# 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, 2024**

**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.)** |
| **99 High Street, 30th Floor Boston, MA** | **02110** |
| **(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** |

Securities registered pursuant to Section 12(g) of the Act: None

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, a 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. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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 June 28, 2024 as reported by the Nasdaq Global Select Market on such date was approximately $733.0 million. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

As of February 26, 2025, the registrant had 20,163,250 shares of common stock, $0.0001 par value per share, outstanding.

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Signatures

## SUMMARY OF THE MATERIAL 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.
- The development and commercialization of drug products is highly uncertain and subject to extensive regulation, and the regulatory approval processes of the U.S. Food and Drug Administration, or the FDA, and comparable foreign regulatory authorities are lengthy, time-consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates on a timely basis if at all, our business will be substantially harmed.
- Preclinical and clinical drug 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 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.
- If we encounter difficulties enrolling patients in our future clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- The markets for our product candidates 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 or otherwise experience disruptions to our business relationships with our current or future licensors, we could lose 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 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.
- Our business is subject to economic, political, regulatory and other risks.
- We depend heavily on our executive officers, principal consultants and others, and the loss of their services would materially harm our business.
- Cyberattacks 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.

- The price of our stock has been and may in the future 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 candidate 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 product candidates, if approved, 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, if approved, commercialization of our product candidates;
- the commercialization of our product candidates, if approved;
- our plans to research, develop and, if approved, commercialize our product candidates;
- future agreements with third parties in connection with the commercialization of our product candidates, if approved, 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, if approved;
- 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; and
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

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 insights from genetic epilepsies into the development of therapies for central nervous system, or CNS, disorders characterized by neuronal excitation-inhibition imbalance. Normal brain function requires a delicate balance of excitation and inhibition in neuronal circuits, which, when dysregulated, can lead to abnormal function and both rare and more prevalent neurological disorders. We are applying genetic insights to the discovery and development of therapies for neurological disorders through two proprietary platforms, using our understanding of shared biological targets and circuits in the brain. Each platform currently has multiple programs, with significant potential for additional program and indication expansion:

- ***Cerebrum***™, our small molecule platform, utilizes deep understanding of neuronal excitability and neuronal networks and applies a series of computational and experimental tools to develop orally available precision therapies
- ***Solidus***™, our antisense oligonucleotide, or ASO, platform, is an efficient, targeted precision medicine discovery and development engine anchored on a proprietary, computational methodology

Our platforms utilize a deliberate, pragmatic and patient-guided 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 diversified, multimodal CNS portfolio with four clinical-stage product candidates across movement disorders and epilepsy.

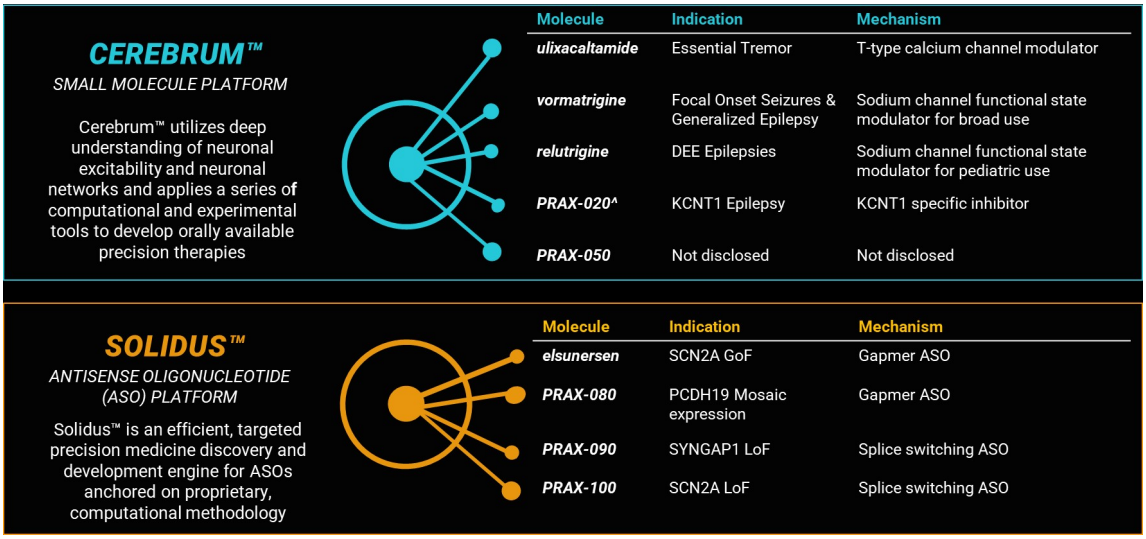
#### Cerebrum™ (small molecule platform)

We have built Cerebrum™, enabled by innovative computational and experimental tools, to discover and develop first- and best-in-class CNS small molecule therapies. Our world-class ion channel discovery science team, along with external collaborators, accelerate our ability to create and execute novel screening cascades for our selected genetic targets. Fundamental to advancement of candidates are our multiscale disease models that link genetic cause to network function to elucidate novel drivers of disease phenotype. We employ translational biomarkers such as quantitative electroencephalography, or qEEG, to guide dose selection, with the goal of improving probability of success in the clinic. The precision application of our candidates is guided by genomics and informatics to identify, stratify and activate patients for trial recruitment and execution. To date, Cerebrum™ has generated three clinical stage product candidates, ulixacaltamide (formerly known as PRAX-944), vormatrigine (formerly known as PRAX-628) and relutrigine (formerly known as PRAX-562), as well as PRAX-020 which has been in-licensed by UCB Biopharma SRL, or UCB. Cerebrum™ has the potential to continue delivering first- and best-in-class orally available therapies for genetic CNS targets.

#### Solidus™ (ASO platform)

We have built Solidus™ to discover and develop first- and best-in-class ASOs with high probability of advancement into the clinic. Solidus™ is enabled by our proprietary, computational workflow to discover ASOs with desired drug-like properties to optimize for up/down-regulation, avoidance of toxic motifs and optimization of binding affinity and specificity. Led by our clinical-stage product candidate, elsunersen (formerly known as PRAX-222), Solidus™ has also generated three novel ASOs with preclinical proof of mechanism that we expect to nominate development candidates for in 2025 — PRAX-080 targeting PCDH19-related developmental epilepsy; PRAX-090 targeting SYNGAP1 loss-of-function, or LoF, mutation driven developmental epilepsy; and PRAX-100 targeting SCN2A LoF mutations, the predominant genetic link to de novo autism spectrum disorders. The platform is uniquely positioned to continue discovering and advancing other new ASOs for novel genetic CNS targets.

Below is a summary of our portfolio:




^PRAX-020 (KCNT1) has been in-licensed by UCB Biopharma SRL

**Our Strategy & Approach to Drug Development**

We leverage the genetics of epilepsy as a gateway for CNS drug discovery and development. Recent investigations have led to the identification of over 900 genes that are causal or risk factors for different forms of epilepsy, providing the field with an outsized understanding of epilepsy genetics relative to other diseases such as Alzheimer's disease, amyotrophic lateral sclerosis, or ALS, and many others. The genetic origin provides clarity around how to address the underlying disease biology and precisely meet the needs of patients not only suffering from epilepsy, but also other neurological disorders of neuronal imbalance with shared pathophysiological mechanisms informed by the same genetics, including movement disorders. It is through our two platforms, Cerebrum™ and Solidus™, that we aim to translate these insights into the discovery, development and potential commercialization of clinically meaningful medicines for patients.

We believe that fostering an ecosystem of collaborators to support our internal research, clinical and commercial efforts is critical to our strategy. Our collaborators include world-renowned research groups and drug developers, clinical research organizations, or CROs, innovative patient mapping database companies, experts in translational tools, next-generation drug delivery technology companies and others. In addition, we are deeply embedded within the communities that we serve and believe that the more we know about the impact on patients, caregivers and communities at large, the better positioned we will be to deliver on what patients actually need.

Underlying each of our programs are four key principles that we believe will increase probability of success and allow us to sustainably and efficiently translate insights into high-impact therapies for patients and society:

1. ***Focus on therapeutic targets identified through human genetics.*** By applying insights derived from the genetics of epilepsies, we have identified biological targets that are implicated in determining neuronal excitability in epilepsies and also in other CNS disorders.

2. ***Utilize translational tools to validate the potential of our targets and product candidates.*** We leverage translational tools to both confirm pharmacodynamic, or PD, effects of our drug product candidates in the brain and establish on-mechanism effects. Our programs utilize target-specific electroencephalogram, or 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 pharmacokinetics, or PK, and PD 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 early and robust demonstration of desired effect in a relatively small patient sample and we focus on clinical endpoints that minimize inter-patient variability. Our global network of CROs and scientists affords us the flexibility to conduct research and development activities in diverse geographic locations to help accelerate development timelines and limit geographic risks. We have also solidified our know-how on running hybrid and decentralized clinical trials, increasing our ability to execute our programs with quality and speed, while being closer to patients needs.

4. ***Apply patient-guided development strategies.*** We pursue the development of candidates that address the treatment needs of patients, caregivers and the treating community, including targeting the underlying disease pathology versus just symptom management. We focus on clinical endpoints that offer a clear connection between PD effects and clinical measures that are meaningful to patients, physicians and regulatory agencies. 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.

## CLINICAL STAGE PROGRAMS

We have advanced four product candidates to clinical stage, including three small molecules through the Cerebrum™ platform and one ASO through the Solidus™ platform:

### Ulixacaltamide for Essential Tremor

Our most advanced program, ulixacaltamide, is a differentiated and highly selective small molecule inhibitor of T-type calcium channels currently in Phase 3 clinical development for the treatment of Essential Tremor, or ET. Additionally, we have an exclusive collaboration and license agreement with Tenacia Biotechnology (Shanghai) Company, Ltd., a China-based portfolio company of Bain Capital, to develop and commercialize ulixacaltamide for the treatment of ET in China, Hong Kong, Macau and Taiwan. Ulixacaltamide has the potential to be developed for other indications, including Parkinson's disease.

#### *Ulixacaltamide Phase 3 Essential3 Program*

Essential3 is a decentralized, Phase 3, multi-study, clinical trial evaluating the safety and efficacy of 60 mg of ulixacaltamide in ET. The trial includes two separate and simultaneous Phase 3 pivotal studies — a 12-week parallel design, placebo-controlled study (N=400), or Study 1, and a 12-week randomized withdrawal study (N=200), or Study 2 — with all participants undergoing one screening process and a long-term safety study, or LTSS. The study uses the modified Activities of Daily Living 11, or mADL11, as the primary endpoint. A pre-planned interim analysis of Study 1 was conducted in the first quarter of 2025. The Independent Data Monitoring Committee, or IDMC, overseeing the interim analysis of Study 1 of the Essential3 program has provided Praxis with the outcome of such analysis. Based on the predefined decision framework for Study 1, the IDMC has recommended that the study be stopped for futility, due to the results being unlikely to meet the primary efficacy endpoint under the parameters set by the statistical model. The committee also indicated that some underlying assumptions of the statistical model might have influenced this outcome and encouraged us to explore alternative analysis methods. Given the advanced state of enrollment for both Study 1 and Study 2 in the Essential3 program, and in the context of the advice received by the IDMC, we have decided to continue both studies to completion, with topline results expected in the third quarter of 2025. The decision about whether the data supports the submission of an NDA will be made after analyzing the final results for Study 1 and Study 2.

#### *Essential1 study*

The Essential1 study was a multi-center, randomized, double-blind, placebo-controlled, dose-range finding Phase 2b clinical trial evaluating the efficacy, safety and tolerability of once-daily treatment of ulixacaltamide compared to placebo after 56 days in participants with moderate-to-severe ET. Topline results for the Phase 2b Essential1 study were announced in the first quarter of 2023. Results of the Essential1 study informed the design of the Phase 3 Essential3 program.

#### *Essential Tremor*

ET is the most common movement disorder with a prevalence of approximately seven million patients in the United States alone, including more than two million diagnosed patients, one million of whom are actively treated for their ET. ET is characterized by involuntary rhythmic movements in the upper limbs that significantly disrupt ability to function and are progressive in nature. There is only one approved pharmacotherapy for ET, a beta blocker (propranolol), approved by the FDA for ET in 1986, that offers limited efficacy and poor tolerability and is contraindicated for comorbidities that affect a significant share of the ET population. Other CNS drugs are used off-label, though similarly are characterized by limited efficacy and poor tolerability. For these reasons, approximately 40% of patients who seek pharmacotherapy treatment discontinue within two years. As a last line therapy, a small subset of patients will opt for invasive procedures such as gamma knife and MRI guided focused ultrasound thalamotomy, where part of the thalamus involved in the cerebello-thalamo-cortical, or CTC, circuit is ablated, or deep brain stimulation, or DBS, where an electrode is implanted to deliver therapeutic electrical stimulation to the thalamus. While these procedures are generally effective, they are associated with significant side effects and risk. Therefore, many patients who are eligible elect not to have these procedures. Key findings from a combined analysis of over 400 ET patients that we conducted included that up to 80% of patients adjust how they complete daily tasks due to burden of the disease, and 77% of patients do not feel their disease is adequately managed with current treatments. In totality, there is significant unmet need for an effective and tolerable pharmacotherapy targeted for ET.

**Vormatrigine for Common Epilepsies (Focal Onset Seizures and Generalized Epilepsy)**

Vormatrigine is a next-generation, functionally selective small molecule targeting the hyperexcitable state of sodium-channels in the brain and is currently being developed as a once daily, oral treatment for adult focal onset epilepsy. Preclinical data demonstrates vormatrigine is differentiated from standard of care, with the potential to be best-in-class for focal epilepsy. In vitro, vormatrigine has demonstrated superior selectivity for disease-state NaV channel hyperexcitability. In vivo studies of vormatrigine have demonstrated unprecedented potency in the maximal electroshock seizure, or MES, model, a highly predictive translational model for efficacy in focal epilepsy. Data from a Phase 1 study demonstrated that vormatrigine was well-tolerated in healthy subjects at greater than 15 times the predicted human equivalent of the mouse MES $EC_{50}$. We initiated our ENERGY program to advance vormatrigine through efficacy and registrational trials in focal onset seizures, or FOS, and generalized epilepsy.

***ENERGY Program***

Our ENERGY program for vormatrigine aims to generate efficacy, safety and PK data to serve as the basis of regulatory registrations globally. The program consists of four studies — EMPOWER, RADIANT, POWER1 and POWER2.

*EMPOWER Observational Study*

EMPOWER is an observational study in partnership with the Epilepsy Study Consortium that aims to better characterize seizure burden. We began enrolling patients in 2024 and we expect to generate standardized, longitudinal data to support planned interventional trials and deepen our understanding of patient experiences with epilepsy. Preliminary findings from EMPOWER revealed a significant disease burden compounded by persistent, uncontrolled and often untracked seizures alongside profound psychosocial impact.

*RADIANT Phase 2 Study*

We have initiated RADIANT, a Phase 2 open-label study to evaluate PK, safety and efficacy of vormatrigine in up to 50 patients with FOS or generalized epilepsy. Patients will be treated with a 30 mg dose over an 8-week period to evaluate the impact of vormatrigine on seizure burden. We anticipate topline results by mid-year 2025.

*POWER1 and POWER 2 Phase 2/3 Registrational Studies*

POWER1 and POWER2 are two 12-week Phase 2/3 studies in patients with FOS to evaluate the efficacy of vormatrigine. We have initiated and plan to enroll approximately 250 patients in POWER1, which is assessing adjunctive treatment that allows dosing of vormatrigine on top of one to three antiseizure medications. POWER1 is a parallel-arm study, comparing a treatment arm of 20 mg for six weeks followed by 30 mg for six weeks versus a placebo arm for 12 weeks. We anticipate topline results in the second half of 2025. POWER2 will be a multi-arm, 12-week registrational study for vormatrigine, and we expect to begin enrollment of the study in the second half of 2025.

***Phase 2a Photo-Paroxysmal Response study***

We conducted a Phase 2a Photo-Paroxysmal Response, or PPR, study to evaluate the efficacy and safety of vormatrigine across two cohorts, dosed at 15 mg and 45 mg. PPR studies measure EEG signatures after intermittent photic stimulation and are widely used as a marker of anti-seizure efficacy and to aid in dose determination. We announced topline results in the first quarter of 2024, with 100% of patients responding in both cohorts. In the 15 mg cohort (n=5), 80% of patients achieved a complete response and 20% achieved a partial response. In the 45 mg cohort (n=3), 100% of patients achieved a complete response. Safety results were consistent with our prior Phase 1 dose escalation study of vormatrigine and PK analysis confirmed therapeutic exposures.

***Vormatrigine Phase 1 studies***

We have conducted Phase 1 healthy volunteer studies of vormatrigine to evaluate the tolerability, PK, PD and food effect of vormatrigine across single and multiple ascending dose cohorts and first announced topline results in the second quarter of 2023. This first clinical study of vormatrigine was a randomized, double-blind, placebo-controlled single ascending dose, or SAD, and multiple ascending dose, or MAD, trial in healthy participants aged 18-55 years. Vormatrigine was generally well-tolerated at all tested doses. PK data demonstrated dose-dependent exposure, supporting once-daily dosing without titration to achieve potentially therapeutically effective drug concentration levels. No adverse events, or AEs, or AEs of special interest led to study drug withdrawal, and no clinically significant findings on vital signs, electrocardiogram or neurological examination were observed. All AEs were mild, mostly transient (lasting minutes to hours), and resolved spontaneously, with the most common AEs being CNS-related. Results from an additional 45 mg MAD cohort showed a dose proportional increase in exposure with favorable tolerability, similar to the 20 and 30 mg MAD cohorts. In addition, a Phase 1 food effect study demonstrated that food intake did not affect vormatrigine absorption, which increases the flexibility in dosing and ease of use of vormatrigine.

***Common Epilepsies (Focal Onset Seizures and Generalized Epilepsy)***

An estimated 3.5 million people in the United States suffer from common epilepsies, with FOS being the most common type of epilepsy, accounting for approximately 60% of all cases. FOS are characterized by seizures that originate in one side or area of the brain and affects one side of the body. Sodium channel therapy is the cornerstone of treatment for patients with epilepsy yet currently approved drugs have significant safety and efficacy limitations. Despite the plethora of marketed treatments, including sodium channel targeting antiepileptic drugs, or AEDs, such as Tegretol (carbamazepine), Lamictal (lamotrigine), Xcopri (cenobamate), at least 30% of patients remain refractory to treatment.

There are two forms of therapeutically relevant sodium current: (1) persistent sodium current and (2) peak sodium current. Standard of care sodium channel targeting AEDs can produce severe toxicity at therapeutic doses from excessive inhibition of peak sodium current, as physiological levels of peak sodium current are required for normal neuronal function. Therefore, novel compounds that inhibit persistent and peak sodium channel hyperexcitability while sparing physiological levels of peak sodium current may improve clinical efficacy and tolerability.

**Relutrigine for Developmental and Epileptic Encephalopathies**

Relutrigine is a first-in-class preferential inhibitor of persistent sodium current, presently in development for the treatment of developmental and epileptic encephalopathies, or DEEs. In-vivo studies of relutrigine have demonstrated dose-dependent block of seizures up to complete inhibition of seizure activity in SCN2A, SCN8A and other DEE mouse models. Relutrigine has been generally well-tolerated in three Phase 1 studies and has demonstrated biomarker changes indicative of voltage-gated sodium channel, or NaV channel, blocking effects. Relutrigine has received Orphan Drug Designation, or ODD, and Rare Pediatric Disease Designation, or RPD, from the FDA, and ODD from the European Medicines Agency, or EMA, for the treatment of SCN2A-DEE and SCN8A-DEE, respectively. Relutrigine has also received RPD from the FDA for the treatment of Dravet Syndrome.

We are currently evaluating relutrigine in the EMBOLD study for SCN2A-DEE and SCN8A-DEE, with plans to initiate the EMERALD study in a broader DEE patient population by mid-year 2025.

***Phase 2 EMBOLD study***

The EMBOLD study is a randomized, double-blind, placebo-controlled Phase 2 clinical trial evaluating the safety, tolerability, efficacy (motor seizure frequency) and PK of relutrigine in pediatric participants aged 2 to 18 years with DEEs, followed by an open-label extension, or OLE. We announced topline results of the first cohort of

the EMBOLD study (n=16) in the third quarter of 2024. Relutrigine was generally safe and well-tolerated with no drug-related serious adverse events or dose reductions required. Patients on relutrigine observed a placebo-adjusted reduction of 46% in monthly motor seizures from baseline over a 16-week period, and there were meaningful gains observed in patients' alertness, communication and seizure severity. Patients continuing into the ongoing OLE (n=13) saw a 77% reduction in motor seizures from baseline through nine months of treatment. Over 30% of patients (n=5) achieved seizure freedom status for a median of 46 days, inclusive of the OLE period, compared to three days at baseline.

Based on these results, we are currently enrolling 80 patients with SCN2A and SCN8A DEEs in a second, registrational cohort for the EMBOLD study and expect topline results in the first half of 2026, followed by a potential NDA filing in 2026.

***Rare, monogenic DEEs***

Epilepsies are common neurological disorders characterized by brain excitation-inhibition, or E/I, imbalance. Hyperexcitability can lead to abnormal synchronization of neurons and neuronal circuits, which is the electrical basis of a seizure. Fundamentals of brain electrophysiology and mechanisms dictating seizure genesis are conserved across species and, consequently, animal models of seizures and epilepsy enable a clinically predictive and therefore efficient drug development path. A subset of epilepsies are rare, monogenic DEEs characterized by early onset (less than 2 years of age), frequent seizures, abnormal epileptiform EEG activity, developmental impairment and resistance to available AEDs. Furthermore, these 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 revealed over 60 genetic causes of epilepsy.

An underlying pathologic feature of many DEEs is 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 PCDH19, SCN8A, SCN2A, KCNT1, KCNQ2, KCNQ1, STXBP1 and SYNGAP1, 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. 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 that can be leveraged within our operating ecosystem to develop meaningful therapies for this group of patients with devastating unmet clinical needs.

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. While standard-of-care sodium channel blockers inhibit persistent sodium current, they also block peak sodium current at therapeutic concentrations, which can cause significant AEs, such as ataxia, drowsiness and dizziness, and therefore have a very narrow Therapeutic Index, or TI, resulting in subpar outcomes for patients and significant need for better therapeutic options.

***SCN2A-DEE***

Early onset SCN2A-DEE is a rare condition caused by a gain-of-function, or GoF, variant in the SCN2A gene. The SCN2A gene encodes the NaV1.2 subunit of brain sodium channels, which control neuronal excitability by regulating the flow of sodium ions into neurons. This movement of sodium ions is a major component of generating electrical signals called action potentials, the way in which the cells communicate. Early-onset SCN2A-DEE presents before three months of life and can lead to profound impact on patients, including drug-resistant seizures, significant cognitive impairment, movement disorders such as dystonia or ataxia, and problems in other body systems such as the gastrointestinal or ocular systems. Currently, there are no approved treatments for SCN2A-DEE, and the standard-of-care typically involves a regimen of many concurrent anti-seizure medications as well as medications for comorbidities. Despite these interventions, it is estimated that more than 80% of early-onset SCN2A-DEE patients live with uncontrolled seizures, and approximately 75% live with severe intellectual disability. It is estimated that there are approximately 2,000 patients in the United States with GoF changes in SCN2A leading to epileptic encephalopathy.

***SCN8A-DEE***

SCN8A-DEE is a rare DEE caused by a GoF variant in the SCN8A gene. Similar to SCN2A-DEE, patients with SCN8A-DEE suffer from recurrent, typically drug-resistant seizures, which start as early as the first day of life. The seizures can be of multiple different types, up to dozens per day, with poor response to current treatment options. Patients with SCN8A-DEE have significant cognitive disabilities, ranging from moderate to severe, often have movement disorders, such as dystonia or ataxia, and have problems in other body systems such as the gastrointestinal or ocular systems. SCN8A-DEE patients also may experience autonomic features such as increases or decreases in heart rate, abnormal breathing and cyanosis. It is estimated that there are approximately 2,000 patients in the United States with SCN8A-DEE.

***Dravet Syndrome***

Dravet syndrome is a severe, progressive genetic epilepsy that typically begins within the first year of life, marked by frequent, prolonged, and treatment-resistant seizures. Beyond seizures, the condition often leads to intellectual disability, developmental delays, movement and balance difficulties, speech and language impairments, growth abnormalities, sleep disturbances, autonomic nervous system dysfunction, and mood disorders. Classified as a developmental and epileptic encephalopathy, Dravet syndrome is associated with significant cognitive and developmental impairments. Patients with this condition also face an elevated risk of early mortality, including due to sudden unexpected death in epilepsy, or SUDEP.

**Elsunersen for SCN2A-DEE**

Elsunersen is a clinical-stage ASO designed to down-regulate 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 is designed to down-regulate 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. Elsunersen has received ODD and RPD from the FDA, and ODD and PRIority MEdicines, or PRIME, designation from the EMA for the treatment of SCN2A-DEE.

We are continuing to evaluate elsunersen in the second cohort of the EMBRAVE study in Brazil, and plan to initiate EMBRAVE3, a Phase 3 registrational study, by mid-year 2025.

***EMBRAVE study***

Part 1 of the EMBRAVE study was a 21-week open label cohort, in which participants received elsunersen for up to 13 weeks, designed to determine the safety and tolerability of intrathecal delivery of elsunersen. No treatment related AEs or SAEs were observed. Additionally, patients observed a marked reduction in seizures and increase in seizure-free days. We are enrolling patients in the second cohort of the EMBRAVE study in Brazil, in which we are evaluating the safety and efficacy of elsunersen versus sham-procedure, and anticipate topline results in the first half of 2026.

***EMBRAVE3 study***

We plan to initiate EMBRAVE3, a global, 24-week, double-blind, sham procedure-controlled clinical trial to assess the efficacy, safety, tolerability and PK of elsunersen by mid-year 2025. We expect this to be a registrational trial consisting of three cohorts. Cohort 1 will enroll approximately 40 patients between 2 and 18 years of age experiencing at least four motor seizures during a four-week baseline period. The primary endpoint will assess the change in seizure frequency. Patients will be randomized 1:1 to a drug arm or a sham procedure arm. Patients in the drug arm will receive 1 mg of elsunersen intrathecally every 4 weeks for 24 weeks. Patients in the sham procedure arm will receive no treatment or intrathecal injection. Cohorts 2 and 3 will enroll patients from age 0 to 2 in a staggered fashion starting with patients ages 1-2 in Cohort 2. Cohort 3 patients will be enrolled following a safety review of the Cohort 2 patients. Patients will receive elsunersen 1.0mg and 0.5mg for Cohorts 2 and 3, respectively, for 24 weeks. All patients will have the option to continue into an open-label extension for an additional 24 weeks.

**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. Additionally, we may face potential challenges in the adoption or acceptance of our product candidates, if approved, by prescribers due to the unfamiliarity of new treatments for previously untreated conditions or conditions where new treatments have not been developed for an extended period of time, such as ET, or unfamiliarity with utilizing new mechanisms such as the precision approach for sodium channel modulation utilized by relutrigine and vormatrigine. We believe continuing to develop medicines that significantly advance the standard of care for patients is the optimal strategy to differentiate us from competitors.

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:

- Approved therapies for ET, such as propranolol, and off-label therapies, such as primidone.
- Sodium channel blocker or similar ion channel-targeting programs in development for common epilepsies, including those of SK-Pharma, Xenon Pharmaceuticals, and Biohaven Pharmaceuticals, as well as other programs in clinical development targeting other mechanisms of action including those from Lundbeck and Stoke Therapeutics, and approved therapies including other existing ion channel blockers.

