	80,507	5.59	06/03/2030
	09/14/2020	09/08/2020	—	93,457	8.91	09/12/2030
Nicole Sweeny	08/19/2020	08/10/2020	—	229,065	8.27	08/17/2030
Kiran Reddy, M.D.	10/19/2018	10/06/2015	230,928	—	2.27	10/16/2028
Stuart Chaffee, Ph.D.(2)	10/19/2018	11/20/2017	134,552	40,002	2.27	10/16/2028
	06/05/2020	05/28/2020	—	65,892	5.59	06/03/2030
	09/14/2020	09/08/2020	—	93,457	8.91	09/12/2030

(1) The stock options vest over four years, with 25% of the total shares vesting on the first anniversary of the vesting commencement date and the remainder vesting in 36 approximately equal monthly installments.
(2) Dr. Chaffee's equity awards were modified in conjunction with the termination of his employment. As a result, 149,669 unexercisable option awards are expected to be forfeited in September 2021.

Compensation Risk Assessment

We believe that although a portion of the compensation provided to our executive officers and other employees is performance-based, our executive compensation program does not encourage excessive or unnecessary risk taking. This is primarily due to the fact that our compensation programs are designed to encourage our executive officers and other employees to remain focused on both short-term and long-term strategic goals. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on us.

Employee Benefit and Equity Compensation Plans

2017 Stock Incentive Plan

The Praxis Precision Medicines, Inc. 2017 Stock Incentive Plan, or our 2017 Plan, was approved by our board of directors and our stockholders in May 2017 and was most recently amended in September 2020. Under the 2017 Plan, as amended through the date hereof, we reserved for issuance an aggregate of 5,937,763 shares of our common stock. The number of shares of common stock reserved for issuance is subject to adjustment in the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event or any dividend or distribution to holders of common stock other than an ordinary cash dividend.

The shares of common stock underlying awards that are expired, lapsed, terminated, surrendered, canceled without having been fully exercised or forfeited in whole or in part (including as a result of shares of common stock subject to such award being repurchased by us at or below the original issuance price), and shares of common stock that are withheld upon exercise of an option or settlement of an award to cover the exercise price or tax withholding are added back to the shares of common stock available for issuance under our 2020 Stock Option and Incentive Plan, or our 2020 Plan.

The 2017 Plan provides that upon the occurrence of a "reorganization event," as defined in the 2017 Plan, our board of directors may take one or more of the following actions as to all or any (or any portion of) awards outstanding under the 2017 Plan other than restricted stock awards: (i) provide that awards will be assumed or substituted by the acquiring or successor corporation, (ii) upon written notice to participants, provide that all unexercised awards will terminate immediately prior to the consummation of the reorganization event unless exercised by the participant within a specified period following the date of such notice, (iii) provide that outstanding awards shall become exercisable, realizable or deliverable, or that all restrictions applicable to such awards shall lapse, in whole or in part, prior to or upon such reorganization event, (iv) make or provide for a cash payment to the award holder equal to the excess, if any, of the per share cash consideration in the reorganization event times the number of shares subject to the participant's award over any aggregate exercise price of such outstanding award and any applicable tax withholdings in exchange for the termination of such awards, (v) provide that, in connection with a liquidation or dissolution of our company, awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise price thereof and any applicable tax withholdings) and (vi) any combination of the foregoing. Upon the occurrence of a reorganization event other than a liquidation or dissolution of the Company, the repurchase and other rights of the Company under each outstanding restricted stock award shall inure to the benefit of our successor and shall, unless our board of directors determines otherwise, apply to the cash, securities or other property which the common stock was converted into or exchanged for pursuant to such reorganization event in the same manner and to the same extent as they applied to the common stock subject to such restricted stock award. Upon the occurrence of a reorganization event involving the liquidation or dissolution of our company (except as otherwise provided for in the award agreement), all restrictions and conditions on all outstanding restricted stock awards will be automatically deemed terminated or satisfied.

The administrator may amend, suspend or terminate the 2017 Plan at any time, subject to stockholder approval where such approval is required by applicable law. The administrator of the 2017 Plan may also amend or cancel any outstanding award, provided that no amendment to an award may adversely affect a participant's rights without his or her consent. The administrator of the 2017 Plan is specifically authorized to exercise its discretion to reduce the exercise price of outstanding awards under the 2017 Plan or effect the repricing of such awards through cancellation and re-grants without stockholder approval.

The 2017 Plan will terminate automatically upon the earlier of 10 years from the date on which the 2017 Plan was adopted by our board of directors or 10 years from the date the 2017 Plan was approved by our stockholders. As of December 31, 2020, options to purchase 5,710,294 shares of common stock were outstanding under the 2017 Plan. Our board of directors determined not to make any further awards under the 2017 Plan following the closing of our initial public offering.

2020 Stock Option and Incentive Plan

Our 2020 Plan was adopted by our board of directors on September 9, 2020, approved by our stockholders on October 8, 2020 and became effective in connection with our initial public offering. The 2020 Plan replaced the 2017 Plan following the closing of our initial public offering. However, the 2017 Plan will continue to govern outstanding equity awards granted thereunder. The 2020 Plan allows us to make equity-based and cash-based incentive awards to our officers, employees, directors and consultants.

We initially reserved 3,271,028 shares of our common stock, or the Initial Limit, for the issuance of awards under the 2020 Plan. The 2020 Plan provides that the number of shares reserved and available for issuance under the 2020 Plan will automatically increase each January 1, beginning on January 1, 2021, by 5% of the outstanding number of shares of our common stock on the immediately preceding December 31, or such lesser number of shares as determined by our compensation committee, or the Annual Increase. These limits are subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The shares we issue under the 2020 Plan are authorized but unissued shares or shares that we reacquire. The shares of common stock underlying awards under the 2020 Plan that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without the issuance of stock, expire or are otherwise terminated (other than by exercise) will be added back to the shares of common stock available for issuance under the 2020 Plan.

The maximum aggregate number of shares that may be issued in the form of incentive stock options shall not exceed the Initial Limit cumulatively increased on January 1, 2021 and on each January 1 thereafter by the lesser of the Annual Increase for such year or 1,635,514 shares of common stock.

The grant date fair value of all awards made under our 2020 Plan and all other cash compensation paid by us to any non-employee director in any calendar year for services as a non-employee director shall not exceed $750,000; provided, however, that such amount shall be $1,000,000 for the calendar year in which the applicable non-employee director is initially elected or appointed to the board of directors and $1,500,000 for the non-executive chair of our board of directors. Notwithstanding the foregoing, the independent members of the board of directors may make exceptions to such limits in extraordinary circumstances.

The 2020 Plan is administered by our compensation committee. Our compensation committee has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted and the number of shares subject to such awards, to make any combination of awards to participants, to accelerate at any time the exercisability or vesting of any award and to determine the specific terms and conditions of each award, subject to the provisions of the 2020 Plan. Persons eligible to participate in the 2020 Plan are those full or part-time officers, employees, non-employee directors and consultants as selected from time to time by our compensation committee in its discretion.

The 2020 Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code, and options that do not so qualify. The option exercise price of each option will be determined by our compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant unless the option is granted (i) pursuant to a transaction described in, and in a manner consistent with, Section 424(a) of the Code or (ii) to individuals who are not subject to U.S. income tax. The term of each option will be fixed by our compensation committee and may not exceed 10 years from the date of grant. Our compensation committee will determine at what time or times each option may be exercised.

Our compensation committee may award stock appreciation rights subject to such conditions and restrictions as it may determine. Stock appreciation rights entitle the recipient to shares of common stock, or cash, equal to the value of the appreciation in our stock price over the exercise price. The exercise price of each stock appreciation right may not be less than 100% of the fair market value of our common stock on the date of grant unless the stock appreciation right is granted (i) pursuant to a transaction described in, and in a manner consistent with, Section 424(a) of the Code or (ii) to individuals who are not subject to U.S. income tax. The term of each stock appreciation right will be fixed by our compensation committee and may not exceed 10 years from the date of grant. Our compensation committee will determine at what time or times each stock appreciation right may be exercised.

Our compensation committee may award restricted shares of common stock and restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and/or continued employment with us through a specified vesting period. Our compensation committee may also grant shares of common stock that are free from any restrictions under the 2020 Plan. Unrestricted stock may be granted to participants in recognition of past services or other valid consideration and may be issued in lieu of cash compensation due to such participant.

Our compensation committee may grant dividend equivalent rights to participants that entitle the recipient to receive credits for dividends that would be paid if the recipient had held a specified number of shares of our common stock.

Our compensation committee may grant cash bonuses under the 2020 Plan to participants, subject to the achievement of certain performance goals.

The 2020 Plan provides that upon the effectiveness of a “sale event,” as defined in the 2020 Plan, an acquirer or successor entity may assume, continue or substitute outstanding awards under the 2020 Plan. To the extent that awards granted under the 2020 Plan are not assumed or continued or substituted by the successor entity, upon the effective time of the sale event, such awards shall terminate. In such case, except as may be otherwise provided in the relevant award certificate, all awards with time-based vesting, conditions or restrictions shall become fully vested and nonforfeitable as of the effective time of the sale event, and all awards with conditions and restrictions relating to the attainment of performance goals may become vested and nonforfeitable in connection with a sale event in the administrator’s discretion or to the extent specified in the relevant award certificate. In the event of such termination, individuals holding options and stock appreciation rights will be permitted to exercise such options and stock appreciation rights (to the extent exercisable) within a specified period of time prior to the sale event. In addition, in connection with the termination of the 2020 Plan upon a sale event, we may make or provide for a payment, in cash or in kind, to participants holding vested and exercisable options and stock appreciation rights equal to the difference between the per share consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights and we may make or provide for a payment, in cash or in kind, to participants holding other vested awards.

Our board of directors may amend or discontinue the 2020 Plan and our compensation committee may amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose but no such action may adversely affect rights under an award without the holder's consent. Certain amendments to the 2020 Plan require the approval of our stockholders. No awards may be granted under the 2020 Plan after the date that is 10 years from the effective date of the 2020 Plan.

As of December 31, 2020, options to purchase 234,252 shares of common stock were outstanding under the 2020 Plan.

2020 Employee Stock Purchase Plan

Our 2020 Employee Stock Purchase Plan, or the 2020 ESPP, was adopted by our board of directors on September 9, 2020, approved by our stockholders on October 8, 2020 and became effective in connection with our initial public offering. The 2020 ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Code. The 2020 ESPP initially reserves and authorizes the issuance of up to a total of 327,102 shares of common stock to participating employees. The 2020 ESPP provides that the number of shares reserved and available for issuance will automatically increase on January 1, 2021 and each January 1 thereafter through January 1, 2030, by the least of (i) 327,102 shares of common stock, (ii) 1% of the outstanding number of shares of our common stock on the immediately preceding December 31 or (iii) such lesser number of shares of common stock as determined by the administrator of the 2020 ESPP. The number of shares reserved under the 2020 ESPP is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

All employees whose customary employment is for more than 20 hours per week are eligible to participate in the 2020 ESPP. However, any employee who owns 5% or more of the total combined voting power or value of all classes of stock will not be eligible to purchase shares under the 2020 ESPP.

We may make one or more offerings each year to our employees to purchase shares under the 2020 ESPP. Offerings will usually begin on or around each May 1 and November 1 and will continue for six-month periods, referred to as offering periods. Each eligible employee may elect to participate in any offering by submitting an enrollment form at least 15 business days before the relevant offering date.

Each employee who is a participant in the 2020 ESPP may purchase shares by authorizing payroll deductions of up to 15% of his or her eligible compensation during an offering period. Unless the participating employee has previously withdrawn from the offering, his or her accumulated payroll deductions will be used to purchase shares of common stock on the last business day of the offering period at a price equal to 85% of the fair market value of the shares on the first business day or the last business day of the offering period, whichever is lower, provided that no more than $25,000 worth of shares of common stock may be purchased by any one employee during any offering period. Under applicable tax rules, an employee may purchase no more than $25,000 worth of shares of common stock, valued at the start of the purchase period, under the 2020 ESPP in any calendar year.

The accumulated payroll deductions of any employee who is not a participant on the last day of an offering period will be refunded. An employee's rights under the 2020 ESPP terminate upon voluntary withdrawal from the plan or when the employee ceases employment with us for any reason.

The 2020 ESPP may be terminated or amended by our board of directors at any time. An amendment that increases the number of shares of common stock authorized under the 2020 ESPP and certain other amendments require the approval of our stockholders.

401(k) Plan

We participate in a retirement savings plan, or 401(k) plan, that is intended to qualify for favorable tax treatment under Section 401(a) of the Code, and contains a cash or deferred feature that is intended to meet the requirements of Section 401(k) of the Code. U.S. employees who are at least 18 years of age are generally eligible to participate in the 401(k) plan, subject to certain criteria. Participants may make pre-tax and certain after-tax (Roth) salary deferral contributions to the plan from their eligible earnings up to the statutorily prescribed annual limit under the Code. Participants who are 50 years of age or older may contribute additional amounts based on the statutory limits for catch-up contributions. Prior to 2021, we made discretionary matching contributions under the 401(k) plan. Beginning in 2021, we began matching up to the first 6% contributed by a participant. Participant contributions are held in trust as required by law. An employee's interest in his or her salary deferral contributions is 100% vested when contributed.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. The director or officer may amend or terminate the plan in limited circumstances. Our directors and executive officers may also buy or sell additional shares of our common stock outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Director Compensation

Non-Employee Director Compensation Policy

In connection with and effective upon the completion of our initial public offering, we adopted a non-employee director compensation policy to enable us to attract and retain, on a long-term basis, highly qualified non-employee directors. Under the policy, each director who is not an employee is paid cash compensation from and after the completion of our initial public offering as set forth below:

	Annual Retainer
Board of Directors:	
Members	$ 40,000
Additional retainer for non-executive chair	$ 30,000
Audit Committee:	
Members (other than chair)	$ 8,000
Retainer for chair	$ 16,000
Compensation Committee:	
Members (other than chair)	$ 6,000
Retainer for chair	$ 12,000
Nominating and Corporate Governance Committee:	
Members (other than chair)	$ 4,000
Retainer for chair	$ 8,000

In addition, the non-employee director compensation policy provides that, upon initial election to our board of directors, each non-employee director will be granted an option to purchase a number of shares equal to 0.1% of the total number of shares of our common stock issued and outstanding on the grant date, or the Initial Grant. The Initial Grant vests in equal monthly installments over three years from the grant date, subject to continued service as a director through the applicable vesting date. Furthermore, on the date of each annual meeting of stockholders following our initial public offering, each non-employee director who continues as a non-employee director following such meeting will be granted an annual option to purchase a number of shares equal to 0.05% of the total number of shares of our common stock issued and outstanding on the grant date, or the Annual Grant. The Annual Grant vests in 12 equal monthly installments, subject to continued service as a director through the applicable vesting date. Such awards are subject to full accelerated vesting upon the sale of the company.

We will reimburse all reasonable out-of-pocket expenses incurred by non-employee directors in attending meetings of the board of directors and committees.

2020 Director Compensation Table

The following table presents the total compensation for each person who served as a non-employee member of our board of directors during the year ended December 31, 2020. Other than as set forth in the table and described more fully below, we did not pay any compensation, make any equity awards or non-equity awards to or pay any other compensation to any of the non-employee members of our board of directors in 2020 for their services as members of the board of directors. Amounts paid to Dr. Reddy, our former President and Chief Executive Officer, for his service as an employee and a director during 2020 are presented in the “2020 Summary Compensation Table” above.

Name	Fees Earned or Paid in Cash ($)	Stock Awards ($)	Option Awards ($)(1)(2)	All Other Compensation ($)	Total ($)
Nicholas Galakatos, Ph.D	10,712	—	—	—	10,712
Dean Mitchell	15,076	—	413,278	—	428,354
Thomas Dyrberg, M.D.(3)	—	—	—	—	—
Stefan Vitorovic	10,315	—	—	—	10,315
Ari Brettman, M.D.(4)	—	—	—	—	—
Paul Medeiros(5)	—	—	—	—	—
Gregory Norden	11,109	—	437,887	—	448,996
Alfred Sandrock(6)	—	—	—	—	—
William Young	12,696	—	448,160	—	460,855

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(1) The amount reported represents the aggregate grant date fair value of stock options awarded during fiscal year 2020, calculated in accordance with FASB ASC Topic 718. Such grant date fair values do not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in this column are set forth in Note 10 of our consolidated financial statements included elsewhere in this Annual Report on Form 10-K. The amounts reported in this column reflect the accounting cost for these stock options and do not correspond to the actual economic value that may be received by our directors upon the exercise of the stock options or any sale of the underlying shares of common stock.

(2) As of December 31, 2020, Mr. Young held options to purchase 102,154 shares of our common stock, Mr. Norden held options to purchase 99,524 shares of our common stock, Mr. Mitchell held options to purchase 65,420 shares of our common stock, and Mr. Sandrock held options to purchase 27,980 shares of our common stock. As of December 31, 2020, none of our other directors (other than Dr. Reddy, whose outstanding equity awards as of December 31, 2020 are set forth in the Outstanding Equity Awards at Fiscal Year-End Table above) held any other outstanding equity awards.

(3) Dr. Dyrberg resigned as a director in October 2020.

(4) Dr. Brettman resigned as a director in October 2020.

(5) Mr. Medeiros resigned as a director in September 2020.

(6) Mr. Sandrock resigned as a director in March 2020.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

Equity Compensation Plan Information

The following table provides information as of December 31, 2020 regarding shares of common stock that may be issued under our equity compensation plans, consisting of our 2017 Stock Incentive Plan, our 2020 Stock Option and Incentive Plan and our 2020 Employee Stock Purchase Plan.

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted Average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plan (excluding securities referenced in column (a)) (c)
Equity compensation plans approved by security holders:	5,944,546(1)	$7.47	3,363,878(2)
Equity compensation plans not approved by security holders:	—	—	—
Total	5,944,546	$7.47	3,363,878

(1) Includes 5,944,546 shares of common stock issuable upon the exercise of outstanding options.
(2) As of December 31, 2020, there were 0 shares available for grant under the 2017 Plan, 3,036,776 shares available for grants under the 2020 Plan and 327,102 shares available for grants under the 2020 ESPP.

Security Ownership of Certain Beneficial Owners

The following table sets forth certain information known to us regarding beneficial ownership of our capital stock outstanding as of March 1, 2021 for:

- each person, or group of affiliated persons, who is known by us to be the beneficial owner of five percent or more of our outstanding common stock;
- each of our directors;
- each of our named executive officers; and
- all of our current directors and executive officers as a group.

We have determined beneficial ownership in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities as well as any shares of common stock that the person has the right to acquire within 60 days of March 1, 2021 through the exercise of stock options or other rights. These shares are deemed to be outstanding and beneficially owned by the person holding those options for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them. Each individual or entity shown on the table has furnished information with respect to beneficial ownership. Except as otherwise indicated below, the address of each officer, director and five percent stockholder listed below is c/o Praxis Precision Medicines, Inc., One Broadway, 16th Floor, Cambridge, MA 02142.

The percentage of beneficial ownership in the table below is based on 38,579,115 shares of common stock deemed to be outstanding as of March 1, 2021.