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 merger and acquisition 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 may also rely on trademarks, copyrights and 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 and other protections afforded through data exclusivity, market exclusivity and patent term extensions, where available.

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. Depending upon the timing, duration and specifics of FDA approval of our drug product candidates, some of our United States, or 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 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.

**T-type Calcium channel blockers**

We own fourteen patent families directed to T-type Calcium channel blockers. One patent family discloses and claims compositions of matter of certain T-type calcium channel modulators, including ulixacaltamide. This patent family has issued in many major pharmaceutical markets and is pending in others and expires in 2029. A second patent family is directed to certain pharmaceutical formulations of ulixacaltamide and methods of use in treating disorders such as essential tremor. Three U.S. patents have issued in this patent family, and expire in 2040, and this family remains pending in multiple jurisdictions of potential commercial interest. A third family is directed to titration methods of using ulixacaltamide and expires in 2041. A fourth patent family is directed to certain analog compounds

of ulixacaltamide and expires in 2040. A fifth patent family is directed to the adjunctive use of a beta blocker and/or certain anticonvulsants with ulixacaltamide and expires in 2043. A sixth patent family is directed to a dosage form of ulixacaltamide and expires in 2044. A seventh patent family is directed to salt forms of ulixacaltamide and expires in 2044. An eighth patent family is directed to crystalline forms of ulixacaltamide and expires in 2044. A ninth patent family is directed to methods of treatment using ulixacaltamide and expires in 2044. A tenth patent family is directed to methods of treatment using ulixacaltamide and expires in 2044. The remaining patent families are directed to other TTCC blockers of various core structures and methods of use in treating diseases such as movement disorders, which expire in 2039 and 2040.

**Persistent sodium current blockers**

We own fifteen patent families directed to persistent sodium current blockers, including a patent family that relates to relutrigine and vormatrigine, two additional patent families that relate to relutrigine, and the remaining patent families relate to other persistent sodium current blockers. One patent family discloses and claims certain persistent sodium current blockers, including relutrigine and vormatrigine, and methods of use in treating diseases such as epilepsy (including pediatric epilepsy), as well as migraine and pain. In this patent family, relutrigine is covered by a patent that has granted in the United States, and patent applications pending in other potentially commercially relevant jurisdictions, which expire in 2039. In this same patent family, vormatrigine is covered by two granted U.S. patents that will expire in 2039. A second family discloses other persistent sodium current blockers and generically claims relutrigine, as well as methods of 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 relutrigine, methods of use in treating diseases such as pediatric epilepsy, cephalgia, short-lasting unilateral neuralgiform headache attacks with conjunctival injection, or SUNCT, and tearing and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms, or SUNA, and methods of making relutrigine, and expires in 2040. The remaining patent families are directed to other persistent sodium current blockers of various core structures and methods of use in treating diseases such as pediatric epilepsy, expiring between 2037 and 2043.

**SCN2A downregulation**

We have exclusively in-licensed three patent families directed to our SCN2A program. Two of these patent families are owned by RogCon, Inc., and disclose and claim certain ASOs targeting SCN2A and methods of use in treating diseases such as epilepsy, including epilepsy having certain SCN2A mutations. One patent family is pending in the United States and expires in 2038. A second patent family is directed to methods of treating SCN1A encephalopathy using ASOs targeting SCN2A and expires in 2039.

The other in-licensed patent family is owned by Ionis Pharmaceuticals, Inc., and is directed to compositions of matter of elsunersen. This family expires in 2041 and one U.S. patent has issued in this family.

We own seven patent families directed to our elsunersen program. The first has claims directed to a method of treating SCN2A gain of function neurological diseases using certain ASOs. This patent family is pending in the United States and expires in 2041. The second is directed to methods of treating SCN2A-related disorders using SCN2A inhibitors and expires in 2043. The third is directed to methods of treating SCN2A-related disorders using SCN2A inhibitors and expires in 2044. The fourth is directed to compositions and methods for treating SCN2A disorders and expires in 2039. The fifth is directed to methods for detecting if a subject with an SCN2A disorder has a gain of function mutation and expires in 2039. The sixth is directed to oligonucleotides targeting SCN2A retained introns and expires in 2039. The seventh is directed to compositions and methods for treating disorders associated with loss-of-function mutations in SCN2A and expires in 2041.

**KCNT1 blockers**

We own twelve patent families directed to KCNT1 blockers. These patent families disclose and claim small molecule KCNT1 blockers and methods of use in treating diseases, such as epilepsy, including epilepsy having certain KCNT1 mutations, and expire between 2040 and 2043.

**GABAA receptor positive allosteric modulators**

We own four patent families directed to GABAA receptor positive allosteric modulators. One patent family discloses and claims salts and polymorphs of PRAX-114. Two patents are granted in the United States, which expire in 2039. A second patent family is directed to alternative salt forms of PRAX-114, and a U.S. patent has

issued, which expires in 2042. Other patent applications cover methods of use in treating diseases (including the use of combination formulations), such as epilepsy, musculoskeletal conditions, motor disorder or essential tremor, which expire from 2042 to 2043.

**PCDH19**

We own one patent family directed to compositions and methods for the treatment of PCDH19 related disorders, which expires in 2042.

**SYNGAP**

We own one patent family directed to compositions and methods for the treatment of disorders associated with loss-of-function mutations in SYNGAP1, which expires in 2041.

**LICENSE AGREEMENTS**

**License Agreement with RogCon**

In September 2019, we and RogCon, Inc., or RogCon, entered into a Cooperation and License Agreement, or the RogCon Agreement, to collaborate to develop ASOs for the treatment of epilepsy caused by mutations of the SCN2A gene. RogCon had an existing collaboration arrangement with Ionis Pharmaceuticals, Inc., or 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. 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. Expenses incurred for all periods presented were not material.

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 ASOs to treat forms of epilepsy caused by mutations of the SCN2A gene. Pursuant to the Ionis Agreement, we and Ionis each conducted certain research activities and Ionis was responsible for identifying a development candidate and conducting an IND-enabling toxicology study. The design of the IND-enabling toxicology study was 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. Ionis granted us an exclusive option 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, following the results of the IND-enabling toxicology study. We exercised this exclusive option in January 2022 and paid a $2.0 million license fee. 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. In the second quarter of 2023, Ionis earned the Additional Milestone fee of $5.0 million, as well as the Initial Interest Amount of $1.9 million. The $6.9 million milestone fee was paid in July 2023.

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. 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. 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.

## 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 rely on CDMOs to manufacture drug substance and drug product in accordance with the FDA's current Good Manufacturing Practices, or cGMP. 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 a 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. 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. 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 process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of certain preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice 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, or ethics committee 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 intended use;
- preparation and submission to the FDA of an NDA;
- a determination by the FDA within 60 days of its receipt of an NDA to file the application for review;
- 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 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 potential FDA audits of clinical trial sites to assess compliance with GCPs and the integrity of the clinical data; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

***Preclinical studies***

Before testing any product candidate in humans, the product candidate must undergo 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. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial. Additionally, the FDA will review any data from clinical trials conducted outside the United States when determining whether to allow an IND to proceed in the United States. Specifically, the FDA's acceptance of data from trials conducted outside of the United States and not under an IND is subject to certain conditions, including that the clinical trial must be conducted in accordance with GCPs, and the FDA must be able to validate the data from the study through an on-site inspection, if necessary. Clinical holds also may be imposed by the FDA at any time before or during studies due to safety concerns or non-compliance.

***Clinical trials***

Clinical trials involve the administration of the product candidate to human subjects under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent 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. While the IND is active, progress reports summarizing the results of clinical trials and nonclinical studies, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and investigators if serious and unexpected suspected adverse events occur, findings from other studies of the same or similar drug or from animal or in vitro testing suggest a significant risk, or there is an increased incidence of a serious suspected adverse reaction compared to that in the protocol or investigator brochure.

Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study, and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. Similarly, 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. An IRB can also 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.

There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries. Specifically, 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 candidate, 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.

Human clinical trials are typically conducted in three phases, which may overlap or be combined. In Phase 1, the product candidate is introduced into healthy human subjects or patients with the target disease or condition to test for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early evaluation of effectiveness. In Phase 2, the product candidate is administered to a limited patient population with a specified disease or condition to evaluate possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for the specified disease or condition, and to determine dosage tolerance and optimal dosage. In Phase 3, the product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to provide substantial evidence of the efficacy and safety of the product candidate, to establish the overall risk-benefit profile of the product candidate, and to provide adequate information for the labeling of the product candidate.

In some cases, the FDA may require, or sponsors may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product in the approved indication. These so-called Phase 4 studies, may be conducted after initial marketing approval, and may be used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition or requirement 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 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 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. The submission of an NDA is subject to a substantial application user fee, unless a waiver or exemption applies.

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. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be withdrawn and resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once an application is accepted for filing, the FDA has a goal of ten months from the date of "filing" to complete a standard review of an NDA for a drug that is a new molecular entity, and six months from the filing date to complete a priority review. The FDA does not always meet its goal dates, and the review process can be extended for a three-month period by the FDA to review information deemed a "major amendment" to the application. This FDA review process typically takes 10 months from the date the NDA is accepted for filing by the FDA (for a standard review) or six months from the filing date (for a priority review). 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 facilities 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 facilities where the product is manufactured. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites and/or the study sponsor 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. A REMS is a safety strategy to manage a known or potential serious risk associated with a drug and to enable patients to have continued access to such medicines by managing their safe use, and 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 sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and any inspection reports regarding the manufacturing facilities, sponsor, 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 will describe all of the deficiencies in the NDA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the NDA in condition for approval, including requests for additional information or clarification. 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 those deficiencies have been addressed to the FDA's satisfaction, the FDA will issue an approval letter. 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 safety, require testing and surveillance programs to monitor the product, 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 sponsor must request orphan drug designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. 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 disease or condition for seven years. If a drug or drug product designated as an orphan product ultimately receives marketing approval for a disease or condition broader than what was designated in its orphan product application, it may not be entitled 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 disease or condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or to provide a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee. Orphan product designation, however, does not convey any advantage in or shorten the duration of the regulatory review and approval process.

***Rare pediatric disease designation and priority review vouchers***

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the United States within one year following the date of approval.

For purposes of this program, a "rare pediatric disease" is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years; and (b) rare diseases or conditions within the meaning of the Orphan Drug Act. Congress has only authorized the Rare Pediatric Disease Priority Review Voucher program until December 20, 2024. Consequently, sponsors of marketing applications approved after that date will not receive the voucher unless Congress reauthorizes the program. If the program is not reauthorized, if a drug candidate receives Rare Pediatric Disease Designation before October 1, 2024, the sponsor of the marketing application for such drug will only be eligible to receive a voucher if the application for the designated drug is approved by the FDA before October 1, 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 that a product candidate 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 candidate. The FDA may also agree to review sections of the NDA for a fast track product candidate on a rolling basis before the complete application is submitted.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation. A product candidate can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Finally, the FDA may designate an NDA for priority review if the product candidate 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 product candidate represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by, among other things, evidence of increased effectiveness, 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 from the filing date for an NDA for a new molecular entity.

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 product candidates can be approved upon a determination that the product candidate has 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 generally requires that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled confirmatory clinical trials to verify and describe the predicted effect on IMM or other clinical endpoint, and may require that such confirmatory trials be underway prior to granting accelerated approval. The FDA may withdraw approval of a drug or indication approved under accelerated approval on an expedited basis if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product or the sponsor fails to conduct such confirmatory trials in a timely manner or in accordance with applicable regulations. 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.

***U.S. drug product marketing exclusivity***

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain marketing applications. For example, the FDCA provides a five-year period of non-patent data 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 non-patent 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 or patent terms. 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. The FDA's issuance of a written request does not obligate the sponsor to complete the requested pediatric studies.

***Post-approval requirements***

Following approval of a 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. 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. 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 program fee requirements for any marketed products.

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, among other things:

- Imposition of post-marketing studies or clinical trials to assess new safety risks, or restrictions under a REMS program;
- Restrictions on the marketing, manufacturing or distribution of the product, complete withdrawal of the product from the market or product recalls;
- Fines, warning letters, untitled 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 revocation of product approvals;
- Consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- Mandated modification of promotional materials and labeling and the issuance of corrective information;

- Issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product;
- Product seizure or detention, or refusal to permit the import or export of products; or
- Injunctions or the imposition of civil or criminal penalties.

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. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested and approved by the FDA. The FDA does not regulate the behavior of physicians in their choice of treatments, but it does restrict the manufacturer's communications on the subject of off-label use of their products. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labeling.

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.

**Healthcare laws and regulations**

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states in which they conduct their business, which may constrain the financial arrangements and relationships through which these companies and their partners research, sell, market and distribute any products for which marketing approval is obtained. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims and transparency laws regarding drug pricing and payments and other transfer of value to physicians and other healthcare providers. If their operations are found to be in violation of any of such laws or any other governmental regulations that apply, they may be subject to penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of operations.

***Current and future healthcare reform legislation***

In the United States, there have been, and likely will continue to be, a number of legislative and regulatory changes regarding the healthcare system directed at broadening the availability of health care, improving the quality of health care and containing or lowering the cost of health care. For example, in March 2010 the Affordable Care Act, or 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, subjected biological products to potential competition by lower-cost biosimilars; expanded 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, which was replaced by a new manufacturer discount program on January 1, 2025 (as discussed below), in which manufacturers were required 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 judicial, administrative, executive and legislative challenges to certain aspects of the ACA. On June 17, 2021 the U.S. Supreme Court dismissed the most recent judicial challenge to the

ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form.

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, included aggregate reductions of Medicare payments to providers. These reductions went into effect on April 1, 2013, and, due to subsequent legislative amendments, will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. 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. Moreover, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminated the statutory Medicaid drug rebate cap for single source and innovator multiple source drugs, beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price.

Payment methodologies may also be subject to changes in healthcare legislation and regulatory initiatives. For example, Centers for Medicare and Medicaid Services 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. By way of example, in August 2022, the Inflation Reduction Act of 2022, or the IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (which began on January 1, 2025). The IRA permits the Secretary of the Department of Health and Human Services, or HHS, to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. These provisions started to take effect progressively starting in fiscal year 2023. On August 15, 2024, HHS announced the agreed-upon prices for the first ten drugs that will be subject to price negotiations, which take effect in January 2026. HHS will select up to fifteen additional products covered under Part D for negotiation in 2025. Each year thereafter, more Part B and Part D products will become subject to the HHS price negotiation program, although the program is currently subject to legal challenges.

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.

We expect that additional federal and state healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in limited coverage and reimbursement and reduced demand for our products, once approved, or additional pricing pressures.

***Coverage, pricing and reimbursement***

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. Sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such drug products. In the United States, third-party payors include federal and state healthcare programs, government authorities, private manage care providers, private health insurers and other organizations. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs.

Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical drug products and medical services, in addition to questioning their safety and efficacy. Such payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our product candidates, if approved, in addition to the costs required to obtain the FDA approvals. Nonetheless, our product candidates may not be considered medically necessary or cost-effective. Moreover, the process for determining whether a third-party payor will provide coverage for a drug product may be separate from the process for setting the price of a drug product or for establishing the reimbursement rate that such a payor will pay for the drug product. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and could increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

***Regulations outside of the United States***

In addition to regulations in the United States, we may be subject to a variety of regulations in foreign jurisdictions that govern, among other things, preclinical and clinical studies, commercial sales and distribution of our future products. Most countries outside of the United States, including the European Union, or the EU, require that clinical trial applications, or CTAs, be submitted to and approved by the local regulatory authority for each clinical study. In addition, whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approval from comparable regulatory authorities outside the United States before we can commence clinical studies or marketing of the product candidate in those countries. The requirements and process governing the conduct of clinical trials, approval, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

*Non-clinical studies and clinical trials in the European Union*

Similar to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new biological substances. Non-clinical (pharmaco-toxicological) studies must be conducted in compliance with the principles of good laboratory practice, or GLP, as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products, e.g., radio-pharmaceutical precursors for radio-labeling purposes). In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use, or ICH, guidelines on good clinical practices, or GCP, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive,

became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, or CTIS, which contains a centralized EU portal and database.

While the EU Clinical Trials Directive required a separate CTA to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR transition period ended on January 31, 2025, and all clinical trials (and related applications) are now fully subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with Good Manufacturing Practice, or GMP. Other national and EU-wide regulatory requirements may also apply.

*Marketing authorization*

In order to market our product candidates in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization, or MA. To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit a MA application, or MAA. The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MAs" are issued by the European Commission through the centralized procedure based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and are valid throughout the EU. The centralized procedure is compulsory for certain types of medicinal products such as (i) medicinal products derived from biotechnological processes, (ii) designated orphan medicinal products, (iii) advanced therapy medicinal products, or ATMPs (such as gene therapy, somatic cell therapy and tissue engineered products) and (iv) medicinal products containing a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative diseases or autoimmune diseases and other immune dysfunctions, and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.
- "National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops. In exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops).

Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIority MEdicines, or PRIME, scheme, which provides incentives similar to the breakthrough therapy designation in the United States. In

March 2016, the EMA launched an initiative, the PRIME scheme, a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Under the above-described procedures, in order to grant the MA, the EMA or the competent authorities of the EU member states make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. MAs have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance.

*Data and market protection*

In the EU, new products authorized for marketing (*i.e.*, reference products) generally receive eight years of data exclusivity and an additional two years of market exclusivity upon MA. If granted, the data exclusivity period prevents generic and biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until ten years have elapsed from the initial MA of the reference product in the EU. The overall ten-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications, which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical or biological entity, and products may not qualify for data exclusivity.

*Orphan medicinal products*

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product can be designated as an orphan if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life threatening or chronically debilitating condition, (2) either (a) such condition affects not more than five in 10,000 persons in the EU when the application is made or (b) the product, without the benefits derived from the orphan status, would not generate sufficient return in the EU to justify the necessary investment and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized for marketing in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition.

Orphan designation must be requested before submitting an MAA. An EU orphan designation entitles a party to incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized procedure. Upon grant of a MA, orphan medicinal products are entitled to ten years of market exclusivity for the approved indication, which means that the competent authorities cannot accept another MAA, or grant a MA, or accept an application to extend a MA for a similar medicinal product for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan, or PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The orphan exclusivity period may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for which it received orphan destination, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. Additionally, MA may be granted to a similar product for the same indication at any time if (i) the second applicant can establish that its product, although similar, is safer, more

effective or otherwise clinically superior; (ii) the applicant consents to a second orphan medicinal product application; or (iii) the applicant cannot supply enough orphan medicinal product.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

*Other healthcare laws*

In the EU, many EU member states have adopted specific anti-gift statutes that further limit commercial practices for medicinal products, in particular vis-à-vis healthcare professionals and organizations. Additionally, there has been a recent trend of increased regulation of payments and transfers of value provided to healthcare professionals or entities and many EU member states have adopted national “Sunshine Acts” which impose reporting and transparency requirements (often on an annual basis), similar to the requirements in the United States, on pharmaceutical companies. Certain countries also mandate implementation of commercial compliance programs, or require disclosure of marketing expenditures and pricing information. Violation of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, disgorgement, additional reporting obligations and oversight if a manufacturer becomes subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and imprisonment.

*Coverage, pricing and reimbursement*

In addition, in many countries, 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.

In the EU, governments influence the price of products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. Member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms. 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 to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. The downward pressure on healthcare costs in general, particularly prescription products, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low priced markets exert a commercial pressure on pricing within a country.

*Healthcare Reform*

The EU is also subject to political, economic and regulatory developments which may affect the ability of pharmaceutical companies to profitably commercialize their products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for

national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could restrict or regulate post-approval activities and affect the ability of pharmaceutical companies to commercialize their products. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

In the EU, potential reductions in prices and changes in reimbursement levels could be the result of different factors, including reference pricing systems, parallel distribution and parallel trade. It could also result from the application of external reference pricing mechanisms, which consist of arbitrage between low-priced and high-priced countries. Reductions in the pricing of our medicinal products in one EU member state could affect the price in other EU member states and, thus, have a negative impact on our financial results.

Health Technology Assessment, or HTA, of medicinal products in the EU is an essential element of the pricing and reimbursement decision-making process in a number of EU member states. The outcome of HTA has a direct impact on the pricing and reimbursement status granted to the medicinal product. A negative HTA by a leading and recognized HTA body concerning a medicinal product could undermine the prospects to obtain reimbursement for such product not only in the EU member state in which the negative assessment was issued, but also in other EU member states.

In 2011, Directive 2011/24/EU was adopted at the EU level. This Directive establishes a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states. The network facilitates and supports the exchange of scientific information concerning HTAs. Further to this, on December 13, 2021, Regulation No 2021/2282 on HTA, amending Directive 2011/24/EU, was adopted. The Regulation entered into force in January 2022 and has been applicable since January 2025, with phased implementation based on the type of product, i.e. oncology and advanced therapy medicinal products as of 2025, orphan medicinal products as of 2028, and all other medicinal products by 2030. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

***Data privacy and security laws***

Numerous state, federal and foreign laws govern the collection, dissemination, use, access to, confidentiality, and security of personal information, including health-related information. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws, including the Health Insurance Portability and Accountability Act of 1996 and regulations promulgated thereunder, or HIPAA, and federal and state consumer protection laws and regulations that govern the collection, use, disclosure, and protection of health-related and other personal information could apply now or in the future to our operations or the operations of our partners. In addition, certain state and non-U.S. laws, such as the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020, collectively, the CCPA, and the General Data Protection Regulation, or GDPR, and the U.K. GDPR, govern the privacy and security of personal information, including health-related information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to make compliance efforts more challenging, and can result in investigations, proceedings, or actions that lead to significant penalties and restrictions on data processing.

***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.

**HUMAN CAPITAL**

At Praxis, our mission is to help patients by delivering life-altering treatments faster and more effectively than has ever been done before. Agnostic to the source of an idea, we work tirelessly to find the most practical solutions for patients as quickly and efficiently as possible.

Our people, the patient communities we serve and their caregivers and families are at the forefront of our efforts. Our approach to building a robust clinical pipeline provides a forum for exploration and innovation where we are all involved in building the company together.

As a flat and agile organization, each employee has an impact. Our ways of working are team-based and focused on co-creation. We respect all opinions and encourage diversity. Discrimination is never tolerated. We are dedicated to developing our culture and our employees through our company core values – ***Trust***, ***Ownership***, ***Curiosity*** and ***Results***. Our ability to deliver life-altering treatments to patients and families affected by and living with complex brain disorders is built on the foundation of our shared core values. More than just statements and ideas, our values provide structure for the way we work as a company and set the expectation for what we can achieve together. By living our values, our teams drive us to deliver positive results for the communities we serve.

It is the strength of our culture and career-defining opportunities that enable us to attract and retain incredible talent to Praxis. As of February 26, 2025, we have 116 employees and plan to grow as we continue to realize the potential of our pipeline. In order to ambitiously deliver results based on the depth of our pipeline, we plan to grow significantly. We provide development opportunities that will stretch and challenge employees to deliver more than they ever thought possible. To support them we offer a world-class portfolio of compensation and benefits, including medical, dental and vision plans, a discretionary bonus program structured to pay on a quarterly basis, 401k plan with match, wellness benefits, eligibility for equity awards and an employee stock purchase plan.

**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' equity and working capital. Our net losses were $182.8 million and $123.3 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $836.7 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 internationally, for our product candidates;
- 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 our product candidates that may 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; and
- acquire or in-license other product candidates and technologies.

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 our product candidates, 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 our current product candidates and other product candidates we may develop and pursue, including drug product manufacturing;
- the timing and uncertainty of, and the costs involved in, obtaining marketing approvals for our current product candidates, 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 our product candidates 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 our product candidates 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 and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications and 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 current cash, cash equivalents and marketable securities will be sufficient to fund our operating expenditures and capital expenditure requirements into 2028. 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, our existing stockholders' ownership interests may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect the rights of our stockholders. 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 a clinical-stage biopharmaceutical company with 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, focused on translating genetic insights into the development of therapies for 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. Our operations have been focused on developing and conducting preclinical and clinical studies of our product candidates. To date, 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 limited 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 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 our product candidates. 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 for product candidates for which we successfully complete clinical development and clinical trials, if any;
- 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 approval, if any, 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, if any;

- 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.

***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.***

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. We are currently evaluating (i) ulixacaltamide for the treatment of essential tremor, or ET, (ii) vormatrigine for the treatment of common epilepsies, including focal onset seizures and generalized epilepsy, (iii) relutrigine for the treatment of SCN2A development and epileptic encephalopathy, or SCN2A-DEE, SCN8A development and epileptic encephalopathy, or SCN8A-DEE, and broader DEEs; and (iv) elsunersen for the treatment of SCN2A-DEE. Our drug development strategy is to clinically test and seek regulatory approval for our product candidates in indications in which we believe we will be able to efficiently generate proof-of-concept data. If any of our product candidates is approved, we then intend to expand to clinical testing and potentially seek regulatory approvals in other neurological 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 gain regulatory approval in another indication or expand to other indications.

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. 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 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

***The development and commercialization of drug products is subject to extensive regulation, and the regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-***

***consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates on a timely basis if at all, our business will be substantially harmed.***

The clinical development, manufacturing, labeling, packaging, storage, recordkeeping, advertising, promotion, export, import, marketing, distribution, adverse event reporting, including the submission of safety and other post-marketing information and reports, and other possible activities relating to our product candidates are subject to extensive regulation. In the United States, obtaining marketing approval for a new drug requires the submission of a New Drug Application, or NDA, to the FDA, and we are not permitted to market any product candidate in the United States until we obtain approval from the FDA of the NDA for that product candidate. An NDA must be supported by extensive clinical and preclinical data, as well as extensive information regarding pharmacology, chemistry, manufacturing, and controls. Outside the United States, many comparable foreign regulatory authorities employ similar approval processes.

We have not previously submitted an NDA to the FDA or similar marketing authorization application to comparable foreign authorities, for any product candidate, and we cannot be certain that any of our product candidates will receive regulatory approval. Obtaining approval of an NDA can be a lengthy, expensive, and uncertain process, and as a company we have no experience with the preparation of an NDA submission or any other marketing authorization application.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere, or regulatory authorities may not accept a submission due to, among other reasons, the content or formatting of the submission;
- the FDA or comparable foreign regulatory authorities may fail to approve our manufacturing processes or facilities or those of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process, and determining when or whether regulatory approval will be obtained for any of our product candidates. For example, regulatory authorities in various jurisdictions have in the past had, and may in the future have, differing requirements for, interpretations of and opinions on our preclinical and clinical data. As a result, we may be required to conduct additional preclinical studies, alter our proposed clinical trial designs, or conduct additional clinical trials to satisfy the regulatory authorities in each of the jurisdictions in which we hope to conduct clinical trials and develop and market our products, if approved. Further, even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA or any comparable foreign regulatory authority.

Even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful

commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

In addition, the FDA and foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may however have a significant impact on the pharmaceutical industry and our business in the long term.

***Preclinical and clinical drug 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 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, pivotal 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. Certain of our product candidates failed to meet the primary endpoint in later stage clinical trials and we may in the future have product candidates that fail to show the desired safety and efficacy results in later stage clinical trials despite having progressed through preclinical studies and initial clinical trials. There can be no assurance that any of our future clinical trials will ultimately be successful or support further clinical development of our product candidates. The commencement and rate of completion of preclinical studies and clinical trials for a product candidate may be delayed by many factors, including, for example:

- inability to generate sufficient preclinical or other in vivo or in vitro data to support the initiation of clinical studies;
- timely completion of preclinical laboratory tests, animal studies and formulation studies in accordance with the Good Laboratory Practice requirements and other applicable regulations of the U.S. Food and Drug Administration, or the FDA, and comparable foreign regulatory authorities;
- delays in obtaining approval from independent Institutional Review Boards, or IRBs, or ethics committees at the clinical sites we intend to utilize in our clinical trials;
- delays in reaching a consensus with regulatory agencies on study design and obtaining regulatory authorization to commence clinical trials; delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;
- delays in recruiting suitable patients to participate in our clinical trials;
- delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing;
- insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- imposition of a temporary or permanent clinical hold by regulatory authorities;
- developments on trials conducted by competitors for related technology that raises FDA or foreign regulatory authority concerns about risk to patients of the technology broadly, or if the FDA or a foreign

regulatory authority finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;

- delays in recruiting, screening and enrolling patients and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- delays caused by operational issues at clinical sites or the use of a decentralized clinical trial model;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties or us to adhere to clinical trial protocols;
- failure to perform in accordance with the FDA's or any other regulatory authority's Good Clinical Practice, or GCP, requirements, or applicable regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits, or occurrence of adverse events in trials of the same class of agents conducted by other companies;
- changes to the clinical trial protocols;
- clinical sites deviating from trial protocol or dropping out of a trial;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data;
- the cost of clinical trials of our product candidates being greater than we anticipated;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates;
- transfer of manufacturing processes to larger-scale facilities operated by a contract development and manufacturing organization, or CDMO, and delays or failure by our CDMOs or us to make any necessary changes to such manufacturing process; and
- third parties being unwilling or unable to satisfy their contractual obligations to us.

Clinical trials must be conducted in accordance with the FDA and other applicable regulatory authorities' legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and ethics committees or IRBs at the medical institutions where the clinical trials are conducted. Before commencing a clinical trial, the FDA or comparable foreign regulatory authorities could raise questions about or concerns with our proposed clinical protocol. For example, the FDA has previously issued clinical holds on certain of our product candidates, and we could not commence the respective clinical trial until such questions or concerns were resolved.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, we may need to amend clinical trial protocols that could require us to resubmit our clinical trial protocols to IRBs or ethics committees for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Some of our trials are, have been, and may in the future 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. 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.

In addition, we plan to conduct clinical trials of certain of our product candidates, including ulixacaltamide, utilizing novel primary endpoints for which the FDA and other regulatory authorities may have limited experience in interpreting and reviewing. Although we have sought consensus with FDA and other regulatory authorities in connection with the design and implementation of our clinical studies, utilizing novel trial endpoints may increase the risk that the FDA and other regulatory authorities will consider the results from such trials, even if successful, insufficient to establish the safety or efficacy of our product candidates, which could require us to conduct additional studies beyond those we currently contemplate for our product candidates.

Further, conducting clinical trials in foreign countries, such as the European Union, or EU, for our product candidates presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

Delays in the completion of any preclinical studies or clinical trials of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate product revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Any delays to our preclinical studies or clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR transition period ended January 31, 2025, and all clinical trials (and related applications) are now fully subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

***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.***

Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates 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 the FDA, the IRBs or DSMBs 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 patient 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.

In addition to side effects caused by our product candidates, the administration process or related procedures of our product candidates could cause adverse side effects, such as the intrathecal or intravitreal administration process or related procedures for antisense oligonucleotide drugs, or ASOs. If any such adverse events occur, our clinical trials could be suspended or terminated. Even if we can demonstrate that adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the clinical trial. Additionally, other ASOs in clinical development utilizing intrathecal delivery could also generate data that could adversely affect the clinical, regulatory or commercial perception of our product candidates.

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;
- the FDA may require a Risk Evaluation and Mitigation Strategy, or 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.

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 have, and may in the future, 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 and nature of the patient population;
- 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;
- 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. Such limitations can also impact the diversity of the patient pool, which may also adversely impact our clinical trials or results.

Our inability to enroll a sufficient number or diversity 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.

***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 publicly disclose preliminary or topline data from our clinical trials, which 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 or preliminary 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 or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the topline or preliminary data we previously reported. As a result, topline and preliminary data should be viewed with caution until the final data are available.

From time to time, we disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we complete are subject to numerous risks, including statistical risks, methodological risks and

operational risks. If interim analyses suggest unexpected results, we may decide to modify the trial design, analytical methods or take other steps in response, which ultimately may or may not lead to a more favorable outcome. Adverse changes between interim data and final data could also significantly harm our business and prospects. 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. 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 interim, preliminary or topline data that we report differ from later, 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 our product candidates may be smaller than we expect.***

Our estimates of the potential market opportunities in each of our platforms include several key assumptions based on our industry knowledge, industry publications and third-party research reports and other data sources and estimates. There can be no assurance that any of these assumptions are, or will remain, accurate. If the actual markets identified for our product candidates, or for any other product candidate we may develop in the future, 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 conduct clinical trials for our product candidates in the United States, Europe and 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.***

The acceptance of study data from preclinical studies and clinical trials conducted outside the United States 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, regardless of whether the trials were subject to an IND, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and the trials were performed by clinical investigators of recognized competence; and the data are considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. For trials that are conducted only at sites outside of the United States and not subject to an IND, the FDA requires the clinical trial to have been conducted in accordance with GCP and the FDA must be able to validate the data from the clinical trial through an on-site inspection if it deems such inspection necessary. For such trials not subject to an IND, the FDA generally does not review the clinical protocols for the trials, and therefore there is an additional potential risk that the FDA could determine that the trial design or protocol for a non-United States clinical trial was inadequate, which could require us to conduct additional clinical trials. 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 obtained orphan drug designation for relutrigine and elsunersen and may 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 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. Orphan drug designation must be requested and granted by the FDA before a new NDA is submitted. After the FDA grants orphan drug designation, it will disclose publicly the generic identity of the drug and its potential orphan use. In the EU, the European Commission grants orphan designation on the basis of the EMA's Committee for Orphan Medicinal Products opinion. A medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from the orphan status, would not generate sufficient return in the EU to justify the necessary investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment, of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition.

In the United States, orphan designation entitles a party to financial incentives such as opportunities for grant funding toward clinical trial costs, tax advantages and user-fee waivers. In addition, if a product candidate that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same product for the same disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity. The applicable exclusivity period is ten years in the EU, but such exclusivity period can be reduced to six years if, at the end of the fifth year, a product no longer meets the criteria for orphan designation or if the product is sufficiently profitable that market exclusivity is no longer justified.

The FDA granted orphan drug designation to relutrigine for the treatment of SCN2A-DEE and SCN8A-DEE, respectively, and to elsunersen for the treatment of SCN2A-DEE. We also obtained orphan designation in the EU for relutrigine for the treatment of SCN2A-DEE and SCN8A-DEE, and for elsunersen for the treatment of SCN2A-DEE. We may seek orphan drug designation for other current and future product candidates.

In the EU, orphan designation entitles a party to financial incentives such as reduction of fees, fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. Moreover, upon grant of a marketing authorization and assuming the requirement for orphan designation are also met at the time the marketing authorization is granted, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan. However, during such period, marketing authorizations may be granted to a similar medicinal product with the same orphan indication if: (i) the applicant can establish that the second medicinal product, although similar to the orphan medicinal product already authorized is safer, more effective or otherwise clinically superior to the orphan medicinal product already authorized; (ii) the marketing authorization holder for the orphan medicinal product grants its consent; or (iii) if the marketing authorization holder of the orphan medicinal product is unable to supply sufficient quantities of product. The European exclusivity period can be reduced to six years, if, at the end of the fifth year a medicine no longer meets the criteria for orphan designation (i.e. the prevalence of the condition has increased above the orphan designation threshold or it is judged that the product is sufficiently profitable so as not to justify maintenance of market exclusivity).

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA or comparable foreign regulatory authority can subsequently approve the same drug for the

same condition if such regulatory authority concludes that the later drug is clinically superior because it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or comparable foreign regulatory authority later determines that the initial request for designation was materially defective. In addition, orphan drug exclusivity does not prevent the FDA from approving competing drugs for the same or similar disease or condition containing a different active ingredient. In addition, if a subsequent drug is approved for marketing for the same or a similar disease or condition as any of our product candidates that receive marketing approval, we may face increased competition and lose market share regardless of orphan drug exclusivity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

***We received rare pediatric disease designation for relutrigine and elsunersen. However, a marketing application for these product candidates, if approved, may not meet the eligibility criteria for a rare pediatric disease priority review voucher.***

In 2012, U.S. Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a “rare pediatric disease” that meets certain criteria may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the United States within one year following the date of approval.

We received rare pediatric disease designation for relutrigine for the treatment of SCN2A-DEE, SCN8A-DEE and Dravet syndrome and for elsunersen 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 December 20, 2024 is currently limited to product candidates that receive rare pediatric disease designation on or prior to December 20, 2024, and the FDA may only award rare pediatric disease priority review vouchers through September 30, 2026. However, it is possible the authority for the FDA to award rare pediatric disease priority review vouchers will be further extended by Congress.

***We received PRIME designation by the EMA for elsunersen and we may seek PRIME or other designations, schemes or tools in the EU for one or more of our product candidates, which we may not receive. Such designations may not lead to a faster development or regulatory review or approval process and do not increase the likelihood that our product candidates will receive marketing authorization.***

We may seek EMA PRIME (PRIority MEdicines) designation or other designations, schemes or tools for one or more of our product candidates. In the EU, innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the Breakthrough Therapy designation in the United States. PRIME is a voluntary scheme aimed at enhancing the EMA’s support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. The benefits of a PRIME designation include the appointment of a rapporteur before submission of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

In November 2023, elsunersen was granted PRIME designation by the EMA’s Committee for Medicinal Products for Human Use, or CHMP, for the treatment of SCN2A-DEE. Acknowledging that elsunersen targets an unmet medical need, the EMA offers enhanced support in the development of the medicinal product through enhanced interaction and early dialogue to optimize our development plans and speed up regulatory evaluation in the EU. The PRIME designation does not, however, guarantee that the regulatory review process in the EU will be

shorter or less demanding. Neither does the PRIME designation guarantee that the European Commission will grant a marketing authorization for elsunersen.

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.

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.

***Our product candidates may be regulated as controlled substances, the making, use, sale, importation, exportation, and distribution of which are subject to significant regulation by the U.S. Drug Enforcement Administration, or DEA, and other regulatory agencies.***

Our product candidates may be classified as controlled substances, which are subject to state, federal, and foreign laws and regulations regarding their manufacture, use, sale, importation, exportation, and distribution. Among other things, controlled substances are regulated under the federal Controlled Substances Act of 1970, and regulations of the DEA.

The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use and may not be marketed or sold in the United States. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. Prior to commercialization, centrally acting drugs, such as those we are developing, are generally subject to review and potential scheduling by the DEA. It is possible that our product candidates may be regulated by the DEA as controlled substances, which would subject such product candidates to additional restrictions regarding their manufacture, shipment, storage, sale and use, depending on the scheduling of the active ingredients, and may limit the commercial potential of any of our product candidates, if approved.

Various states also independently regulate controlled substances. Though state controlled substances laws often mirror federal law, because the states are separate jurisdictions, they may separately schedule drugs as well. While some states automatically schedule a drug when the DEA does so, in other states there must be rule making or a legislative action. State scheduling may delay commercial sale of any controlled substance drug product for which we obtain federal regulatory approval and adverse scheduling could impair the commercial attractiveness of such product. We or our collaborators must also obtain separate state registrations in order to be able to obtain, handle and distribute controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions from the states in addition to those from the DEA or otherwise arising under federal law.

For any of our product candidates classified as controlled substances, we and our suppliers, manufacturers, contractors, customers and distributors are required to obtain and maintain applicable registrations from state, federal and foreign law enforcement and regulatory agencies and comply with state, federal and foreign laws and regulations regarding the manufacture, use, sale, importation, exportation and distribution of controlled substances. There is a risk that DEA regulations may limit the supply of the compounds used in clinical trials for our product candidates, and, in the future, the ability to produce and distribute our products in the volume needed to meet commercial demand. Regulations associated with controlled substances govern manufacturing, labeling, packaging, testing, dispensing, production and procurement quotas, recordkeeping, reporting, handling, shipment and disposal.

These regulations increase the personnel needs and the expense associated with development and commercialization of product candidates including controlled substances. The DEA, and some states, conduct periodic inspections of registered establishments that handle controlled substances. Failure to obtain and maintain required registrations or comply with any applicable regulations could delay or preclude us from developing and commercializing our product candidates containing controlled substances and subject us to enforcement action. The DEA may seek civil penalties, refuse to renew necessary registrations or initiate proceedings to revoke those registrations. In some circumstances, violations could lead to criminal proceedings. Because of their restrictive nature, these regulations could limit commercialization of any of our product candidates that are classified as controlled substances.

***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 approved therapies for ET, such as propranolol, and off-label therapies, such as primidone; and sodium channel blocker or similar ion channel-targeting programs in development for common epilepsies, including those of SK-Pharma, Xenon Pharmaceuticals, and Biohaven Pharmaceuticals, as well as other programs in clinical development targeting other mechanisms of action including those from Lundbeck, and Stoke Therapeutics, 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 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 or similar regulatory requirements outside the United States 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 or other similar regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP or similar regulatory requirements 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. Similar requirements may apply in foreign jurisdictions. 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 and elsewhere, the FDA and foreign regulatory authorities 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 or similar 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 or foreign regulatory authorities 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.

Violations of the FDCA 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. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products, if approved. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

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 be subject to enforcement action and we may not achieve or sustain profitability.

***The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found or alleged to have improperly promoted off-label uses, we may become subject to significant liability.***

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about drug products. These regulations include standards and restrictions for direct-to-consumer advertising, industry-sponsored scientific and educational activities, promotional activities involving the internet and off-label promotion. For example, any regulatory approval that the FDA grants is limited to those indications and patient populations for which a drug is deemed to be safe and effective by the FDA.

While physicians in the United States may choose, and are generally permitted, to prescribe products for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, our ability to promote any of our products candidates, if approved, will be narrowly limited to those indications and populations that are specifically approved by the FDA or such other regulatory agencies, and if we are found to have promoted such off-label uses, we may become subject to significant liability. For example, the federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The government has also required companies to enter into consent decrees or imposed permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

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 Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS, determines whether and to what extent new 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 EU, 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 reimbursed 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 EU 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 Europe, 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 healthcare 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 remuneration is to induce referrals, the federal Anti-Kickback statute is violated. 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. In addition, 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;

- 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;
- the federal Physician Payments Sunshine Act 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), certain non-physician providers including physician providers including physician assistants and nurse practitioners, and teaching hospitals, as well as ownership and investment interests held by the physicians and their immediate family members;
- 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; and 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.

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. 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.

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.***

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information, such as information that we may collect in connection with clinical trials in the United States and abroad. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perceptions of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulations, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business.

In Europe, the GDPR took effect in May 2018. The GDPR imposes stringent requirements on entities that process personal data of individuals in the European Economic Area, or EEA. These requirements include, for example, establishing a legal basis for processing, providing notice to data subjects about how personal data is collected and processed, developing procedures to vindicate expanded data subject rights, implementing appropriate technical and organizational measures to safeguard personal data, introducing the obligation to notify data protection regulators or supervisory authorities (and in certain cases, affected individuals) of significant data breaches, imposing limitations on retention of personal data, maintaining a record of data processing and complying with the principal of accountability and the obligation to demonstrate compliance through policies, procedures, training and audit. In addition, the GDPR establishes 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 processing of personal data collected during the course of clinical trials is therefore subject to heightened protections under the GDPR. Violations of the GDPR can lead to potential fines of up to €20 million or 4% of the annual global revenues of the noncompliant undertaking, whichever is greater. In addition to the foregoing, a breach of the GDPR could result in regulatory investigations, reputational damage, orders to cease/change our processing of our data, enforcement notices, and/or assessment notices (for a compulsory audit). We may also face civil claims including representative actions and other class action type litigation (where individuals have suffered harm), potentially amounting to significant compensation or damages liabilities, as well as associated costs, diversion of internal resources, and reputational harm.

Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United

States, and the efficacy and longevity of current transfer mechanisms between the EEA and the United States remains uncertain. Case law from the Court of Justice of the European Union, or the CJEU, states that reliance on the standard contractual clauses, or SCCs — a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism — alone may not necessarily be sufficient in all circumstances. Use of the SCCs must now be assessed on a case-by-case basis. The European Commission adopted its Adequacy Decision in relation to the new EU-U.S. Data Privacy Framework, or DPF, on July 10, 2023, rendering the DPF effective as a GDPR transfer mechanism to U.S. entities self-certified under the DPF. The existing legal complexity and uncertainty regarding international personal data transfers may continue, and in particular, the DPF Adequacy Decision could be challenged and international transfers to the United States and to other jurisdictions more generally could continue to be subject to enhanced scrutiny by regulators. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Further, since January 2021, we may also be subject to the UK GDPR, which, together with the UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, meaning the potential of parallel fines of up to the greater of £17.5 million or 4% of a non-compliant undertaking's global annual revenue for the preceding financial year. On October 12, 2023, the UK Extension to the DPF came into effect (as approve by the UK government) as a data transfer mechanism from the UK to U.S. entities self-certified under the DPF.

In the United States, 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, as well as their covered subcontractors. While we do not believe that we are currently acting as a covered entity or business associate under HIPAA, we may receive individually identifiable health information from these entities. Failure to receive this information properly could subject us to HIPAA's criminal penalties. Further, any person may be prosecuted under HIPAA’s criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA’s requirements for disclosure of individually identifiable health information.

Various states have also implemented similar privacy laws and regulations, such as the California Confidentiality of Medical Information Act, or the CMIA, that impose restrictive requirements regulating the use and disclosure of health information and other personally identifiable information. In addition to imposing fines and penalties, some of these state laws afford private rights of action to individuals who believe their personal information has been misused. California’s patient privacy laws, for example, provide for significant penalties and permit injured parties to sue for damages. In addition to the CMIA, California also enacted the CCPA, which requires covered businesses that process the personal information of California residents to, among other things: (i) provide certain disclosures to California residents regarding the business’s collection, use, and disclosure of their personal information; (ii) receive and respond to requests from California residents to access, delete, and correct their personal information, or to opt out of certain disclosures of their personal information; and (iii) enter into specific contractual provisions with service providers that process California resident personal information on the business’s behalf. Similar laws have been passed in other states and are continuing to be proposed at the state and federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by the CCPA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

In addition, we use artificial intelligence, or AI, machine learning, and automated decision-making technologies, collectively, AI Technologies, in our business from time to time. The regulatory framework for AI Technologies is rapidly evolving as many federal, state, and foreign government bodies and agencies have introduced or are currently considering additional laws and regulations. Additionally, existing laws and regulations may be interpreted in ways that would affect the operation of AI Technologies. As a result, implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine

the impact future laws, regulations, standards, or market perception of their requirements may have on our business and may not always be able to anticipate how to respond to these laws or regulations.

It is possible that new laws and regulations will be adopted in the United States and in other non-U.S. jurisdictions, or that existing laws and regulations, including competition and antitrust laws, may be interpreted in ways that would limit our ability to use AI Technologies for our business, or require us to change the way we use AI Technologies in a manner that negatively affects the performance of our products, services, and business and the way in which we use AI Technologies. We may need to expend resources to adjust our products or services in certain jurisdictions if the laws, regulations, or decisions are not consistent across jurisdictions. Further, the cost to comply with such laws, regulations, or decisions and/or guidance interpreting existing laws, could be significant and would increase our operating expenses (such as by imposing additional reporting obligations regarding our use of AI Technologies). Such an increase in operating expenses, as well as any actual or perceived failure to comply with such laws and regulations, could adversely affect our business, financial condition and results of operations.

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. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties 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.***

In the United States 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, which was replaced by a new manufacturer discount program on January 1, 2025 (as discussed below), in which manufacturers were required 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. On June 17, 2021 the U.S. Supreme Court dismissed the recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form.

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, included aggregate reductions of Medicare payments to providers. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. 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. Moreover, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminated the statutory Medicaid drug rebate cap for single source and innovator multiple source drugs, beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price.

Payment methodologies may also 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. By way of example, in August 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (which began on January 1, 2025). The IRA permits the Secretary of the Department of Health and Human Services, or HHS, to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. These provisions started to take effect progressively starting in fiscal year 2023. On August 15, 2024, HHS announced the agreed-upon prices for the first ten drugs that are subject to price negotiations, which take effect in January 2026. HHS will select up to fifteen additional products covered under Part D for negotiation in 2025. Each year thereafter, more Part B and Part D products will become subject to the HHS price negotiation program.

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.

***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 and foreign regulatory authorities 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 FDA and foreign regulatory authorities 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. In addition, government funding of other government agencies 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 and or modifications to approved drugs or to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. If a prolonged government shutdown occurs, or if global health concerns hinder or 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 or other regulatory

authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

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 laws of EU member states, and in respect of the United Kingdom (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 must often be subject to a prior notification and/or 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, 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.

In the EU, similar developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and EU, reimbursement and healthcare payment

systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

In December 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA, amending Directive 2011/24/EU, was adopted. The Regulation entered into force in January 2022 and has been applicable since January 2025, with phased implementation based on the type of product, i.e., oncology and advanced therapy medicinal products as of 2025, orphan medicinal products as of 2028, and all other medicinal products by 2030. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (*e.g.*, economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

***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. Certain of these laws impose joint and several liability, including in some instances regardless of fault or legality at

the time of occurrence. 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. The trend has generally been for such laws and regulations, and associated interpretations, to become more stringent over time. For example, various policymakers have adopted or are considering adopting, requirements for various climate- or other sustainability-related disclosures or other actions. 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 depends 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, or obtain, maintain and/or enforce patents or trademarks that may issue or be registered based on our applications, at a reasonable cost or in a timely manner. In addition, our pending and future patent applications may not result in issued patents that protect our technology or products, in whole or in part, or may not effectively prevent others from commercializing competitive technologies and products. Changes in either patent laws or interpretation of patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. Further, 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. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such results before a patent application is filed, thereby jeopardizing our ability 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 that we hold with respect to our product candidates is threatened, it could

dissuade companies from collaborating with us to develop new or improved products 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 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 or duplicate any of our technologies without infringing our intellectual property rights;
- 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 may 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 are likely to 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 that 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 or otherwise experience disruptions to our business relationships with our current or future licensors, we could lose 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 reporting, 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, or to pursue other remedies.

We may not be able to obtain licenses at a reasonable cost or on reasonable terms, if at all. Furthermore, if we lose intellectual property rights licensed under existing agreements or fail to obtain future licenses, we may be required to expend considerable time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected proprietary technologies and product candidates, which could harm our business significantly. Third-party patents may exist which might be enforced against our current or future proprietary technologies and product candidates, resulting in either an injunction

prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties

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 could 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. If any of our current or future licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business and our competitors could market competing products using the intellectual property. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners, including loss of our right to prosecute the licensed patent applications or early termination of the license by our licensor. We also may 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.

***Our technology licensed from third parties may be subject to retained rights.***

Any license we may enter into could provide for the retention by the licensor of certain rights under their agreements with us, including for example, the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether any future licensors will limit their use of the technology to these uses, and we may incur substantial expenses to enforce our rights to our licensed technology in the event of misuse.

In addition, the U.S. government retains certain rights in inventions produced with its financial assistance under the Patent and Trademark Law Amendments Act, or the Bayh-Dole Act. The U.S. government retains a "nonexclusive, nontransferable, irrevocable, paid-up license" for its own benefit. The Bayh-Dole Act also provides federal agencies with "march-in rights". March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a "nonexclusive, partially exclusive, or exclusive license" to a "responsible applicant or applicants". If the patent owner refuses to do so, the government may grant the license itself. The Bayh-Dole Act also imposes other obligations, including the requirement that products covered by the government funded patents be manufactured in the United States. We sometimes collaborate with academic institutions to accelerate our preclinical research or development. In the future, we may own or license technology

which is critical to our business that is developed in whole or in part with federal funds subject to the Bayh-Dole Act. If the federal government exercises its rights under the Bayh-Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected.

***We may rely on trade secrets and proprietary know-how, which can be difficult to trace and enforce and, if we are unable to protect the confidentiality of our trade secrets and proprietary know-how, 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. Additionally, because we expect to rely on third parties in the development and manufacture of our product candidates, we must, at times, share trade secrets with them. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements.

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.

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, or threatened with, 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 slowing or halting the progress of our clinical development and commercialization efforts.

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 that 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.

If we are found to infringe a third-party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing technologies, product candidates or products. Alternatively, we may be required to obtain a license from such third-party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing technologies, product candidates or products. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. A finding of infringement could prevent us from commercializing our technologies, product candidates or products or force us to cease some of our business operations, and could divert the time and attention of our technical personnel and management, cause development delays, and/or require us to develop non-infringing technology, which may not be possible on a cost-effective basis, any of which could materially harm our business. In the event of a successful claim of infringement against us, we may have to pay substantial monetary damages, including treble damages and attorneys' fees for willful infringement, pay royalties and other fees, redesign our infringing drug or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

***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 various 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, in cases where written agreements either do or do not exist, we may be limited in our ability to capitalize on the market potential of these inventions or developments.

Additionally, our licensors may have relied on third-party consultants or collaborators or on funds from third parties, such as the U.S. government, such that our licensors are not the sole and exclusive owners of the patents we in-license. If other third parties have ownership rights or other rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

***We may become subject to claims challenging the inventorship or ownership of our patents and other intellectual property.***

We may be subject to claims that employees, former employees or third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors or not named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, or portion of such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

In addition, while we require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

***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 compounds, compositions of matter, materials, formulations, methods of manufacture or methods of use 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. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates and other proprietary technologies we may develop, could be found to be infringed by our product candidates. 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. A court could also prohibit us from using technologies or features that are essential to our product candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. 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 compounds, compositions, formulations, 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 compounds, compositions formulations, methods of use or processes 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 different or 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 other intellectual property, or the patents or intellectual property of our licensors, which could be expensive, time-consuming and unsuccessful.***

Competitors or other third parties may infringe our patents, trademarks, copyrights or other intellectual property, or the intellectual property 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 and divert time and attention of our management and scientific personnel. Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In addition, in any infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable, in whole or in part, and that we do not have the right 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 or, in some cases, not at all, 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. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. 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.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. 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 litigation. There could also 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 material adverse effect on the price of shares of our common stock. Moreover, we may not have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

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, renewal fees, annuities fees and various other governmental fees on any issued patent and/or patent application are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and/or patent application. 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. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or insufficient written description. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during patent prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention, or decide that the other party's use of our patented technology falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1). An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive position, business, financial

conditions, and prospects. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

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 2043, 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 2043, 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 not already granted or that a court will uphold any patents already issued.

***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.***

Our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. 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. 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.

Further, on June 1, 2023, the European Union Patent Package, or the EU Patent Package, regulations were implemented with the goal of providing a single pan-European Unitary Patent and a new European Unified Patent Court, or UPC, for litigation involving European patents. As a result, all European patents, including those issued prior to ratification of the EU Patent Package, now by default automatically fall under the jurisdiction of the UPC. It is uncertain how the UPC will impact granted European patents in the biotechnology and pharmaceutical industries. Our European patent applications, if issued, could be challenged in the UPC. During the first seven years of the UPC's existence, the UPC legislation allows a patent owner to opt its European patents out of the jurisdiction of the UPC. We may decide to opt out our future European patents from the UPC , but doing so may preclude us from realizing the benefits of the UPC. Moreover, if we do not meet all of the formalities and requirements for opt-out under the UPC, our future European could remain under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum to centrally revoke our European patents, and allow for the possibility of a competitor to obtain pan-European injunction. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize our technology and product candidates and, resultantly, on our business, financial condition, prospects and results of operations.