	COMMON STOCK BENEFICIALLY OWNED	
	SHARES	PERCENTAGE
5% or Greater Stockholders		
Entities affiliated with Blackstone (1)	8,501,487	22.0 %
FMR LLC (2)	4,163,834	10.8 %
Entities affiliated with Eventide (3)	3,513,081	9.1 %
Vida Ventures, LLC (4)	2,939,329	7.6 %
Novo Holdings A/S (5)	2,442,080	6.3 %
Directors, Named Executive Officers and Other Executive Officers		
Dean Mitchell	—	—
Nicholas Galakatos, Ph.D. (1)	—	—
Stefan Vitorovic (4)	2,939,329	7.6 %
Gregory Norden (6)	16,294	*
Kiran Reddy, M.D. (1)(7)	698,217	1.8 %
William Young (8)	27,980	*
Marcio Souza (9)	263,287	*
Bernard Ravina (10)	130,335	*
Nicole Sweeny	0	—
All executive officers and directors as a group (10 persons) (11)	4,083,479	10.4 %

* Represents beneficial ownership of less than one percent.

(1) Based solely on information contained in a Schedule 13G filed jointly by Clarus Lifesciences III, L.P., or Clarus, BSOF Parallel Master Fund L.P., Clarus Ventures III GP, L.P., Blackstone Clarus III L.L.C., Blackstone Strategic Opportunity Associates L.L.C., Blackstone Alternative Solutions L.L.C., Blackstone Holdings I L.P., Blackstone Holdings II L.P., Blackstone Holdings I/II GP L.L.C., The Blackstone Group Inc., Blackstone Group Management L.L.C. and Stephen A. Schwarzman with the SEC on February 16, 2021. Clarus directly holds 7,594,109 shares of common stock and BSOF Parallel Master Fund L.P. directly holds 907,378 shares of common stock. Clarus Ventures III GP, L.P. is the general partner of Clarus. Blackstone Clarus III L.L.C. is the general partner of Clarus GP. The sole member of Blackstone Clarus III L.L.C. is Blackstone Holdings II L.P. Blackstone Strategic Opportunity Associates L.L.C. is the general partner of BSOF Parallel Master Fund L.P. Blackstone Holdings II L.P. is the sole member of Blackstone Strategic Opportunity Associates L.L.C. Blackstone Alternative Solutions L.L.C. is the investment manager of BSOF Parallel Master Fund L.P. Blackstone Holdings I L.P. is the sole member of Blackstone Alternative Solutions L.L.C. The general partner of Blackstone Holdings I L.P. and Blackstone Holdings II L.P. is Blackstone Holdings I/II GP L.L.C. The sole member of Blackstone Holdings I/II GP L.L.C. is The Blackstone Group Inc. The sole holder of the Class C common stock of The Blackstone Group Inc. is Blackstone Group Management L.L.C. Blackstone Group Management L.L.C. is wholly-owned by Blackstone's senior managing directors and controlled by its founder, Stephen A. Schwarzman. Each of such entities and Mr. Schwarzman may be deemed to beneficially own the shares beneficially owned by the Blackstone Funds controlled by it or him, but each (other than the Blackstone Funds to the extent of their direct ownership) disclaims beneficial ownership of such shares. Each of Nicholas Galakatos, Ph.D. and Kiran Reddy, M.D., members of our board of directors, is an employee of an entity affiliated with the Blackstone Funds and each disclaims beneficial ownership of the shares beneficially owned by the Blackstone Funds. The address for each of Clarus and Clarus Ventures III GP, L.P. is c/o Clarus Ventures LLC, 101 Main Street, Suite 1210, Cambridge, MA 02142. The address for each of the other Blackstone entities and Mr. Schwarzman is c/o The Blackstone Group Inc., 345 Park Avenue, New York, NY 10154.

(2) Based solely on information contained in a Schedule 13G/A filed by FMR LLC with the SEC on February 10, 2021. FMR LLC has sole voting power with respect to 1,564,801 shares of common stock and sole dispositive power with respect to 4,163,834 shares of common stock. Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of

voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act ("Fidelity Funds") advised by Fidelity Management & Research Company ("FMR Co"), a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. FMR Co carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees. The address of FMR LLC is 245 Summer Street, Boston, MA 02210.

(3) Based solely on information contained in a Schedule 13G filed by Eventide Asset Management, LLC with the SEC on February 12, 2021. Eventide Asset Management, LLC, a Delaware limited liability company, is the beneficial owner of 3,513,081 common shares by virtue of being the investment adviser to registered investment companies. Mutual Fund Series Trust, On Behalf Of Eventide Gilead Fund, or Eventide Gilead, directly holds 1,566,708 shares of common stock and the Mutual Fund Series Trust, On Behalf Of Eventide Healthcare & Life Sciences Fund, or Eventide Healthcare, directly holds 1,946,373 shares of common stock. The address for both Eventide Healthcare and Eventide Gilead is One International Place, Suite 4210, Boston, Massachusetts 02110.

(4) Based solely on information contained in a Schedule 13G filed by Vida Ventures, LLC with the SEC on February 16, 2021. All shares are held directly by Vida Ventures, LLC, a United States limited liability company. Stefan Vitorovic is the Co-Founder and Managing Director of Vida Ventures, LLC and is also a member of our board of directors. VV Manager, LLC, or VV Manager, is the managing member of Vida. Stefan Vitorovic, Arjun Goyal, Fred Cohen, Arie Belldegrun and Leonard Potter are managers of VV Manager, and may be deemed to share voting and dispositive power over the shares held by Vida. The address of Vida is 40 Broad Street, Suite 201, Boston, Massachusetts 02109.

(5) Based solely on information contained in a Schedule 13G filed by Novo Holdings A/S, or Novo, with the SEC on February 8, 2021. All shares are held directly by Novo Holdings A/S, a Danish limited liability company that manages investments and financial assets. Novo Holdings A/S is wholly owned by Novo Nordisk Foundation, or the Foundation, a Danish commercial foundation. Novo Holdings A/S is the holding company in the group of Novo companies (currently comprised of Novo Nordisk A/S and Novozymes A/S) and is responsible for managing the Foundation's assets, including its financial assets. Based on the governance structure of Novo Holdings A/S and the Foundation, the Foundation is not deemed to have any beneficial ownership of the shares held by Novo Holdings A/S. The address for Novo Holdings A/S is Tuborg Havnevej 19, DK-2900 Hellerup, Denmark.

(6) Consists of 16,294 shares of common stock underlying options exercisable within 60 days of March 1, 2021.

(7) Consists of (i) 467,289 shares of common stock and (ii) 230,928 shares of common stock underlying options exercisable within 60 days of March 1, 2021.

(8) Consists of 27,980 shares of common stock underlying options exercisable within 60 days of March 1, 2021.

(9) Consists of (i) 24,450 shares of common stock and (ii) 238,837 shares of common stock underlying options exercisable within 60 days of March 1, 2021.

(10) Consists of (i) 56,021 shares of common stock and (ii) 74,314 shares of common stock underlying options exercisable within 60 days of March 1, 2021.

(11) Consists of (i) 3,487,089 shares of common stock and (ii) 596,390 shares of common stock underlying options exercisable within 60 days of March 1, 2021.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The following is a description of transactions or series of transactions since January 1, 2019 through the year ended December 31, 2020, to which we were or will be a party, in which:

- the amount involved in the transaction exceeds, or will exceed, $120,000; and
- in which any of our executive officers, directors or holders of five percent or more of any class of our capital stock, including their immediate family members or affiliated entities, had or will have a direct or indirect material interest.

Compensation arrangements for our named executive officers and our directors are described elsewhere in this Annual Report under "Executive Compensation" and "Director Compensation."

Series B-1 Preferred Stock Financing

In June 2019, we issued and sold to investors in a private placement an aggregate of 2,666,666 shares of our Series B-1 preferred stock at a price of $3.75 per share, for aggregate consideration of approximately $10.0 million, or our Series B-1 Preferred Stock Financing. The following table sets forth the aggregate number and purchase price of shares of our Series B-1 preferred stock purchased by related persons:

Purchaser	Shares of Series B-1 Preferred Stock Purchased	Aggregate Purchase Price ($)
Entities affiliated with Blackstone(1)	1,410,477	5,289,288
Novo Holdings A/S(2)	551,794	2,069,228
Vida Ventures, LLC(3)	551,794	2,069,228
Purdue Neuroscience Company(4)	133,334	500,003
Total	2,647,399	9,927,747

(1) Nicholas Galakatos, Ph.D., a member of our board of directors, was a managing director of Clarus, prior to its acquisition by Blackstone, and is a senior managing director of Blackstone. Ari Brettman, M.D., a former member of our board of directors, was a principal at Clarus, prior to its acquisition by Blackstone, and is a managing director of Blackstone.
(2) Thomas Dyrberg, M.D., a former member of our board of directors, is employed as a Managing Partner of Novo. Dr. Dyrberg is not deemed to hold any beneficial ownership or reportable pecuniary interest in the shares held by Novo.
(3) Stefan Vitorovic, a member of our board of directors, is a managing director of Vida Ventures, LLC.
(4) Purdue Neuroscience Company became a holder of five percent or more of our capital stock pursuant to our Series B-1 Preferred Financing, but is no longer a holder of five percent or more of our capital stock as of December 2021. Paul Medeiros, a former member of our board of directors, served as a senior vice president of Purdue Pharma L.P., an affiliate of Purdue Neuroscience Company, and resigned in September 2020.

Series C Preferred Stock Financing

From November 2019 through May 2020, we issued and sold to investors in a private placement an aggregate of 14,368,935 shares of our Series C preferred stock at a price of $5.15 per share, for aggregate consideration of approximately $74.0 million, or our Series C Preferred Stock Financing. The following table sets forth the aggregate number and purchase price of shares of our Series C preferred stock purchased by related persons:

Purchaser	Shares of Series C Preferred Stock Purchased	Aggregate Purchase Price ($)
Entities affiliated with Blackstone (1)	2,500,956	12,879,923
Novo Holdings A/S(2)	171,410	882,762
Vida Ventures, LLC(3)	171,410	882,762
Entities affiliated with Eventide(4)	3,883,496	20,000,004
Purdue Neuroscience Company(5)	59,333	305,565
Total	6,786,605	34,951,016

(1) Ari Brettman, M.D., a former member of our board of directors, and Nicholas Galakatos, Ph.D., a member of our board of directors, are a managing director and senior managing director, respectively, of Blackstone, an affiliate of Clarus and BSOF Parallel Master Fund L.P., or BSOF. Kiran Reddy, M.D., a member of our board of directors and our former president and chief executive officer, is a managing director of Blackstone, an affiliate of Clarus and BSOF.
(2) Thomas Dyrberg, M.D., a former member of our board of directors, is employed as a Managing Partner of Novo. Dr. Dyrberg is not deemed to hold any beneficial ownership or reportable pecuniary interest in the shares held by Novo.
(3) Stefan Vitorovic, a member of our board of directors, is a managing director of Vida Ventures, LLC.
(4) Mutual Fund Series Trust, On Behalf of Eventide Healthcare & Life Sciences Fund, or Eventide Healthcare, and Mutual Fund Series Trust, On Behalf of Eventide Gilead Fund, or Eventide Gilead, together became a holder of five percent or more of our capital stock pursuant to our Series C Preferred Stock Financing.
(5) Purdue Neuroscience Company is no longer a holder of five percent or more of our capital stock as of December 2020. Paul Medeiros, a former member of our board of directors, served as a senior vice president of Purdue Pharma L.P., an affiliate of Purdue Neuroscience Company, and resigned in September 2020.

Series C Repurchase

In February 2020 and March 2020, we repurchased from certain holders of five percent or more of our capital stock an aggregate of 5,825,243 shares of our Series C preferred stock at a price of $5.15 per share, for an aggregate consideration of approximately $30.0 million, or the Series C Repurchase. The following table sets forth the aggregate number and purchase price of shares of our Series C preferred stock repurchased by us from related persons:

Name of Holder	Shares of Series C Preferred Stock Repurchased	Aggregate Purchase Price ($)
Entities affiliated with RTW	2,912,622	15,000,003
Entities affiliated with Venrock	2,912,621	14,999,998
Total	5,825,243	30,000,001

Series C-1 Preferred Stock Financing

From July to August 2020, we issued and sold to investors in a private placement an aggregate of 19,444,453 shares of our Series C-1 preferred stock at a price of $5.67 per share, for aggregate consideration of approximately $110.3 million, or our Series C-1 Preferred Stock Financing. The following table sets forth the aggregate number and purchase price of shares of our Series C-1 preferred stock purchased by related persons:

Purchaser	Shares of Series C-1 Preferred Stock Purchased	Aggregate Purchase Price ($)
Entities affiliated with Blackstone (1)	352,734	2,000,002
Novo Holdings A/S (2)	352,734	2,000,002
Vida Ventures, LLC (3)	881,835	5,000,004
Entities affiliated with Eventide (4)	3,527,337	20,000,001
Marcio Souza (5)	44,092	250,002
Total	5,158,732	29,250,011

(1) Ari Brettman, M.D., a former member of our board of directors, and Nicholas Galakatos, Ph.D., a member of our board of directors, are a managing director and senior managing director, respectively, of Blackstone, an affiliate of Clarus and BSOF Parallel Master Fund L.P., or BSOF. Kiran Reddy, M.D. a member of our board of directors and our former president and chief executive officer, is a managing director of Blackstone, an affiliate of Clarus and BSOF.
(2) Thomas Dyrberg, M.D., a former member of our board of directors, is employed as a Managing Partner of Novo. Dr. Dyrberg is not deemed to hold any beneficial ownership or reportable pecuniary interest in the shares held by Novo.
(3) Stefan Vitorovic, a member of our board of directors, is a managing director of Vida Ventures, LLC.
(4) Mutual Fund Series Trust, On Behalf of Eventide Healthcare & Life Sciences Fund, or Eventide Healthcare, and Mutual Fund Series Trust, On Behalf of Eventide Gilead Fund, or Eventide Gilead, together hold five percent or more of our capital stock pursuant to our Series C-1 Preferred Stock Financing.
(5) Marcio Souza serves on our board of directors and is our President and Chief Executive Officer.

Participation in our Initial Public Offering

Certain holders of 5% or more of our capital stock purchased shares of our common stock in our initial public offering at the initial public offering price. The underwriting discount for the shares sold to such stockholders in the initial public offering was the same as the underwriting discount for the shares sold to the public. The following table sets forth the number of shares of our common stock purchased by 5% stockholders and their affiliate and the aggregate purchase price paid for such shares.

Purchaser	Shares of Common Stock Purchased	Aggregate Purchase Price ($)
Vida Ventures, LLC(1)	250,000	4,750,000
Entities affiliated with Eventide(2)	50,000	950,000
Total	300,000	5,700,000

(1) Stefan Vitorovic, a member of our board of directors, is a managing director of Vida Ventures, LLC.
(2) Mutual Fund Series Trust, On Behalf of Eventide Healthcare & Life Sciences Fund, or Eventide Healthcare, and Mutual Fund Series Trust, On Behalf of Eventide Gilead Fund, or Eventide Gilead, together hold five percent or more of our capital stock.

Agreements with Stockholders

In connection with our Series A preferred stock financing, our Series B preferred stock financing, our Series B-1 preferred stock financing, our Series C preferred stock financing and our Series C-1 preferred stock financing, we entered into investors' rights, voting and right of first refusal and co-sale agreements containing registration rights, information rights, voting rights and rights of first refusal, among other things, with certain holders of our preferred stock and certain holders of our common stock. All of the material provisions of these agreements terminated immediately prior to the completion of our initial public offering, other than the provisions relating to registration rights, which continued in effect following the completion of our initial public offering and entitle the holders of such rights to have us register their shares of our common stock for sale in the United States.

Commercial Agreements with Related Parties

Purdue

In December 2017, we and Purdue Neuroscience Company, or Purdue, a former holder of five percent or more of our capital stock, entered into a license agreement, described in the section of this Annual Report on Form 10-K captioned “Business—License Agreements.” Paul Medeiros, a former member of our board of directors, served as a senior vice president of Purdue Pharma L.P., an affiliate of Purdue Neuroscience Company, and resigned in September 2020.

RogCon

In December 2018, we entered into an agreement with RogCon Inc., or RogCon, pursuant to which we agreed to advance RogCon a deposit of up to $1.0 million related to the cooperation and license agreement described below. The amounts funded to RogCon under this agreement were applied towards the purchase price of the license agreement with RogCon described below.

In September 2019, we entered into a cooperation and license agreement with RogCon, described in the section of this Annual Report on Form 10-K captioned “Business—License Agreements.”

Alex Nemiroff, our General Counsel and Secretary, is a co-founder and chief executive officer of RogCon.

Other Arrangements

In March 2020, we reimbursed an affiliate of Blackstone approximately $164,000 in third-party expenses related to the recruitment of our chief executive officer.

Indemnification Agreements

We have entered into, and in the future plan to enter into, agreements to indemnify our directors and executive officers. These agreements, among other things, require us to indemnify these individuals for certain expenses (including attorneys’ fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on behalf of our company or that person’s status as a member of our board of directors to the maximum extent allowed under Delaware law.

Policies for Approval of Related Party Transactions

Our board of directors reviews and approves transactions with directors, officers and holders of five percent or more of our voting securities and their affiliates, each a related party. Prior to our initial public offering, the material facts as to the related party’s relationship or interest in the transaction are disclosed to our board of directors prior to their consideration of such transaction, and the transaction is not considered approved by our board of directors unless a majority of the directors who are not interested in the transaction approve the transaction. Further, when stockholders are entitled to vote on a transaction with a related party, the material facts of the related party’s relationship or interest in the transaction are disclosed to the stockholders, who must approve the transaction in good faith.

In connection with our initial public offering, we adopted a formal written policy that our executive officers, directors, holders of more than five percent of any class of our voting securities, and any member of the immediate family of and any entity affiliated with any of the foregoing persons, are not permitted to enter into a related party transaction with us without the prior consent of our audit committee, or other independent members of our board of directors in the event it is inappropriate for our audit committee to review such transaction due to a conflict of interest. Any request for us to enter into a transaction with an executive officer, director, holders of more than 5% of any class of our voting securities, or any of their immediate family members or affiliates, in which the amount involved exceeds $120,000 must first be presented to our audit committee for review, consideration and approval. In approving or rejecting any such proposal, our audit committee considers the relevant facts and circumstances available and deemed relevant to our audit committee, including, but not limited to, whether the transaction will be on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related party’s interest in the transaction.

Director Independence

The Nasdaq Stock Market LLC, or Nasdaq, Marketplace Rules, or the Nasdaq Listing Rules, require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq Listing Rules require that, subject to specified exceptions and phase in periods following the initial public offering, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under the Nasdaq Listing Rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee: (1) accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries; or (2) otherwise be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of the director, including any consulting, advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In connection with our initial public offering, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors, with the exception of Marcio Souza and Kiran Reddy, is an "independent director" as defined under the Nasdaq Listing Rules. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our common stock by each non-employee director.

Item 14. Principal Accounting Fees and Services

The Audit Committee has selected Ernst & Young LLP as our independent registered public accounting firm for the years ended December 31, 2020 and 2019. In addition to retaining Ernst & Young LLP to audit our consolidated financial statements for years ended December 31, 2020 and 2019, we may engage the firm from time to time during the year to perform other services.

	For the Year Ended	
	2020	2019
Audit fees(1)	$1,297,000	$206,000
Audit-related fees(2)	—	—
Tax fees(3)	14,000	12,000
All other fees(4)	—	—
Total fees	$1,311,000	$218,000

(1) ***Audit fees*** consist of fees for professional services rendered in connection with the audit of our annual consolidated financial statements, the review of the interim consolidated financial statements included in quarterly reports, services rendered in connection with the our initial public offering, and services that are normally provided by Ernst & Young LLP, such as comfort letters, in connection with statutory and regulatory filings or engagements.

(2) There were no ***audit-related fees*** billed in 2020 or 2019.

(3) ***Tax fees*** consist of fees for professional services rendered for tax return preparation and tax advisory services.

(4) There were no ***other fees*** billed in 2020 or 2019.

Audit Committee Pre-Approval Policy and Procedures

The Audit Committee has adopted a policy requiring pre-approval of all audit and non-audit related services to be performed by our independent auditor regardless of amount. These services may include audit services, audit-related services, tax services and other related services. Ernst & Young LLP and management are required to periodically report to the Audit Committee regarding the extent of services provided by Ernst & Young LLP in accordance with this pre-approval and the fees for the services performed to date. The Audit Committee may also pre-approve particular services on a case-by-case basis.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

1. Financial Statements

For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page 139 of this Annual Report on Form 10-K, incorporated into this Item by reference.

2. Financial Statement Schedules

Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

3. Exhibits

The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K. The exhibits listed in the Exhibit Index are incorporated by reference herein.

Item 16. Form 10–K Summary

None.

Exhibit Index

3.1	Amended and Restated Certificate of Incorporation of Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on October 20, 2020)
3.2	Amended and Restated Bylaws of Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on October 20, 2020)
4.1	Specimen Stock Certificate Evidencing the Shares of Common Stock (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
4.2	Fourth Amended and Restated Investors' Rights Agreement among Praxis Precision Medicines, Inc. and certain of its stockholders, effective as of July 24, 2020 (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)
4.3*	Description of Securities of Praxis Precision Medicines, Inc.
10.1	Form of Director Indemnification Agreement, as amended (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.2	Form of Officer Indemnification Agreement (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)
10.3#*	Praxis Precision Medicines, Inc. 2017 Stock Incentive Plan, as amended, and form of award agreements thereunder
10.4#	Praxis Precision Medicines, Inc. 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.5#	Form of Incentive Stock Option Agreement under the 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.6#	Form of Non-Qualified Stock Option Agreement for Company Employees under the 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.7#	Form of Non-Qualified Stock Option Agreement for Non-Employee Directors under the 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.8#	Form of Restricted Stock Award Agreement under the 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.9#	Form of Restricted Stock Award Agreement for Company Employees under the 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.10#	Form of Restricted Stock Award Agreement for Non-Employee Directors under the 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.11#	Praxis Precision Medicines, Inc. 2020 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.12#	Form of Amended and Restated Employment Agreement (incorporated by reference to Exhibit 10.11 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39620) filed on November 23, 2020)
10.13#	Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.14†	License Agreement, dated December 31, 2017, by and between Purdue Neuroscience Company and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)
10.15†	Cooperation and License Agreement, dated September 11, 2019, by and between RogCon Inc. and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.15 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)

10.16†	Research Collaboration, Option and License Agreement, dated September 11, 2019, by and between Ionis Pharmaceuticals, Inc. and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.16 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)
10.17	Sublease, dated October 4, 2018, by and between Highland Capital Partners, LLC and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.17 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)
10.18	Consent to Sublease, First Amendment of Lease and Amendment, dated November 2, 2018, by and among Highland Capital Partners, LLC, MIT One Broadway, LLC and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.18 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)
21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)
23.1*	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Interim Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1**	Certification of Principal Executive Officer and Interim Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS*	Inline XBRL Instance Document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

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*	Filed herewith.
**	The certifications furnished in Exhibit 32.1 hereto are deemed to accompany this Annual Report on Form 10-K and will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended. Such certifications will not be deemed to be incorporated by reference into any filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.
#	Indicates a management contract or any compensatory plan, contract or arrangement.
†	Portions of this exhibit (indicated by asterisks) have been omitted in accordance with the rules of the Securities and Exchange Commission.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

PRAXIS PRECISION MEDICINES, INC.

Date: March 17, 2021

By: /s/ Marcio Souza
Marcio Souza
Chief Executive Officer

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Marcio Souza and Alex Nemiroff, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Name	Title	Date
/s/ Marcio Souza Marcio Souza	Chief Executive Officer and Director (Principal Executive Officer)	March 17, 202
/s/ Lauren Mastrocola Lauren Mastrocola	Principal Accounting Officer and Interim Principal Financial Officer	March 17, 202
/s/ Dean Mitchell Dean Mitchell	Chairman of the Board	March 17, 202
/s/ Nicholas Galakatos Nicholas Galakatos, Ph.D.	Director	March 17, 202
/s/ Gregory Norden Gregory Norden	Director	March 17, 202
/s/ Kiran Reddy Kiran Reddy, M.D.	Director	March 17, 202
/s/ Stefan Vitorovic Stefan Vitorovic	Director	March 17, 202
/s/ William Young William Young	Director	March 17, 202

Exhibit 4.3

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

The common stock, par value $0.0001 per share ("common stock"), of Praxis Precision Medicines, Inc. ("Praxis," "we," or "our") is registered under Section 12 of the Securities Exchange Act of 1934, as amended. The following description sets forth certain general terms and provisions of our common stock. These descriptions are in all respects subject to and qualified in their entirety by, and should be read in conjunction with, the applicable provisions of our amended and restated certificate of incorporation (our "certificate of incorporation") and our amended and restated bylaws (our "bylaws"), each of which is incorporated herein by reference and copies of which are incorporated by reference as exhibits to our most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission, and the applicable provisions of General Corporation Law of the State of Delaware (the "DGCL").

Authorized Capital Stock

We are authorized to issue 150,000,000 shares of common stock and 10,000,000 shares of preferred stock, par value $0.0001 per share ("preferred stock").

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock.

Preferred Stock

Our board of directors is authorized, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our Company or other corporate action.

Registration Rights

Pursuant to the terms of our Fourth Amended and Restated Investors' Rights Agreement, dated as of July 24, 2020 (our "Investors' Rights Agreement"), certain of our stockholders are entitled to rights with respect to the registration of their shares (which we refer to herein as "registrable securities") under the Securities Act of 1933, as amended (the "Securities Act"), including demand registration rights, short-form registration rights and piggyback registration rights.

Demand Registration Rights

The holders of our registrable securities are entitled to demand registration rights. Under the terms of the Investors' Rights Agreement, we will be required, upon the written request of holders of at least a majority of the securities eligible for registration then outstanding, and if anticipated aggregate offering price, net of related fees and expenses, would exceed $5 million, we will be required to file a registration statement covering all securities eligible

for registration that our stockholders request to be included in such registration. We are required to effect only two registrations pursuant to this provision of the Investors' Rights Agreement in any twelve-month period.

Short-Form Registration Rights

The holders of our registrable securities are also entitled to short form registration rights. Pursuant to the Investors' Rights Agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of stockholders holding at least a majority of the securities eligible for registration then outstanding, we will be required to file a Form S-3 registration restatement with respect to outstanding securities of such stockholders having an anticipated aggregate offering, net of related fees and expenses, of at least $3 million. We are required to effect only two registrations in any twelve-month period pursuant to this provision of the Investors' Rights Agreement. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Piggyback Registration Rights

The holders of our registrable securities are also entitled to piggyback registration rights. If we register any of our securities either for our own account or for the account of other security holders, the holders of these shares are entitled to include their shares in the registration. Subject to certain exceptions contained in the Investors' Rights Agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

The Investors' Rights Agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The demand registration rights and short-form registration rights granted under the Investors' Rights Agreement will terminate on the earliest to occur of: (i) on the fifth anniversary of the completion of our initial public offering or (ii) a merger, sale or liquidation of our company.

Anti-Takeover Effects of our Certificate of Incorporation and Bylaws and Delaware Law

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Undesignated Preferred Stock

Our certificate of incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control.

Exclusive Jurisdiction for Certain Actions

Our bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers and employees to us or our stockholders, (iii) any action asserting a claim against us or any of our current or former directors, officers, or other employees or stockholders arising pursuant to any provision of the DGCL, our certificate of incorporation or our bylaws, (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or our bylaws or (v) any action asserting a claim against us or any of our current or former directors or officers or other employees that is governed by the internal affairs doctrine.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the DGCL. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

In general, Section 203 defines a business combination to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an "interested stockholder" as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Certificate of Incorporation and Bylaws

Provisions of our certificate of incorporation and our bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our certificate of incorporation and bylaws:

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that the authorized number of directors may be changed only by resolution adopted by a majority of the board of directors;
- provide that the board of directors or any individual director may only be removed with cause and the affirmative vote of the holders of at least 66.67% of the voting power of all of our then outstanding common stock;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law or subject to the rights of holders of preferred stock as designated from time to time, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide our board of directors into three classes;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent or electronic transmission;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner and also specify requirements as to the form and content of a stockholder's notice;
- do not provide for cumulative voting rights (therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- provide that special meetings of our stockholders may be called only by our board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office; and
- provide that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers and employees to us or our stockholders, (iii) any action asserting a claim against us or any of our current or former directors, officers, or other employees or stockholders arising pursuant to any provision of the DGCL, our certificate of incorporation or our bylaws, (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or our bylaws or (v) any action asserting a claim against us or any of our current or former directors or officers or other employees that is governed by the internal affairs doctrine.

The amendment of any of these provisions included in our certificate of incorporation, with the exception of the ability of our board of directors to issue shares of preferred stock and designate any rights, preferences and privileges thereto, would require the affirmative vote of the majority of all of our then outstanding common stock. The amendment of any of these provisions included in our bylaws would require the affirmative vote of the holders of at least 66.67% of the voting power of our then outstanding common stock.

Exhibit 10.3

PRAXIS PRECISION MEDICINES, INC.

2017 STOCK INCENTIVE PLAN

1. Purpose

The purpose of this 2017 Stock Incentive Plan (the "Plan") of Praxis Precision Medicines, Inc., a Delaware corporation (the "Company"), is to advance the interests of the Company's stockholders by enhancing the Company's ability to attract, retain and motivate persons who are expected to make important contributions to the Company and by providing such persons with equity ownership opportunities and performance-based incentives that are intended to better align the interests of such persons with those of the Company's stockholders. Except where the context otherwise requires, the term "Company" shall include any of the Company's present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "Code") and any other business venture (including, without limitation, joint venture or limited liability company) in which the Company has a controlling interest, as determined by the Board of Directors of the Company (the "Board").

2. Eligibility

All of the Company's employees, officers, directors, consultants and advisors are eligible to be granted options, restricted stock, restricted stock units ("RSUs") and other stock-based awards (each, an "Award") under the Plan. Each person who receives an Award under the Plan is deemed a "Participant".

3. Administration and Delegation

(a) Administration by Board of Directors. The Plan will be administered by the Board. The Board shall have authority to grant Awards and to adopt, amend and repeal such administrative rules, guidelines and practices relating to the Plan as it shall deem advisable. The Board may construe and interpret the terms of the Plan and any A ward agreements entered into under the Plan. The Board may correct any defect, supply any omission or reconcile any inconsistency in the Plan or any Award in the manner and to the extent it shall deem expedient to carry the Plan into effect and it shall be the sole and final judge of such expediency. All decisions by the Board shall be made in the Board's sole discretion and shall be final and binding on all persons having or claiming any interest in the Plan or in any Award. No director or person acting pursuant to the authority delegated by the Board shall be liable for any action or determination relating to or under the Plan made in good faith.

(b) Appointment of Committees. To the extent permitted by applicable law, the Board may delegate any or all of its powers under the Plan to one or more committees or subcommittees of the Board (a "Committee"). All references in the Plan to the "Board" shall mean the Board or a Committee of the Board or the officers referred to in Section 3(c) to the extent that the Board's powers or authority under the Plan have been delegated to such Committee or officers. The Board may abolish any Committee at any time and re-vest in itself any previously delegated authority.

(c) Delegation to Officers. To the extent permitted by applicable law, the Board may delegate to one or more officers of the Company the power to grant Awards (subject to any limitations under the Plan) to employees or officers of the Company or any of its present or future subsidiary corporations and to exercise such other powers under the Plan as the Board may determine, *provided* that the Board shall fix the terms of the Awards to be granted by such officers (including the exercise price of such Awards, which may include a formula by which the exercise price will be determined) and the maximum number of shares subject to Awards that the officers may grant; *provided further, however*, that no officer shall be authorized to grant Awards to any "executive officer" of the Company (as defined by Rule 3b-7 under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) or to any "officer" of the Company (as defined by Rule 16a-1 under the Exchange Act). The Board may rescind any such delegation at any time and re-vest in itself any previously delegated authority.

4. Stock Available for Awards.

(a) Number of Shares. Subject to adjustment under Section 8 hereof, Awards may be made under the Plan covering up to five hundred twenty-five thousand (525,000) shares of common stock of the Company (the "Common Stock"). If any Award expires, lapses, or is terminated, surrendered or canceled without having been fully exercised or is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at or below the original issuance price), in any case in a manner that results in any shares of Common Stock covered by such Award not being issued or being so reacquired by the Company, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock delivered (whether by actual delivery or attestation) or tendered to the Company by a Participant to satisfy the applicable exercise or purchase price of an Award and/or to satisfy any applicable tax withholding obligation (including shares retained by the Company from the Award being exercised or purchased and/or creating the tax obligation) shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options (as hereinafter defined), the foregoing provisions shall be subject to any limitations under the Code. Shares of Common Stock issued under the Plan may consist in whole or in part of authorized but unissued shares, shares purchased on the open market, or treasury shares. At no time while there is any Option (as defined below) outstanding and held by a Participant who was a resident of the State of California on the date of grant of such Option, shall the total number of shares of Common Stock issuable upon exercise of all outstanding options and the total number of shares provided for under any stock bonus or similar plan or agreement of the Company exceed the applicable percentage as calculated in accordance with the conditions and exclusions of Section 260.140.45 of the California Code of Regulations (the "California Regulations"), based on the shares of the Company which are outstanding at the time the calculation is made.

(b) Substitute Awards. In connection with a merger or consolidation of an entity with the Company or the acquisition by the Company of property or stock of an entity, the Board may grant Awards in substitution for any options or other stock or stock-based awards granted prior to such merger or consolidation by such entity or an affiliate thereof. Substitute Awards may be granted on such terms as the Board deems appropriate in the circumstances, notwithstanding any limitations on Awards contained in the Plan. Substitute Awards shall not count against the overall share limit set forth in Section 4(a) hereof, except as may be required by reason of Section 422 and related provisions of the Code.

5. Stock Options

(a) General. The Board may grant options to purchase Common Stock (each, an "Option") and determine the number of shares of Common Stock to be covered by each Option, the exercise price of each Option and the conditions and limitations applicable to the exercise of each Option, including conditions relating to applicable federal or state securities laws, as it considers necessary or advisable. An Option that is not intended to be an Incentive Stock Option (as hereinafter defined) shall be designated a "Nonstatutory Stock Option".

(b) Incentive Stock Options. An Option that the Board intends to be an "incentive stock option" as defined in Section 422 of the Code (an "Incentive Stock Option") shall only be granted to employees of the Company, any of the Company's present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Code, and any other entities the employees of which are eligible to receive Incentive Stock Options under the Code. All Options intended to qualify as Incentive Stock Options shall be subject to and shall be construed consistently with the requirements of Section 422 of the Code, and without limiting generality of the foregoing, such Options shall be deemed to include terms that comply with the eligibility standards described section 422(b) of the Code. Subject to the remaining provisions of this Section 5(b), if an Option intended to qualify as an Incentive Stock Option does not so qualify, the Board may, at its discretion, amend the Plan and Award with respect to such Option so that such Option qualifies as an Incentive Stock Option. To the extent that the aggregate Fair Market Value (determined at the time of grant) of Common Stock with respect to which Incentive Stock Options are exercisable for the first time by any Participant during any calendar year (under all plans of the Company and any affiliates) exceeds $100,000 (or such other limit established in the Code) or otherwise does not comply with the rules governing Incentive Stock Options, the Options or portions thereof that exceed such limit (according to the order in which they were granted) or otherwise do not comply with the rules will be treated as Nonstatutory Stock Options, notwithstanding any contrary provision of the applicable Award. Neither the Company nor the Board shall have any liability to a Participant, or any other party, (i) if an Option (or any part thereof) which is intended to qualify as an Incentive

Stock Option fails to qualify as such or (ii) for any action or omission by the Company or Board that causes an Option not to qualify as an Incentive Stock Option, including without limitation the conversion of an Incentive Stock Option to a Nonstatutory Stock Option or the grant of an Option intended as an Incentive Stock Option that fails to satisfy the requirements under the Code applicable to an Incentive Stock Option.

(c) Exercise Price. The Board shall establish the exercise price of each Option and specify the exercise price in the applicable option agreement. The exercise price shall be not less than 100% of the Fair Market Value on the date the Option is granted. In the case of an Incentive Stock Option granted to an employee who, at the time of grant of the Option, owns (or is treated as owning under Section 424 of the Code) stock representing more than 10% of the voting power of all classes of stock of the Company (or a "parent corporation" or "subsidiary corporation" thereof within the meaning of Sections 424(e) or 424(f) of the Code, respectively), the per share exercise price shall be no less than 110% of the Fair Market Value on the date the Option is granted

(d) Duration of Options. Each Option shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable option agreement, *provided* that the term of any Option shall not exceed ten years. In the case of an Incentive Stock Option granted to an employee who, at the time of grant of the Option, owns (or is treated as owning under Section 424 of the Code) stock representing more than 10% of the voting power of all classes of stock of the Company (or a "parent corporation" or "subsidiary corporation" thereof within the meaning of Sections 424(e) or 424(f) of the Code, respectively), the term of the Option shall not exceed five years.

(e) Exercise of Option; Notification of Disposition. Options may be exercised by delivery to the Company of a written notice of exercise signed by the proper person or by any other form of notice (including electronic notice) approved by the Board together with payment in full as specified in Section 5(f) for the number of shares for which the Option is exercised. Unless otherwise determined by the Board, an Option may not be exercised for a fraction of a share of Common Stock. Shares of Common Stock subject to the Option will be delivered by the Company as soon as practicable following exercise. If an Option is designated as an Incentive Stock Option, the Participant shall give prompt notice to the Company of any disposition or other transfer of any shares of Common Stock acquired from the Option if such disposition or transfer is made (i) within two years from the grant date with respect to such Option or (ii) within one year after the transfer of such shares to the Participant (other than any such disposition made in connection with a Reorganization Event). Such notice shall specify the date of such disposition or other transfer and the amount realized, in cash, other property, assumption of indebtedness or other consideration, by the Participant in such disposition or other transfer.