***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.

In addition, geo-political actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia's conflict in Ukraine may limit or prevent filing, prosecution, and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our

patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees from the United States without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

***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 technologies and 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, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration and may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to launch their product earlier than might otherwise be the case.

***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 current or future 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. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. We may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks that may be costly and time-consuming, and our trademarks may not survive such proceedings. 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. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and tradenames.

**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. Moreover, 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.

Risks Related to Third-Party Manufacturers

***We contract with third parties for the manufacture of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.***

We do not currently have the infrastructure or internal capability to manufacture supplies of our product candidates for use in development and commercialization. We rely, and expect to continue to rely, on third-party manufacturers for the production of our product candidates for preclinical studies and clinical trials under the

guidance of members of our organization. If we were to experience an unexpected loss of supply of any of our product candidates or any of our future product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials.

We expect to continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third party to manufacture our product candidates according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms;
- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the failure of the third party to manufacture our product candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or study drug or placebo not being properly identified;
- clinical supplies not being delivered to clinical sites on time and at expected cost due to inflationary impacts, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the misappropriation of our proprietary information, including our trade secrets and know-how.

We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP or similar regulations for manufacturing both active drug substances and finished drug products. Third-party manufacturers may not be able to comply with cGMP or similar regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain approval for the use of their manufacturing facilities in connection with any of our product candidates that may receive marketing approval. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

***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 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 have, and may seek in the future, 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, such as The Florey Institute of Neuroscience. 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

***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, including our ability to prosecute or maintain patents in Russia due to the sanctions imposed by the United States and other countries on Russia as a result of Russia's invasion of Ukraine and our ability to enforce patents due to Russia's March 2022 decree that allows the use of inventions, utility models and industrial designs that are held by intellectual property owners from "unfriendly countries," including the United States, without the consent of or payment of any compensation to such owners;
- 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 Foreign Corrupt Practices Act, U.K. Bribery Act of 2010 or comparable foreign laws, including expanded sanctions imposed by the United States and other countries on Russia due to Russia's invasion of Ukraine;
- business interruptions resulting from geo-political actions, including war and terrorism, such as Russia's invasion of Ukraine, 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, including an increased likelihood that Russia's invasion of Ukraine could result in more cyberattacks or cybersecurity incidents.

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

***We or the third parties upon whom we depend may be adversely affected by natural disasters, health epidemics or other business interruptions and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

Natural disasters or health epidemics could severely disrupt our operations, and have a material adverse impact on our business, results of operations, financial condition, and prospects. If a natural disaster, power outage, health epidemic or other event occurred that prevented us from conducting our clinical trials, releasing clinical trial results or delaying our ability to obtain regulatory approval for our product candidates, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The extent to which these events will impact our business will depend on future developments, which are highly uncertain and cannot be predicted, including with regard to their impact on economic conditions and social activity, including with respect to inflationary pressures and supply chain shortages and disruptions, among others.

For example, since December 2019, several novel strains of coronavirus have been identified and continue to spread globally, including in the United States, and the disease they cause, COVID-19, has been declared a pandemic by the World Health Organization. At present, we are not experiencing significant impact or delays from the COVID-19 pandemic on our business, operations and, if our product candidates are approved, commercialization plans. 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 strains, and of any future-identified novel coronavirus strains, the effectiveness of actions taken in the United States and other countries to contain the coronavirus strains or treat their impact, including the adoption and effectiveness of vaccines and vaccine distribution efforts and the extent and duration of the pandemic's impact on economic conditions and social activity, including with respect to inflationary pressures and supply chain shortages and disruptions, among others.

Climate change and other environmental or social pressures are expected to increase the frequency or intensity of certain such events, and to contribute to chronic effects (e.g., sea-level rise or changes in meteorological or hydrological patterns), which may result in various adverse impacts to our business or those of third parties upon whom we depend, including in ways that may not be known to us. Increasing stakeholder scrutiny on such environmental and social matters may also require us to incur costs or otherwise devote resources to address such issues, and any failure to successfully navigate such considerations may also adversely impact our business.

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 retain the services of our current executive officers, principal consultants and others, including Marcio Souza, our President and Chief Executive Officer, and Timothy Kelly, our Chief Financial Officer. We have entered into employment agreements with Mr. Souza and Mr. Kelly, 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 significant demand for, and 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.

In addition, we have a limited number of employees to manage and operate our business. We cannot ensure that we will be able to maintain adequate staff to develop our product candidates, to run our operations or accomplish our objectives. If we are unable to maintain adequate staffing levels, our business and operations could be materially adversely affected.

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.

***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, quality 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. 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 and Cybersecurity

***Cyberattacks 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, our IT systems and those of such third parties, are increasingly vulnerable to attack, damage and interruption from natural disasters, terrorism, war, telecommunication and electrical failures, hacking, cyber incidents, including third parties gaining access to employee accounts using stolen or inferred credentials, malicious code, malware, viruses (e.g., ransomware), spamming, phishing attacks and other social engineering schemes, employee theft or misuse, human error, fraud, denial or degradation of service attacks, and sophisticated nation-state and nation-state-supported actors or other deliberate attacks and attempts to gain unauthorized access to IT systems and networks, as such attacks have increased in frequency and sophistication. Attacks upon IT systems are also increasing in their levels of persistence and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. We may also face increased cybersecurity risks due to our reliance on internet technology and our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence.

We and certain of our service providers are from time to time subject to cyberattacks and security incidents. While we do not believe that we have 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 business operations and 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 our cybersecurity risk management program and processes, including our policies, controls or procedures, will be fully implemented, complied with or successful in preventing cyberattacks or other IT disruptions, or in 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. Further, the costs associated with the investigation, remediation and potential notification of a breach to counterparties and data subjects could be material. Any cyberattack, 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 cyberattacks or other data security breaches and may incur significant additional expense to implement further data protection measures. Our insurance coverage may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

***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.

Risks Related to Tax Laws

***Legislation or other changes in tax laws could adversely affect our business and financial condition.***

The legislation, regulations and rules regarding U.S. federal, state and local and non-U.S. taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department and by state and local and non-U.S. tax agencies. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. Changes have been made to applicable tax laws from time to time and changes are expected to occur in the future as a result of recent U.S. presidential and congressional elections.

It cannot be predicted whether, when, in what form or with what effective dates changes in tax laws, regulations or rules promulgated or issued under existing or new tax laws may take place. Any such changes 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. If any such changes are enacted or implemented, we are currently unable to predict the ultimate impact on our business or holders of our common stock.

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

Our ability to use our U.S. federal and state net operating losses and tax credits is dependent upon our generation of future taxable income and income tax liabilities. We cannot predict with certainty when, or whether, we will generate sufficient taxable income or income tax liabilities to use any or all of our net operating losses or tax credits.

Our U.S. federal net operating losses generated in tax years beginning before January 1, 2018, and state net operating losses subject to expiration, will carry forward to offset future taxable income, if any, until such net operating losses expire. Such U.S. federal and state net operating losses could expire unused and be unavailable to offset future taxable income. Our U.S. federal net operating losses generated in tax years beginning after December 31, 2017 are not subject to expiration and may be carried forward indefinitely. However, such U.S. federal net operating losses may only be used to offset 80% of taxable income in each taxable year for U.S. federal income tax purposes. As a result, we may be required to pay U.S. federal income taxes in future years even if we generated net losses for U.S. federal income tax purposes in prior years. Although our U.S. federal and state tax credits generally will carry forward and be available to offset future income tax liabilities, certain of such tax credits may be subject to expiration. Accordingly, our U.S. federal and state net operating losses and tax credits subject to expiration could expire unused.

In addition, both our current and future U.S. federal net operating losses and U.S. federal tax credits may be subject to limitation under Sections 382 and 383 of the United States Internal Revenue Code of 1986, as amended, or the Code. Under Sections 382 and 383 of the Code, if a corporation undergoes an “ownership change,” generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders or groups of stockholders over a rolling three-year period, the corporation’s ability to use its pre-change U.S. federal net operating losses and U.S. federal tax credits to offset its post-change U.S. federal taxable income or U.S. federal income tax liabilities may be limited. We have not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception, and our existing U.S. federal net operating losses and U.S. federal tax credits may be subject to limitations arising from previous ownership changes. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change. Our net operating losses and tax credits may be similarly limited under state law.

We have established a full valuation allowance against our U.S. federal and state deferred tax assets due to the uncertainty surrounding the realization of such assets.

**Risks Related to Our Common Stock**

Risks Related to Investment in Securities

***The price of our stock has been and may in the future be volatile, and you could lose all or part of your investment.***

The trading price of our common stock has been and is likely to continue to be highly volatile and has been 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, factors that may affect the trading price of our common stock include:

- the commencement, enrollment, completion or results of our current clinical trials of our product candidates;
- any delay in identifying and advancing a clinical candidate for our other programs;
- any delay in our regulatory filings for our 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 any of our product candidates 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 our product candidates, 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 our product candidates;
- 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 and general economic conditions. Broad market and industry factors have negatively affected and may continue to 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.

***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.

***Future issuances of our common stock or the issuance of shares of common stock upon the exercise or conversion of securities that are exercisable or convertible into shares of common stock, such as our pre-funded warrants, or upon the exercise or vesting of incentive awards, may result in dilution for our stockholders.***

We have needed and anticipate we will need additional capital in the future to continue our planned operations. To the extent that we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities, or other equity securities in one or more transactions at prices and in a manner we determine from time to time. We also expect to issue common stock to employees, directors, and consultants pursuant to our equity incentive plans. If we sell common stock, convertible securities, or other equity securities in subsequent transactions, or common stock is issued pursuant to equity incentive plans, investors may be materially diluted. New investors in such subsequent transactions could gain rights, preferences, and privileges senior to those of holders of our common stock.

As of December 31, 2024, we have outstanding pre-funded warrants to purchase 1,125,818 shares of common stock at an exercise price of $0.0001 per share, which may be paid by way of a cashless exercise, meaning that the holder may not pay a cash purchase price upon exercise, but instead would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. Accordingly, we will not receive a significant amount, or potentially any, additional funds upon the exercise of the pre-funded warrants. To the extent such pre-funded warrants are exercised, additional shares of common stock will be issued for nominal or no additional consideration, which could result in dilution to then existing holders of our common stock and will increase the number of shares eligible for resale in the public market. Sales of substantial numbers of such shares in the public market could adversely affect the market price of the common stock, causing our stock price to decline.

***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 and directors and principal stockholders own a significant percentage of our stock and will be able to exert significant influence over matters subject to stockholder approval.***

Based on shares outstanding as of December 31, 2024, our executive officers and directors, combined with our stockholders who own more than 5% of our outstanding common stock and their affiliates, beneficially hold, in the aggregate, approximately 52.3% of our outstanding voting stock. These stockholders, acting together, would be able to exert significant influence over 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.***

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. 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.

***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 are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. 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, or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware, or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated bylaws also specify that unless we consent in writing to the selection of an alternate forum, the federal district courts of the United States shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. 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. 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 enforceability of similar choice of forum provisions in other companies' governing documents has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our bylaws to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition, or results of operations.

**Item 1B. Unresolved Staff Comments**

None.

**Item 1C. Cybersecurity**

**Risk Management and Strategy**

We have developed and implemented a cybersecurity risk management program intended to protect the confidentiality, integrity and availability of our critical systems and information. Our cybersecurity risk-management program includes a cybersecurity incident response plan.

We design and assess our program based on the National Institute of Standards and Technology Cybersecurity Framework, or NIST CSF, also integrating security best practices typically used to support the Health Insurance Portability and Accountability Act, or HIPAA, and General Data Protection Regulation, or GDPR, implementations. We use the NIST CSF and such security best practices as a guide to help us monitor, identify, assess and manage cybersecurity risks relevant to our business; however, this does not imply that we meet any particular technical standards, specifications or compliance requirements.

Our cybersecurity risk management program is integrated into our overall enterprise risk management program, and shares common methodologies, reporting channels and governance processes that apply across the enterprise risk management program to other legal, compliance, strategic, operational and financial risk areas.

Key elements of our cybersecurity risk management program include but are not limited to:

- risk assessments designed to help identify material risks from cybersecurity threats to our critical systems and information;
- adoption of various cybersecurity software, including but not limited to cloud-based malware, ransomware and antivirus software, phishing monitoring and artificial intelligence-based anomaly detection;
- a security team principally responsible for managing (1) our cybersecurity risk-assessment processes, (2) our security controls, and (3) our response to cybersecurity incidents;

- the use of external service providers, where appropriate, to assess, test or otherwise assist with aspects of our security processes;
- cybersecurity awareness training of our employees, incident response personnel and senior management;
- a cybersecurity incident response plan that includes procedures for responding to cybersecurity incidents; and
- security audits and a third-party risk assessment process for key service providers, suppliers and vendors.

We have not identified risks from known cybersecurity threats, including as a result of any prior cybersecurity incidents, that have materially affected or are reasonably likely to materially affect us, including our operations, business strategy, results of operations or financial condition. For more information, see the section titled “Risk Factor—Risks Related to Data Privacy and Cybersecurity—Cyberattacks or other failures in our telecommunications or information technology, or IT, 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.”

**Governance**

Our Board of Directors considers cybersecurity risk as part of its risk oversight function and has delegated to the Audit Committee oversight of cybersecurity and risks, including oversight of management’s implementation of our cybersecurity risk management program. The Audit Committee receives periodic reports from management on our cybersecurity risks. In addition, management updates the Audit Committee, when it deems appropriate, regarding cybersecurity incidents it considers to be significant or potentially significant. The Audit Committee reports to the full Board regarding its activities, including those related to cybersecurity.

We have an internal cybersecurity team, reporting to our Chief Financial Officer, who is responsible for (i) managing our overall cybersecurity risk-management program; (ii) assessing and managing our risks from cybersecurity threats; and (iii) overseeing retained cybersecurity consultants and providers for additional external expertise. This internal team is led by our Vice President of Information Technology, who has over 20 years of experience managing cybersecurity, systems architecture and complex data operations for biotechnology and pharmaceutical companies. Additional team members have between 12 to 15 years of experience each in cybersecurity, IT management and cloud architecture. The internal team works closely with external network operations and cybersecurity teams who provide 24/7 network operations and cybersecurity review and response capabilities.

We have an Executive Compliance Committee consisting of executive officers and members from senior management across the regulatory, quality, legal, finance and people operations functions that takes steps to stay informed about and monitor efforts to prevent, detect, mitigate and remediate cybersecurity risks and incidents through various means, which includes updates from our internal cybersecurity team, as relevant; review of any threat intelligence and other information obtained from governmental, public or private sources, including external consultants engaged by us; and alerts and reports produced by security tools deployed in the IT environment.

## Item 2. Properties

**Facilities**

We sublease a facility containing 25,445 square feet of office space, which is located at 99 High Street, Boston, Massachusetts 02110. Our sublease expires on January 31, 2026. We believe that our current facility is 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.

***Holders of Our Common Stock***

As of February 26, 2025, there were approximately two holders of record of shares of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

***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***

We did not make any sales of unregistered securities during the three months ended December 31, 2024.

***Purchases of Equity Securities by the Issuer and Affiliated Purchasers***

There were no repurchases of shares of common stock made during the three months ended December 31, 2024.

### Item 6. [Reserved]

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 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 financing needs, 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

As noted in our Company Overview in Part I of this report, we are a clinical-stage biopharmaceutical company translating insights from genetic epilepsies into the development of therapies for central nervous system, or CNS, disorders characterized by neuronal excitation-inhibition imbalance. Normal brain function requires a delicate balance of excitation and inhibition in neuronal circuits, which, when dysregulated, can lead to abnormal function and both rare and more prevalent neurological disorders. We are applying genetic insights to the discovery and development of therapies for neurological disorders through two proprietary platforms, using our understanding of shared biological targets and circuits in the brain. Each platform currently has multiple programs, with significant potential for additional program and indication expansion:

- ***Cerebrum***™, our small molecule platform, utilizes deep understanding of neuronal excitability and neuronal networks and applies a series of computational and experimental tools to develop orally available precision therapies
- ***Solidus***™, our antisense oligonucleotide, or ASO, platform, is an efficient, targeted precision medicine discovery and development engine anchored on a proprietary, computational methodology

Our platforms utilize a deliberate, pragmatic and patient-guided 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 diversified, multimodal CNS portfolio with four clinical-stage product candidates across movement disorders and epilepsy.

For our most advanced product candidate under the Cerebrum™ platform, ulixacaltamide, our Phase 3 Essential3 clinical trials in essential tremor, or ET, are ongoing. A pre-planned interim analysis of Study 1 was conducted in the first quarter of 2025. The Independent Data Monitoring Committee, or IDMC, overseeing the interim analysis of Study 1 of the Essential3 program has provided Praxis with the outcome of such analysis. Based on the predefined decision framework for Study 1, the IDMC has recommended that the study be stopped for futility, due to the results being unlikely to meet the primary efficacy endpoint under the parameters set by the statistical model. The committee also indicated that some underlying assumptions of the statistical model might have influenced this outcome and encouraged us to explore alternative analysis methods. Given the advanced state of enrollment for both Study 1 and Study 2 in the Essential3 program, and in the context of the advice received by the IDMC, we have decided to continue both studies to completion, with topline results expected in the third quarter of 2025. The decision about whether the data supports the submission of an NDA will be made after analyzing the final results for Study 1 and Study 2.

Within our vormatrigine program (formerly known as PRAX-628), we announced positive results from our Photo-Paroxysmal Response ("PPR") study in the first quarter of 2024, and have initiated or plan to initiate four studies to generate patient eligibility, efficacy, safety and pharmacokinetics (PK) data for the program. We initiated the EMPOWER study, an observational study of vormatrigine in patients with epilepsy, in the third quarter of 2024, and initiated or plan to initiate three efficacy studies. The first efficacy study, RADIANT, is an open label eight-week study in patients with focal onset seizures or generalized epilepsy that is currently enrolling, with topline results expected by mid-year 2025. We have also initiated the POWER1 study, a double-blind, placebo-controlled, 12-week study in focal onset seizures, with topline results expected in the second half of 2025, and plan to begin enrollment in the POWER2 study, a third efficacy study, in the second half of 2025. Within our relutrigine program (formerly known as PRAX-562), we announced positive topline results from the first cohort of our EMBOLD study in the third quarter of 2024 and have initiated enrollment of the second cohort, with topline results expected in the first half of 2026. We also plan to initiate the EMERALD study in a broader developmental and epileptic encephalopathies, or

DEE, patient population by mid-year 2025. For our most advanced product candidate under the Solidus™ platform, elsunersen (formerly known as PRAX-222), we shared results from Part 1 of the EMBRAVE study in the fourth quarter of 2023. We are currently enrolling the second cohort of the EMBRAVE study in Brazil, with topline results expected in the first half of 2026, and plan to initiate EMBRAVE3, a Phase 3 registrational study, by mid-year 2025. For further details on our business, refer to the Business section of Part I of this report.

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, or IP, 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, contract development and manufacturing organizations and contract research organizations, or CROs, to conduct our preclinical and clinical activities. Since inception, we have financed our operations primarily with proceeds from the sale and issuance of equity securities.

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 product candidates 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 $182.8 million and $123.3 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $836.7 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 be maintained or increased in connection with our ongoing activities, as we:

- advance our lead product candidate, ulixacaltamide, through completion of the Phase 3 Essential3 clinical trial program for ET;
- advance relutrigine (formally PRAX-562) in the EMBOLD and EMERALD clinical trials;
- advance vormatrigine (formerly PRAX-628) in efficacy clinical trials for focal onset seizures or generalized epilepsy;
- advance elsunersen (formerly PRAX-222) into the pivotal stage of the program;
- advance our preclinical candidates to clinical trials;
- further invest in our pipeline;
- further invest in our manufacturing capabilities;
- seek regulatory approval for our product candidates;
- maintain, expand, protect and defend our IP portfolio;
- acquire or in-license technology;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; and
- when needed, increase our headcount to support our development efforts and any future commercialization efforts.

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.

In November 2021, we entered into an Open Market Sale Agreement, or the 2021 Sales Agreement, with Jefferies LLC, or Jefferies, to provide for the offering, issuance and sale of up to an aggregate amount of $125.0 million of common stock from time to time in at-the-market offerings for which Jefferies acted as sales agent. We terminated the 2021 Sales Agreement in June 2023. During the year ended December 31, 2023, we issued and sold an aggregate of 952,794 shares under the 2021 Sales Agreement for aggregate net proceeds of $24.1 million, after deducting commissions and offering expenses payable by us.

In June 2023, we completed a public offering of: (i) an aggregate of 4,296,646 shares of common stock at a public offering price of $14.25 per share, including the underwriters' full exercise of their option to purchase 619,979 additional shares of common stock, and (ii) pre-funded warrants to purchase 470,000 shares of common stock at a public offering price of $14.2485 per share. The purchase price per share for each pre-funded warrant represents the per share offering price for the common stock, less the $0.0015 per share exercise price for each underlying share. Total net proceeds generated from the offering were approximately $63.4 million, after deducting underwriting discounts, commissions and other offering expenses payable by us. As of December 31, 2024, all warrants associated with this offering were exercised on a cashless basis with no proceeds received by us.

In December 2023, we entered into an Open Market Sale Agreement, or the 2023 Sales Agreement, with Jefferies, to provide for the offering, issuance and sale of up to an aggregate amount of $75.0 million of common stock from time to time in at-the-market offerings. The 2023 Sales Agreement was terminated in January 2024. During the year ended December 31, 2024, we issued and sold an aggregate of 192,190 shares under the 2023 Sales Agreement for aggregate net proceeds of $5.3 million, after deducting commissions and offering expenses payable by us. During the year ended December 31, 2023, we issued and sold an aggregate of 212,453 shares under the 2023 Sales Agreement for aggregate net proceeds of $4.0 million, after deducting commissions and offering expenses payable by us.

In January 2024, we completed a public offering of: (i) an aggregate of 3,802,025 shares of our common stock at a public offering price of $35.50 per share, including the underwriters' full exercise of their option to purchase 633,750 additional shares of common stock, and (ii) pre-funded warrants to purchase 1,056,725 shares of common stock at a public offering price of $35.4999 per share of common stock underlying the warrants. The purchase price per share for each pre-funded warrant represents the per share offering price for the common stock, less the $0.0001 per share exercise price of each underlying share. Total net proceeds generated from the offering were approximately $161.6 million, after deducting underwriting discounts, commissions and other offering expenses payable by us. As of December 31, 2024, 152,145 warrants associated with this offering were exercised on a cashless basis with no cash proceeds received by us.

In March 2024, we entered into an Open Market Sale Agreement, or the March 2024 Sales Agreement, with Jefferies, to provide for the offering, issuance, and sale of up to an aggregate amount of $150.0 million of common stock from time to time in at-the-market offerings. During the year ended December 31, 2024, we issued and sold an aggregate of 1,614,975 shares under the March 2024 Sales Agreement for aggregate net proceeds of $113.1 million, after deducting commissions and offering expenses payable by us.

In April 2024, we completed a public offering of: (i) an aggregate of 3,849,558 shares of our common stock at a public offering price of $56.50 per share, including the underwriters' full exercise of their option to purchase 530,973 additional shares of common stock, and (ii) pre-funded warrants to purchase 221,238 shares of common stock at a public offering price of $56.4999 per share of common stock underlying the warrants. The purchase price per share for each pre-funded warrant represents the per share offering price for the common stock, less the $0.0001 per share exercise price of each underlying share. Total net proceeds generated from the offering were approximately $216.0 million, after deducting underwriting discounts, commissions and other offering expenses payable by us.

In December 2024, we entered into an amendment to the March 2024 Sales Agreement with Jefferies, to provide for the offering, issuance, and sale of up to an aggregate amount of $250.0 million of common stock from time to time in at-the-market offerings. During the year ended December 31, 2024, we issued and sold an aggregate

of 16,487 shares under the amended March 2024 Sales Agreement for aggregate net proceeds of $1.0 million, after deducting commissions and offering expenses payable by us.

As of December 31, 2024, we had cash, cash equivalents and marketable securities of $469.5 million. We expect that our cash, cash equivalents, and marketable securities as of December 31, 2024 will be sufficient to fund our operating expenditures and capital expenditure requirements necessary to advance our research efforts and clinical trials into 2028. The analysis included consideration of our current financial needs and ongoing research and development plans. We have based this estimate on assumptions that may provide to be wrong, and we could exhaust our available capital resources sooner than we expect. See "—Liquidity and Capital Resources."

***Reverse Stock Split***

On November 28, 2023, we filed a Certificate of Amendment to our Amended and Restated Certificate of Incorporation with the Secretary of State of the State of Delaware to effect a 1-for-15 reverse stock split of our common stock, or the Reverse Stock Split. The Reverse Stock Split became effective at 5:00 p.m., Eastern Time, on November 28, 2023, or the Effective Time.

As a result of the Reverse Stock Split, every 15 shares of our issued and outstanding common stock were automatically reclassified into one validly issued, fully-paid and non-assessable share of common stock, subject to the treatment of fractional shares as described below, without any action on the part of the holders thereof. The Reverse Stock Split did not affect the number of authorized shares of common stock or the par value of the common stock.

No fractional shares were issued in connection with the Reverse Stock Split. Stockholders who would otherwise be entitled to receive fractional shares as a result of the Reverse Stock Split were entitled to a cash payment in lieu thereof at a price equal to the fraction to which the stockholder would otherwise be entitled multiplied by the closing price per share of the common stock (as adjusted for the Reverse Stock Split) on the Nasdaq Global Select Market on November 28, 2023, the last trading day immediately preceding the Effective Time.

**Financial Operations Overview**

***Revenue***

We have not generated any revenue from the sale of products since inception and do not expect to generate any revenue from the sale of products for several years, if at all. As discussed in Note 9 to our audited consolidated financial statements, we entered into an Option and License Agreement, or the Collaboration Agreement, with UCB Biopharma SRL, or UCB, in December 2022. We recognized $8.6 million and $2.4 million, respectively, of collaboration revenue from the Collaboration Agreement during the years ended December 31, 2024 and 2023. In December 2024, UCB exercised its option to in-license global development and commercialization rights under the terms of the Collaboration Agreement.

***Operating Expenses***

*Research and Development Expenses*

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 product candidates; 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 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 to acquire, develop and manufacture materials for preclinical and clinical studies; and
- depreciation, amortization and other direct and allocated expenses, including rent and other operating costs, such as information technology, 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 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.

As a company operating in a virtual environment, a significant portion of our research and development costs have been external costs incurred by third-parties. We track direct external research and development expenses to specific platforms and product candidates upon commencement. Due to the number of ongoing studies and our ability to use resources across platforms, indirect or shared operating costs incurred for our research and development platforms, such as personnel, facility costs and certain consulting costs, are not recorded or maintained on a platform-specific basis.

The following table reflects our research and development expenses, including direct expenses summarized by platform and indirect or shared operating costs recognized as research and development expenses during each period presented (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Cerebrum™ | $ 93,591 | $ 31,680 |
| Solidus™ | 5,738 | 19,009 |
| Personnel-related (including stock-based compensation) | 43,407 | 28,904 |
| Other indirect research and development expenses | 9,677 | 7,173 |
| Total research and development expenses | $ 152,413 | $ 86,766 |

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 be maintained or 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 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 IP protection and regulatory exclusivity for our product candidates, if approved;
- our receipt of marketing approvals from applicable regulatory authorities;
- our ability to commercialize products, if approved, whether alone or in collaboration with others; and
- the continued acceptable safety profiles of our product candidates.

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 require significant 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, commercial 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; commercial-related costs to support market assessments and scenario planning; insurance costs; administrative travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for office rent and other operating costs, such as information technology. Costs to secure and defend our IP are expensed as incurred and are classified as general and administrative expenses. These costs relate to the operation of the business and are unrelated to the research and development function or any individual platform or product candidate.

We anticipate that our general and administrative expenses may increase in the future as we increase our headcount, when needed, to support the expected growth in our research and development activities and the potential commercialization of our product candidates. We also expect to incur additional IP-related expenses as we file patent applications to protect innovations arising from our research and development activities.

***Other Income***

*Other Income, Net*

Other income, net consists of interest income from our cash, cash equivalents and marketable securities and amortization of investment premiums and discounts.

***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, 2024 and 2023, we had U.S. federal and state net operating loss carryforwards which may be available to offset future taxable income and which begin to expire in 2035. As of December 31, 2024 and 2023, we also had federal and state research and development tax credit carryforwards which may be available to offset future income tax liabilities and which begin to expire in 2032.

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. There was no income tax provision recognized for the years ended December 31, 2024 and 2023.

## Results of Operations

### *Comparison of the Years Ended December 31, 2024 and 2023*

The following table summarizes our consolidated statements of operations for each period presented (in thousands):

| | Year Ended December 31, | | Change |
|---|---|---|---|
| | 2024 | 2023 | |
| Collaboration revenue | $ 8,553 | $ 2,447 | $ 6,106 |
| Operating expenses: | | | |
| Research and development | 152,413 | 86,766 | 65,647 |
| General and administrative | 56,305 | 42,054 | 14,251 |
| Total operating expenses | 208,718 | 128,820 | 79,898 |
| Loss from operations | (200,165) | (126,373) | (73,792) |
| Other income: | | | |
| Other income, net | 17,346 | 3,096 | 14,250 |
| Total other income | 17,346 | 3,096 | 14,250 |
| Net loss | $ (182,819) | $ (123,277) | $ (59,542) |

*Collaboration Revenue*

The $6.1 million increase in collaboration revenue is associated with an increase in revenue recorded under the Collaboration Agreement with UCB that was executed in December 2022. In December 2024, UCB exercised its option to in-license global development and commercialization rights for a development candidate as part of the Collaboration Agreement. Upon notice of the exercise, we recognized a $6.0 million option exercise fee, and also recognized the remaining $2.6 million of collaboration revenue associated with the $5.0 million up front payment earned upon execution of the Collaboration Agreement. We have no further research service obligations under the terms of the Collaboration Agreement.

*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 |
|---|---|---|---|
| | 2024 | 2023 | |
| Cerebrum™ | $ 93,591 | $ 31,680 | $ 61,911 |
| Solidus™ | 5,738 | 19,009 | (13,271) |
| Personnel-related (including stock-based compensation) | 43,407 | 28,904 | 14,503 |
| Other indirect research and development expenses | 9,677 | 7,173 | 2,504 |
| Total research and development expenses | $ 152,413 | $ 86,766 | $ 65,647 |

The $65.6 million increase in research and development expenses was primarily attributable to the following:

- $61.9 million increase in expense related to our Cerebrum™ platform, driven primarily by:
  - $49.8 million increase in spend for our ulixacaltamide program, primarily due to Essential3 study spend and Phase 1 trial spend, partially offset by completion of the Essential1 study in the prior year;

- $11.4 million increase in spend for our vormatrigine program, primarily driven by spend for our ENERGY program and manufacturing-related spend;
- $2.3 million increase in spend for our relutrigine program, primarily related to EMBOLD Phase 2 clinical trial spend; partially offset by
- $1.6 million decrease in activities for our earlier stage assets;

- $14.5 million increase in personnel-related costs mainly due to increased headcount and stock-based compensation expense;
- $2.5 million increase in indirect expenses, primarily driven by increased consulting spend to support operations; partially offset by
- $13.3 million decrease in expense related to our Solidus™ platform, primarily related to our elsunersen program, driven by a $6.9 million milestone payment to Ionis Pharmaceuticals Inc. upon initiation of our EMBRAVE study in the prior year, as well as prior year study activity.

*General and Administrative Expense*

The $14.3 million increase in general and administrative expenses was primarily attributable to the following:

- $11.7 million increase in personnel-related costs mainly due to increased stock-based compensation expense;
- $1.7 million increase in professional fees; and
- $0.9 million increase in other general and administrative expenses, none of which were individually significant.

**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 may not generate revenue from sales of any products for several years, if at all.

To date, we have financed our operations primarily with proceeds from the issuance of redeemable convertible preferred stock and from the sale of common stock through an initial public offering, common stock and pre-funded warrants through follow-on public offerings and common stock from at-the-market offerings under our shelf registration statement. From inception through December 31, 2024, we have raised $1.1 billion in aggregate cash proceeds from such transactions, net of issuance costs. As of December 31, 2024, we had cash, cash equivalents, and marketable securities of $469.5 million.

In November 2021, we entered into the 2021 Sales Agreement with Jefferies to provide for the offering, issuance and sale of up to an aggregate amount of $125.0 million of common stock from time to time in at-the-market offerings for which Jefferies acted as sales agent. We terminated the 2021 Sales Agreement in June 2023. During the year ended December 31, 2023, we issued and sold an aggregate of 952,794 shares under the 2021 Sales Agreement for aggregate net proceeds of $24.1 million, after deducting commissions and offering expenses payable by us.

In June 2023, we completed a public offering of: (i) an aggregate of 4,296,646 shares of common stock at a public offering price of $14.25 per share, including the underwriters' full exercise of their option to purchase 619,979 additional shares of common stock, and (ii) pre-funded warrants to purchase 470,000 shares of common stock at a public offering price of $14.2485 per share. The purchase price per share for each pre-funded warrant represents the per share offering price for the common stock, less the $0.0015 per share exercise price for each underlying share. Total net proceeds generated from the offering were approximately $63.4 million, after deducting underwriting discounts, commissions and other offering expenses payable by us. As of December 31, 2024, all warrants associated with this offering were exercised on a cashless basis with no proceeds received by us.

In December 2023, we entered into the 2023 Sales Agreement with Jefferies to provide for the offering, issuance and sale of up to an aggregate amount of $75.0 million of common stock from time to time in at-the-market offerings. The 2023 Sales Agreement was terminated in January 2024. During the year ended December 31, 2024, we issued and sold an aggregate of 192,190 shares under the 2023 Sales Agreement for aggregate net proceeds of $5.3 million, after deducting commissions and offering expenses payable by us. During the year ended December 31, 2023, we issued and sold an aggregate of 212,453 shares under the 2023 Sales Agreement for aggregate net proceeds of $4.0 million, after deducting commissions and offering expenses payable by us.

In January 2024, we completed a public offering of: (i) an aggregate of 3,802,025 shares of our common stock at a public offering price of $35.50 per share, including the underwriters' full exercise of their option to purchase 633,750 additional shares of common stock, and (ii) pre-funded warrants to purchase 1,056,725 shares of common stock at a public offering price of $35.4999 per share of common stock underlying the warrants. The purchase price per share for each pre-funded warrant represents the per share offering price for the common stock, less the $0.0001 per share exercise price of each underlying share. Total net proceeds generated from the offering were approximately $161.6 million, after deducting underwriting discounts, commissions and other offering expenses payable by us. As of December 31, 2024, 152,145 warrants associated with this offering were exercised on a cashless basis with no cash proceeds received by us.

In March 2024, we entered into the March 2024 Sales Agreement with Jefferies to provide for the offering, issuance and sale of up to an aggregate amount of $150.0 million of common stock from time to time in at-the-market offerings. During the year ended December 31, 2024, we issued and sold an aggregate of 1,614,975 shares under the March 2024 Sales Agreement for aggregate net proceeds of $113.1 million, after deducting commissions and offering expenses payable by us.

In April 2024, we completed a public offering of: (i) an aggregate of 3,849,558 shares of our common stock at a public offering price of $56.50 per share, including the underwriters' full exercise of their option to purchase 530,973 additional shares of common stock, and (ii) pre-funded warrants to purchase 221,238 shares of common stock at a public offering price of $56.4999 per share of common stock underlying the warrants. The purchase price per share for each pre-funded warrant represents the per share offering price for the common stock, less the $0.0001 per share exercise price of each underlying share. Total net proceeds generated from the offering were approximately $216.0 million, after deducting underwriting discounts, commissions and other offering expenses payable by us.

In December 2024, we entered into an amendment to the March 2024 Sales Agreement with Jefferies to provide for the offering, issuance and sale of up to an aggregate amount of $250.0 million of common stock from time to time in at-the-market offerings. During the year ended December 31, 2024, we issued and sold an aggregate of 16,487 shares under the amended March 2024 Sales Agreement for aggregate net proceeds of $1.0 million, after deducting commissions and offering expenses payable by us.

***Cash Flows***

The following table provides information regarding our cash flows for each period presented (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | **2024** | **2023** |
| Net cash (used in) provided by: | | |
| Operating activities | $ (131,757) | $ (111,136) |
| Investing activities | (248,494) | 38,950 |
| Financing activities | 514,323 | 91,871 |
| Net increase in cash, cash equivalents and restricted cash | $ 134,072 | $ 19,685 |

*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 have 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 operating assets and liabilities.

During the year ended December 31, 2024, net cash used in operating activities of $131.8 million was primarily due to our $182.8 million net loss and $10.9 million in changes in operating assets and liabilities primarily related to an increase in accrued expenses and accounts payable, partially offset by $40.1 million of non-cash charges primarily related to stock-based compensation.

During the year ended December 31, 2023, net cash used in operating activities of $111.1 million was primarily due to our $123.3 million net loss and $14.0 million in changes in operating assets and liabilities primarily related to a decrease in accrued expenses and accounts payable, partially offset by $26.2 million of non-cash charges primarily related to stock-based compensation.

*Investing Activities*

During the year ended December 31, 2024, net cash used in investing activities of $248.5 million primarily related to purchases of marketable securities, partially offset by maturities of marketable securities.

During the year ended December 31, 2023, net cash provided by investing activities of $39.0 million primarily related to maturities of marketable securities.

*Financing Activities*

During the year ended December 31, 2024, net cash provided by financing activities of $514.3 million consisted primarily of net proceeds from our January 2024 and April 2024 follow-on public offerings, our at-the-market offerings and our collaboration and license agreement with Tenacia.

During the year ended December 31, 2023, net cash provided by financing activities of $91.9 million consisted primarily of net proceeds from our June 2023 follow-on public offering of $63.4 million and from at-the-market offerings of $28.2 million.

***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. 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 clinical-stage product candidates within our Cerebrum™ and Solidus™ platforms;
- 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 IP portfolio and opportunistically acquire complementary IP;
- seek to obtain regulatory approvals for our product candidates;
- establish a sales, marketing, technology and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- when needed, 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 operations as 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 current operating plan, we believe that our current cash, cash equivalents and marketable securities will be sufficient to fund our operating expenditures and capital expenditure requirements into 2028. However, we have based this estimate on assumptions that may prove to be wrong and we could exhaust our capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with product development and potential collaborations with third parties for the development of our product candidates, 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 platforms and product candidates;
- the number and characteristics of product candidates 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 IP rights and defending any IP-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; 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 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, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of holders of our common stock. Additional debt financing and preferred 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 result in dilution to the holders of our common stock.

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**

We have entered into certain agreements under which we have incurred or may in the future incur obligations and commitments that could have a material impact on our capital resources.

We sublease building space in Boston, Massachusetts. Our sublease will expire on January 31, 2026. As of December 31, 2024, our operating lease commitments for the remainder of the lease term were $1.4 million.

In addition, we have entered into collaboration and license agreements with 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 RogCon, we are obligated to reimburse RogCon for its out-of-pocket costs incurred for activities performed under the license agreement. Additionally, we may be obligated to pay RogCon a milestone payment of $3.0 million and profit share payments. The $3.0 million milestone payment is 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 are 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. See “Business—License Agreements—License Agreement with RogCon.”

Under our collaboration agreement with Ionis, we reimbursed Ionis for identifying a development candidate and conducting an investigational new drug application, or IND, enabling toxicology study, as well as out of pocket costs incurred by Ionis related to research activities. Ionis granted us an exclusive option to obtain the rights and license to further develop and commercialize the development candidate in the field of epilepsy and neurodevelopmental disorders, other than Dravet Syndrome, following the results of the IND-enabling toxicology study. We exercised this exclusive option in January 2022 and paid a $2.0 million license fee. In July 2023, upon initiation of the elsunersen EMBRAVE study in the second quarter of 2023, we paid a milestone payment of $6.9 million to Ionis. Ionis may be entitled to additional development milestone payments, additional milestone payments, and sales royalties or sublicense fees. We may be required to make additional payments to Ionis including development milestone payments, additional milestone payments and sales royalties or sublicense fees. Either party may terminate the collaboration agreement upon material breach or insolvency of the other party. Ionis may terminate if we fail to achieve a performance milestone. See “Business—License Agreements—Ionis Collaboration Agreement.”

We have also entered into multiple agreements with third parties under which we may be obligated to make future development, regulatory and commercial milestone payments and royalty payments on future sales of specified product candidates. Payments under these agreements generally become due and payable upon achievement of such milestones and sales. When the achievement of these milestones or sales have not occurred, such contingencies are not recorded in our financial statements.

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.

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 collaborators, in connection with any U.S. patent or any copyright or other IP infringement claim by any third party with respect to our product candidates. 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.

**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. 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 and Prepaids***

Research and development expenses include costs directly attributable to the conduct of research and development activities, 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 and prepaid 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 in determining our accrued and prepaid research and development 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 and prepaid expenses, we analyze progress of the studies or trials related to these services, including the phase or completion of events, invoices received and contracted costs. Examples of estimated accrued and prepaid 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 expensing 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 expense accordingly. Significant judgments and estimates are made in determining the accrued and prepaid research and development expenses 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.

**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 consolidated financial statements or do not otherwise apply to our current operations.

**Item 7A. Quantitative and Qualitative Disclosures About Market Risk**

We are not required to provide the information required by this Item 7A until our Quarterly Report on Form 10-Q for the first quarter after the fiscal year in which it is determined that we are no longer a smaller reporting company.

**Item 8. Financial Statements and Supplementary Data**

**INDEX TO CONSOLIDATED FINANCIAL STATEMENTS**

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15, Exhibits and Financial Statement Schedules, of this Annual Report on Form 10-K.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## 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, 2024 and 2023, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2024, 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, 2024 and 2023, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 28, 2025 expressed an unqualified opinion thereon.

**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 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. 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.

**Critical Audit Matter**

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

**Cerebrum Platform Accrued and Prepaid Research and Development Costs**

*Description of the Matter*

The Company's accrued costs for research and development expenses totaled $13.4 million at December 31, 2024, including accruals related to the Company's Cerebrum Platform research and development costs. In addition, the Company's prepaid expenses and other current assets were $11.8 million which included amounts that were paid in advance of services incurred pursuant to the Cerebrum Platform research and development costs. As discussed in Note 2 to the consolidated financial statements, the Company analyzes the 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 and prepaid balances at the end of any reporting period for the Company's Cerebrum Platform research and development costs. The Company is required to estimate such accruals and prepaids using judgment based on certain information, including actual costs incurred or level of effort expended, as provided by its vendors. Payments for such activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected on the consolidated balance sheet within accrued or prepaid expenses and other current assets.

Auditing the Company's accrued and prepaid research and development costs for the Cerebrum Platform costs was complex, as accounting for the costs associated with these studies or clinical trials required subjective estimates of the level of services performed and the associated costs incurred by vendors. Furthermore, due to the duration of the Company's Cerebrum Platform research and development costs, and the timing of information received from third parties, the actual amounts incurred are not typically known at the time the consolidated financial statements are issued.

*How We Addressed the Matter in Our Audit*

We obtained an understanding, evaluated the design, and tested the operating effectiveness of internal controls over accrued and prepaid research and development costs for the Cerebrum Platform, including assessing management's controls over the significant judgments and estimates regarding costs incurred or level of effort expended by vendors. To evaluate the accrued and prepaid research and development costs for the Cerebrum Platform research and development costs, our audit procedures included, among others, testing the accuracy and completeness of the underlying data used in the estimates and evaluating the significant judgments and estimates made by management to determine the recorded accruals and prepayments. To test the significant judgments and estimates, we discussed the progress of research and development activities with the Company's research and development personnel that oversee the research and development projects and inspected the Company's contracts with vendors and pending change orders to assess the impact on amounts recorded. In addition, we inspected information obtained by the Company from vendors, which included the vendors' estimate of costs incurred to date. We also obtained vendor confirmations, analyzed fluctuations in accruals by vendor and by trial throughout the period subject to audit, evaluated the costs incurred per trial, site and/or patient for reasonableness and tested subsequent invoices received from vendors.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2019.
Boston, Massachusetts
February 28, 2025

**PRAXIS PRECISION MEDICINES, INC.**

**CONSOLIDATED BALANCE SHEETS**

**(Amounts in thousands, except share and per share data)**

| | December 31, | |
|---|---|---|
| | **2024** | **2023** |
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 215,372 | $ 81,300 |
| Marketable securities | 177,195 | — |
| Prepaid expenses and other current assets | 11,805 | 3,580 |
| Total current assets | 404,372 | 84,880 |
| Long-term marketable securities | 76,961 | — |
| Property and equipment, net | 230 | 588 |
| Operating lease right-of-use assets | 1,131 | 2,064 |
| Other non-current assets | 416 | 416 |
| Total assets | $ 483,110 | $ 87,948 |
| **Liabilities and stockholders' equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 12,528 | $ 5,815 |
| Accrued expenses | 23,763 | 7,416 |
| Operating lease liabilities | 1,259 | 1,126 |
| Current portion of deferred revenue | — | 1,392 |
| Total current liabilities | 37,550 | 15,749 |
| Long-term liabilities: | | |
| Non-current portion of operating lease liabilities | 110 | 1,369 |
| Non-current portion of deferred revenue | — | 1,161 |
| Total liabilities | 37,660 | 18,279 |
| Commitments and contingencies (Note 8) | | |
| Stockholders' equity: | | |
| Preferred stock, $0.0001 par value; 10,000,000 shares authorized and no shares issued or outstanding as of December 31, 2024 and December 31, 2023 | — | — |
| Common stock, $0.0001 par value; 150,000,000 shares authorized; 19,422,358 shares issued and outstanding as of December 31, 2024, and 8,791,877 shares issued and outstanding as of December 31, 2023 | 14 | 13 |
| Additional paid-in capital | 1,281,522 | 723,577 |
| Accumulated other comprehensive gain | 654 | — |
| Accumulated deficit | (836,740) | (653,921) |
| Total stockholders' equity | 445,450 | 69,669 |
| Total liabilities and stockholders' equity | $ 483,110 | $ 87,948 |

The accompanying notes are an integral part of these consolidated financial statements.

**PRAXIS PRECISION MEDICINES, INC.**

**CONSOLIDATED STATEMENTS OF OPERATIONS**

**(Amounts in thousands, except share and per share data)**

| | Year Ended December 31, | |
|---|---|---|
| | **2024** | **2023** |
| Collaboration revenue | $ 8,553 | $ 2,447 |
| Operating expenses: | | |
| Research and development | 152,413 | 86,766 |
| General and administrative | 56,305 | 42,054 |
| Total operating expenses | 208,718 | 128,820 |
| Loss from operations | (200,165) | (126,373) |
| Other income: | | |
| Other income, net | 17,346 | 3,096 |
| Total other income | 17,346 | 3,096 |
| Net loss | $ (182,819) | $ (123,277) |
| Net loss per share attributable to common stockholders, basic and diluted | $ (10.21) | $ (18.69) |
| Weighted average common shares outstanding, basic and diluted | 17,906,794 | 6,594,316 |

*The accompanying notes are an integral part of these consolidated financial statements.*

**PRAXIS PRECISION MEDICINES, INC.**

**CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS**

**(Amounts in thousands, except share and per share data)**

| | Year Ended December 31, | |
|---|---|---|
| | **2024** | **2023** |
| Net loss | $ (182,819) | $ (123,277) |
| Change in unrealized gain (loss) on marketable securities, net of tax | 654 | 173 |
| Comprehensive loss | $ (182,165) | $ (123,104) |

The accompanying notes are an integral part of these consolidated financial statements.

**PRAXIS PRECISION MEDICINES, INC.**

**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY**

**(Amounts in thousands, except share data)**

| | Common Stock | | Additional Paid-In Capital | Accumulated Deficit | Accumulated Other Comprehensive Gain (Loss) | Total Stockholders' Equity |
|---|---|---|---|---|---|---|
| | Shares | Amount | | | | |
| **Balance at December 31, 2023** | 8,791,877 | $ 13 | $ 723,577 | $ (653,921) | $ — | $ 69,669 |
| Stock-based compensation expense | — | — | 14,475 | — | — | 14,475 |
| Issuance of common stock from follow-on public offering and accompanying pre-funded warrants, net of underwriting discounts, commissions and offering costs of $10,836 | 3,802,025 | — | 161,649 | — | — | 161,649 |
| Issuance of common stock from at-the-market public offerings, net of issuance and commission costs of $376 | 209,852 | — | 6,169 | — | — | 6,169 |
| Issuance of common stock from a collaboration and license agreement | 443,253 | — | 17,265 | — | — | 17,265 |
| Vesting of restricted stock units | 11,095 | — | — | — | — | — |
| Shares withheld for taxes for vesting of restricted stock units | (3,689) | — | (137) | — | — | (137) |
| Issuance of common stock upon exercise of stock options | 3,634 | — | 143 | — | — | 143 |
| Change in unrealized gain (loss) on marketable securities, net of tax | — | — | — | — | 3 | 3 |
| Net loss | — | — | — | (39,553) | — | (39,553) |
| **Balance at March 31, 2024** | 13,258,047 | $ 13 | $ 923,141 | $ (693,474) | $ 3 | $ 229,683 |
| Stock-based compensation expense | — | — | 5,878 | — | — | 5,878 |
| Issuance of common stock from follow-on public offering and accompanying pre-funded warrants, net of underwriting discounts, commissions and offering costs of $14,013 | 3,849,558 | 1 | 215,987 | — | — | 215,988 |
| Issuance of common stock from exercise of pre-funded warrants | 622,123 | — | — | — | — | — |
| Issuance of common stock under employee stock purchase plan | 25,146 | — | 311 | — | — | 311 |
| Vesting of restricted stock units | 726 | — | — | — | — | — |
| Shares withheld for taxes for vesting of restricted stock units | (242) | — | (13) | — | — | (13) |
| Issuance of common stock upon exercise of stock options | 148 | — | 4 | — | — | 4 |
| Change in unrealized gain (loss) on marketable securities, net of tax | — | — | — | — | (74) | (74) |
| Net loss | — | — | — | (32,677) | — | (32,677) |
| **Balance at June 30, 2024** | 17,755,506 | $ 14 | $ 1,145,308 | $ (726,151) | $ (71) | $ 419,100 |
| Stock-based compensation expense | — | — | 12,432 | — | — | 12,432 |
| Issuance of common stock from at-the-market public offerings, net of issuance and commission costs of $70 | 25,189 | — | 1,442 | — | — | 1,442 |
| Issuance of common stock from exercise of stock options | 4,971 | — | 201 | — | — | 201 |
| Vesting of restricted stock units | 51 | — | — | — | — | — |
| Shares withheld for taxes for vesting of restricted stock units | (20) | — | (1) | — | — | (1) |
| Change in unrealized gain (loss) on marketable securities, net of tax | — | — | — | — | 1,402 | 1,402 |
| Net loss | — | — | — | (51,910) | — | (51,910) |
| **Balance at September 30, 2024** | 17,785,697 | $ 14 | $ 1,159,382 | $ (778,061) | $ 1,331 | $ 382,666 |
| Stock-based compensation expense | — | — | 8,575 | — | — | 8,575 |
| Issuance of common stock from at-the-market public offerings, net of issuance and commission costs of $2,812 | 1,588,611 | — | 111,748 | — | — | 111,748 |
| Issuance of common stock under employee stock purchase plan | 6,235 | — | 233 | — | — | 233 |
| Issuance of common stock from exercise of stock options | 36,424 | — | 1,741 | — | — | 1,741 |
| Vesting of restricted stock units | 7,603 | — | — | — | — | — |
| Shares withheld for taxes for vesting of restricted stock units | (2,212) | — | (157) | — | — | (157) |
| Change in unrealized gain (loss) on marketable securities, net of tax | — | — | — | — | (677) | (677) |
| Net loss | — | — | — | (58,679) | — | (58,679) |
| **Balance at December 31, 2024** | 19,422,358 | $ 14 | $ 1,281,522 | $ (836,740) | $ 654 | $ 445,450 |

The accompanying notes are an integral part of these consolidated financial statements.