(f) Payment Upon Exercise. Common Stock purchased upon the exercise of an Option granted under the Plan shall be paid for as follows:

(1) in cash or by check, payable to the order of the Company;

(2) when the Common Stock is registered under the Exchange Act, except as may otherwise be provided in the applicable option agreement, by (i) delivery of an irrevocable and unconditional undertaking by a creditworthy broker acceptable to the Company to deliver promptly to the Company sufficient funds to pay the exercise price and any required tax withholding or (ii) delivery by the Participant to the Company of a copy of irrevocable and unconditional instructions to a creditworthy broker acceptable to the Company to deliver promptly to the Company cash or a check sufficient to pay the exercise price and any required tax withholding;

(3) when the Common Stock is registered under the Exchange Act and to the extent provided for in the applicable option agreement or approved by the Board, in its sole discretion, by delivery (either by actual delivery or attestation) of shares of Common Stock owned by the Participant valued at their fair market value as determined by (or in a manner approved by) the Board ("Fair Market Value"), *provided* (i) such method of payment is then permitted under applicable law, (ii) such Common Stock, if acquired directly from the Company, was owned by the Participant for such minimum period of time, if any, as may be established by the Board in its discretion and (iii) such Common Stock is not subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements;

(4) to the extent permitted by applicable law and provided for in the applicable option agreement or approved by the Board, in its sole discretion, by (i) delivery of a promissory note of the Participant to the Company on terms determined by the Board, or (ii) payment of such other lawful consideration as the Board may determine; or

(5) by any combination of the above permitted forms of payment.

(g) Early Exercise of Options. The Board may provide in the terms of an option agreement that the Participant may exercise an Option in whole or in part prior to the full vesting of the Option in exchange for unvested shares of Restricted Stock (as defined below) with respect to any unvested portion of the Option so exercised. Shares of Restricted Stock acquired upon the exercise of any unvested portion of an Option shall be subject to such terms and conditions as the Board shall determine.

6. Restricted Stock; Restricted Stock Units

(a) General. The Board may grant Awards entitling recipients to acquire shares of Common Stock ("Restricted Stock"), subject to the right of the Company to repurchase all or part of such shares at their issue price or other stated or formula price (or to require forfeiture of such shares if issued at no cost) from the recipient in the event that conditions specified by the Board in the applicable Award are not satisfied prior to the end of the applicable restriction period or periods established by the Board for such Award. Instead of granting Awards for Restricted Stock, the Board may grant Awards entitling the recipient to receive shares of Common Stock or cash to be delivered at the time such Award vests ("Restricted Stock Units") (Restricted Stock and Restricted Stock Units are each referred to herein as a "Restricted Stock Award").

(b) Terms and Conditions for All Restricted Stock Awards. The Board shall determine and set forth in the applicable award agreement the terms and conditions of a Restricted Stock Award, including the conditions for vesting and repurchase (or forfeiture) and the issue price, if any.

(c) Additional Provisions Relating to Restricted Stock.

(1) Dividends. Participants holding shares of Restricted Stock will be entitled to all ordinary cash dividends paid with respect to such shares to the extent such dividends have a record date that is on or after the date on which the Participant to whom such Restricted Stock is granted becomes the record holder of such Restricted Stock, unless otherwise provided by the Board. Unless otherwise provided by the Board, if any dividends or distributions are paid in shares, or consist of a dividend or distribution to holders of Common Stock other than an ordinary cash dividend, the shares or other property will be subject to the same restrictions on transferability and forfeitability as the shares of Restricted Stock with respect to which they were paid. Each dividend payment will be made as provided in the applicable award agreement, but no later than the end of the calendar year in which the dividends are paid to shareholders of that class of stock or, if later, the 15th day of the third month following the later of (A) the date the dividends are paid to shareholders of that class of stock and (B) the date the dividends are no longer subject to forfeiture.

(2) Stock Certificates. The Company may require that any stock certificates issued in respect of shares of Restricted Stock shall be deposited in escrow by the Participant, together with a stock power endorsed in blank, with the Company (or its designee). At the expiration of the applicable restriction periods, the Company (or such designee) shall deliver the certificates no longer subject to such restrictions to the Participant or if the Participant has died, to the beneficiary designated, in a manner determined by the Board, by a Participant to receive amounts due or exercise rights of the Participant in the event of the Participant's death (the "Designated Beneficiary"). In the absence of an effective designation by a Participant, "Designated Beneficiary" shall mean the Participant's estate.

(d) Additional Provisions Relating to Restricted Stock Units.

(1) Settlement. Upon the vesting of a Restricted Stock Unit, the Participant shall be entitled to receive from the Company one share of Common Stock or an amount of cash or other property equal to the Fair Market Value of one share of Common Stock on the settlement date, as the Board shall determine and as provided in the applicable award agreement. The Board may provide that settlement of Restricted Stock Units shall occur upon or as soon as reasonably practicable after the vesting of the Restricted Stock Units or

shall instead be deferred, on a mandatory basis or at the election of the Participant, in a manner that complies with Section 409A of the Code.

(2) Voting Rights. A Participant shall have no voting rights with respect to any Restricted Stock Units unless and until shares are delivered in settlement thereof.

(3) Dividend Equivalents. To the extent provided by the Board, a grant of Restricted Stock Units may provide a Participant with the right to receive Dividend Equivalents. Dividend Equivalents may be paid currently or credited to an account for the Participant, may be settled in cash and/or shares of Common Stock and may be subject to the same restrictions on transfer and forfeitability as the Restricted Stock Units with respect to which the Dividend Equivalents are paid, as determined by the Board, subject, in each case, to such terms and conditions as the Board shall establish and set forth in the applicable award agreement. "Dividend Equivalents" means a right granted to a Participant to receive the equivalent value (in cash or shares of Common Stock) of dividends paid on shares of Common Stock.

7. Other Stock-Based Awards

Other Awards of shares of Common Stock, and other Awards that are valued in whole or in part by reference to, or are otherwise based on, shares of Common Stock or other property, may be granted hereunder to Participants ("Other Stock-Based Awards"), including without limitation stock appreciation rights ("SARs") and Awards entitling recipients to receive shares of Common Stock to be delivered in the future. Such Other Stock-Based Awards shall also be available as a form of payment in the settlement of other Awards granted under the Plan or as payment in lieu of compensation to which a Participant is otherwise entitled. Other Stock-Based Awards may be paid in shares of Common Stock or cash, as the Board shall determine. Subject to the provisions of the Plan, the Board shall determine the terms and conditions of each Other Stock-Based Award, including any purchase price, transfer restrictions, vesting conditions and other terms and conditions applicable thereto.

8. Adjustments for Changes in Common Stock and Certain Other Events

(a) In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of Common Stock other than an ordinary cash dividend, (i) the number and class of securities available under this Plan, (ii) the number and class of securities and exercise price per share of each outstanding Option, (iii) the number of shares subject to and the repurchase price per share subject to each outstanding Restricted Stock Award, and (iv) the terms of each other outstanding Award shall be equitably adjusted by the Company (or substituted Awards may be made, if applicable) in the manner determined by the Board; *provided* that, unless otherwise determined by the Board, such changes to the Options shall comply with section 1.424-1 of the Treasury Regulations. Without limiting the generality of the foregoing, in the event the Company effects a split of the Common Stock by means of a stock dividend and the exercise price of and the number of shares subject to an outstanding Option are adjusted as of the date of the distribution of the dividend (rather than as of the record date for such dividend), then an optionee who exercises an Option between the record date and the distribution date for such stock dividend shall be entitled to receive, on the distribution date, the stock dividend with respect to the shares of Common Stock acquired upon such Option exercise, notwithstanding the fact that such shares were not outstanding as of the close of business on the record date for such stock dividend.

(b) Reorganization Events.

(1) Definition. A "Reorganization Event" means the consummation of: (i) the dissolution or liquidation of the Company, (ii) the sale of all or substantially all of the assets of the Company on a consolidated basis to an unrelated person or entity, (iii) a merger, reorganization or consolidation pursuant to which the holders of the Company's outstanding voting power immediately prior to such transaction do not own a majority of the outstanding voting power of the surviving or resulting entity (or its ultimate parent, if applicable), (iv) the acquisition of all or a majority of the outstanding voting stock of the Company in a single transaction or a series of a related transactions by a person or group of persons, or (v) any other acquisition of the business of the Company, as determined by the Board; *provided*, *however*, that the first firm commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, covering the offer and sale by the Company of its equity securities,

as a result of or following which the Common Stock shall be public, any subsequent public offering or another capital raising event, or a merger effected solely to change the Company's domicile shall not constitute a "Reorganization Event."

(2) Consequences of a Reorganization Event on Awards Other than Restricted Stock Awards. In connection with a Reorganization Event, the Board may take any one or more of the following actions as to all or any (or any portion of) outstanding Awards other than Restricted Stock Awards on such terms as the Board determines: (i) provide that Awards shall be assumed, or substantially equivalent Awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof); provided that, unless otherwise determined by the Board, such assumption or substitution of the Options shall comply with section 1.424-1 of the Treasury Regulations, (ii) upon written notice to a Participant, provide that the Participant's unexercised Awards will terminate immediately prior to the consummation of such Reorganization Event unless exercised by the Participant within a specified period following the date of such notice, (iii) provide that outstanding Awards shall become exercisable, realizable, or deliverable, or restrictions applicable to an Award shall lapse, in whole or in part prior to or upon such Reorganization Event, (iv) in the event of a Reorganization Event under the terms of which holders of Common Stock will receive upon consummation thereof a cash payment for each share surrendered in the Reorganization Event (the "Acquisition Price"), make or provide for a cash payment to a Participant equal to the excess, if any, of (A) the Acquisition Price times the number of shares of Common Stock subject to the Participant's Awards (to the extent the exercise price does not exceed the Acquisition Price) over (B) the aggregate exercise price of all such outstanding Awards and any applicable tax withholdings, in exchange for the termination of such Awards, (v) provide that, in connection with a liquidation or dissolution of the Company, Awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise price thereof and any applicable tax withholdings) and (vi) any combination of the foregoing. In taking any of the actions permitted under this Section 8(b), the Board shall not be obligated by the Plan to treat all Awards, all Awards held by a Participant, or all Awards of the same type, identically.

For purposes of clause (i) above, an Option shall be considered assumed if, following consummation of the Reorganization Event, the Option confers the right to purchase, for each share of Common Stock subject to the Option immediately prior to the consummation of the Reorganization Event, the consideration (whether cash, securities or other property) received as a result of the Reorganization Event by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Reorganization Event (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Common Stock); *provided*, *however*, that if the consideration received as a result of the Reorganization Event is not solely common stock of the acquiring or succeeding corporation (or an affiliate thereof), the Company may, with the consent of the acquiring or succeeding corporation, provide for the consideration to be received upon the exercise of Options to consist solely of common stock of the acquiring or succeeding corporation (or an affiliate thereof) equivalent in value (as determined by the Board) to the per share consideration received by holders of outstanding shares of Common Stock as a result of the Reorganization Event.

(3) Consequences of a Reorganization Event on Restricted Stock Awards. Upon the occurrence of a Reorganization Event other than a liquidation or dissolution of the Company, the repurchase and other rights of the Company under each outstanding Restricted Stock Award shall inure to the benefit of the Company's successor and shall, unless the Board determines otherwise, apply to the cash, securities or other property which the Common Stock was converted into or exchanged for pursuant to such Reorganization Event in the same manner and to the same extent as they applied to the Common Stock subject to such Restricted Stock Award. Upon the occurrence of a Reorganization Event involving the liquidation or dissolution of the Company, except to the extent specifically provided to the contrary in the instrument evidencing any Restricted Stock Award or any other agreement between a Participant and the Company, all restrictions and conditions on all Restricted Stock A wards then outstanding shall automatically be deemed terminated or satisfied.

9. General Provisions Applicable to Awards

(a) Transferability of Awards. Except as the Board may otherwise determine or provide in an Award, Awards shall not be sold, assigned, transferred, pledged or otherwise encumbered by the person to whom they are granted, either voluntarily or by operation of law, except by will or the laws of descent and distribution or, other than in the case of an Incentive Stock Option, pursuant to a qualified domestic relations order, and, during the life of the Participant, shall be exercisable only by the Participant. References to a Participant, to the extent relevant in the context, shall include references to authorized transferees.

(b) Documentation. Each Award shall be evidenced in such form (written, electronic or otherwise) as the Board shall determine. Each Award may contain terms and conditions in addition to those set forth in the Plan.

(c) Board Discretion. Except as otherwise provided by the Plan, each Award may be made alone or in addition or in relation to any other Award. The terms of each Award need not be identical, and the Board need not treat Participants uniformly.

(d) Termination of Status. The Board shall determine the effect on an Award of the disability, death, retirement, termination or other cessation of employment, authorized leave of absence or other change in the employment or other status of a Participant and the extent to which, and the period during which, the Participant, or the Participant's legal representative, conservator, guardian or Designated Beneficiary, may exercise rights under the Award.

(e) Withholding. The Company shall not be obligated to deliver certificates, release from forfeiture, otherwise recognize a Participant's unrestricted ownership in an Award or the cash or property proceeds therefrom, until the Company satisfies all applicable federal, state, and local or other income and employment tax withholding obligations. In its sole discretion, the Company may satisfy such withholding obligations by any of the following means or by a combination of such means: (i) causing the Participant to tender to the Company cash payment; (ii) withholding cash from an Award settled in cash; (iii) withholding from amounts otherwise payable by the Company to the Participant, including but not limited to additional withholding on the Participant's salary or wages, or from proceeds from the sale of Common Stock issued pursuant to an Award; (iv) delivery of shares of Common Stock, including shares retained from the Award creating the tax obligation, valued at their Fair Market Value; *provided*, *however*, except as otherwise provided by the Board, that the total tax withholding where stock is being used to satisfy such tax obligations cannot exceed the Company's minimum statutory withholding obligations (based on minimum statutory withholding rates for federal and state tax purposes, including payroll taxes, that are applicable to such supplemental taxable income), and *provided*, *further*, shares surrendered to satisfy tax withholding requirements cannot be subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements; or (v) by such other method as determined by the Board.

(f) Amendment of Award.

(1) The Board may amend, modify or terminate any outstanding Award, including but not limited to, substituting therefor another Award of the same or a different type, changing the date of exercise or settlement, and converting an Incentive Stock Option to a Nonstatutory Stock Option. The Participant's consent to such action shall be required unless (i) the Board determines that the action, taking into account any related action, would not materially and adversely affect the Participant's rights under the Plan, (ii) the change is permitted under Section 8 hereof, or (iii) the change is to ensure that an Option intended to qualify as an Incentive Stock Option qualifies as such.

(2) The Board may, without stockholder approval, amend any outstanding Award granted under the Plan to provide an exercise price per share that is lower than the then-current exercise price per share of such outstanding Award. The Board may also, without stockholder approval, cancel any outstanding award (whether or not granted under the Plan) and grant in substitution therefor new Awards under the Plan covering the same or a different number of shares of Common Stock and having an exercise price per share lower than the then-current exercise price per share of the cancelled award.

(g) Conditions on Delivery of Stock. The Company will not be obligated to deliver any shares of Common Stock pursuant to the Plan or to remove restrictions from shares previously delivered under the Plan until (i) all conditions of the Award have been met or removed to the satisfaction of the Company, (ii) in the opinion of the Company's counsel, all other legal matters in connection with the issuance and delivery of such shares have been

satisfied, including any applicable securities laws and any applicable stock exchange or stock market rules and regulations, and (iii) the Participant has executed and delivered to the Company such representations or agreements as the Company may consider appropriate to satisfy the requirements of any applicable laws, rules or regulations. The inability of the Company to obtain authority from any regulatory body having jurisdiction, which authority is determined by the Board to be necessary to the lawful issuance and sale of any securities hereunder, shall relieve the Company of any liability in respect of the failure to issue or sell such shares at to which such requisite authority shall not have been obtained.

(h) Acceleration. The Board may at any time provide that any Award shall become immediately exercisable in full or in part, free of some or all restrictions or conditions, or otherwise realizable in full or in part, as the case may be.

10. Miscellaneous

(a) No Right To Employment or Other Status. No person shall have any claim or right to be granted an Award, and the grant of an Award shall not be construed as giving a Participant the right to continued employment or any other relationship with the Company. The Company expressly reserves the right at any time to dismiss or otherwise terminate its relationship with a Participant free from any liability or claim under the Plan, except as expressly provided in the applicable Award.

(b) No Rights As Stockholder. Subject to the provisions of the applicable Award, no Participant or Designated Beneficiary shall have any rights as a stockholder with respect to any shares of Common Stock to be distributed with respect to an Award until becoming the record holder of such shares. Notwithstanding any other provision of the Plan, unless otherwise determined by the Board or required by any applicable laws, the Company shall not be required to deliver to any Participant certificates evidencing shares of Common Stock issued in connection with any Award and instead such shares of Common Stock may be recorded in the books of the Company (or, as applicable, its transfer agent or stock plan administrator). The Company may place legends on any stock certificates issued under the Plan deemed necessary or appropriate by the Board in order to comply with applicable laws.

(c) Effective Date and Term of Plan. The Plan shall become effective on the date on which it is adopted by the Board. No Awards shall be granted under the Plan after the expiration of 10 years from the earlier of (i) the date on which the Plan was adopted by the Board or (ii) the date the Plan was approved by the Company's stockholders, but Awards previously granted may extend beyond that date.

(d) Amendment of Plan. The Board may amend, suspend or terminate the Plan or any portion thereof at any time; *provided* that if at any time the approval of a Company stockholder is required as to any modification or amendment under Section 422 of the Code or any successor provision with respect to Incentive Stock Options, the Board may not effect such modification or amendment without the consent of the affected Participant. Unless otherwise specified in the amendment, any amendment to the Plan adopted in accordance with this Section 10(d) shall apply to, and be binding on the holders of, all Awards outstanding under the Plan at the time the amendment is adopted, provided the Board determines that such amendment does not materially and adversely affect the rights of Participants under the Plan.

(e) Authorization of Sub-Plans. The Board may from time to time establish one or more sub-plans under the Plan for purposes of satisfying applicable blue sky, securities or tax laws of various jurisdictions. The Board shall establish such sub-plans by adopting supplements to this Plan containing (i) such limitations on the Board's discretion under the Plan as the Board deems necessary or desirable or (ii) such additional terms and conditions not otherwise inconsistent with the Plan as the Board shall deem necessary or desirable. All supplements adopted by the Board shall be deemed to be part of the Plan, but each supplement shall apply only to Participants within the affected jurisdiction and the Company shall not be required to provide copies of any supplement to Participants in any jurisdiction which is not the subject of such supplement.

(f) Compliance with Code Section 409A. Unless otherwise expressly provided for in an Award, the Plan and Award will be interpreted to the greatest extent possible in a manner that makes the Plan and the Awards granted hereunder exempt from Section 409A of the Code, and, to the extent not so exempt, in compliance with Section 409A of the Code. If the Board determines that any Award granted hereunder is not exempt from and is

therefore subject to Section 409A of the Code, the Award will incorporate the terms and conditions necessary to avoid the consequences specified in Section 409A(a)(1) of the Code, and to the extent an Award is silent on terms necessary for compliance, such terms as deemed necessary by the Board in its sole discretion are hereby incorporated by reference into the Award. Without limiting the generality of the foregoing, if shares of Common Stock are publicly traded, and if a Participant holding an Award that constitutes "deferred compensation" under Section 409A of the Code is a "specified employee" for purposes of Section 409A of the Code, no distribution or payment of any amount that is due because of a "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) will be issued or paid before the date that is six (6) months following the date of such Participant's "separation from service" or, if earlier, the date of the Participant's death, unless such distribution or payment can be made in a manner that complies with Section 409A of the Code, and any amounts so deferred will be paid in a lump sum on the day after such six (6) month period elapses, with the balance paid thereafter on the original schedule. The Company shall have no liability to a Participant, or any other party, if an Award that is intended to be exempt from, or compliant with, Section 409A of the Code is not so exempt or compliant or for any other action taken by the Board.

(g) Governing Law. The provisions of the Plan and all Awards made hereunder shall be governed by and interpreted in accordance with the laws of the State of Delaware, excluding choice-of-law principles of the law of such state that would require the application of the laws of a jurisdiction other than such state.

(h) Data Privacy. As a condition of receipt of any Award, each Participant explicitly and unambiguously consents to the collection, use and transfer, in electronic or other form, of personal data as described in this paragraph by and among, as applicable, the Company and its subsidiaries and affiliates for the exclusive purpose of implementing, administering and managing the Participant's participation in the Plan. The Company and its subsidiaries and affiliates may hold certain personal information about a Participant, including but not limited to, the Participant's name, home address and telephone number, date of birth, social security or insurance number or other identification number, salary, nationality, job title(s), any shares of stock held in the Company or any of its subsidiaries and affiliates, details of all Awards, in each case, for the purpose of implementing, managing and administering the Plan and Awards (the "Data"). The Company and its subsidiaries and affiliates may transfer the Data amongst themselves as necessary for the purpose of implementation, administration and management of a Participant's participation in the Plan, and the Company and its subsidiaries and affiliates may each further transfer the Data to any third parties assisting the Company in the implementation, administration and management of the Plan. These recipients may be located in the Participant's country, or elsewhere, and the Participant's country may have different data privacy laws and protections than the recipients' country. Through acceptance of an Award, each Participant authorizes such recipients to receive, possess, use, retain and transfer the Data, in electronic or other form, for the purposes of implementing, administering and managing the Participant's participation in the Plan, including any requisite transfer of such Data as may be required to a broker or other third party with whom the Company or the Participant may elect to deposit any shares of Common Stock. The Data related to a Participant will be held only as long as is necessary to implement, administer, and manage the Participant's participation in the Plan. A Participant may, at any time, view the Data held by the Company with respect to such Participant, request additional information about the storage and processing of the Data with respect to such Participant, recommend any necessary corrections to the Data with respect to the Participant or refuse or withdraw the consents herein in writing, in any case without cost, by contacting his or her local human resources representative. The Company may cancel Participant's ability to participate in the Plan and, in the Board's discretion, the Participant may forfeit any outstanding Awards if the Participant refuses or withdraws his or her consents as described herein. For more information on the consequences of refusal to consent or withdrawal of consent, Participants may contact their local human resources representative.

(i) Restrictions on Shares; Claw-back Provisions. Shares of Common Stock acquired in respect of Awards shall be subject to such terms and conditions as the Board shall determine, including, without limitation, restrictions on the transferability of shares of Common Stock, the right of the Company to repurchase shares of Common Stock, the right of the Company to require that shares of Common Stock be transferred in the event of certain transactions, tag-along rights, bring-along rights, redemption and co-sale rights and voting requirements. Such terms and conditions may be additional to those contained in the Plan and may, as determined by the Board, be contained in the applicable Award Agreement or in an exercise notice, stockholders' agreement or in such other agreement as the Board shall determine, in each case in a form determined by the Board. The issuance of such shares of Common

Stock shall be conditioned on the Participant's consent to such terms and conditions and the Participant's entering into such agreement or agreements. All Awards (including any proceeds, gains or other economic benefit actually or constructively received by Participant upon any receipt or exercise of any Award or upon the receipt or resale of any shares of Common Stock underlying the Award) shall be subject to the provisions of any claw-back policy implemented by the Company, including, without limitation, any claw-back policy adopted to comply with the requirements of the Dodd-Frank Wall Street Reform and Consumer Protection Act and any rules or regulations promulgated thereunder, to the extent set forth in such claw-back policy and/or in the applicable Award Agreement.

PRAXIS PRECISION MEDICINES, INC.

2017 STOCK INCENTIVE PLAN

CALIFORNIA SUPPLEMENT

Pursuant to Section 10(e) of the Plan, the Board has adopted this supplement for purposes of satisfying the requirements of Section 25102(o) of the California Law:

Any Awards granted under the Plan to a Participant who is a resident of the State of California on the date of grant (a "California Participant") shall be subject to the following additional limitations, terms and conditions:

1. Additional Limitations on Options.

(a) Minimum Vesting Rate. Except in the case of Options granted to California Participants who are officers, directors, managers, consultants or advisors of the Company or its affiliates (which Options may become exercisable at whatever rate is determined by the Board), Options granted to California Participants shall become exercisable at a rate of not less than 20% per year over five years from the date of grant; *provided*, *that*, such Options may be subject to such reasonable forfeiture conditions as the Board may choose to impose and which are not inconsistent with Section 260.140.41 of the California Regulations.

(b) Minimum Exercise Price. The exercise price of Options granted to California Participants may not be less than 85% of the Fair Market Value of the Common Stock on the date of grant in the case of a Nonstatutory Stock Option or less than 100% of the Fair Market Value of the Common Stock on the date of grant in the case of an Incentive Stock Option; *provided*, *however*, that if the California Participant is a person who owns stock possessing more than 10% of the total combined voting power of all classes of stock of the Company or its parent or subsidiary corporations, the exercise price shall be not less than 110% of the Fair Market Value of the Common Stock on the date of grant.

(c) Maximum Duration of Options. No Options granted to California Participants shall have a term in excess of 10 years measured from the Option grant date.

(d) Minimum Exercise Period Following Termination. Unless a California Participant's employment is terminated for cause (as defined by applicable law, the terms of any contract of employment between the Company and such Participant, or in the instrument evidencing the grant of such Participant's Option), in the event of termination of employment of such Participant, such Participant shall have the right to exercise an Option, to the extent that he or she was otherwise entitled to exercise such Option on the date employment terminated, as follows: (i) at least six months from the date of termination, if termination was caused by such Participant's death or "permanent and total disability" (within the meaning of Section 22(e)(3) of the Code) and (ii) at least 30 days from the date of termination, if termination was caused other than by such Participant's death or "permanent and total disability" (within the meaning of Section 22(e)(3) of the Code).

(e) Limitation on Repurchase Rights. If an Option granted to a California Participant gives the Company the right to repurchase shares of Common Stock issued pursuant to the Plan upon termination of employment of such Participant, the terms of such repurchase right must comply with Section 260.140.41(k) of the California Regulations.

2. Additional Limitations for Restricted Stock Awards.

(a) Minimum Purchase Price. The purchase price for a Restricted Stock Award granted to a California Participant shall be not less than 85% of the Fair Market Value of the Common Stock at the time such Participant is granted the right to purchase shares under the Plan or at the time the purchase is consummated; *provided*, *however*, that if such Participant is a person who owns stock possessing more than 10% of the total combined voting power or value of all classes of stock of the Company or its parent or subsidiary corporations, the purchase price shall be not less than 100% of the Fair Market Value of the Common Stock at the time such Participant is granted the right to purchase shares under the Plan or at the time the purchase is consummated.

(b) Limitation of Repurchase Rights. If a Restricted Stock Award granted to a California Participant gives the Company the right to repurchase shares of Common Stock issued pursuant to the Plan upon termination of

employment of such Participant, the terms of such repurchase right must comply with Section 260.140.42(h) of the California Regulations.

3. Additional Limitations for Other Stock-Based Awards. The terms of all Awards granted to a California Participant under Section 7 of the Plan shall comply, to the extent applicable, with Section 260.140.41 or Section 260.140.42 of the California Regulations.

4. Additional Requirement to Provide Information to California Participants. The Company shall provide to each California Participant and to each California Participant who acquires Common Stock pursuant to the Plan, not less frequently than annually, copies of annual financial statements (which need not be audited). The Company shall not be required to provide such statements to key employees whose duties in connection with the Company assure their access to equivalent information.

5. Additional Limitations on Timing of Awards. No Award granted to a California Participant shall become exercisable, vested or realizable, as applicable to such Award, unless the Plan has been approved by the holders of a majority of the Company's outstanding voting securities within 12 months before or after the date the Plan was adopted by the Board.

6. Additional Limitations Relating to Definition of Fair Market Value. For purposes of Section 1(b) and 2(a) of this supplement, "Fair Market Value" shall be determined in a manner not inconsistent with Section 260.140.50 of the California Regulations.

7. Additional Restriction Regarding Recapitalizations, Stock Splits, Etc. For purposes of Section 8 of the Plan, in the event of a stock split, reverse stock split, stock dividend, recapitalization, combination, reclassification or other distribution of the Company's securities, the number of securities allocated to each California Participant must be adjusted proportionately and without the receipt by the Company of any consideration from any California Participant.

PRAXIS PRECISION MEDICINES, INC.
AMENDMENT NO. 1 TO
2017 STOCK INCENTIVE PLAN

The Praxis Precision Medicines, Inc. 2017 Stock Incentive Plan, as amended (the "Plan") is hereby amended by the Board of Directors as follows:

Section 4(a) of the Plan is hereby amended to increase the total number of Shares (as defined in the Plan) reserved and available for issuance under the Plan such that Section 4(a) of the Plan, as so amended, shall read in its entirety as follows:

4. Stock Available for Awards.

(a) Number of Shares. Subject to adjustment under Section 8 hereof, Awards may be made under the Plan covering up to 4,794,211 shares of common stock of the Company (the "Common Stock"). If any Award expires, lapses, or is terminated, surrendered or canceled without having been fully exercised or is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at or below the original issuance price), in any case in a manner that results in any shares of Common Stock covered by such Award not being issued or being so reacquired by the Company, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock delivered (whether by actual delivery or attestation) or tendered to the Company by a Participant to satisfy the applicable exercise or purchase price of an Award and/or to satisfy any applicable tax withholding obligation (including shares retained by the Company from the Award being exercised or purchased and/or creating the tax obligation) shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options (as hereinafter defined), the foregoing provisions shall be subject to any limitations under the Code. Shares of Common Stock issued under the Plan may consist in whole or in part of authorized but unissued shares, shares purchased on the open market, or treasury shares. At no time while there is any Option (as defined below) outstanding and held by a Participant who was a resident of the State of California on the date of grant of such Option, shall the total number of shares of Common Stock issuable upon exercise of all outstanding options and the total number of shares provided for under any stock bonus or similar plan or agreement of the Company exceed the applicable percentage as calculated in accordance with the conditions and exclusions of Section 260.140.45 of the California Code of Regulations (the "California Regulations"), based on the shares of the Company which are outstanding at the time the calculation is made.

ADOPTED BY BOARD OF DIRECTORS: October 2, 2018

ADOPTED BY STOCKHOLDERS: October 2, 2018

PRAXIS PRECISION MEDICINES, INC.
AMENDMENT NO. 2 TO
2017 STOCK INCENTIVE PLAN

The Praxis Precision Medicines, Inc. 2017 Stock Incentive Plan, as amended (the "Plan") is hereby amended by the Board of Directors as follows:

Section 4(a) of the Plan is hereby amended to increase the total number of Shares (as defined in the Plan) reserved and available for issuance under the Plan such that Section 4(a) of the Plan, as so amended, shall read in its entirety as follows:

"4. Stock Available for Awards.

(a) Number of Shares. Subject to adjustment under Section 8 hereof, Awards may be made under the Plan covering up to 5,043,824 shares of common stock of the Company (the "Common Stock"). If any Award expires, lapses, or is terminated, surrendered or canceled without having been fully exercised or is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at or below the original issuance price), in any case in a manner that results in any shares of Common Stock covered by such Award not being issued or being so reacquired by the Company, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock delivered (whether by actual delivery or attestation) or tendered to the Company by a Participant to satisfy the applicable exercise or purchase price of an Award and/or to satisfy any applicable tax withholding obligation (including shares retained by the Company from the Award being exercised or purchased and/or creating the tax obligation) shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options (as hereinafter defined), the foregoing provisions shall be subject to any limitations under the Code. Shares of Common Stock issued under the Plan may consist in whole or in part of authorized but unissued shares, shares purchased on the open market, or treasury shares. At no time while there is any Option (as defined below) outstanding and held by a Participant who was a resident of the State of California on the date of grant of such Option, shall the total number of shares of Common Stock issuable upon exercise of all outstanding options and the total number of shares provided for under any stock bonus or similar plan or agreement of the Company exceed the applicable percentage as calculated in accordance with the conditions and exclusions of Section 260.140.45 of the California Code of Regulations (the "California Regulations"), based on the shares of the Company which are outstanding at the time the calculation is made."

ADOPTED BY BOARD OF DIRECTORS: November 18, 2019

ADOPTED BY STOCKHOLDERS: November 18, 2019

PRAXIS PRECISION MEDICINES, INC.
AMENDMENT NO. 3 TO
2017 STOCK INCENTIVE PLAN

The Praxis Precision Medicines, Inc. 2017 Stock Incentive Plan, as amended (the "Plan") is hereby amended by the Board of Directors as follows:

A. Section 8(b)(2) of the Plan is hereby amended by adding the following sentence at the end of such Section 8(b)(2):

For purposes of clauses (i) and (iv) above, any escrow, holdback, indemnification, earn-out or similar provisions in the definitive documents effecting such Reorganization Event may apply to any assumed Awards or payments in respect of Awards to the same extent and in the same manner as such provisions apply to holders of Common Stock.

ADOPTED BY BOARD OF DIRECTORS: December 10, 2019

ADOPTED BY STOCKHOLDERS: December 10, 2019

PRAXIS PRECISION MEDICINES, INC.
AMENDMENT NO. 4 TO
2017 STOCK INCENTIVE PLAN

The Praxis Precision Medicines, Inc. 2017 Stock Incentive Plan, as amended (the "Plan") is hereby amended by the Board of Directors as follows:

Section 4(a) of the Plan is hereby amended to increase the total number of Shares (as defined in the Plan) reserved and available for issuance under the Plan such that Section 4(a) of the Plan, as so amended, shall read in its entirety as follows:

4. Stock Available for Awards.

(a) Number of Shares. Subject to adjustment under Section 8 hereof, Awards may be made under the Plan covering up to 8,366,813 shares of common stock of the Company (the "Common Stock"). If any Award expires, lapses, or is terminated, surrendered or canceled without having been fully exercised or is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at or below the original issuance price), in any case in a manner that results in any shares of Common Stock covered by such Award not being issued or being so reacquired by the Company, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock delivered (whether by actual delivery or attestation) or tendered to the Company by a Participant to satisfy the applicable exercise or purchase price of an Award and/or to satisfy any applicable tax withholding obligation (including shares retained by the Company from the Award being exercised or purchased and/or creating the tax obligation) shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options (as hereinafter defined), the foregoing provisions shall be subject to any limitations under the Code. Shares of Common Stock issued under the Plan may consist in whole or in part of authorized but unissued shares, shares purchased on the open market, or treasury shares. At no time while there is any Option (as defined below) outstanding and held by a Participant who was a resident of the State of California on the date of grant of such Option, shall the total number of shares of Common Stock issuable upon exercise of all outstanding options and the total number of shares provided for under any stock bonus or similar plan or agreement of the Company exceed the applicable percentage as calculated in accordance with the conditions and exclusions of Section 260.140.45 of the California Code of Regulations (the "California Regulations"), based on the shares of the Company which are outstanding at the time the calculation is made.

ADOPTED BY BOARD OF DIRECTORS: June 3, 2020

ADOPTED BY STOCKHOLDERS: June 5, 2020

CHARTER AMENDMENT APPROVED: June 5, 2020

PRAXIS PRECISION MEDICINES, INC.
AMENDMENT NO. 5 TO
2017 STOCK INCENTIVE PLAN

The Praxis Precision Medicines, Inc. 2017 Stock Incentive Plan, as amended (the "Plan") is hereby amended by the Board of Directors as follows:

Section 4(a) of the Plan is hereby amended to increase the total number of Shares (as defined in the Plan) reserved and available for issuance under the Plan such that Section 4(a) of the Plan, as so amended, shall read in its entirety as follows:

4. Stock Available for Awards.

(a) Number of Shares. Subject to adjustment under Section 8 hereof, Awards may be made under the Plan covering up to 12,706,813 shares of common stock of the Company (the "Common Stock"). If any Award expires, lapses, or is terminated, surrendered or canceled without having been fully exercised or is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at or below the original issuance price), in any case in a manner that results in any shares of Common Stock covered by such Award not being issued or being so reacquired by the Company, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock delivered (whether by actual delivery or attestation) or tendered to the Company by a Participant to satisfy the applicable exercise or purchase price of an Award and/or to satisfy any applicable tax withholding obligation (including shares retained by the Company from the Award being exercised or purchased and/or creating the tax obligation) shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options (as hereinafter defined), the foregoing provisions shall be subject to any limitations under the Code. Shares of Common Stock issued under the Plan may consist in whole or in part of authorized but unissued shares, shares purchased on the open market, or treasury shares. At no time while there is any Option (as defined below) outstanding and held by a Participant who was a resident of the State of California on the date of grant of such Option, shall the total number of shares of Common Stock issuable upon exercise of all outstanding options and the total number of shares provided for under any stock bonus or similar plan or agreement of the Company exceed the applicable percentage as calculated in accordance with the conditions and exclusions of Section 260.140.45 of the California Code of Regulations (the "California Regulations"), based on the shares of the Company which are outstanding at the time the calculation is made.

ADOPTED BY BOARD OF DIRECTORS: September 2, 2020

ADOPTED BY STOCKHOLDERS: September 2, 2020

CHARTER AMENDMENT APPROVED: September 2, 2020

PRAXIS PRECISION MEDICINES, INC.

Restricted Stock Agreement
Granted Under 2017 Stock Incentive Plan

AGREEMENT made this [____] day of [_____, 20[●], between Praxis Precision Medicines, Inc., a Delaware corporation (the "Company"), and [_____] (the "Participant").

For valuable consideration, receipt of which is acknowledged, the parties hereto agree as follows:

1. Purchase of Shares.

The Company shall issue and sell to the Participant, and the Participant shall purchase from the Company, subject to the terms and conditions set forth in this Agreement and in the Company's 2017 Stock Incentive Plan (the "Plan"), [_____] shares (the "Shares") of common stock of the Company ("Common Stock"), at a purchase price of $[___] per share. The aggregate purchase price for the Shares shall be paid by the Participant by check payable to the order of the Company or such other method as may be acceptable to the Company. Upon receipt by the Company of payment for the Shares, the Company shall issue to the Participant one or more certificates in the name of the Participant for that number of Shares purchased by the Participant. The Participant agrees that the Shares shall be subject to the purchase options set forth in Sections 2 and 5 of this Agreement and the restrictions on Transfer (as defined below) set forth in Section 4 of this Agreement. Subject to applicable law, the Participant agrees to become party to any voting agreement, drag along agreement, right of first refusal and co-sale agreement, or any other agreement approved by the Board of Directors of the Company and creating obligations of or among any stockholder of the Company that holds in the aggregate shares of Common Stock equal to or greater than the aggregate number of shares of Common Stock held by the Participant, in each case calculated on a fully-diluted basis, as the Company may request.

2. Purchase Option.

(a) In the event that the Participant ceases to be employed by the Company for any reason or no reason, with or without cause, prior to the fourth anniversary of the Vesting Commencement Date (as defined below), the Company shall have the right and option (the "Purchase Option") to purchase from the Participant, for a sum of $[_____] per share (the "Option Price"), some or all of the Unvested Shares (as defined below).