## PRAXIS PRECISION MEDICINES, INC.

## CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (continued)

## (Amounts in thousands, except share data)

| | Common Stock | | Additional Paid-In Capital | Accumulated Deficit | Accumulated Other Comprehensive Loss | Total Stockholders' Equity |
|---|---|---|---|---|---|---|
| | Shares | Amount | | | | |
| **Balance at December 31, 2022** | 3,292,163 | $ 5 | $ 606,918 | $ (530,644) | $ (173) | $ 76,106 |
| Stock-based compensation expense | — | — | 7,593 | — | — | 7,593 |
| Issuance of common stock from at-the-market public offerings net of commission costs of $560 | 560,253 | 1 | 18,095 | — | — | 18,096 |
| Vesting of restricted stock units | 11,516 | — | — | — | — | — |
| Shares withheld for taxes for vesting of restricted stock units | (2,875) | — | (127) | — | — | (127) |
| Issuance of common stock upon exercise of stock options | 2,970 | — | 101 | — | — | 101 |
| Change in unrealized gain (loss) on marketable securities, net of tax | — | — | — | — | 154 | 154 |
| Net loss | — | — | — | (37,455) | — | (37,455) |
| **Balance at March 31, 2023** | 3,864,027 | $ 6 | $ 632,580 | $ (568,099) | $ (19) | $ 64,468 |
| Stock-based compensation expense | — | — | 5,775 | — | — | 5,775 |
| Issuance of common stock from follow-on public offering and accompanying pre-funded warrants, net of underwriting discounts, commissions and offering costs of $4,484 | 4,296,646 | 6 | 63,433 | — | — | 63,439 |
| Issuance of common stock from at-the-market public offerings, net of issuance costs | 392,541 | 1 | 6,031 | — | — | 6,032 |
| Issuance of common stock under employee stock purchase plan | 15,663 | — | 208 | — | — | 208 |
| Vesting of restricted stock units | 720 | — | — | — | — | — |
| Shares withheld for taxes for vesting of restricted stock units | (249) | — | (4) | — | — | (4) |
| Change in unrealized gain (loss) on marketable securities, net of tax | — | — | — | — | 19 | 19 |
| Net loss | — | — | — | (34,312) | — | (34,312) |
| **Balance at June 30, 2023** | 8,569,348 | $ 13 | $ 708,023 | $ (602,411) | $ — | $ 105,625 |
| Stock-based compensation expense | — | — | 5,763 | — | — | 5,763 |
| Vesting of restricted stock units | 233 | — | — | — | — | — |
| Shares withheld for taxes for vesting of restricted stock units | (70) | — | (1) | — | — | (1) |
| Issuance of common stock upon exercise of stock options | 311 | — | 1 | — | — | 1 |
| Net loss | — | — | — | (24,632) | — | (24,632) |
| **Balance at September 30, 2023** | 8,569,822 | $ 13 | $ 713,786 | $ (627,043) | $ — | $ 86,756 |
| Stock-based compensation expense | — | — | 5,726 | — | — | 5,726 |
| Issuance of common stock under employee stock purchase plan | 9,027 | — | 106 | — | — | 106 |
| Issuance of common stock from at-the-market public offerings, net of issuance costs of $123 | 212,453 | — | 3,964 | — | — | 3,964 |
| Vesting of restricted stock units | 824 | — | — | — | — | — |
| Shares withheld for taxes for vesting of restricted stock units | (249) | — | (5) | — | — | (5) |
| Net loss | — | — | — | (26,878) | — | (26,878) |
| **Balance at December 31, 2023** | 8,791,877 | $ 13 | $ 723,577 | $ (653,921) | $ — | $ 69,669 |

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, | |
|---|---|---|
| | **2024** | **2023** |
| **Cash flows from operating activities:** | | |
| Net loss | $ (182,819) | $ (123,277) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Depreciation expense | 358 | 432 |
| Stock-based compensation expense | 41,360 | 24,857 |
| Non-cash operating lease expense | 933 | 837 |
| Amortization of premiums and discounts on marketable securities, net | (5,010) | 47 |
| Non-cash collaboration and license agreement expense | 2,500 | — |
| Changes in operating assets and liabilities: | | |
| Prepaid expenses and other current assets | (8,225) | 6,772 |
| Accounts payable | 6,713 | (8,855) |
| Accrued expenses | 16,110 | (8,497) |
| Operating lease liabilities | (1,126) | (1,005) |
| Deferred revenue | (2,553) | (2,447) |
| Other | 2 | — |
| Net cash used in operating activities | (131,757) | (111,136) |
| **Cash flows from investing activities:** | | |
| Purchases of property and equipment | — | (50) |
| Purchases of marketable securities | (371,519) | — |
| Maturities of marketable securities | 123,025 | 39,000 |
| Net cash (used in) provided by investing activities | (248,494) | 38,950 |
| **Cash flows from financing activities:** | | |
| Issuance of common stock from follow-on public offering and accompanying pre-funded warrants, net of underwriting discounts, commissions and offering costs | 377,636 | 63,439 |
| Issuance of common stock from collaboration and license agreement | 14,765 | — |
| Proceeds from at-the-market offerings, net of issuance and commission costs | 119,597 | 28,153 |
| Payments of tax withholdings related to vesting of restricted stock units | (308) | (137) |
| Proceeds from exercise of options and employee stock purchase plan purchases | 2,633 | 416 |
| Net cash provided by financing activities | 514,323 | 91,871 |
| Increase in cash, cash equivalents and restricted cash | 134,072 | 19,685 |
| Cash, cash equivalents and restricted cash, beginning of period | 81,716 | 62,031 |
| Cash, cash equivalents and restricted cash, end of period | $ 215,788 | $ 81,716 |
| **Reconciliation of cash, cash equivalents and restricted cash:** | | |
| Cash and cash equivalents | 215,372 | 81,300 |
| Restricted cash | 416 | 416 |
| Total cash, cash equivalents and restricted cash | $ 215,788 | $ 81,716 |
| **Supplemental disclosures of non-cash activities:** | | |
| Issuance costs from at-the-market offerings included in accrued expenses | $ 238 | $ 63 |
| Offering costs from follow-on public offering included in accounts payable | $ — | $ 184 |

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 insights from genetic epilepsies into the development of therapies for central nervous system ("CNS"), disorders characterized by neuronal excitation-inhibition imbalance. Normal brain function requires a delicate balance of excitation and inhibition in neuronal circuits, which, when dysregulated, can lead to abnormal function and both rare and more prevalent neurological disorders. The Company is applying genetic insights to the discovery and development of therapies for neurological disorders through two proprietary platforms, using its understanding of shared biological targets and circuits in the brain. Each platform has multiple programs currently, with significant potential for additional program and indication expansion:

- ***Cerebrum***™, the Company's small molecule platform, utilizes deep understanding of neuronal excitability and neuronal networks and applies a series of computational and experimental tools to develop orally available precision therapies
- ***Solidus***™, the Company's antisense oligonucleotide ("ASO"), platform, is an efficient, targeted precision medicine discovery and development engine anchored on a proprietary, computational methodology

The Company's platforms utilize a deliberate, pragmatic and patient-guided 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, the Company has established a diversified, multimodal CNS portfolio with four clinical-stage product candidates across movement disorders and epilepsy.

Praxis was incorporated in 2015 and commenced operations in 2016. The Company has funded its operations primarily with proceeds from the issuance of redeemable convertible preferred stock, from the sale of common stock through an initial public offering ("IPO"), at-the-market offerings under its shelf registration statement, and follow-on public offerings of common stock and pre-funded warrants to purchase common stock. From inception through December 31, 2024, the Company raised $1.1 billion in aggregate cash proceeds from these transactions, net of issuance costs.

The Company is subject to risks and uncertainties common to clinical-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 a net loss of $182.8 million for the year ended December 31, 2024. In addition, as of December 31, 2024, the Company had an accumulated deficit of $836.7 million. The Company expects to continue to generate operating losses for the foreseeable future.

The Company expects that its cash, cash equivalents and marketable securities as of December 31, 2024 of $469.5 million will be sufficient to fund its operating expenditures and capital expenditure requirements necessary to advance its research efforts and clinical trials for at least one year from the date of the issuance of these consolidated financial statements. The future viability of the Company 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 subsidiary, Praxis Security Corporation. 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, accrued and prepaid research and development expense, collaboration revenue, stock-based compensation expense 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.

### *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 insured liquid deposit funds and interest-bearing money market funds. Cash equivalents are carried at cost, which approximates their fair market value.

Restricted cash comprises letters of credit for the benefit of the landlord in connection with the Company's lease facilities. Restricted cash is classified as either current or non-current based on the terms of the underlying lease arrangement.

The following table presents cash and 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, | |
|---|---|---|
| | 2024 | 2023 |
| Cash and cash equivalents | $ 215,372 | $ 81,300 |
| Restricted cash | 416 | 416 |
| Total cash, cash equivalents and restricted cash as shown on the consolidated statements of cash flows | $ 215,788 | $ 81,716 |

### *Marketable Securities*

The Company may invest its excess cash in money market funds and debt instruments of the U.S. Treasury, financial institutions, corporations and U.S. government agencies with strong credit ratings and an investment grade rating at or above A-1 or P-1 by two of the three nationally recognized statistical rating organizations. The Company does not believe that it is exposed to more than a nominal amount of credit risk related to any marketable securities it may invest in. The Company has established guidelines relative to diversification and maturities that maintain safety and liquidity, and periodically reviews and modifies these guidelines to maximize trends in yields and interest rates without compromising safety and liquidity.

The Company classifies its investments in debt instruments as available-for-sale. Available-for-sale investments are reported at fair value at each balance sheet date, and include any unrealized holding gains and losses in accumulated other comprehensive loss, a component of stockholders' equity. Realized gains and losses are included in the Company's consolidated statements of operations. All of the Company's available-for-sale securities are available for use in its current operations. The Company classifies marketable securities as either cash equivalents, short-term or long-term based on their stated maturity dates as it is more-likely-than-not that the Company will hold these assets through to their maturity dates. The Company held $254.2 million of marketable securities as of December 31, 2024. The Company did not hold any marketable securities as of December 31, 2023.

The Company evaluates securities for impairment at the end of each reporting period. Impairment is evaluated considering numerous factors, and their relative significance varies depending on the situation. Factors considered include whether a decline in fair value below the amortized cost basis is due to credit-related factors or non-credit-related factors, the financial condition and near-term prospects of the Company, and the Company's intent and ability to hold the investment to allow for an anticipated recovery in fair value. A credit-related impairment is recognized as an allowance on the balance sheet with a corresponding adjustment to earnings. Any impairment that is not credit-related is recognized in other comprehensive loss, net of applicable taxes unless deemed other than temporary.

***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, restricted cash and marketable securities. The Company's investment portfolio may include money market funds, marketable debt securities, including debt securities issued by U.S. government agencies and corporations, and commercial paper. The Company's investments are limited to investment-grade securities with strong credit ratings with the objective of maintaining safety and liquidity. The Company also 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, 2024 and 2023, 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, 2024 and 2023, 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 reflect 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.

Items measured at fair value on a recurring basis include cash equivalents and marketable securities (Note 4 and Note 5). The carrying amounts reflected in the consolidated balance sheets for cash, 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 during the years ended December 31, 2024 and 2023.

***Leases***

The Company accounts for leases in accordance with ASC 842. 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, 2024 and 2023 did not include any lease incentives. Lease expense for future lease payments is recognized on a straight-line basis over the lease term.

***Collaboration Agreements***

The Company analyzes its collaboration arrangements to assess whether they are within the scope of ASC Topic 808, *Collaborative Arrangements (*"ASC 808"), to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards that are dependent on the commercial success of such activities. To the extent the arrangement is within the scope of ASC 808, the Company assesses whether aspects of the arrangement between the Company and its collaboration partner are within the scope of other accounting literature, including ASC Topic 606, *Revenue from Contracts with Customers (*"ASC 606"). If it is concluded that some or all aspects of the arrangement represent a transaction with a customer, the Company will account for those aspects of the arrangement within the scope of ASC 606.

ASC 808 provides guidance for the presentation and disclosure of transactions in collaborative arrangements, but it does not provide recognition or measurement guidance. Therefore, if the Company concludes a counterparty to a transaction is not a customer or otherwise not within the scope of ASC 606, the Company considers the guidance in other accounting literature as applicable or by analogy to account for such transaction. The classification of transactions under the Company's arrangements is determined based on the nature and contractual terms of the arrangement along with the nature of the operations of the participants.

***Revenue Recognition***

The Company enters into collaboration agreements which are within the scope of ASC 606 under which the Company may license or provide options to license certain development or product candidates and, in certain

cases, may perform research and development services. The terms of these agreements may include payment of non-refundable, upfront fees, option exercise fees, development and commercial milestone payments and royalties on net sales of licensed products.

Under ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine the appropriate amount of revenue to be recognized for agreements determined to be within the scope of ASC 606, the Company performs the following five steps: (1) identify the contract with a customer; (2) identify the performance obligations in the contract; (3) determine the transaction price; (4) allocate the transaction price to the performance obligations in the contract; and (5) recognize revenue when or as the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when it is probable that the Company will collect consideration it is entitled to in exchange for the goods or services it transfers to the customer.

At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations. The Company then assesses whether each promised good or service is distinct. When the Company offers options for additional goods or services, such as an option to obtain a license, it evaluates whether such options are material rights that should be treated as separate performance obligations.

The Company estimates the transaction price based on the amount expected to be received for transferring the promised goods or services in the contract. The consideration may include fixed consideration or variable consideration. At the inception of each agreement that includes variable consideration, the Company evaluates the amount of potential payments and the likelihood that the payments will be received to estimate the amount expected to be received. The amount of variable consideration included in the transaction price may be constrained and is included in the transaction price only to the extent that it is probable that a significant reversal of the cumulative revenue recognized will not occur in a future period.

The Company recognizes as revenue the amount of the transaction price that it allocated to the respective performance obligation when or as each performance obligation is satisfied, either at a point in time or over time. If the performance obligation is satisfied over time, the Company recognizes revenue based on the use of an output or input method. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. For example, for research and development services that are recognized over time, the Company measures its progress using an input method. The input methods used are based on the effort the Company expends or costs it incurs toward the satisfaction of its performance obligation. The Company estimates the amount of effort it expends, including the time it estimates it will take to complete the activities, or costs it incurs in a given period, relative to the estimated total effort or costs to satisfy the performance obligation. This results in a percentage that is multiplied by the transaction price to determine the amount of revenue recognized each period. If the estimates or judgements change over the course of the collaboration, they may affect the timing and amount of revenue that is recognized in the current and future periods.

Upfront payments are recorded as contract liabilities within deferred revenue on the consolidated balance sheets until the Company performs its obligations under these agreements. Amounts are recorded as accounts receivable when the Company’s right to consideration is unconditional.

As of December 31, 2024, the Company had an option and license agreement with UCB Biopharma SRL ("UCB"), which it entered into in December 2022. Additionally, it had a collaboration and license agreement with Tenacia Biotechnology (Shanghai) Co., Ltd ("Tenacia"), which it entered into in January 2024. The accounting related to these agreements is outlined in Note 9, Collaboration and License Agreements.

***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 and prepaid expenses for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities and prepaid expenses, 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 and prepaid balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical 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.

***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 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 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. 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.

The grant date fair value of restricted stock units is estimated based on the fair value of the Company's underlying common stock on the date of grant.

***Foreign Currency***

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, 2024 and 2023.

***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' equity that are excluded from net loss. For the years ended December 31, 2024 and 2023, comprehensive loss consists of net loss and changes in unrealized gains and losses on marketable securities.

***Common Stock Warrants***

The Company accounts for warrants to purchase shares of its common stock in accordance with the guidance in FASB ASC No. 480, *Distinguishing Liabilities from Equity* ("ASC 480") and ASC No. 815, *Derivatives and Hedging* ("ASC 815"). The Company classifies warrants issued for the purchase of shares of its common stock as either equity or liability instruments based on an assessment of the specific terms and conditions of each respective contract. Such assessment includes determining whether the warrants are freestanding financial instruments or embedded in a host instrument, whether the warrants are liabilities within the scope of ASC 480, whether the warrants meet the definition of a derivative in ASC 815 and whether the warrants meet the requirements for equity classification pursuant to the indexation and equity classification criteria in ASC 815. The Company determines the classification for its warrants at the time of issuance and updates its assessment, as necessary. Warrants that meet all of the criteria for equity classification are recorded as a component of additional paid-in capital. Equity classified warrants are accounted for at fair value on the issuance date with no changes in fair value recognized after the issuance date.

***Net Loss per Share***

Basic net loss per share is computed by dividing net loss by the weighted average number of common shares outstanding for the period. The calculation of weighted average number of common shares outstanding excludes shares of restricted common stock that are not vested but includes shares of common stock underlying pre-funded warrants. Diluted net loss per share is computed by dividing net loss 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 potential shares issuable under the 2020 ESPP 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 are the same, as the inclusion of the potentially dilutive securities would be anti-dilutive.

***Recent Accounting Pronouncements***

*Recently Adopted Accounting Pronouncements*

In November 2023, the FASB issued ASU No. 2023-07, *Segment Reporting (Topic 280) - Improvements to Reportable Segment Disclosures* ("ASU 2023-07"). ASU 2023-07 improves reportable segment disclosure requirements, primarily through enhanced disclosures about significant segment expenses. The amendments included in this ASU apply to all public entities that are required to report segment information in accordance with Topic 280, including those with a single reportable segment. The amendments are effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024. The Company adopted ASU 2023-07 as of December 31, 2024. The amendments were applied retroactively to all prior periods presented in the consolidated financial statements and are reflected within Note 17.

*Recently Issued Accounting Pronouncements*

In December 2023, the FASB issued ASU No. 2023-09, *Income Taxes (Topic 740) - Improvements to Income Tax Disclosures* ("ASU 2023-09"). ASU 2023-09 provides more transparency about income tax information through improvements to income tax disclosures primarily related to the rate reconciliation and incomes taxes paid information. For public companies, the amendments are effective for annual periods beginning after December 15, 2024 and should be applied prospectively. The Company has determined that the effects of adopting the amendments in ASU 2023-09 will only impact its disclosures and not have a material impact on its consolidated financial position and the results of its operations when such amendment is adopted.

In November 2024, the FASB issued ASU No. 2024-03, *Income Statement-Reporting Comprehensive Income-Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses* ("ASU 2024-03"), requiring public entities to disclose additional information about specific expense categories in the notes to the financial statements on an interim and annual basis. ASU 2024-03 is effective for fiscal years beginning after December 15, 2026, and for interim periods beginning after December 15, 2027, with early adoption permitted. The amendments in this update should be applied either prospectively to financial statements issued for reporting periods after the effective date of this update, or retrospectively to any or all prior periods presented in the financial statements. The Company is currently evaluating the impact of adopting ASU 2024-03 on its consolidated financial statements.

**3. Restricted Cash**

As of December 31, 2024 and 2023, the Company had restricted cash of $0.4 million and $0.4 million, respectively, held as letters of credit for the benefit of its current landlord. The Company's Boston, Massachusetts sublease expires on January 31, 2026, and the related letter of credit of $0.4 million was classified within other non-current assets on the consolidated balance sheet as of December 31, 2024 and 2023.

**4. Cash Equivalents and Marketable Securities**

The following is a summary of the Company's investment portfolio as of December 31, 2024 (in thousands). The Company did not hold any cash equivalents or marketable securities as of December 31, 2023.

| | As of December 31, 2024 | | | |
|---|---|---|---|---|
| | Cost | Gross Unrealized Gains | Gross Unrealized Losses | Estimated Fair Value |
| Cash equivalents: | | | | |
| Money market funds | $ 128,652 | $ — | $ — | $ 128,652 |
| Debt securities issued by U.S. government agencies | 15,953 | 2 | — | 15,955 |
| Available-for-sale securities: | | | | |
| Debt securities issued by U.S. government agencies | 128,215 | 475 | — | 128,690 |
| Corporate debt securities | 107,695 | 157 | — | 107,852 |
| Commercial paper | 8,775 | 19 | — | 8,794 |
| Other debt securities | 8,819 | 1 | — | 8,820 |
| Total cash equivalents and marketable securities | $ 398,109 | $ 654 | $ — | $ 398,763 |

Contractual maturities of the marketable securities at each balance sheet are as follows (in thousands):

| | December 31, 2024 | December 31, 2023 |
|---|---|---|
| Within one year | $ 177,195 | $ — |
| After one year through five years | 76,961 | — |
| Total | $ 254,156 | $ — |

Securities are evaluated for impairment at the end of each reporting period. The Company did not record any impairment related to its available-for-sale securities during the years ended December 31, 2024 and 2023.

### 5. Fair Value of Financial Assets

The following table presents 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 as of December 31, 2024 (in thousands). The Company did not hold any financial assets measured at fair value on a recurring basis as of December 31, 2023.

| | As of December 31, 2024 | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| **Assets:** | | | | |
| Money market funds | $ 128,652 | $ — | $ — | $ 128,652 |
| | | | | |
| Debt securities issued by U.S. government agencies | 144,644 | — | — | 144,644 |
| Corporate debt securities | — | 107,852 | — | 107,852 |
| Commercial paper | — | 8,794 | — | 8,794 |
| Other debt securities | — | 8,821 | — | 8,821 |
| | $ 273,296 | $ 125,467 | $ — | $ 398,763 |

The Company estimates the fair value of its marketable securities classified as Level 2 by taking into consideration valuations obtained from third-party pricing sources. These pricing sources utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include market pricing based on real-time trade data for the same or similar securities, issuer credit spreads, benchmark yields, and other observable inputs. The Company validates the prices provided by its third-party pricing sources by understanding the models used, obtaining market values from other pricing sources and analyzing pricing data in certain instances.

## 6. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Computer equipment | $ 689 | $ 689 |
| Office furniture and equipment | 545 | 545 |
| Laboratory equipment | 359 | 359 |
| Total property and equipment | 1,593 | 1,593 |
| Less: Accumulated depreciation | (1,363) | (1,005) |
| Property and equipment, net | $ 230 | $ 588 |

Depreciation expense was $0.4 million and $0.4 million for the years ended December 31, 2024 and 2023, respectively.

## 7. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Accrued external research and development expenses | $ 13,363 | $ 2,957 |
| Accrued personnel-related expenses | 9,365 | 3,716 |
| Accrued other expenses | 1,035 | 743 |
| Total accrued expenses | $ 23,763 | $ 7,416 |

## 8. Commitments and Contingencies

### *Leases*

In May 2021, the Company entered into a sublease agreement for office space located in Boston, Massachusetts. The sublease expires on January 31, 2026, with no option to renew or terminate early. The base rent increases by approximately 2% 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. At inception, the Company recorded an operating lease right-of-use asset and operating lease liability of $4.1 million.

The following table summarizes the presentation of the operating lease in the Company's consolidated balance sheets (in thousands):

| | As of December 31, | |
|---|---|---|
| | 2024 | 2023 |
| **Assets:** | | |
| Operating lease right-of-use assets | $ 1,131 | $ 2,064 |
| **Liabilities:** | | |
| Current operating lease liabilities | $ 1,259 | $ 1,126 |
| Non-current portion of operating lease liabilities | 110 | 1,369 |
| Total lease liabilities | $ 1,369 | $ 2,495 |

The following table summarizes total lease costs recognized in the Company's consolidated statements of operations (in thousands):

| | For the year ended December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Operating lease cost | $ 1,102 | $ 1,102 |
| Variable lease costs | 33 | 14 |
| Total lease costs | $ 1,135 | $ 1,116 |

Variable lease costs were primarily related to operating expenses, taxes and insurance associated with the operating leases, 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 were 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, 2024 were as follows (in thousands):

| Year Ended December 31, | Future Lease Payments |
|---|---|
| 2025 | $ 1,321 |
| 2026 | 110 |
| Total future lease payments | 1,431 |
| Less: interest | (62) |
| Present value of operating lease liabilities | $ 1,369 |

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, | |
|---|---|---|
| | 2024 | 2023 |
| Weighted average remaining lease term (in years) | 1.1 | 2.1 |
| Weighted average incremental borrowing rate | 9.0 % | 9.0 % |

***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 material legal proceedings during the years ended December 31, 2024 and 2023, 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.

***Agreements***

The Company has entered into multiple agreements with third parties under which it may be obligated to make future development, regulatory and commercial milestone payments and royalty payments on future sales of specified product candidates. Payments under these agreements generally become due and payable upon achievement of such milestones and sales. When the achievement of these milestones or sales have not occurred, such contingencies are not recorded in the Company's financial statements.

**9. Collaboration and License Agreements**

***UCB Option and License Agreement***

In December 2022, the Company entered into an Option and License Agreement ("the Collaboration Agreement") with UCB for the discovery of small molecule therapeutics as potential treatments of KCNT1-related epilepsies. Under the terms of the Collaboration Agreement, the Company has agreed to perform general biology-related research services as part of a mutually agreed upon research plan in exchange for a $5.0 million upfront payment. In addition, the Company provided UCB an exclusive option to in-license global development and commercialization rights to any resulting KCNT1 small molecule development candidate identified as part of the research plan. If UCB exercises its option to in-license global development and commercialization rights, the Collaboration Agreement stipulates that UCB will assume research, development, manufacturing and commercialization responsibilities and costs. Under the terms of the Collaboration Agreement, the Company will be eligible to receive an option fee and future success-based development and commercialization milestone payments, totaling up to $98.5 million, in addition to tiered royalties on net sales of any resulting products from the Collaboration Agreement.

The Company concluded that UCB is a customer, and as such, the arrangement falls within the scope of Topic 606. At the commencement of the Collaboration Agreement, the Company identified one performance obligation, which was to perform the research services for UCB. The Company determined the transaction price to be $5.0 million, comprised of the upfront payment it received. The option provided to UCB was determined not to be a material right.

The Company recognizes revenue for its research services performance obligation over time using an input method over the duration of the research services. In December 2024, UCB exercised its option to in-license global development and commercialization rights for a KCNT1 development candidate as part of the Collaboration Agreement. Upon notice of the exercise, the Company recognized the $6.0 million option exercise fee as collaboration revenue within the consolidated statement of operations. The Company also recognized the $2.6 million of remaining collaboration revenue associated with the $5.0 million up front payment, as the Company will have no further research service obligations under the terms of the Collaboration Agreement.

During the years ended December 31, 2024 and 2023, the Company recognized $8.6 million and $2.4 million respectively, in collaboration revenue related to the Collaboration Agreement in the consolidated statement of operations. As of December 31, 2024, there was no deferred revenue included in the consolidated balance sheet.

***Tenacia Collaboration and License Agreement***

On January 4, 2024, the Company entered into an exclusive collaboration and license Agreement ("the License Agreement") with Tenacia, a China-based portfolio company of Bain Capital, which provides Tenacia an exclusive license to use certain intellectual property for the development and commercialization of ulixacaltamide and products containing ulixacaltamide in China, Hong Kong, Macau and Taiwan. Tenacia is solely responsible for the development and commercialization under the arrangement, with the exception of the associated manufacturing. The Company also entered into a Stock Purchase Agreement ("the Stock Purchase Agreement") with BCPE Tenet Holdings Cayman, Ltd. ("BCPE"), a related party of Tenacia. Pursuant to the terms of the License Agreement, the Company was entitled to an up-front, non-refundable and non-creditable cash payment of $5.0 million, net of certain tax withholdings. In addition, the Company is eligible to receive $264.0 million in success-based development and commercialization milestone payments as well as tiered royalties on net sales. Pursuant to the terms of the Stock Purchase Agreement, the Company issued and sold 443,253 shares of its common stock to BCPE at a price per share of $22.5605 for aggregate gross proceeds of $10.0 million. The per share price was based on a 20% premium over the 30-day volume-weighted average price.

Under the terms of the License Agreement, the Company granted to Tenacia an exclusive license to use certain intellectual property for the development and commercialization of ulixacaltamide and products containing ulixacaltamide in China, Hong Kong, Macau and Taiwan. Tenacia is solely responsible for the development and commercialization under the arrangement, with the exception of the associated manufacturing.

The Company concluded that the License Agreement and the Stock Purchase Agreement is a combined arrangement since they were executed at the same time and in contemplation of each other with the same counterparty or a related party thereof and the combined arrangement falls within the scope of Topic 606.

The Company's obligations under the arrangement comprise a single promise, or one performance obligation, related to the exclusive development and commercialization license granted to Tenacia. Total proceeds associated with the combined arrangement at inception were $14.8 million consisting of the following: (i) $10.0 million gross proceeds from the sale of common stock under the Stock Purchase Agreement and (ii) $4.8 million, net of tax, related to the up-front payment under the License Agreement, both of which were received in January 2024. During the year ended December 31, 2024, the Company had not achieved any development or sales milestones or earned any royalties under the License Agreement.

The Company recorded the common stock sold to BCPE at its issuance date fair value of $38.95 per share, or $17.3 million in the aggregate, which exceeded the proceeds received which were calculated based on the 20% premium over the prior 30-day volume-weighted average price. Accordingly, there is no transaction price allocable to the performance obligation. The Company accounted for the excess of the fair value of the equity securities issued over the total proceeds received as consideration paid to a customer for which no distinct good or service was transferred in exchange. As a result, the transaction gives rise to negative revenue on a cumulative basis in the amount of $2.5 million, which was recorded at the inception of the collaboration and license agreement in research and development expense in the accompanying consolidated statement of operations. For agreements where the licenses are considered separate performance obligations or represent the only performance obligation, the Company recognizes revenue at the point in time that the Company effectively grants the license, as the licenses or assignments represent functional intellectual property.

As of December 31, 2024, the Company did not have any receivables or deferred revenue related to the arrangement with Tenacia. The Company did not recognize any contract assets related to costs to obtain a contract with a customer or costs to fulfill a contract with a customer through December 31, 2024 because no qualifying costs were incurred. During the year ended December 31, 2024, the Company did not recognize any revenue associated with the combined arrangement.

**10. Common Stock and Preferred Stock**

***Common Stock***

In November 2021, the Company entered into an Open Market Sale Agreement (the "2021 Sales Agreement") with Jefferies LLC ("Jefferies"), to provide for the offering, issuance and sale of up to an aggregate amount of $125.0 million of common stock from time to time in at-the-market offerings for which Jefferies acted as sales agent. The Company terminated the 2021 Sales Agreement in June 2023. During the year ended December 31, 2023, the Company issued and sold an aggregate of 952,794 shares under the 2021 Sales Agreement for aggregate net proceeds of $24.1 million, after deducting commissions and offering expenses payable by the Company.