"Unvested Shares" means the total number of Shares multiplied by the Applicable Percentage at the time the Purchase Option becomes exercisable by the Company, with the resulting number of Shares rounded down to the nearest whole Share. The "Applicable Percentage" shall be (i) 100% during the period ending on the first anniversary of the Vesting Commencement Date, (ii) 75% less 2.0833% for each month of employment completed by the Participant with the Company from and after the first anniversary of the Vesting Commencement Date, and (iii) zero on or after the fourth anniversary of the Vesting Commencement Date. For purposes of this Agreement, "Vesting Commencement Date" shall mean [_____].

[*Additional provision at the discretion of the Board:* Additionally, if following a Company Sale (as defined below), the Participant is terminated without Cause (as defined below), then 100% of the Shares that are not then vested shall become vested. If the Participant is party to an employment or severance agreement with the Company that contains a definition of "cause" for termination of employment, "Cause" shall have the meaning ascribed to such term in such agreement. Otherwise, "Cause" shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant shall be considered to have been discharged for Cause if the Company determines, within 30 days after the Participant's resignation, that discharge for cause was warranted.]

(b) If the Participant is employed by a parent or subsidiary of the Company, any references in this Agreement to employment with the Company or termination of employment by or with the Company shall instead be deemed to refer to such parent or subsidiary.

3. Exercise of Purchase Option and Closing.

(a) The Company may exercise the Purchase Option by delivering or mailing to the Participant (or his estate) a written notice of exercise of the Purchase Option in connection with or following Participant's termination of employment or service with the Company (an "Exercise Notice"). Such Exercise Notice shall specify the number of Shares to be purchased and may not be given after the 90 day period following a written request from the Participant (following Participant's termination of employment or service with the Company) that the Company indicate whether or not it plans to exercise the Purchase Option. If and to the extent the Purchase Option is not exercised within such 90-day period (if requested by the Participant pursuant to the foregoing sentence), the Purchase Option shall expire and terminate effective upon the expiration of such 90-day period.

(b) Within 10 days after delivery to the Participant of the Exercise Notice pursuant to subsection (a) above, the Participant (or his estate) shall, pursuant to the provisions of the Joint Escrow Instructions referred to in Section 7 below, tender to the Company at its principal offices the certificate or certificates representing the Shares which the Company has elected to purchase in accordance with the terms of this Agreement, duly endorsed in blank or with duly endorsed stock powers attached thereto, all in form suitable for the Transfer of such Shares to the Company. Promptly following its receipt of such certificate or certificates, the Company shall pay to the Participant the aggregate Option Price for such Shares (provided that any delay in making such payment shall not invalidate the Company's exercise of the Purchase Option with respect to such Shares).

(c) After the time at which any Shares are required to be delivered to the Company for Transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Shares, but shall, in so far as permitted by law, treat the Company as the owner of such Shares.

(d) The Option Price may be payable, at the option of the Company, in cancellation of all or a portion of any outstanding indebtedness of the Participant to the Company or in cash (by check) or both.

(e) The Company shall not purchase any fraction of a Share upon exercise of the Purchase Option, and any fraction of a Share resulting from a computation made pursuant to Section 2 of this Agreement shall be rounded to the nearest whole Share (with any one-half Share being rounded upward).

(f) The Company may assign its Purchase Option to one or more persons or entities.

4. Restrictions on Transfer.

(a) The Participant shall not sell, assign, transfer, pledge, hypothecate or otherwise dispose of, by operation of law or otherwise (collectively "Transfer") any Shares, or any interest therein, that are subject to the Purchase Option, except that the Participant may Transfer such Shares (i) to or for the benefit of any spouse, children, parents, uncles, aunts, siblings, grandchildren and any other relatives approved by the Board of Directors (collectively, "Approved Relatives") or to a trust established solely for the benefit of the Participant and/or Approved Relatives, provided that such Shares shall remain subject to this Agreement (including without limitation the restrictions on Transfer set forth in this Section 4, the Purchase Option and the right of first refusal set forth in Section 5) and such permitted transferee shall, as a condition to such Transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Agreement or (ii) subject to Section 9(b) hereof, as part of the sale of all or substantially all of the shares of capital stock of the Company (including pursuant to a merger or consolidation), provided that, in accordance with the Plan, the securities or other property received by the Participant in connection with such transaction shall remain subject to this Agreement.

(b) The Participant shall not Transfer any Shares, or any interest therein, that are no longer subject to the Purchase Option, except in accordance with Section 5 below.

(c) The Company shall not be required (1) to Transfer on its books any of the Shares which shall have been sold or Transferred in violation of any of the provisions set forth in this Agreement or the Company's Bylaws, or (2) to treat as owner of such Shares or to pay dividends to any transferee to whom any such Shares shall have been so sold or Transferred.

5. Right of First Refusal.

(a) If the Participant proposes to Transfer any Shares that are no longer subject to the Purchase Option (either because they are no longer Unvested Shares or because the Purchase Option expired unexercised), then the Participant shall first give written notice of the proposed Transfer (the "Transfer Notice") to the Company. The Transfer Notice shall name the proposed transferee and state the number of such Shares the Participant proposes to Transfer (the "Offered Shares"), the price per share and all other material terms and conditions of the Transfer.

(b) For 30 days following its receipt of such Transfer Notice, the Company shall have the option to purchase all or part of the Offered Shares at the price and upon the terms set forth in the Transfer Notice. In the event the Company elects to purchase all or part of the Offered Shares, it shall give written notice of such election to the Participant within such 30-day period. Within 10 days after his or her receipt of such notice, the Participant shall tender to the Company at its principal offices the certificate or certificates representing the Offered Shares to be purchased by the Company, duly endorsed in blank by the Participant or with duly endorsed stock powers attached thereto, all in a form suitable for Transfer of the Offered Shares to the Company. Promptly following receipt of such certificate or certificates, the Company shall deliver or mail to the Participant a check in payment of the purchase price for such Offered Shares; provided that if the terms of payment set forth in the Transfer Notice were other than cash against delivery, the Company may pay for the Offered Shares on the same terms and conditions as were set forth in the Transfer Notice; and provided further that any delay in making such payment shall not invalidate the Company's exercise of its option to purchase the Offered Shares.

(c) If the Company does not elect to acquire all of the Offered Shares, the Participant may, within the 30-day period following the expiration of the option granted to the Company under subsection (b) above, Transfer the Offered Shares which the Company has not elected to acquire to the proposed transferee, provided that such Transfer shall not be on terms and conditions more favorable to the transferee than those contained in the Transfer Notice. Notwithstanding any of the above, all Offered Shares Transferred pursuant to this Section 5 shall remain subject to this Agreement (including without limitation the restrictions on Transfer set forth in Section 4 and the right of first refusal set forth in this Section 5) and such transferee shall, as a condition to such Transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Agreement.

(d) After the time at which the Offered Shares are required to be delivered to the Company for Transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Offered Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Offered Shares, but shall, insofar as permitted by law, treat the Company as the owner of such Offered Shares.

(e) The following transactions shall be exempt from the provisions of this Section 5:

(1) a Transfer of Shares to or for the benefit of any Approved Relatives, or to a trust established solely for the benefit of the Participant and/or Approved Relatives;

(2) any Transfer pursuant to an effective registration statement filed by the Company under the Securities Act of 1933, as amended (the "Securities Act"); and

(3) the sale of all or substantially all of the outstanding shares of capital stock of the Company (including pursuant to a merger or consolidation);

provided, however, that in the case of a Transfer pursuant to clause (1) above, such Shares shall remain subject to this Agreement (including without limitation the restrictions on Transfer set forth in Section 4 and the right of first refusal set forth in this Section 5) and such transferee shall, as a condition to such Transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Agreement.

(f) The Company may assign its rights to purchase Offered Shares in any particular transaction under this Section 5 to one or more persons or entities.

(g) The provisions of this Section 5 shall terminate upon the earlier of the following events:

(1) the closing of the sale of shares of Common Stock in an underwritten public offering pursuant to an effective registration statement filed by the Company under the Securities Act; or

(2) the sale of all or substantially all of the outstanding shares of capital stock, assets or business of the Company, by merger, consolidation, sale of assets or otherwise (other than a merger or consolidation in which all or substantially all of the individuals and entities who were beneficial owners of the Company's voting securities immediately prior to such transaction beneficially own, directly or indirectly, a majority (determined on an as-converted basis) of the outstanding securities entitled to vote generally in the election of directors of the resulting, surviving or acquiring corporation in such transaction) (a "Company Sale").

6. Agreement in Connection with Initial Public Offering.

The Participant hereby agrees that it will not, without the prior written consent of the managing underwriter, during the period commencing on the effective date of any registration statement of the Company filed under the Securities Act and ending on the date specified by the Company and the representative of the underwriters of Common Stock (or other securities) of the Company (such period not to exceed one hundred eighty (180) days, or such other period as may be requested by the Company or an underwriter to accommodate regulatory restrictions on (1) the publication or other distribution of research reports, and (2) analyst recommendations and opinions, including, but not limited to, the restrictions contained in FINRA Rule 2711(f)(4) or NYSE Rule 472(f)(4), or any successor provisions or amendments thereto), (i) lend; offer; pledge; sell; contract to sell; sell any option or contract to purchase; purchase any option or contract to sell; grant any option, right, or warrant to purchase; or otherwise Transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into or exercisable or exchangeable (directly or indirectly) for Common Stock held immediately before the effective date of the registration statement for such offering or (ii) enter into any swap or other arrangement that Transfers to another, in whole or in part, any of the economic consequences of ownership of such securities, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of Common Stock or other securities, in cash, or otherwise.

Participant agrees to execute and deliver such other agreements as may be reasonably requested by the Company or the representative of the underwriters of Common Stock (or other securities) which are consistent with the foregoing or which are necessary to give further effect thereto. In addition, if requested by the Company or the representative of the underwriters of Common Stock (or other securities) of the Company, Participant shall provide, within ten days of such request, such information as may be required by the Company or such representative in connection with the completion of any public offering of the Company's securities pursuant to a registration statement filed under the Securities Act. The obligations described in this Section 6 shall not apply to a registration relating solely to employee benefit plans on Form S-1 or Form S-8 or similar forms that may be promulgated in the future, or a registration relating solely to a Securities and Exchange Commission ("SEC") Rule 145 transaction on Form S-4 or similar forms that may be promulgated in the future. The Company may impose stop-transfer instructions with respect to the shares of Common Stock (or other securities) subject to the foregoing restriction until the end of said one hundred and eighty (180) day (or other) period. Participant agrees that any transferee of the Shares shall be bound by this Section 6.

The foregoing provisions of this Section 6 shall not apply to the sale of any shares to an underwriter pursuant to an underwriting agreement, or the Transfer of any shares to any trust for the direct or indirect benefit of the Participant or the immediate family of the Participant, provided that the trustee of the trust agrees to be bound in writing by the restrictions set forth herein, and provided further that any such Transfer shall not involve a disposition for value. The underwriters in connection with such registration are intended third party beneficiaries of this Section 6 and shall have the right, power and authority to enforce the provisions hereof as though they were a party hereto.

7. Escrow.

The Participant shall, upon the execution of this Agreement, execute Joint Escrow Instructions in the form attached to this Agreement as Exhibit A. The Joint Escrow Instructions shall be delivered to the Secretary of the Company, as escrow agent thereunder. The Participant shall deliver to such escrow agent a stock assignment duly endorsed in blank, in the form attached to this Agreement as Exhibit B, and hereby instructs the Company to deliver to such escrow agent, on behalf of the Participant, the certificate(s) evidencing the Shares issued hereunder. Such

materials shall be held by such escrow agent pursuant to the terms of such Joint Escrow Instructions. As a further condition to the Company's obligations under this Agreement, the spouse or registered domestic partner of Participant, if any, shall execute and deliver to the Company the Consent of Spouse or Domestic Partner attached hereto as Exhibit C.

8. Restrictive Legends.

All certificates representing Shares shall have affixed thereto legends in substantially the following form, in addition to any other legends that may be required under federal or state securities laws:

"The shares of stock represented by this certificate are subject to restrictions on transfer and an option to purchase set forth in a certain Restricted Stock Agreement between the Company and the registered owner of these shares (or his predecessor in interest). Such restrictions on transfer and option to purchase are binding upon transferees of these securities, and such Restricted Stock Agreement is available for inspection without charge at the office of the Secretary of the company."

"The shares represented by this certificate have not been registered under the Securities Act of 1933, as amended (the "Act"), and may not be sold, transferred or otherwise disposed of in the absence of an effective registration statement related thereto under the Act or an opinion of counsel in a form satisfactory to the company to the effect that such registration is not required under the Act."

The Company may be authorized from time to time pursuant to its certificate of incorporation to issue more than one (1) class or series of stock. In such case and at any time or from time to time thereafter the Company will furnish without charge to you upon request the powers, designations, preferences and relative participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

9. Provisions of the Plan.

(a) This Agreement is subject to the provisions of the Plan, a copy of which is furnished to the Participant with this Agreement.

(b) As provided in the Plan, upon the occurrence of a Reorganization Event (as defined in the Plan), the repurchase and other rights of the Company hereunder shall inure to the benefit of the Company's successor and shall apply to the cash, securities or other property into which the Shares were converted or for which the Shares were exchanged pursuant to such Reorganization Event, in the same manner and to the same extent as they applied to the Shares under this Agreement. If, in connection with a Reorganization Event, a portion of the cash, securities and/or other property received upon the conversion or exchange of the Shares is to be placed into escrow to secure indemnification or similar obligations, the mix between the vested and unvested portion of such cash, securities and/or other property that is placed into escrow shall be the same as the mix between the vested and unvested portion of such cash, securities and/or other property that is not subject to escrow.

10. Investment Representations.

The Participant represents, warrants and covenants as follows:

(a) The Participant is purchasing the Shares for his own account for investment only, and not with a view to, or for sale in connection with, any distribution of the Shares in violation of the Securities Act, or any rule or regulation under the Securities Act.

(b) The Participant has had such opportunity as he has deemed adequate to obtain from representatives of the Company such information as is necessary to permit him to evaluate the merits and risks of his investment in the Company.

(c) The Participant has sufficient experience in business, financial and investment matters to be able to evaluate the risks involved in the purchase of the Shares and to make an informed investment decision with respect to such purchase.

(d) The Participant can afford a complete loss of the value of the Shares and is able to bear the economic risk of holding such Shares for an indefinite period.

(e) The Participant understands that (i) the Shares have not been registered under the Securities Act and are "restricted securities" within the meaning of Rule 144 under the Securities Act; (ii) the Shares cannot be sold, transferred or otherwise disposed of unless they are subsequently registered under the Securities Act or an exemption from registration is then available; (iii) in any event, the exemption from registration under Rule 144 will not be available for at least one year and even then will not be available unless a public market then exists for the Common Stock, adequate information concerning the Company is then available to the public, and other terms and conditions of Rule 144 are complied with; and (iv) there is now no registration statement on file with the Securities and Exchange Commission with respect to any stock of the Company and the Company has no obligation or current intention to register the Shares under the Securities Act.

11. Withholding Taxes; Section 83(b) Election.

(a) The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state or local taxes of any kind required by law to be withheld with respect to the purchase of the Shares by the Participant or the lapse of the Purchase Option. No Shares will be released from the Purchase Option pursuant to this Agreement unless and until the Company satisfies all applicable federal, state, and local or other income and employment tax withholding obligations as described in the Plan.

(b) The Participant has reviewed with the Participant's own tax advisors the federal, state, local and foreign tax consequences of this investment and the transactions contemplated by this Agreement. The Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's own tax liability that may arise as a result of this investment or the transactions contemplated by this Agreement. The Participant understands that it may be beneficial in many circumstances to elect to be taxed at the time the Shares are purchased rather than when and as the Company's Purchase Option expires by electing to be taxed currently on the difference between the purchase price of the Shares and their Fair Market Value on the date of purchase by filing an election under Section 83(b) of the Internal Revenue Code of 1986 with the I.R.S. within 30 days from the date of purchase of the Shares.

PARTICIPANT ACKNOWLEDGES THAT IT IS PARTICIPANT'S SOLE RESPONSIBILITY AND NOT THE COMPANY'S TO FILE TIMELY THE ELECTION UNDER SECTION 83(b), EVEN IF PARTICIPANT REQUESTS THE COMPANY OR ITS REPRESENTATIVES TO MAKE THIS FILING ON PARTICIPANT'S BEHALF.

12. Miscellaneous.

(a) No Rights to Employment. The Participant acknowledges and agrees that the vesting of the Shares pursuant to Section 2 hereof is earned only by continuing service as an employee at the will of the Company (not through the act of being hired or purchasing shares hereunder). The Participant further acknowledges and agrees that the transactions contemplated hereunder and the vesting schedule set forth herein do not constitute an express or implied promise of continued engagement as an employee or consultant for the vesting period, for any period, or at all.

(b) Severability. The invalidity or unenforceability of any provision of this Agreement shall not affect the validity or enforceability of any other provision of this Agreement, and each other provision of this Agreement shall be severable and enforceable to the extent permitted by law.

(c) Waiver. Any provision for the benefit of the Company contained in this Agreement may be waived, either generally or in any particular instance, by the Board of Directors of the Company.

(d) Binding Effect. This Agreement shall be binding upon and inure to the benefit of the Company and the Participant and their respective heirs, executors, administrators, legal representatives, successors and assigns, subject to the restrictions on Transfer set forth in Sections 4 and 5 of this Agreement.

(e) Notice. All notices required or permitted hereunder shall be in writing and deemed effectively given upon personal delivery or five days after deposit in the United States Post Office, by registered or certified mail, postage prepaid, addressed to the other party hereto at the address shown beneath his or its respective signature to this Agreement, or at such other address or addresses as either party shall designate to the other in accordance with this Section 12(e).

(f) Pronouns. Whenever the context may require, any pronouns used in this Agreement shall include the corresponding masculine, feminine or neuter forms, and the singular form of nouns and pronouns shall include the plural, and vice versa.

(g) Entire Agreement. This Agreement and the Plan constitute the entire agreement between the parties, and supersedes all prior agreements and understandings, relating to the subject matter of this Agreement.

(h) Amendment. This Agreement may be amended or modified only by a written instrument executed by both the Company and the Participant.

(i) Further Instruments. Participant hereby agrees to execute such further instruments and to take such further action as may be reasonably necessary to carry out the purposes and intent of this Agreement.

(j) Governing Law. This Agreement shall be construed, interpreted and enforced in accordance with the internal laws of the State of Delaware without regard to any applicable conflicts of laws.

(k) Tax Indemnity. Participant shall, if required by the Company, enter into an election with the Company or a subsidiary (in a form approved by the Company) under which any liability to the Company's (or a subsidiary's) Tax Liability, including, but not limited to, National Insurance Contributions ("NICs") and Fringe Benefit Tax ("FBT"), is transferred to and met by Participant. For purposes of this Section 13(k), Tax Liability shall mean any and all liability under applicable non-U.S. laws, rules or regulations from any income tax, the Company's (or a subsidiary's) NICs, FBT or similar liability and Participant's NICs, FBT or similar liability under non-U.S. laws that are attributable to: (A) the grant of, or any other benefit derived by the Participant from the Shares; (B) the acquisition by Participant of the Shares; or (C) the disposal of any Shares acquired. Participant shall indemnify and hold harmless the Company and any of its subsidiaries from any and all Tax Liability.