In December 2023, the Company entered into an Open Market Sale Agreement (the "2023 Sales Agreement"), with Jefferies, to provide for the offering, issuance and sale of up to an aggregate amount of $75.0 million of common stock from time to time in at-the-market offerings. The 2023 Sales Agreement was terminated in January 2024. During the year ended December 31, 2024, the Company issued and sold an aggregate of 192,190 shares under the 2023 Sales Agreement for aggregate net proceeds of $5.3 million, after deducting commissions and offering expenses payable by the Company.

In March 2024, the Company entered into an Open Market Sale Agreement (the "March 2024 Sales Agreement"), with Jefferies, to provide for the offering, issuance, and sale of up to an aggregate amount of $150.0 million of common stock from time to time in at-the-market offerings. During the year ended December 31, 2024, the Company issued and sold an aggregate of 1,614,975 shares under the March 2024 Sales Agreement for aggregate net proceeds of $113.1 million, after deducting commissions and offering expenses payable by the Company.

In December 2024, the Company entered into an amendment to the March Sales Agreement with Jefferies, to provide for the offering, issuance, and sale of up to an aggregate amount of $250.0 million of common stock from time to time in at-the-market offerings. During the year ended December 31, 2024, the Company issued and sold an aggregate of 16,487 shares under the amended March 2024 Sales Agreement for aggregate net proceeds of $1.0 million, after deducting commissions and offering expenses payable by the Company.

As of December 31, 2024 and 2023, 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, 2024, the Company did not hold any treasury shares.

***Follow-On Public Offerings***

*June 2023 Public Offering*

On June 21, 2023, the Company completed a public offering of: (i) an aggregate of 4,296,646 shares of its common stock at a public offering price of $14.25 per share, including the underwriters' full exercise of their option to purchase 619,979 additional shares of common stock, and (ii) pre-funded warrants to purchase 470,000 shares of common stock at a public offering price of $14.2485 per share of common stock underlying the warrants. The purchase price per share for each pre-funded warrant represents the per share offering price for the common stock, less the $0.0015 per share exercise price for each underlying share. Total net proceeds generated from the offering were approximately $63.4 million, after deducting underwriting discounts, commissions and other offering expenses payable by the Company.

During the year ended December 31, 2024, all pre-funded warrants associated with this offering were exercised via a cashless exercise, resulting in 469,981 shares of common stock issued. No cash proceeds associated with the exercise were received by the Company. As of December 31, 2024, there were no pre-funded warrants associated with this offering outstanding.

*January 2024 Public Offering*

On January 16, 2024, the Company completed a public offering of: (i) an aggregate of 3,802,025 shares of its common stock at a public offering price of $35.50 per share, including the underwriters' full exercise of their option to purchase 633,750 additional shares of common stock, and (ii) pre-funded warrants to purchase 1,056,725 shares of common stock at a public offering price of $35.4999 per share of common stock underlying the warrants. The purchase price per share of each pre-funded warrant represents the per share offering price for the common stock, less the $0.0001 per share exercise price of each underlying share. Total net proceeds generated from the offering were approximately $161.6 million, after deducting underwriting discounts, commissions and other offering expenses payable by the Company.

The pre-funded warrants are exercisable at any time on or after the date of issuance at the option of the holder, subject to a beneficial ownership blocker that may limit exercisability. No holder may exercise any portion of the warrants that would cause the aggregate number of shares of common stock beneficially owned by such holder, together with its affiliates, to exceed 4.99% (or 9.99%) of the issued and outstanding common stock. A holder of a pre-funded warrant may increase or decrease this percentage up to 19.99% by providing at least 61 days' prior notice to the Company. The pre-funded warrants do not expire. The pre-funded warrants may be settled through either physical or net share settlement. Following the occurrence of certain fundamental transactions, the holders of the pre-funded warrants have the right to receive upon exercise of the warrants the same amount and kind of securities, cash, or property as they would have been entitled to receive if they had been holders of the common shares issuable under the warrants immediately prior to such transaction. During the year ended December 31, 2024, 152,145 pre-funded warrants were exercised via a cashless exercise, resulting in 152,142 shares of common stock issued. No cash proceeds associated with the exercise were received by the Company. As of December 31, 2024, a total of 904,580 pre-funded warrants associated with this offering remained outstanding.

*April 2024 Public Offering*

On April 2, 2024 the Company completed a public offering of: (i) an aggregate of 3,849,558 shares of its common stock at a public offering price of $56.50 per share, including the underwriters' full exercise of their option to purchase 530,973 additional shares of common stock, and (ii) pre-funded warrants to purchase 221,238 shares of common stock at a public offering price of $56.4999 per share of common stock underlying the warrants. The purchase price per share for each pre-funded warrant represents the per share offering price for the common stock, less the $0.0001 per share exercise price of each underlying share. Total net proceeds generated from the offering were approximately $216.0 million, after deducting underwriting discounts, commissions and other offering expenses payable by the Company.

The pre-funded warrants are exercisable at any time on or after the date of issuance at the option of the holder, subject to a beneficial ownership blocker that may limit exercisability. No holder may exercise any portion of the warrants that would cause the aggregate number of shares of common stock beneficially owned by such holder, together with its affiliates, to exceed 4.99% (or 9.99%) of the issued and outstanding common stock. A holder of a pre-funded warrant may increase or decrease this percentage up to 19.99% by providing at least 61 days' prior notice to the Company. The pre-funded warrants do not expire. The pre-funded warrants may be settled through either physical or net share settlement. Following the occurrence of certain fundamental transactions, the holders of the pre-funded warrants have the right to receive upon exercise of the warrants the same amount and kind of securities, cash, or property as they would have been entitled to receive if they had been holders of the common shares issuable under the warrants immediately prior to such transaction. As of December 31, 2024, none of the pre-funded warrants had been exercised and all remained outstanding.

The Company determined that the pre-funded warrants related to the June 2023, January 2024, and April 2024 public offerings are freestanding financial instruments because they are both legally detachable and separately exercisable from the common stock sold in the offering. As such, the Company evaluated the pre-funded warrants to determine whether they represent instruments that require liability classification pursuant to the guidance in ASC 480. However, the Company concluded that the pre-funded warrants are not a liability within the scope of ASC 480 due to their characteristics. Further, the Company determined that the pre-funded warrants do not meet the definition of a derivative under ASC 815 because they do not meet the criteria regarding no or little initial net investment. Accordingly, the Company assessed the pre-funded warrants relative to the guidance in ASC No. 815-40, *Contracts in Entity's Own Equity*, to determine the appropriate treatment. The Company concluded that

the pre-funded warrants are both indexed to its own stock and meet all other conditions for equity classification. Accordingly, the Company has classified the pre-funded warrants as permanent equity.

***Shares Reserved for Future Issuance***

The Company had reserved the following shares of common stock for future issuance:

| | December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Shares reserved for exercise of outstanding stock options | 1,809,343 | 666,163 |
| Shares reserved for exercise of pre-funded warrants related to the June 2023 Financing | — | 470,000 |
| Shares reserved for exercise of pre-funded warrants related to the January 2024 Financing | 904,580 | — |
| Shares reserved for exercise of pre-funded warrants related to the April 2024 Financing | 221,238 | — |
| Shares reserved for future awards under the 2020 Stock Option and Incentive Plan | 91,343 | 148,264 |
| Shares reserved for future awards under the 2020 Employee Stock Purchase Plan | 109,648 | 53,111 |
| Shares reserved for future awards under the 2024 Inducement Plan | 112,774 | — |
| Shares reserved for vesting of restricted stock units | 224,473 | 47,145 |
| Total shares of authorized common stock reserved for future issuance | 3,473,399 | 1,384,683 |

***Preferred Stock***

As of December 31, 2024 and 2023, 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. As of December 31, 2024 and 2023, the Company had no shares of undesignated preferred stock issued or outstanding.

**11. Stock-Based Compensation**

***Equity Incentive Plans***

In January 2024, the Board of Directors ("the Board") adopted the 2024 Inducement Plan (the "Inducement Plan") without stockholder approval pursuant to Rule 5635(c)(4) of the Nasdaq Stock Market LLC listing rules ("Rule 5635(c)(4)"). In accordance with Rule 5635(c)(4), the Inducement Plan allows the Company to grant awards only to a newly hired employee who was not previously an employee or non-employee director or to an employee who is being rehired following a bona fide period of non-employment if such award is a material inducement to such employee entering into employment. The total shares of common stock initially authorized for issuance under the Inducement Plan was 1,000,000. In June 2024, the shares of common stock authorized for issuance under the Inducement Plan was reduced by 870,000 shares following stockholder approval of an amendment and restatement of the 2020 Stock Option and Incentive Plan ("the 2020 Plan"). The total number of shares of common stock authorized for issuance under the Inducement Plan as of December 31, 2024 was 130,000 shares.

The total number of shares of common stock authorized for issuance under the 2020 Plan as of December 31, 2024 and December 31, 2023 was 1,970,833 shares and 661,240 shares, respectively. The total number of shares of common stock authorized for issuance under the 2017 Stock Incentive Plan (the "2017 Plan") as of December 31, 2024 and 2023 was 395,850 shares. 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.

Stock options issued under the 2024 Inducement, 2020 Plan and 2017 Plan expire ten years from the date of grant. Shares that expire, are terminated, surrendered or canceled under the 2024 Inducement, 2020 Plan and 2017 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.

The total shares authorized for issuance under the 2020 Employee Stock Purchase Plan (the "2020 ESPP") as of December 31, 2024 and 2023 was 175,145 shares and 87,227 shares, respectively. During the years ended December 31, 2024 and 2023, the Company issued 31,381 and 24,690 shares, respectively, under the 2020 ESPP.

***Restricted Stock Units***

The following table summarizes the Company's restricted stock unit activity:

| | Shares | Weighted Average Grant Date Fair Value |
|---|---|---|
| Unvested as of December 31, 2023 | 47,145 | $ 202.27 |
| Issued | 208,997 | 53.35 |
| Vested | (19,576) | 201.07 |
| Forfeited | (12,093) | 53.90 |
| Unvested as of December 31, 2024 | 224,473 | $ 71.71 |

As of December 31, 2024, total unrecognized compensation cost related to unvested restricted stock units was $10.6 million, which is expected to be recognized over a weighted-average period of 2.72 years.

The total fair value of restricted stock units that vested during the years ended December 31, 2024 and 2023 was $1.0 million and $0.5 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, 2023 | 666,163 | $ 160.19 | 7.79 | $ 254 |
| Granted | 1,221,746 | 51.59 | | |
| Exercised | (45,177) | 46.24 | | $ 1,231 |
| Cancelled or Forfeited | (33,389) | 108.85 | | |
| Outstanding as of December 31, 2024 | 1,809,343 | $ 90.84 | 8.47 | $ 39,989 |
| Exercisable as of December 31, 2024 | 933,936 | $ 120.30 | 7.77 | $ 19,033 |
| Vested and expected to vest as of December 31, 2024 | 1,809,343 | $ 90.84 | 8.47 | $ 39,989 |

The aggregate intrinsic value of stock options exercised for the years ended December 31, 2024 and 2023 was $1.2 million and $0.1 million, respectively. The aggregate intrinsic value of stock options outstanding, exercisable, and vested and expected to vest 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, 2024. The aggregate intrinsic value of stock options exercised 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 on the date of exercise for those stock options that had exercise prices lower than the fair value of the Company's common stock on the exercise date.

***Valuation of Stock Options***

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 for the for the years ended December 31, 2024 and 2023:

| | Year Ended December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Risk-free interest rate | 4.01 % | 3.60 % |
| Expected term (in years) | 6.03 | 6.00 |
| Expected volatility | 96.60 % | 88.40 % |
| Expected dividend yield | — % | — % |
| Weighted average grant-date fair value per share | $ 41.25 | $ 29.73 |

As of December 31, 2024, total unrecognized compensation cost related to unvested stock options was $38.4 million, which is expected to be recognized over a weighted-average period of 2.49 years.

***Stock-Based Compensation***

Stock-based compensation expense was allocated as follows (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Research and development | $ 15,620 | $ 8,055 |
| General and administrative | 25,740 | 16,802 |
| Total stock-based compensation expense | $ 41,360 | $ 24,857 |

**12. Significant Agreements**

***RogCon and Ionis Agreements***

On September 11, 2019, the Company entered into both a Cooperation and License Agreement (the “License Agreement”) with RogCon, Inc. ("RogCon"), and a Research, Collaboration, Option and License Agreement (the “Ionis Collaboration Agreement”) with Ionis Pharmaceuticals, Inc. ("Ionis"). The agreements were entered into contemporaneously to enable the parties to advance their collective efforts related to SCN2A.

*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.

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. Expenses incurred for all periods presented were not material.

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 Ionis 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 Ionis Collaboration Agreement, both parties participated 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 was also responsible for identifying a development candidate and conducting an IND-enabling toxicology study. The Company reimbursed Ionis for out-of-pocket costs incurred related to the research activities, identification of a development candidate and conducting an IND-enabling toxicology study. The reimbursement of out-of-pocket costs was recognized as research and development expense as incurred. Expense for the years ended December 31, 2024 and 2023 was immaterial.

Ionis granted the Company an exclusive option 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, following the results of the investigational new drug application-enabling toxicology study. The Company exercised this exclusive option in January 2022, paid a $2.0 million license fee and recognized the license fee in research and development expenses in the consolidated statement of operations during the year ended December 31, 2022. After option exercise, the Company is responsible for clinical development and commercialization of the development candidate.

Additionally, in July 2023, the Company paid a milestone payment of $6.9 million to Ionis, which was earned in the second quarter of 2023 upon initiation of the Company's elsunersen EMBRAVE study, and was recognized in research and development expenses in the consolidated statement of operations during the year ended December 31, 2023. Ionis may be entitled to additional development milestone payments, additional milestone payments, and sales royalties or sublicense fees.

The Ionis Collaboration Agreement will continue until the expiration of all payment obligations to Ionis, unless earlier terminated. Either party may terminate the Ionis Collaboration Agreement upon material breach or insolvency of the other party. 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.

## 13. Net Loss per Share

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, | |
|---|---|---|
| | 2024 | 2023 |
| Outstanding stock options | 1,809,343 | 666,163 |
| Unvested restricted stock units | 224,473 | 47,145 |
| Potential shares issuable under the ESPP | 7,315 | 24,972 |
| | 2,041,131 | 738,280 |

Common shares issuable upon exercise of the pre-funded warrants that were sold and remain outstanding in connection with the January 2024 and April 2024 underwritten public offerings are included in the calculation of weighted average number of common shares outstanding for the year ended December 31, 2024. Consistent with the guidance in ASC 260-10-45-13, the underlying common shares are issuable for little to no consideration and there are no vesting conditions or contingencies associated with the warrants. Accordingly, the aggregate number of common shares underlying the pre-funded warrants have been considered outstanding for purposes of the calculation of net loss per share from the date of issuance.

## 14. 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, 2024 or 2023 related to its U.S. operations due to the uncertainty regarding future taxable income. In the years ended December 31, 2024 and 2023, 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 (provision) recognized for the years ended December 31, 2024 and 2023 was not material.

The reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate is as follows:

| | Year Ended December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Federal statutory income tax rate | 21.0 % | 21.0 % |
| Federal and state research and development credits | 3.9 % | 3.5 % |
| State taxes, net of federal benefit | 3.5 % | 4.3 % |
| Changes in tax rates | (3.2)% | 2.9 % |
| Non-deductible executive compensation | (2.6)% | (1.4)% |
| Non-deductible items | (0.8)% | — % |
| Stock-based compensation | (0.9)% | (1.3)% |
| Change in valuation allowance | (20.7)% | (29.7)% |
| Other | (0.2)% | 0.7 % |
| Effective income tax rate | — % | — % |

Net deferred tax assets consisted of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Deferred tax assets: | | |
| Net operating loss carryforwards | $ 90,108 | $ 74,528 |
| Capitalized research expenditures | 65,836 | 48,954 |
| Research and development credits | 30,582 | 23,451 |
| Amortization | 20,600 | 23,929 |
| Stock-based compensation | 8,784 | 7,697 |
| Accrued expenses | 2,333 | 1,147 |
| Leases | 344 | 676 |
| Deferred revenue | — | 692 |
| Total gross deferred tax assets | 218,587 | 181,074 |
| Less: Valuation allowance | (218,303) | (180,515) |
| Net deferred tax assets | $ 284 | $ 559 |
| Deferred tax liabilities: | | |
| Operating lease right-of-use asset | (284) | (559) |
| Total gross deferred tax liabilities | (284) | (559) |
| Net deferred tax assets | $ — | $ — |

As of December 31, 2024 and 2023, the Company had U.S. federal net operating loss carryforwards which may be able to offset future income tax liabilities of approximately $342.4 million and $282.8 million, respectively. Federal net operating loss carryforwards of $7.7 million will expire at various dates from 2035 through 2037 and approximately $334.7 million may be carried forward indefinitely. As of December 31, 2024 and 2023, the Company also had state net operating loss carryforwards of approximately $289.7 million and $239.4 million, respectively, which may be available to offset future income tax liabilities and expire at various dates from 2036 through 2044.

As of December 31, 2024 and 2023, the Company had federal research and development tax credit carryforwards of approximately $27.3 million and $20.4 million, respectively, available to reduce future tax liabilities which expire at various dates from 2039 through 2044. As of December 31, 2024 and 2023, the Company had state research and development tax credit carryforwards of approximately $4.1 million and $3.8 million, respectively, available to reduce future tax liabilities which expire at various dates from 2032 through 2039. 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, 2024 and 2023 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 $218.3 million and $180.5 million has been established at December 31, 2024 and 2023, respectively. Management reevaluates the positive and negative evidence at each reporting period. The valuation allowance increased by approximately $37.8 million and $36.6 million during the years ended December 31, 2024 and 2023, 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, 2024 and 2023. 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, 2024 and 2023, 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 for either year ended December 31, 2024 or 2023. The statute of limitations for federal and the majority of state tax authorities is open for tax years ended December 31, 2021 through December 31, 2024. The statute of limitation for the remaining state tax authorities is open for tax years ended December 31, 2020 through December 31, 2024. 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.

**15. Related Party Transactions**

One of the founders of RogCon is the Company's General Counsel. During the years ended December 31, 2024 and 2023, the Company reimbursed RogCon for its out-of-pocket costs incurred for activities performed under the License Agreement (Note 12).

**16. 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 $1.2 million and $1.0 million during the years ended December 31, 2024 and 2023, respectively.

**17. Segment Information**

The Company has one operating segment. The Company's operating segment discovers and develops therapies for CNS disorders. The Company's chief operating decision maker ("CODM"), its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purposes of assessing performance and allocating resources based on net loss that also is reported on the consolidated statement of operations as consolidated net loss. Net loss is used by the CODM to make key strategic and operational decisions. The operating segment's revenue is derived from a single domestic collaboration agreement from which the segment licenses certain development or product candidates and has performed research and development services. The measure of segment assets is reported on the balance sheet as total consolidated assets. The majority of the Company's long-lived assets are held in the United States.

The following table presents selected financial information about the Company's single operating segment for the year ended December 31, 2024 (in thousands):

| | December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Collaboration revenue | $ 8,553 | $ 2,447 |
| Program-specific expenses: | | |
| Ulixacaltamide[(a)] | 69,172 | 19,464 |
| Vormatrigine | 18,360 | 6,275 |
| Relutrigine | 6,273 | 3,996 |
| Elsunersen | 2,135 | 14,595 |
| Other early stage assets | 4,634 | 7,055 |
| Personnel-related expenses | 42,853 | 33,160 |
| Stock-based compensation expense | 41,361 | 24,857 |
| Depreciation expense | 358 | 432 |
| Other segment expenses[(b)] | 23,572 | 18,986 |
| Interest income | 17,346 | 3,096 |
| Consolidated net loss | $ (182,819) | $ (123,277) |

(a) Includes non-cash research and development of $2.5 million in the year ended December 31, 2024 associated with the Company's collaboration with Tenacia
(b) Other segment expenses includes research and development and general and administrative costs not attributable to a specific program.

## 18. Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the consolidated financial statements to provide additional evidence for certain estimates or to identify matters that require additional disclosure. The Company has concluded that no subsequent events have occurred that require disclosure other than those noted below.

### *At-the-Market Offerings*

Subsequent to December 31, 2024, the Company issued and sold a total of 694,212 shares under the amended March 2024 Sales Agreement for aggregate net proceeds of $54.9 million after deducting commissions and offering expenses payable by the Company.

## Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosures

None.

## Item 9A. Controls and Procedures

### *Limitations on Effectiveness of Controls and Procedures*

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

### *Evaluation of 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, as controls and other procedures of an issuer that are designed to ensure that information required to be disclosed by the issuer in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by an issuer in the reports that it files or submits under the Exchange Act is accumulated and communicated to the issuer's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

Our management, with the participation of our Chief Executive Officer (our principal executive officer) and Chief Financial Officer (our principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2024. Based on the evaluation of our disclosure controls and procedures as of December 31, 2024, our Chief Executive Officer and Chief Financial Officer 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 three months ended December 31, 2024 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*

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Exchange Act Rules 13a-15(f), to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Management assessed our internal control over financial reporting as of December 31, 2024. Management based its assessment on criteria established in "Internal Control - Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on that assessment, our management concluded that our internal control over financial reporting was effective as of December 31, 2024.

### *Attestation Report of the Independent Registered Public Accounting Firm*

Ernst & Young LLP, an independent registered public accounting firm, audited the effectiveness of our internal control over financial reporting as of December 31, 2024, as stated in their attestation report included in this Annual Report on Form 10-K.

**Report of Independent Registered Public Accounting Firm**

To the Stockholders and the Board of Directors of Praxis Precision Medicines, Inc.

**Opinion on Internal Control Over Financial Reporting**

We have audited Praxis Precision Medicines, Inc.'s internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Praxis Precision Medicines, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2024 and 2023, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2024, and the related notes and our report dated February 28, 2025 expressed an unqualified opinion thereon.

**Basis for Opinion**

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

**Definition and Limitations of Internal Control Over Financial Reporting**

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 28, 2025

**Item 9B. Other Information**

(a) Disclosure in lieu of a Current Report on Form 8-K.

None.

(b) Material changes to the procedures by which security holders may recommend nominees to the board of directors.

None.

(c) Insider Trading Arrangements and Policies.

During the three months ended December 31, 2024, no director or officer of the Company adopted or terminated a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement," as each term is defined in Item 408(a) of Regulation S-K.

**Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections**

Not Applicable.

## 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 February 28, 2025:

| Name | Age | Position |
|---|---|---|
| **Executive Officers:** | | |
| Marcio Souza | 45 | President, Chief Executive Officer, Director |
| Timothy Kelly | 52 | Chief Financial Officer |
| Alex Nemiroff, J.D. | 46 | General Counsel, Corporate Secretary |
| **Non-Employee Directors:** | | |
| Dean Mitchell(2)(4) | 69 | Chairman, Director |
| Jeffrey Chodakewitz, M.D.(3)(4) | 69 | Director |
| Merit Cudkowicz, M.D.(1)(4) | 61 | Director |
| Jill DeSimone(1)(2)(3) | 69 | Director |
| Gregory Norden(1)(2) | 67 | Director |
| William Young(2)(3) | 80 | Director |

(1) Member of the Audit Committee.

(2) Member of the Compensation Committee.

(3) Member of the Nominating and Corporate Governance Committee.

(4) Member of the Science and Technology Committee

**Executive Officers**

***Marcio Souza*** has served as a member of our Board of Directors 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. Mr. Souza currently serves on the board of directors of Remagine Labs, a private company. Mr. Souza previously served on the boards of directors of Spyre Therapeutics, Inc. (previously Aeglea BioTherapeutics, Inc.) and Clearpoint Neuro, Inc. (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

***Timothy Kelly*** has served as our Chief Financial Officer since May 2021. Prior to his role as Chief Financial Officer, Mr. Kelly served as Chief Financial Officer of Foundation Medicine, Inc. from 2019 to April 2021. In this position, he led the finance and corporate management teams, providing strategic leadership and oversight for the corporate functions, which included accounting and tax, billing and reimbursement, procurement, corporate development, project management and financial planning and analysis. Prior to his time at Foundation Medicine, Mr. Kelly served in several finance roles of increasing responsibility at the F. Hoffman-La Roche AG, or Roche, and Genentech (before being acquired by Roche in 2009) from 2003 to 2019, including finance and corporate services director for Roche Pharma in the United Kingdom from 2017 to 2019 and head of group strategic planning for the Roche Group in Switzerland from 2013 to 2017. Mr. Kelly holds a B.A. in economics from the College of William and Mary and an M.B.A. from the Columbia Business School.

***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 Vice President 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.

**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 S.à.r.l., a specialty pharmaceutical company, from August 2013 until its sale in March 2020 and was chairman of PaxVax Corporation, a biotechnology company, 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. Prior to 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 boards of directors of Theravance Biopharma, Inc. (NASDAQ: TBPH) and Precigen Inc. (formerly Intrexon Inc.) (NASDAQ: PGEN). Mr. Mitchell previously served on the boards of directors of ImmunoGen Inc. (acquired by Abbvie Inc. in 2024) and Kinnate Biopharma Inc. (acquired by XOMA Corporation in 2024). 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.

***Jeffrey Chodakewitz, M.D.,*** has served as a member of our Board of Directors since April 2021. Dr. Chodakewitz has served as an advisory partner for Ascenta Capital, a life sciences investment firm, since December 2022. He previously served as a senior advisor to Blackstone Life Sciences, a life sciences private equity firm from March 2019 to January 2022. From April 2018 through March 2019, he served as Executive Vice President, Clinical Medicine and External Innovation, at Vertex Pharmaceuticals, Inc., or Vertex. Prior to that role, Dr. Chodakewitz held the roles of Chief Medical Officer and Executive Vice President, Global Medicines Development and Medical Affairs at Vertex from January 2014 to April 2018 and was a member of the Vertex Executive Committee. Prior to Vertex, Dr. Chodakewitz spent over 20 years at Merck & Co. serving in several positions, including leadership roles as Head of Infectious Diseases and Vaccines Global Development, Senior Vice President of Global Scientific Strategy (infectious disease, respiratory & immunology), Vice President of Early-Stage Development and Senior Vice President of Late-Stage Development. Dr. Chodakewitz currently serves on the boards of directors of Adicet Bio, Inc. (NASDAQ: ACET) and Schrödinger, Inc. (NASDAQ:SDGR). Dr. Chodakewitz previously served on the board of directors of Freeline Therapeutics Holdings plc. (acquired by Syncona Ltd in 2024). Dr. Chodakewitz received a B.S. in Biochemistry cum laude from Yale University and an M.D. from the Yale University School of Medicine. We believe Dr. Chodakewitz is qualified to serve on our Board of Directors because of his extensive business and leadership experience working in the biotechnology industry.

***Merit Cudkowicz, M.D.,*** has served as a member of our Board of Directors since April 2021. Dr. Cudkowicz has served as the Chief of Neurology at Massachusetts General Hospital since 2012 and is the Director of the Sean M. Healey & AMG Center for ALS and Director and the Julieanne Dorn Professor of Neurology at Harvard Medical School. A member of the National Academy of Medicine, she has led innovations to accelerate the development of treatments for people with neurological disorders such as ALS, including the first platform trial in ALS, and serving in a senior role in the research and development of the first antisense oligonucleotide treatment for a neurological disorder. Dr. Cudkowicz is also the principal investigator of the Clinical Coordination Center for the National Institute of Neurological Disorders and Stroke's Neurology Network of Excellence in Clinical Trials, or NeuroNEX. Dr. Cudkowicz received a B.S. in Chemical Engineering from Massachusetts Institute of Technology, an M.D. from Harvard Medical School and a MSc. in Clinical Epidemiology from Harvard School of Public Health. We believe Dr. Cudkowicz is qualified to serve on our Board of Directors because of her extensive medical background and experience.