(l) Participant's Acknowledgments. The Participant acknowledges that he or she: (i) has read this Agreement; (ii) has been represented in the preparation, negotiation, and execution of this Agreement by legal counsel of the Participant's own choice or has voluntarily declined to seek such counsel; (iii) understands the terms and consequences of this Agreement; (iv) is fully aware of the legal and binding effect of this Agreement; (v) to the extent the Shares are issued in uncertificated form, agrees that this Agreement constitutes the notice required by Section 151(f) of the Delaware General Corporation Law; (vi) understands that the law firm of Faber Daeufer & Itrato PC, is acting as counsel to the Company in connection with the transactions contemplated by the Agreement, and is not acting as counsel for the Participant, and (vii) if Participant is married or in a registered domestic partnership, his or her spouse or registered domestic partner has signed the Consent of Spouse or Domestic Partner attached to this Agreement as Exhibit C.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the day and year first above written.

PRAXIS PRECISION MEDICINES, INC.

By: _____
Title: _____
Address: _____
_____

_____
Name of Participant

Address: _____

Exhibit A

PRAXIS PRECISION MEDICINES, INC.

Joint Escrow Instructions

_____, [●]

Precision Medicines, Inc.
[Address]
Attn: Secretary

Dear Sir:

As Escrow Agent for Praxis Precision Medicines, Inc., a Delaware corporation, and its successors in interest under the Restricted Stock Agreement (the "Agreement") of even date herewith, to which a copy of these Joint Escrow Instructions is attached (the "Company"), and the undersigned person ("Holder"), you are hereby authorized and directed to hold the documents delivered to you pursuant to the terms of the Agreement in accordance with the following instructions:

1. Appointment. Holder irrevocably authorizes the Company to deposit with you any certificates evidencing Shares (as defined in the Agreement) to be held by you hereunder and any additions and substitutions to said Shares. For purposes of these Joint Escrow Instructions, "Shares" shall be deemed to include any additional or substitute property. Holder does hereby irrevocably constitute and appoint you as his attorney-in-fact and agent for the term of this escrow to execute with respect to such Shares all documents necessary or appropriate to make such Shares negotiable and to complete any transaction herein contemplated. Subject to the provisions of this Section 1 and the terms of the Agreement, Holder shall exercise all rights and privileges of a stockholder of the Company while the Shares are held by you.

2. Closing of Purchase.

(a) Upon any purchase by the Company of the Shares pursuant to the Agreement, the Company shall give to Holder and you a written notice specifying the number of Shares to be purchased, the purchase price for the Shares, as determined pursuant to the Agreement, and the time for a closing hereunder (the "Closing") at the principal office of the Company. Holder and the Company hereby irrevocably authorize and direct you to close the transaction contemplated by such notice in accordance with the terms of said notice.

(b) At the Closing, you are directed (i) to date the stock assignment form or forms necessary for the Transfer of the Shares, (ii) to fill in on such form or forms the number of Shares being Transferred, and (iii) to deliver the same, together with the certificate or certificates evidencing the Shares to be Transferred, to the Company against the simultaneous delivery to you of the purchase price for the Shares being purchased pursuant to the Agreement.

3. Withdrawal. The Holder shall have the right to withdraw from this escrow any Shares as to which the Purchase Option (as defined in the Agreement) has terminated or expired.

4. Duties of Escrow Agent.

(a) Your duties hereunder may be altered, amended, modified or revoked only by a writing signed by all of the parties hereto.

(b) You shall be obligated only for the performance of such duties as are specifically set forth herein and may rely and shall be protected in relying or refraining from acting on any instrument reasonably believed by you to be genuine and to have been signed or presented by the proper party or parties. You shall not be personally liable for any act you may do or omit to do hereunder as Escrow Agent or as attorney-in-fact of Holder while acting in good faith and in the exercise of your own good judgment, and any act done or omitted by you pursuant to the advice of your own attorneys shall be conclusive evidence of such good faith.

(c) You are hereby expressly authorized to disregard any and all warnings given by any of the parties hereto or by any other person or entity, excepting only orders or process of courts of law, and are hereby expressly authorized to comply with and obey orders, judgments or decrees of any court. If you are uncertain of any actions to

be taken or instructions to be followed, you may refuse to act in the absence of an order, judgment or decrees of a court. In case you obey or comply with any such order, judgment or decree of any court, you shall not be liable to any of the parties hereto or to any other person or entity, by reason of such compliance, notwithstanding any such order, judgment or decree being subsequently reversed, modified, annulled, set aside, vacated or found to have been entered without jurisdiction.

(d) You shall not be liable in any respect on account of the identity, authority or rights of the parties executing or delivering or purporting to execute or deliver the Agreement or any documents or papers deposited or called for hereunder.

(e) You shall be entitled to employ such legal counsel and other experts as you may deem necessary properly to advise you in connection with your obligations hereunder and may rely upon the advice of such counsel.

(f) Your rights and responsibilities as Escrow Agent hereunder shall terminate if (i) you cease to be Secretary of the Company or (ii) you resign by written notice to each party. In the event of a termination under clause (i), your successor as Secretary shall become Escrow Agent hereunder; in the event of a termination under clause (ii), the Company shall appoint a successor Escrow Agent hereunder.

(g) If you reasonably require other or further instruments in connection with these Joint Escrow Instructions or obligations in respect hereto, the necessary parties hereto shall join in furnishing such instruments.

(h) It is understood and agreed that if you believe a dispute has arisen with respect to the delivery and/or ownership or right of possession of the securities held by you hereunder, you are authorized and directed to retain in your possession without liability to anyone all or any part of said securities until such dispute shall have been settled either by mutual written agreement of the parties concerned or by a final order, decree or judgment of a court of competent jurisdiction after the time for appeal has expired and no appeal has been perfected, but you shall be under no duty whatsoever to institute or defend any such proceedings.

(i) These Joint Escrow Instructions set forth your sole duties with respect to any and all matters pertinent hereto and no implied duties or obligations shall be read into these Joint Escrow Instructions against you.

(j) The Company shall indemnify you and hold you harmless against any and all damages, losses, liabilities, costs, and expenses, including attorneys' fees and disbursements, (including without limitation the fees of counsel retained pursuant to Section 4(e) above, for anything done or omitted to be done by you as Escrow Agent in connection with this Agreement or the performance of your duties hereunder, except such as shall result from your gross negligence or willful misconduct.

5. Notice. Any notice required or permitted hereunder shall be given in writing and shall be deemed effectively given upon personal delivery or upon deposit in the United States Post Office, by registered or certified mail with postage and fees prepaid, addressed to each of the other parties thereunto entitled at the following addresses, or at such other addresses as a party may designate by ten days' advance written notice to each of the other parties hereto.

COMPANY:	Notices to the Company shall be sent to the address set forth in the salutation hereto, Attn: President
HOLDER:	Notices to Holder shall be sent to the address set forth below Holder's signature below.
ESCROW AGENT:	Notices to the Escrow Agent shall be sent to the address set forth in the salutation hereto.

6. Miscellaneous.

(a) By signing these Joint Escrow Instructions, you become a party hereto only for the purpose of said Joint Escrow Instructions, and you do not become a party to the Agreement.

(b) This instrument shall be binding upon and inure to the benefit of the parties hereto and their respective successors and permitted assigns.

Very truly yours,

PRAXIS PRECISION MEDICINES, INC.

By:_____
Title:_____

HOLDER:

(Signature)

Print Name

Address:_____
_____

Date Signed:_____

ESCROW AGENT:

_____
Secretary

Exhibit B

(STOCK ASSIGNMENT SEPARATE FROM CERTIFICATE)

FOR VALUE RECEIVED, I hereby sell, assign and transfer unto _____ (_____) shares of Common Stock, $0.0001 par value per share, of Precision Medicines, Inc. (the "Company") standing in my name on the books of the Company represented by Certificate(s) Number _____ herewith, and do hereby irrevocably constitute and appoint _____ attorney to transfer the said stock on the books of the Company with full power of substitution in the premises.

Dated:

IN PRESENCE OF

NOTICE: The signature(s) to this assignment must correspond with the name as written upon the face of the certificate, in every particular, without alteration, enlargement, or any change whatever and must be guaranteed by a commercial bank, trust company or member firm of the Boston, New York or Midwest Stock Exchange.

Exhibit C

CONSENT OF SPOUSE OR DOMESTIC PARTNER

I, _____, spouse or registered domestic partner of _____, have read and approve the Restricted Stock Agreement dated _____, _____, between my spouse or registered domestic partner and Praxis Precision Medicines, Inc. In consideration of granting of the right to my spouse or registered domestic partner to purchase shares of common stock of Precision Medicines, Inc. set forth in the Restricted Stock Agreement, I hereby appoint my spouse or registered domestic partner as my attorney-in-fact in respect to the exercise of any rights under the Agreement and agree to be bound by the provisions of the Restricted Stock Agreement insofar as I may have any rights in said Restricted Stock Agreement or any shares issued pursuant thereto under the community property laws or similar laws relating to marital property in effect in the state of our residence as of the date of the signing of the foregoing Restricted Stock Agreement.

Dated:_____,_____

_____

Signature of Spouse or Registered Domestic Partner

PRAXIS PRECISION MEDICINES, INC.

Nonstatutory Stock Option Agreement

Granted Under 2017 Stock Incentive Plan

1. Grant of Option.

This agreement evidences the grant by Praxis Precision Medicines, Inc., a Delaware corporation (the "Company"), on [_____] (the "Grant Date") to [_], an employee, consultant or director of the Company (the "Participant"), of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2017 Stock Incentive Plan (the "Plan"), a total of [_] shares (the "Shares") of common stock of the Company ("Common Stock") at $[_] per Share. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on [_____] (the "Final Exercise Date").

It is intended that the option evidenced by this agreement shall not be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "Code"). Except as otherwise indicated by the context, the term "Participant", as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

[Subject to Section 3(b) below, this option will become exercisable ("vest") as to 25% of the original number of Shares on the first anniversary of the Vesting Commencement Date (as defined below) and as to an additional 2.0833% of the original number of Shares at the end of each successive month following the first anniversary of the Vesting Commencement Date until the fourth anniversary of the Vesting Commencement Date.] In determining the number of vested Shares at the time of any exercise, the number of Shares shall be rounded down to the nearest whole Share. For purposes of this Agreement, "Vesting Commencement Date" shall mean [_____].

[Additionally, if within 12 months following a Company Sale (as defined below), the Participant is terminated without Cause (as defined below), then 100% of the Shares that are not then vested shall become vested.]

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

(a) Exercise. Each election to exercise this option shall be accompanied by a completed Notice of Stock Option Exercise in the form attached hereto as Exhibit A and signed by the Participant, and when applicable, a signed and completed Consent of Spouse or Domestic Partner in the form attached hereto as Exhibit B, and received by the Company at its principal office, accompanied by this agreement, and payment in full in the manner provided in the Plan. The Participant may purchase less than the number of Shares covered hereby, provided that no partial exercise of this option may be for any fractional share or for fewer than ten whole shares. Subject to applicable law and as a condition to the exercise of this option and the issuance of any shares hereunder, the Participant agrees to become party to any voting agreement, drag along agreement, right of first refusal and co-sale agreement, or any other agreement approved by the Board of Directors of the Company (the "Board") and creating obligations of or among any stockholder of the Company that holds in the aggregate shares of Common Stock equal to or greater than the aggregate number of shares of Common Stock held by the Participant, in each case calculated on a fully-diluted basis, as the Company may request.

(b) Time for Exercise of Certain Options. With respect to any option that constitutes a plan for the deferral of compensation within the meaning of Section 409A of the Code, such option may only be exercised for vested Shares upon the earliest to occur of the following events (all terms within the meaning of Section 409A of the Code): (i) the Participant's separation from service; (ii) the Participant's death or disability; or (iii) a change in the ownership or effective control of the Company, or in the ownership of a substantial portion of the assets of the Company.

(c) Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee, officer or director of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants, or advisors of which are eligible to receive option grants under the Plan (an "Eligible Participant").

(d) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (e) and (f) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

(e) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for Cause (as defined below), this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(f) Termination for Cause. If, prior to the Final Exercise Date, the Participant's employment is terminated by the Company for Cause, the right to exercise this option shall terminate immediately upon the effective date of such termination of employment. If, prior to the Final Exercise Date, the Participant is given notice by the Company of the termination of his or her employment by the Company for Cause, and the effective date of such employment termination is subsequent to the date of delivery of such notice, the right to exercise this option shall be suspended from the time of the delivery of such notice until the earlier of (i) such time as it is determined or otherwise agreed that the Participant's employment shall not be terminated for Cause as provided in such notice or (ii) the effective date of such termination of employment (in which case the right to exercise this option shall, pursuant to the preceding sentence, terminate upon the effective date of such termination of employment). If the Participant is party to an employment or severance agreement with the Company that contains a definition of "cause" for termination of employment, "Cause" shall have the meaning ascribed to such term in such agreement. Otherwise, "Cause" shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant shall be considered to have been discharged for Cause if the Company determines, within 30 days after the Participant's resignation, that discharge for cause was warranted.

4. Company Right of First Refusal.

(a) Notice of Proposed Transfer. If the Participant proposes to sell, assign, transfer, pledge, hypothecate or otherwise dispose of, by operation of law or otherwise (collectively, "transfer") any Shares acquired upon exercise of this option, then the Participant shall first give written notice of the proposed transfer (the "Transfer Notice") to the Company. The Transfer Notice shall name the proposed transferee and state the number of such Shares the Participant proposes to transfer (the "Offered Shares"), the price per share and all other material terms and conditions of the transfer.

(b) Company Right to Purchase. For 30 days following its receipt of such Transfer Notice, the Company shall have the option to purchase all or part of the Offered Shares at the price and upon the terms set forth in the Transfer Notice. In the event the Company elects to purchase all or part of the Offered Shares, it shall give written notice of such election to the Participant within such 30-day period. Within 10 days after his or her receipt of such notice, the Participant shall tender to the Company at its principal offices the certificate or certificates representing the Offered Shares to be purchased by the Company, duly endorsed in blank by the Participant or with duly endorsed stock powers attached thereto, all in a form suitable for transfer of the Offered Shares to the Company. Promptly

following receipt of such certificate or certificates, the Company shall deliver or mail to the Participant a check in payment of the purchase price for such Offered Shares; provided that if the terms of payment set forth in the Transfer Notice were other than cash against delivery, the Company may pay for the Offered Shares on the same terms and conditions as were set forth in the Transfer Notice; and provided further that any delay in making such payment shall not invalidate the Company's exercise of its option to purchase the Offered Shares.

(c) Shares Not Purchased By Company. If the Company does not elect to acquire all of the Offered Shares, the Participant may, within the 30-day period following the expiration of the option granted to the Company under subsection (b) above, transfer the Offered Shares which the Company has not elected to acquire to the proposed transferee, provided that such transfer shall not be on terms and conditions more favorable to the transferee than those contained in the Transfer Notice. Notwithstanding any of the above, all Offered Shares transferred pursuant to this Section 4 shall remain subject to the right of first refusal set forth in this Section 4 and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Section 4.

(d) Consequences of Non-Delivery. After the time at which the Offered Shares are required to be delivered to the Company for transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Offered Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Offered Shares, but shall, insofar as permitted by law, treat the Company as the owner of such Offered Shares.

(e) Exempt Transactions. The following transactions shall be exempt from the provisions of this Section 4:

(1) any transfer of Shares to or for the benefit of any spouse, child or grandchild of the Participant, or to a trust for their benefit;

(2) any transfer pursuant to an effective registration statement filed by the Company under the Securities Act of 1933, as amended (the "Securities Act"); and

(3) the sale of all or substantially all of the outstanding shares of capital stock of the Company (including pursuant to a merger or consolidation);

provided, however, that in the case of a transfer pursuant to clause (1) above, such Shares shall remain subject to the right of first refusal set forth in this Section 4 and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Section 4.

(f) Assignment of Company Right. The Company may assign its rights to purchase Offered Shares in any particular transaction under this Section 4 to one or more persons or entities.

(g) Termination. The provisions of this Section 4 shall terminate upon the earlier of the following events:

(1) the closing of the sale of shares of Common Stock in an underwritten public offering pursuant to an effective registration statement filed by the Company under the Securities Act; or

(2) the sale of all or substantially all of the outstanding shares of capital stock, assets or business of the Company, by merger, consolidation, sale of assets or otherwise (other than a merger or consolidation in which all or substantially all of the individuals and entities who were beneficial owners of the Company's voting securities immediately prior to such transaction beneficially own, directly or indirectly, a majority (determined on an as-converted basis) of the outstanding securities entitled to vote generally in the election of directors of the resulting, surviving or acquiring corporation in such transaction) (a "Company Sale").

(h) No Obligation to Recognize Invalid Transfer. The Company shall not be required (1) to transfer on its books any of the Shares which shall have been sold or transferred in violation of any of the provisions set forth in this Section 4, or (2) to treat as owner of such Shares or to pay dividends to any transferee to whom any such Shares shall have been so sold or transferred.

(i) Legends. The certificate representing Shares shall bear a legend substantially in the following form (in addition to, or in combination with, any legend required by applicable federal and state securities laws and agreements relating to the transfer of the Company securities):

"The shares represented by this certificate are subject to a right of first refusal in favor of the Company, as provided in a certain stock option agreement with the Company."

5. Agreement in Connection with Initial Public Offering.

The Participant agrees, in connection with the initial underwritten public offering of the Common Stock pursuant to a registration statement under the Securities Act, (i) not to (a) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any other securities of the Company or (b) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of shares of Common Stock or other securities of the Company, whether any transaction described in clause (a) or (b) is to be settled by delivery of securities, in cash or otherwise, during the period beginning on the date of the filing of such registration statement with the Securities and Exchange Commission and ending 180 days after the date of the final prospectus relating to the offering (plus up to an additional 34 days to the extent requested by the managing underwriters for such offering in order to address Rule 2711(f) of the National Association of Securities Dealers, Inc. or any similar successor provision), and (ii) to execute any agreement reflecting clause (i) above as may be requested by the Company or the managing underwriters at the time of such offering. The Company may impose stop-transfer instructions with respect to the shares of Common Stock or other securities subject to the foregoing restriction until the end of the "lock-up" period.

6. Withholding.

No Shares will be issued pursuant to the exercise of this option unless and until the Company satisfies all applicable federal, state, and local or other income and employment tax withholding obligations as described in the Plan.

7. Transfer Restrictions.

(a) This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

(b) The Participant agrees that he or she will not transfer any Shares issued pursuant to the exercise of this option unless the transferee, as a condition to such transfer, delivers to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of Section 4 and Section 5; provided that such a written confirmation shall not be required with respect to (1) Section 4 after such provision has terminated in accordance with Section 4(g) or (2) Section 5 after the completion of the lock-up period in connection with the Company's initial underwritten public offering.

8. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

IN WITNESS WHEREOF, the Company has caused this option to be executed under its corporate seal by its duly authorized officer. This option shall take effect as a sealed instrument.

PRAXIS PRECISION MEDICINES, INC.

By:

Name:

Title:

PARTICIPANT'S ACCEPTANCE

The undersigned hereby accepts the foregoing option and agrees to the terms and conditions thereof. The undersigned hereby acknowledges receipt of a copy of the Company's 2017 Stock Incentive Plan.

PARTICIPANT:

Address:

Exhibit A

NOTICE OF STOCK OPTION EXERCISE

Date: _____[1]

Praxis Precision Medicines, Inc.

Attention: Treasurer

Dear Sir or Madam:

I am the holder of _____[2] Stock Option granted to me under the Praxis Precision Medicines, Inc. (the "Company") 2017 Stock Incentive Plan on _____[3] for the purchase of _____[4] shares of Common Stock of the Company at a purchase price of $_____[5] per share.

I hereby exercise my option to purchase _____[6] shares of Common Stock (the "Shares"), for which I have enclosed _____[7] in the amount of _____[8]. Please register my stock certificate as follows:

Name(s): _____ [9]

_____

Address: _____

Tax I.D. #: _____ [10]

_____

[1] Enter the date of exercise.
[2] Enter either "an Incentive" or "a Nonstatutory".
[3] Enter the date of grant.
[4] Enter the total number of shares of Common Stock for which the option was granted.
[5] Enter the option exercise price per share of Common Stock.
[6] Enter the number of shares of Common Stock to be purchased upon exercise of all or part of the option.
[7] Enter "cash", "personal check" or if permitted by the option or Plan, "stock certificates No. XXXX and XXXX".
[8] Enter the dollar amount (price per share of Common Stock times the number of shares of Common Stock to be purchased), or the number of shares tendered. Fair market value of shares tendered, together with cash or check, must cover the purchase price of the shares issued upon exercise.
[9] Enter name(s) to appear on stock certificate: (a) Your name only; (b) Your name and other name (i.e., John Doe and Jane Doe, Joint Tenants With Right of Survivorship); or (c) In the case of a Nonstatutory option only, a Child's name, with you as custodian (i.e., Jane Doe, Custodian for Tommy Doe). Note: There may be income and/or gift tax consequences of registering shares in a Child's name.
[10] Social Security Number of Holder(s).

I represent, warrant and covenant as follows:

1. I am purchasing the Shares for my own account for investment only, and not with a view to, or for sale in connection with, any distribution of the Shares in violation of the Securities Act of 1933 (the “Securities Act”), or any rule or regulation under the Securities Act.

2. I have had such opportunity as I have deemed adequate to obtain from representatives of the Company such information as is necessary to permit me to evaluate the merits and risks of my investment in the Company.

3. I have sufficient experience in business, financial and investment matters to be able to evaluate the risks involved in the purchase of the Shares and to make an informed investment decision with respect to such purchase.

4. I can afford a complete loss of the value of the Shares and am able to bear the economic risk of holding such Shares for an indefinite period.

5. I understand that (i) the Shares have not been registered under the Securities Act and are “restricted securities” within the meaning of Rule 144 under the Securities Act, (ii) the Shares cannot be sold, transferred or otherwise disposed of unless they are subsequently registered under the Securities Act or an exemption from registration is then available; (iii) in any event, the exemption from registration under Rule 144 will not be available for at least one year and even then will not be available unless a public market then exists for the Common Stock, adequate information concerning the Company is then available to the public, and other terms and conditions of Rule 144 are complied with; and (iv) there is now no registration statement on file with the Securities and Exchange Commission with respect to any stock of the Company and the Company has no obligation or current intention to register the Shares under the Securities Act.

Very truly yours,

(Signature)

Exhibit B

CONSENT OF SPOUSE OR DOMESTIC PARTNER

I, _____, spouse or registered domestic partner of _____, have read and approve the Nonstatutory Stock Option Agreement dated _____, _____, between my spouse or registered domestic partner and Praxis Precision Medicines, Inc. (the "Agreement"). In consideration of granting an option to my spouse or registered domestic partner to purchase shares of Common Stock of Praxis Precision Medicines, Inc. set forth in the Agreement, I hereby appoint my spouse or registered domestic partner as my attorney-in-fact in respect to the exercise of any rights under the Agreement and agree to be bound by the provisions of the Agreement insofar as I may have any rights in said Agreement or any shares issued pursuant thereto under the community property laws or similar laws relating to marital property in effect in the state of our residence as of the date of the signing of the foregoing Agreement.

Dated: ,

Signature of Spouse or Registered Domestic Partner

PRAXIS PRECISION MEDICINES, INC.

Incentive Stock Option Agreement

Granted Under 2017 Stock Incentive Plan

1. Grant of Option.

This agreement evidences the grant by Praxis Precision Medicines, Inc., a Delaware corporation (the "Company"), on [_____] (the "Grant Date") to [ ], an employee of the Company (the "Participant"), of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2017 Stock Incentive Plan (the "Plan"), a total of [ ] shares (the "Shares") of common stock of the Company ("Common Stock") at $[ ]per Share. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on [_____] (the "Final Exercise Date").

It is intended that the option evidenced by this agreement shall be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "Code"). Except as otherwise indicated by the context, the term "Participant", as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

[This option will become exercisable ("vest") as to 25% of the original number of Shares on the first anniversary of the Vesting Commencement Date (as defined below) and as to an additional 2.0833% of the original number of Shares at the end of each successive month following the first anniversary of the Vesting Commencement Date until the fourth anniversary of the Vesting Commencement Date.] In determining the number of vested Shares at the time of any exercise, the number of Shares shall be rounded down to the nearest whole Share. For purposes of this Agreement, "Vesting Commencement Date" shall mean [_____].

[Additionally, if within 12 months following a Company Sale (as defined below), the Participant is terminated without Cause (as defined below), then 100% of the Shares that are not then vested shall become vested.]

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

(a) Exercise. Each election to exercise this option shall be accompanied by a completed Notice of Stock Option Exercise in the form attached hereto as Exhibit A and signed by the Participant, and when applicable, a signed and completed Consent of Spouse or Domestic Partner in the form attached hereto as Exhibit B, and received by the Company at its principal office, accompanied by this agreement, and payment in full in the manner provided in the Plan.

The Participant may purchase less than the number of Shares covered hereby, provided that no partial exercise of this option may be for any fractional share or for fewer than ten whole shares. Subject to applicable law and as a condition to the exercise of this option and the issuance of any shares hereunder, the Participant agrees to become party to any voting agreement, drag along agreement, right of first refusal and co-sale agreement, or any other agreement approved by the Board of Directors of the Company (the "Board") and creating obligations of or among any stockholder of the Company that holds in the aggregate shares of Common Stock equal to or greater than the aggregate number of shares of Common Stock held by the Participant, in each case calculated on a fully-diluted basis, as the Company may request.

(b) Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee, officer or director of, or consultant or advisor to, the Company or any parent or subsidiary of the Company as defined in Section 424(e) or (f) of the Code (an "Eligible Participant").

(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate

three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

(d) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for Cause (as defined below), this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e) Termination for Cause. If, prior to the Final Exercise Date, the Participant's employment is terminated by the Company for Cause, the right to exercise this option shall terminate immediately upon the effective date of such termination of employment. If, prior to the Final Exercise Date, the Participant is given notice by the Company of the termination of his or her employment by the Company for Cause, and the effective date of such employment termination is subsequent to the date of delivery of such notice, the right to exercise this option shall be suspended from the time of the delivery of such notice until the earlier of (i) such time as it is determined or otherwise agreed that the Participant's employment shall not be terminated for Cause as provided in such notice or (ii) the effective date of such termination of employment (in which case the right to exercise this option shall, pursuant to the preceding sentence, terminate upon the effective date of such termination of employment). If the Participant is party to an employment or severance agreement with the Company that contains a definition of "cause" for termination of employment, "Cause" shall have the meaning ascribed to such term in such agreement. Otherwise, "Cause" shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant shall be considered to have been discharged for Cause if the Company determines, within 30 days after the Participant's resignation, that discharge for cause was warranted.

4. Company Right of First Refusal.

(a) Notice of Proposed Transfer. If the Participant proposes to sell, assign, transfer, pledge, hypothecate or otherwise dispose of, by operation of law or otherwise (collectively, "transfer") any Shares acquired upon exercise of this option, then the Participant shall first give written notice of the proposed transfer (the "Transfer Notice") to the Company. The Transfer Notice shall name the proposed transferee and state the number of such Shares the Participant proposes to transfer (the "Offered Shares"), the price per share and all other material terms and conditions of the transfer.

(b) Company Right to Purchase. For 30 days following its receipt of such Transfer Notice, the Company shall have the option to purchase all or part of the Offered Shares at the price and upon the terms set forth in the Transfer Notice. In the event the Company elects to purchase all or part of the Offered Shares, it shall give written notice of such election to the Participant within such 30-day period. Within 10 days after his or her receipt of such notice, the Participant shall tender to the Company at its principal offices the certificate or certificates representing the Offered Shares to be purchased by the Company, duly endorsed in blank by the Participant or with duly endorsed stock powers attached thereto, all in a form suitable for transfer of the Offered Shares to the Company. Promptly following receipt of such certificate or certificates, the Company shall deliver or mail to the Participant a check in payment of the purchase price for such Offered Shares; provided that if the terms of payment set forth in the Transfer Notice were other than cash against delivery, the Company may pay for the Offered Shares on the same terms and conditions as were set forth in the Transfer Notice; and provided further that any delay in making such payment shall not invalidate the Company's exercise of its option to purchase the Offered Shares.

(c) Shares Not Purchased By Company. If the Company does not elect to acquire all of the Offered Shares, the Participant may, within the 30-day period following the expiration of the option granted to the Company under

subsection (b) above, transfer the Offered Shares which the Company has not elected to acquire to the proposed transferee, provided that such transfer shall not be on terms and conditions more favorable to the transferee than those contained in the Transfer Notice. Notwithstanding any of the above, all Offered Shares transferred pursuant to this Section 4 shall remain subject to the right of first refusal set forth in this Section 4 and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Section 4.

(d) Consequences of Non-Delivery. After the time at which the Offered Shares are required to be delivered to the Company for transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Offered Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Offered Shares, but shall, insofar as permitted by law, treat the Company as the owner of such Offered Shares.

(e) Exempt Transactions. The following transactions shall be exempt from the provisions of this Section 4:

(1) any transfer of Shares to or for the benefit of any spouse, child or grandchild of the Participant, or to a trust for their benefit;

(2) any transfer pursuant to an effective registration statement filed by the Company under the Securities Act of 1933, as amended (the "Securities Act"); and

(3) the sale of all or substantially all of the outstanding shares of capital stock of the Company (including pursuant to a merger or consolidation);

provided, however, that in the case of a transfer pursuant to clause (1) above, such Shares shall remain subject to the right of first refusal set forth in this Section 4 and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Section 4.

(f) Assignment of Company Right. The Company may assign its rights to purchase Offered Shares in any particular transaction under this Section 4 to one or more persons or entities.

(g) Termination. The provisions of this Section 4 shall terminate upon the earlier of the following events:

(1) the closing of the sale of shares of Common Stock in an underwritten public offering pursuant to an effective registration statement filed by the Company under the Securities Act; or

(2) the sale of all or substantially all of the outstanding shares of capital stock, assets or business of the Company, by merger, consolidation, sale of assets or otherwise (other than a merger or consolidation in which all or substantially all of the individuals and entities who were beneficial owners of the Company's voting securities immediately prior to such transaction beneficially own, directly or indirectly, a majority (determined on an as-converted basis) of the outstanding securities entitled to vote generally in the election of directors of the resulting, surviving or acquiring corporation in such transaction) (a "Company Sale").

(h) No Obligation to Recognize Invalid Transfer. The Company shall not be required (1) to transfer on its books any of the Shares which shall have been sold or transferred in violation of any of the provisions set forth in this Section 4, or (2) to treat as owner of such Shares or to pay dividends to any transferee to whom any such Shares shall have been so sold or transferred.

(i) Legends. The certificate representing Shares shall bear a legend substantially in the following form (in addition to, or in combination with, any legend required by applicable federal and state securities laws and agreements relating to the transfer of the Company securities):

"The shares represented by this certificate are subject to a right of first refusal in favor of the Company, as provided in a certain stock option agreement with the Company."

5. Agreement in Connection with Initial Public Offering.

The Participant agrees, in connection with the initial underwritten public offering of the Common Stock pursuant to a registration statement under the Securities Act, (i) not to (a) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any

option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any other securities of the Company or (b) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of shares of Common Stock or other securities of the Company, whether any transaction described in clause (a) or (b) is to be settled by delivery of securities, in cash or otherwise, during the period beginning on the date of the filing of such registration statement with the Securities and Exchange Commission and ending 180 days after the date of the final prospectus relating to the offering (plus up to an additional 34 days to the extent requested by the managing underwriters for such offering in order to address Rule 2711(f) of the National Association of Securities Dealers, Inc. or any similar successor provision), and (ii) to execute any agreement reflecting clause (i) above as may be requested by the Company or the managing underwriters at the time of such offering. The Company may impose stop-transfer instructions with respect to the shares of Common Stock or other securities subject to the foregoing restriction until the end of the "lock-up" period.

6. Tax Matters.

(a) Withholding. No Shares will be issued pursuant to the exercise of this option unless and until the Company satisfies all applicable federal, state, and local or other income and employment tax withholding obligations as described in the Plan.

(b) Disqualifying Disposition. If the Participant disposes of Shares acquired upon exercise of this option within two years from the Grant Date or one year after such Shares were acquired pursuant to exercise of this option, the Participant shall notify the Company in writing of such disposition.

7. Transfer Restrictions.

(a) This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

(b) The Participant agrees that he or she will not transfer any Shares issued pursuant to the exercise of this option unless the transferee, as a condition to such transfer, delivers to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of Section 4 and Section 5; provided that such a written confirmation shall not be required with respect to (1) Section 4 after such provision has terminated in accordance with Section 4(g) or (2) Section 5 after the completion of the lock-up period in connection with the Company's initial underwritten public offering.

8. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

IN WITNESS WHEREOF, the Company has caused this option to be executed under its corporate seal by its duly authorized officer. This option shall take effect as a sealed instrument.

PRAXIS PRECISION MEDICINES, INC.

By: _____

Name:

Title:

PARTICIPANT'S ACCEPTANCE

The undersigned hereby accepts the foregoing option and agrees to the terms and conditions thereof. The undersigned hereby acknowledges receipt of a copy of the Company's 2017 Stock Incentive Plan.

PARTICIPANT:

Address:

Exhibit A

NOTICE OF STOCK OPTION EXERCISE

Date: _____[11]

Praxis Precision Medicines, Inc.

Attention: Treasurer

Dear Sir or Madam:

I am the holder of _____[12] Stock Option granted to me under the Praxis Precision Medicines, Inc. (the "Company") 2017 Stock Incentive Plan on _____[13] for the purchase of _____[14] shares of Common Stock of the Company at a purchase price of $_____[15] per share.

I hereby exercise my option to purchase _____[16] shares of Common Stock (the "Shares"), for which I have enclosed _____[17] in the amount of _____[18]. Please register my stock certificate as follows:

Name(s): _____[19]

Address:

Tax I.D. #: _____[20]

10 Social Security Number of Holder(s).

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[11] Enter the date of exercise.
[12] Enter either "an Incentive" or "a Nonstatutory".
[13] Enter the date of grant.
[14] Enter the total number of shares of Common Stock for which the option was granted.
[15] Enter the option exercise price per share of Common Stock.
[16] Enter the number of shares of Common Stock to be purchased upon exercise of all or part of the option.
[17] Enter "cash", "personal check" or if permitted by the option or Plan, "stock certificates No. XXXX and XXXX".
[18] Enter the dollar amount (price per share of Common Stock times the number of shares of Common Stock to be purchased), or the number of shares tendered. Fair market value of shares tendered, together with cash or check, must cover the purchase price of the shares issued upon exercise.
[19] Enter name(s) to appear on stock certificate: (a) Your name only; (b) Your name and other name (i.e., John Doe and Jane Doe, Joint Tenants With Right of Survivorship); or (c) In the case of a Nonstatutory option only, a Child's name, with you as custodian (i.e., Jane Doe, Custodian for Tommy Doe). Note: There may be income and/or gift tax consequences of registering shares in a Child's name.
[20] Social Security Number of Holder(s).

I represent, warrant and covenant as follows:

1. I am purchasing the Shares for my own account for investment only, and not with a view to, or for sale in connection with, any distribution of the Shares in violation of the Securities Act of 1933 (the “Securities Act”), or any rule or regulation under the Securities Act.

2. I have had such opportunity as I have deemed adequate to obtain from representatives of the Company such information as is necessary to permit me to evaluate the merits and risks of my investment in the Company.

3. I have sufficient experience in business, financial and investment matters to be able to evaluate the risks involved in the purchase of the Shares and to make an informed investment decision with respect to such purchase.

4. I can afford a complete loss of the value of the Shares and am able to bear the economic risk of holding such Shares for an indefinite period.

5. I understand that (i) the Shares have not been registered under the Securities Act and are “restricted securities” within the meaning of Rule 144 under the Securities Act, (ii) the Shares cannot be sold, transferred or otherwise disposed of unless they are subsequently registered under the Securities Act or an exemption from registration is then available; (iii) in any event, the exemption from registration under Rule 144 will not be available for at least one year and even then will not be available unless a public market then exists for the Common Stock, adequate information concerning the Company is then available to the public, and other terms and conditions of Rule 144 are complied with; and (iv) there is now no registration statement on file with the Securities and Exchange Commission with respect to any stock of the Company and the Company has no obligation or current intention to register the Shares under the Securities Act.

Very truly yours,

(Signature)

Exhibit B

CONSENT OF SPOUSE OR DOMESTIC PARTNER

I, _____, spouse or registered domestic partner of _____, have read and approve the Incentive Stock Option Agreement dated _____, _____, between my spouse or registered domestic partner and Praxis Precision Medicines, Inc. (the "Agreement"). In consideration of granting an option to my spouse or registered domestic partner to purchase shares of Common Stock of Praxis Precision Medicines, Inc. set forth in the Agreement, I hereby appoint my spouse or registered domestic partner as my attorney-in-fact in respect to the exercise of any rights under the Agreement and agree to be bound by the provisions of the Agreement insofar as I may have any rights in said Agreement or any shares issued pursuant thereto under the community property laws or similar laws relating to marital property in effect in the state of our residence as of the date of the signing of the foregoing Agreement.

Dated: _____, _____

Signature of Spouse or Registered Domestic Partner

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333-249522) pertaining to the 2017 Stock Incentive Plan, 2020 Stock Option and Incentive Plan, and 2020 Employee Stock Purchase Plan of Praxis Precision Medicines, Inc. of our report dated March 17, 2021, with respect to the consolidated financial statements of Praxis Precision Medicines, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2020.

/s/ Ernst & Young, LLP

Boston, Massachusetts
March 17, 2021

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Marcio Souza, certify that:

1. I have reviewed this Annual Report on Form 10-K of Praxis Precision Medicines, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 17, 2021

By: /s/ MARCIO SOUZA

Marcio Souza
Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Lauren Mastrocola, certify that:

1. I have reviewed this Annual Report on Form 10-K of Praxis Precision Medicines, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 17, 2021

By: /s/ LAUREN MASTROCOLA

Lauren Mastrocola

Principal Accounting Officer and Interim Principal Financial Officer

Exhibit 32.1

CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND INTERIM PRINCIPAL FINANCIAL OFFICER PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Praxis Precision Medicines, Inc. (the "Company") for the fiscal year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of their knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 17, 2021 By: /s/ MARCIO SOUZA

Marcio Souza
Chief Executive Officer
(Principal Executive Officer)

Date: March 17, 2021 By: /s/ LAUREN MASTROCOLA

Lauren Mastrocola
Principal Accounting Officer and Interim Principal Financial Officer