***Jill DeSimone*** has served as a member of our Board of Directors since May 2022. Ms. DeSimone served as President of U.S. Oncology at Merck & Co., Inc., or Merck, from 2014 to May 2022. During her time at Merck, Ms. DeSimone also temporarily served as Interim President of U.S. Pharma to help navigate the business through the COVID-19 pandemic. Prior to joining Merck, she served as Senior Vice President of Global Women's Health at Teva Pharmaceutical Industries Ltd, or Teva, from 2012 to 2014. Prior to her time at Teva, Ms. DeSimone served in several roles of increasing responsibility at Bristol Myers-Squibb from 1980 to 2012, including Senior Vice President

of Oncology and Senior Vice President of Commercial Operations. Ms. DeSimone currently serves on the board of directors of Oncternal Therapeutics, Inc. (NASDAQ: ONCT), iTeos Therapeutics, Inc. (NASDAQ: ITOS) and Affini-T Therapeutics, Inc., a private company. Ms. DeSimone previously served on the board of directors of Kinnate Biopharma, Inc. (acquired by XOMA Corporation in 2024). Ms. DeSimone also serves as a board member for the Florida Cancer Specialists Foundation and Swim Across America, nonprofit organizations focused on cancer patient support and research. Ms. DeSimone received a B.S. in pharmacy from Northeastern University and completed a fellowship with the Wharton School of the University of Pennsylvania. We believe Ms. DeSimone is qualified to serve on our Board of Directors because of her leadership and extensive business experience in the pharmaceutical industry.

***Gregory Norden*** has served as a member of our Board of Directors since March 2019. Mr. Norden is the former Chief Financial Officer of Wyeth Pharmaceuticals Inc. and has served as the Managing Director of G9 Capital Group LLC, which invests in early stage ventures and provides corporate advisory services, since 2010. Mr. Norden currently serves on the boards of directors of Zoetis Inc. (NYSE: ZTS) and Royalty Pharma plc (NASDAQ: RPRX). Mr. Norden previously served on the boards of directors of Human Genome Sciences, Inc., Univision, Welch Allyn and NanoString Technologies, Inc. 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 LIU 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.

***William Young*** has served as a member of our Board of Directors since December 2016. Mr. Young is a Senior Advisor with Blackstone Life Sciences, which he joined in November 2018. Prior to its acquisition by Blackstone, Mr. Young joined Clarus Ventures LLC in March 2010 and held various roles, including Venture Partner, Senior Advisor and portfolio company board member. Prior to joining Clarus, Mr. Young was chairman of the board of directors and Chief Executive Officer of Monogram Biosciences Inc. from 2000 until its acquisition by Laboratory Corporation of America Holdings in 2009. Previously, Mr. Young spent 20 years at Genentech, Inc. in roles of increasing responsibility, culminating as Chief Operating Officer from 1997 to 1999. Mr. Young currently serves as a member of the board of directors of Autolus Therapeutics plc (NASDAQ: AUTL). Mr. Young previously served as the chairman of the board of directors of Annexon, Inc., and as a member of the boards of directors of Vertex Pharmaceuticals Inc., BioMarin Pharmaceutical Inc., Theravance BioPharma, Inc. and NanoString Technologies, Inc. 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.

**Code of Business Conduct and Ethics**

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the code is posted on the corporate governance section of our website, which is located at https://investors.praxismedicines.com/corporate-governance/governance-overview. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a Form 8-K.

The remainder of the information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

## Item 11. Executive Compensation

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

## 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, 2024 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, our 2020 Employee Stock Purchase Plan and our 2024 Inducement Plan.

| Plan Category | Number of securities to be issued upon exercise of outstanding options, restricted stock units, warrants and rights (a) | Weighted average exercise price of outstanding options (b) | Number of securities remaining available for future issuance under equity compensation plan (excluding securities reflected in column (a)) (c) |
|---|---|---|---|
| Equity compensation plans approved by security holders(1): | 2,016,590(2) | $91.04(3) | 200,991(4) |
| Equity compensation plans not approved by security holders(5): | 17,226(6) | $53.13(7) | 112,774 (8) |
| Total | 2,033,816 | $90.84 | 313,765 |

(1) The 2020 Stock Option and Incentive Plan provides for an annual increase in the number of securities available for future issuance on each January 1 by an amount equal to 5% of the number of shares of common stock outstanding as of the immediately preceding December 31 or such lesser number of shares as determined by the administrator of such plan. The 2020 Employee Stock Purchase Plan provides for an annual increase in the number of securities available for future issuance on each January 1 by an amount equal to the lesser of (i) 1% of the number of shares of common stock outstanding as of the immediately preceding December 31, (ii) 327,102 shares of common stock, or (iii) such number of shares of common stock as determined by the administrator of such plan.

(2) Includes 1,799,643 shares of common stock issuable upon the exercise of outstanding options under the 2017 and 2020 Stock Option and Incentive Plans and 216,947 shares subject to restricted stock units that will entitle the holder to one share of common stock for each unit that vests.

(3) The calculation does not take into account the 216,947 shares of common stock subject to outstanding restricted stock units under the 2020 Stock Option and Incentive Plan. Such shares will be issued at the time the restricted stock unit vests, without any cash consideration payable for those shares.

(4) As of December 31, 2024, there were no shares available for grant under the 2017 Stock Incentive Plan, 91,343 shares available for grants under the 2020 Stock Option and Incentive Plan and 109,648 shares available for grants under the 2020 Employee Stock Purchase Plan (of which 7,315 shares were subject to outstanding purchase rights).

(5) The 2024 Inducement Plan was adopted in January 2024. Awards issued under the 2024 Inducement Plan may only be made to a newly hired employee who was not previously an employee or non-employee director or to an employee who is being rehired following a bona fide period of non-employment if such award is a material inducement to such employee entering into employment. The material terms of the 2024 Inducement Plan are described in Note 11 to the consolidated financial statements included herein.

(6) Includes 9,700 shares of common stock issuable upon the exercise of outstanding options under the 2024 Inducement Plan and 7,526 shares subject to restricted stock units that will entitle the holder to one share of common stock for each unit that vests.

(7) The calculation does not take into account the 7,526 shares of common stock subject to outstanding restricted stock units under the 2024 Inducement Plan. Such shares will be issued at the time the restricted stock unit vests, without any cash consideration payable for those shares.

(8) As of December 31, 2024, there were 112,774 shares available for grant under the 2024 Inducement Plan. In January 2025, the number of shares of the Company's common stock reserved for issuance under the 2024 Inducement Plan was increased by 870,000 shares.

The remainder of the information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

**Item 13. Certain Relationships and Related Transactions, and Director Independence**

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

**Item 14. Principal Accounting Fees and Services**

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

## PART IV

**Item 15. Exhibits and Financial Statement Schedules.**

*(a)(1) Financial Statements.*

For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page 100 of this Annual Report on Form 10-K, incorporated into this Item by reference.

*(a)(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.

*(a)(3) List of Exhibits*

| | |
|---|---|
| 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 | Certificate of Amendment to the Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on December 1, 2023) |
| 3.3 | Amended and Restated Bylaws 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 January 7, 2022) |
| 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, as amended (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-3 (File No. 333-260726) filed on November 3, 2021) |
| 4.3 | Description of Securities of Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 4.3 to the Registrant's Annual Report on Form 10-K (File No. 001-39620) filed on February 28, 2022) |
| 4.4 | Form of Pre-funded Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on January 12, 2024) |
| 4.5 | Form of Pre-funded Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on March 29, 2024) |
| 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 (incorporated by reference to Exhibit 10.3 to the Registrant's Annual Report on Form 10-K (File No. 001-39620) filed on March 17, 2021) |
| 10.4# | Praxis Precision Medicines, Inc. 2020 Stock Option and Incentive Plan, as amended and restated (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on June 6, 2024) |
| 10.5# | Form of Incentive Stock Option Agreement under the 2020 Stock Option and Incentive Plan, as amended and restated (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, as amended and restated (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, as amended and restated (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, as amended and restated (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 Unit Award Agreement for Company Employees under the 2020 Stock Option and Incentive Plan, as amended and restated (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 Unit Award Agreement for Non-Employee Directors under the 2020 Stock Option and Incentive Plan, as amended and restated (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# | Praxis Precision Medicines, Inc. 2024 Inducement Plan and Forms of Award Agreements thereunder (incorporated by reference to Exhibit 99.1 to the Registrant's Registration Statement on Form S-8 (File No. 333-276786) filed on January 31, 2024) |
| 10.13# | Amended and Restated Employment Agreement, dated October 20, 2020, by and between Praxis Precision Medicines, Inc. and Marcio Souza (incorporated by reference to Exhibit 10.12 to the Registrant's Annual Report on Form 10-K (File No. 001-39620) filed on February 28, 2022) |
| 10.14# | Amended and Restated Employment Agreement, dated May 13, 2021, by and between Praxis Precision Medicines, Inc. and Timothy Kelly (incorporated by reference to Exhibit 10.13 to the Registrant's Annual Report on Form 10-K (File No. 001-39620) filed on February 7, 2023) |
| 10.15# | Amended and Restated Employment Agreement, dated October 20, 2020, by and between Praxis Precision Medicines, Inc. and Alex Nemiroff (incorporated by reference to Exhibit 10.15 to the Registrant's Annual Report on Form 10-K (File No. 001-39620) filed on March 5, 2024) |
| 10.16# | Employment Agreement Amendment Letter, dated October 11, 2024, by and between Marcio Souza and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on October 15, 2024) |
| 10.17# | Employment Agreement Amendment Letter, dated October 11, 2024, by and between Timothy Kelly and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on October 15, 2024) |
| 10.18# | Employment Agreement Amendment Letter, dated October 11, 2024, by and between Alex Nemiroff and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on October 15, 2024) |
| 10.19# | Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-39620) filed on August 13, 2024) |
| 10.20† | 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) |
| 10.21† | 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) |
| 10.22 | Sublease, dated May 27, 2021, by and between CBRE, Inc. and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on June 2, 2021) |
| 19* | Praxis Precision Medicines, Inc. Insider Trading Policy |
| 21.1* | Subsidiaries of the Registrant |
| 23.1* | Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm |
| 24.1* | Power of Attorney (included on signature page hereto) |
| 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 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 Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 |

| | |
|---|---|
| 97 | Praxis Precision Medicines, Inc. Policy for Recovery of Erroneously Awarded Compensation (incorporated by reference to Exhibit 97 to the Registrant's Annual Report on Form 10-K (File No. 001-39620) filed on March 5, 2024) |
| 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 |
| 104 | Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101) |

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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.

**Item 16. Form 10–K Summary**

None.

## 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: February 28, 2025

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 Timothy Kelly, 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<br>Marcio Souza | Chief Executive Officer and Director (Principal Executive Officer) | February 28, 2025 |
| /s/ Timothy Kelly<br>Timothy Kelly | Chief Financial Officer (Principal Financial Officer) | February 28, 2025 |
| /s/ Lauren Mastrocola<br>Lauren Mastrocola | Principal Accounting Officer | February 28, 2025 |
| /s/ Dean Mitchell<br>Dean Mitchell | Chairman of the Board | February 28, 2025 |
| /s/ Jeffrey Chodakewitz<br>Jeffrey Chodakewitz, M.D. | Director | February 28, 2025 |
| /s/ Merit Cudkowicz<br>Merit Cudkowicz, M.D. | Director | February 28, 2025 |
| /s/ Jill DeSimone<br>Jill DeSimone | Director | February 28, 2025 |
| /s/ Gregory Norden<br>Gregory Norden | Director | February 28, 2025 |
| /s/ William Young<br>William Young | Director | February 28, 2025 |

**Praxis Precision Medicines, Inc.**
**Insider Trading Policy**

In order to mitigate the risk of insider trading violations by officers, directors, employees and other related individuals of Praxis Precision Medicines, Inc. (the “Company”) and its subsidiaries, the Company has adopted this Insider Trading Policy (the “Policy”).

**Statement of Intent**

The Company opposes the misuse of material nonpublic information in the trading of securities and it is the intent of this Policy to implement procedures designed to prevent trading based on material nonpublic information regarding the Company, including any of its subsidiaries. The Company also wishes to discourage certain trading in its securities by its officers, directors, employees and other related individuals that may be contrary to the interests of our shareholders. The term "officers" herein shall be defined as under Rule 16a-1(f) of the Securities Exchange Act of 1934, as amended (the “Exchange Act”).

**Covered Parties**

The Policy covers officers, directors and all other employees of, or consultants or contractors to, the Company or its subsidiaries, as well as their immediate families, and members of their households, and any entities controlled by individuals subject to the Policy, including any corporations, partnerships or trusts (“Insider(s)”). Directors, officers, employees, consultants and contractors subject to this Policy are responsible for ensuring that members of their immediate families and households comply with this Policy.

This Policy shall not apply to any entity controlled by an Insider that engages in the investment of securities in the ordinary course of its business if such entity has established its own insider trading controls and procedures in compliance with applicable securities laws and an Insider has represented to the Company that such entity: (a) engages in the investment of securities in the ordinary course of its business; (b) has established insider trading controls and procedures in compliance with applicable securities laws; and (c) is aware such securities laws prohibit any person or entity who has material nonpublic information concerning the Company from purchasing or selling securities of the Company or from communicating such information to any other person under circumstances in which it is reasonably foreseeable that such person is likely to purchase or sell securities.

**Covered Transactions**

This Policy applies to all transactions in the Company’s securities, including common stock, options for common stock and any other securities the Company may issue from time to time, such as preferred stock, warrants and convertible debentures, as well as to derivative securities relating to the Company’s stock, whether or not issued by the Company, such as publicly-traded options.

**Prohibited Transactions**

No Insider shall engage in any transaction involving a purchase or sale of the Company's securities, including any offer to purchase or offer to sell, while in possession of material nonpublic information relating to the Company and/or its securities.

No Insider shall disclose ("tip") material nonpublic information about the Company or its subsidiaries to any other person where such information may be used by such person to his or her profit by trading in the securities of companies to which such information relates, nor shall such Insider or related person make recommendations or express opinions on the basis of material nonpublic information as to trading in the Company's securities.

No Insider shall engage in any transaction involving the purchase or sale of another company's securities while in possession of material nonpublic information about such company when that information is obtained in the course of employment with, or the performance of services on behalf of, the Company and for which there is a relationship of trust and confidence concerning the information.

**Permitted Transactions**

The prohibition on transactions in the Company's securities under this Policy do not apply to the following permitted transactions:

- purchases of the Company's securities by an Insider from the Company, including without limitation pursuant to an employee stock purchase plan, or sales of the Company's securities by an Insider to the Company;
- exercises of stock options or other equity awards or the surrender of shares to the Company in payment of the exercise price or in satisfaction of any tax withholding obligations in a manner permitted by the applicable equity award agreement, or vesting of equity-based awards, that in each case do not involve a market sale of the Company's securities (the "cashless exercise" of a Company stock option through a broker does involve a market sale of the Company's securities, and therefore would not qualify under this exception);
- *bona fide* gifts of the Company's securities, unless the person making the gift has reason to believe, or is reckless in not determining, that the recipient intends to sell the securities while the donor is in possession of material nonpublic information about the Company; or
- purchases or sales of the Company's securities made pursuant to a plan entered into and conducted in good faith in accordance with the Exchange Act Rule 10b5-1 ("Rule 10b5-1"). For more information about Rule 10b5-1 trading plans, see "10b5-1 Trading Plans" below.

**Other Prohibited Transactions**

No officer or director shall, at any time, engage in any transactions involving any short sales, hedging or derivatives of Company securities, including trading in futures and derivative securities and engaging in hedging activities relating to Company securities, including exchange traded options, puts, calls, collars, forward sale contracts, equity swaps, exchange funds or other arrangements or instruments designed to hedge or offset decreases in the market value of our securities, purchases of the Company's securities on margin (other than in connection with a cashless exercise of stock options through a broker under the Company's equity plans), or pledge of the Company's securities as collateral to secure loans. While employees (other than officers) are not prohibited by this Policy from engaging in these transactions, the Company discourages employees from such activity because there is a heightened legal risk and/or the appearance of improper or inappropriate conduct if Insiders engage in these transactions. In addition, these types of transactions may result in transactions in Company securities during a Closed Window (defined below). Limit orders with brokers should not extend into a Closed Window and be cancellable upon an imposition of a Closed Window. Employees interested in trading during a Closed Window should look into adopting a 10b5-1 trading plan, as described in "10b5-1 Trading Plans" below.

**Trading Window**

The Company has determined that all officers, directors, and those other persons identified on Attachment 1 hereto (as may be amended from time to time by the Compliance Officer (as defined below)), shall be prohibited from buying, selling or otherwise effecting transactions in any stock or other securities of the Company or derivative securities thereof during a "Closed Window," except for purchases and sales made pursuant to the permitted transactions described in "Permitted Transactions" above. The Closed Window shall remain in effect until the Company communicates that it is opening the window to permit trading in any stock or other securities of the Company or derivative securities thereof, which the Company anticipates will occur each fiscal quarter. In addition, from time to time, the Company, through the Company's Board of Directors (the "Board of Directors"), the Company's disclosure committee or the Compliance Officer, may recommend that officers, directors, employees or others suspend trading in the Company's securities because of developments that have not yet been disclosed to the public. All of those affected should not trade in the Company's securities while the suspension is in effect, and should not disclose to others that the Company has suspended trading.

Exceptions to a Closed Window may be approved only by the Compliance Officer or, in the case of an exception for the Compliance Officer or persons or entities subject to this policy as a result of their relationship with the Compliance Officer, the Chief Executive Officer or, in the case of exceptions for directors or persons or entities subject to this policy as a result of their relationship with a director, the Board of Directors.

It should be noted that even outside of a Closed Window, any person possessing material nonpublic information should not engage in any transactions in the Company's securities.

**Pre-clearance of Trades and Other Transactions by Officers and Directors**

All officers, directors, employees, consultants and contractors of the Company (the "Pre-Clearance Persons") must refrain from all transactions (including without limitation, acquisitions and dispositions of Company stock (including by gift), the exercise of stock options and the sale of Company stock issued upon exercise of stock options) in the Company's securities, even outside of a Closed Window, without first seeking pre-clearance from the Compliance Officer or his/her designee, or, in the event the Compliance Officer is seeking pre-clearance, the Company's Chief Financial Officer, and obtaining pre-clearance to effect a transaction in the Company's securities.

In addition, all officers and directors are required to comply with Section 16 of the Exchange Act, and related rules and regulations which set forth reporting obligations as well as limitations on "short swing" transactions. The Company is available to assist in filing Section 16 reports, however, the obligation to comply with Section 16 is personal. Please direct any inquiries concerning compliance to the Compliance Officer. Officers and directors who wish to pledge the Company's stock as collateral after October 15, 2020 must first contact the Company's Compliance Officer to request an exemption and pre-clearance to enter into the transaction.

**Post-Termination Transactions**

If an individual is in possession of material nonpublic information when his or her service terminates, that individual may not trade in the Company's securities until that information has become public or is no longer material.

**10b5-1 Trading Plans**

The Company permits all directors, officers and other employees to adopt trading plans in accordance with Rule 10b5-1 and otherwise pursuant to the Company's procedure for adopting such a trading plan (a "Trading Plan"), including the Company's guidelines for such plans attached hereto as Attachment 2 (the "Guidelines"). The restrictions on trading set forth in this Policy, including pre-clearance and Closed Windows, shall not apply to trades made pursuant to a 10b5-1 trading plan.

The Compliance Officer may impose such other conditions on the implementation and operation of the Trading Plan as the Compliance Officer deems necessary or advisable. Compliance of a Trading Plan with the terms of Rule 10b5-1 and the execution of transactions pursuant to the Trading Plan are the sole responsibility of the person initiating the Trading Plan, and none of the Company, the Compliance Officer, or the Company's other employees assumes any liability for any delay in reviewing and/or refusing to approve a Trading Plan submitted for approval, nor the legality or consequences relating to a person entering into, informing the Company of, or trading under, a Trading Plan.

For more information concerning Trading Plans, contact the Compliance Officer.

**Consequences for Violation**

Employees who violate this Policy shall be subject to disciplinary action by the Company, which may include termination of employment, or ineligibility for future participation in the Company's equity stock option and other incentive plans.

Pursuant to U.S. federal and state securities laws, Insiders may be subject to criminal and civil fines and penalties as well as imprisonment for engaging in transactions in the Company's securities at a time when they have knowledge of material nonpublic information regarding the Company or its subsidiaries. In addition, Insiders may be liable for improper transactions by any person (commonly referred to as a "tippee") to whom they have disclosed material nonpublic information regarding the Company or its subsidiaries or to whom they have made recommendations or expressed opinions on the basis of such information as to trading in the Company's securities.

**Individual Responsibility and Limitation of Liability**

Every officer, director and other employee, consultant and contractor has the individual responsibility to comply with this Policy, and the applicable laws of their jurisdiction. An Insider may, from time to time, have to forego a proposed transaction in the Company's securities even if he or she planned to make the transaction before learning of the material nonpublic information and even though the Insider believes he or she may suffer an economic loss or forego anticipated profit by waiting. **Trading in the Company's securities outside of a Closed Window should not be considered a "safe harbor," and all directors, officers and other persons should use good judgment at all times.**

**Compliance Officer**

The Company's General Counsel, or such other person as the Board of Directors may designate from time to time, shall serve as the Insider Trading Compliance Officer (the "Compliance Officer"). The duties of the Compliance Officer shall include, but not be limited to, the following:

- Pre-clearing transactions and 10b5-1 trading plans as required under this Policy.
- Assisting, as requested, in the preparation and filing of Section 16 reports (Forms 3, 4 and 5) for Section 16 reporting persons.
- Serving as the designated recipient at the Company of copies of reports filed with the Securities and Exchange Commission ("SEC") by Section 16 reporting persons under Section 16 of the Exchange Act.
- Periodically reminding all Section 16 reporting persons regarding their obligations to report and quarterly reminders of the dates that the Closed Windows described above begin and end.
- Circulating this Policy to all employees, including Section 16 reporting persons, on an annual basis.
- Assisting the Company in implementation of this Policy.

- Coordinating with Company counsel regarding compliance activities with respect to Rule 144 requirements and regarding changing requirements and recommendations for compliance with Section 16 of the Exchange Act and insider trading laws to ensure that this Policy is amended as necessary to comply with such requirements.

The duties may be delegated by the Compliance Officer to such other individuals as the Compliance Officer deems appropriate.

**Definition of Material Nonpublic Information**

It is not possible to define all categories of material information. However, information should be regarded as material if there is a substantial likelihood that it would be considered important to a reasonable investor in making an investment decision regarding the purchase or sale of the Company's securities or if the information is likely to have a significant effect on the market price of the Company's securities. Put another way, there must be a substantial likelihood that the information would be viewed by the reasonable investor as having significantly altered the total mix of information available in the market concerning the Company. Either positive or negative information may be material. Information is "nonpublic" if it is not available to the general public.

Questions concerning whether information is material nonpublic information can be directed to the Compliance Officer.

**Attachment 1**

Praxis employees

Praxis consultants and contractors

**Attachment 2**

Praxis Precision Medicines, Inc.: 10b5-1 Plan Guidelines

**Praxis Precision Medicines, Inc.: 10b5-1 Plan Guidelines**

| Issue | Guidelines |
|---|---|
| **Generally Applicable Guidelines** | The 10b5-1 trading plan (a "Plan") must be a written, binding agreement, which the Company may retain a copy of. The Compliance Officer must approve, in writing, each Plan, including any amendment or termination. Participants must enter into a Plan in good faith and not as part of a plan or scheme to evade the prohibitions of Rule 10b5. |
| **Designated Broker** | Plans with respect to PRAX equity awards must be adopted through Fidelity. |
| **Timing of Entering Into a Plan** | There are limits on when a Plan can be adopted, so plan ahead. In short, a participant can only set up a Plan when: (1) the trading window under the Company's Insider Trading Policy is open and (2) the participant does not possess material non-public information ("MNPI") about the Company. The Plan must include a representation that, at the time of adoption, the participant does not possess any MNPI about the Company and is adopting the Plan in good faith and not as part of a plan or scheme to evade Rule 10b-5. |
| **Preclearance of Plan** | Before a Company insider adopts a Plan, the Compliance Officer (currently Alex Nemiroff) must pre-clear the Plan to ensure that the Company's policies are being complied with and the selling stockholder does not have MNPI at the time the Plan is put into place. The pre-clearance review will focus on (i) the existence of MNPI, (ii) the Plan provisions regarding allocation of risk and responsibilities of broker, (iii) trading schedule and share amounts and (iv) termination and suspension rights and responsibilities of both the Company and the participant.<br>In order to use the affirmative defense provided by Rule 10b5-1, a Plan must be put in place while the insider does not have any MNPI and must be entered into in "good faith." A participant does *not* get the benefit of the affirmative defense if a Plan is entered into while aware of MNPI, even if no trades will occur until that MNPI becomes public. |
| **Number of Plans** | A participant may have only one active Plan in place at a time. However, a single Plan may contain multiple trading strategies.<br>A participant may adopt a new Plan to replace an existing one, but only if the first scheduled trade under the new 10b5-1 trading plan does not occur before the last scheduled trade of the existing 10b5-1 trading plan. |
| **Duration of Plan** | Each 10b5-1 trading plan must have a term of at least 6 months but no longer than 24 months. |

| | |
|---|---|
| **Cooling-Off Period** | **Section 16 reporting persons**: A Plan must include a cooling-off period that extends to the later of 90 days after adoption or modification of a Plan or two business days after filing the Form 10-K or Form 10-Q covering the fiscal quarter in which the Plan was adopted, up to a maximum of 120 days.<br>**Non-Section 16 employees and any other persons:** A Plan must include a cooling-off period that extends 30 days after adoption or modification of a Plan. |
| **Trading Schedule** | The timing of trades under a Plan must be designed to avoid raising "red flags" and assist the insider in disputing a claim that the Plan was not entered into in good faith.<br>In designing the Plan, avoid setting trade dates that occur in close proximity to earnings releases or other known significant corporate developments or announcements. |
| **Modifications and Terminations** | Modifications to Plans are permitted only when the participant is not aware of any MNPI. Modifications to, and terminations of, a Trading Plan are subject to preapproval by the Compliance Officer and modifications of a Trading Plan that change the amount, price, or timing of the purchase or sale of the securities underlying a Trading Plan will trigger a new cooling-off period (as described above). . |
| **Sales Outside of Existing Plan** | Each individual cannot complete sales of shares subject to an active Plan ("Active Shares") outside of the Plan. Note that sales of such Active Shares outside of a 10b5-1 plan could be viewed as "altering or deviating" from the approved 10b5-1 plan. |
| **Compliance with Rule 144** | Each Plan must provide for specific procedures to comply with Rule 144 under the Securities Act of 1933, as amended, including the filing of Forms 144, when applicable. |
| **Section 16 Filings** | Sales made on behalf of Section 16 filers pursuant to a Plan are required to be reported on Form 4 within two days of the sale. Each Plan must provide that the broker will promptly notify the participant and the Company of any trades under the plan so that, where required, the insider can make timely filings under the Exchange Act (*i.e.*, no later than the close of business on the day of the trade).<br><br>The Form 4 must clearly indicate in footnotes that the sales were made pursuant to a Plan. |
| **Public Disclosure of a Plan** | The Company reserves the right to publicly disclose, announce, or respond to inquiries from the media regarding the adoption, modification, or termination of a Trading Plan and non-Rule 10b5-1 trading arrangements, or the execution of transactions made under a Trading Plan. |

| | |
|---|---|
| **Automatic Suspensions and Terminations** | Each Plan must suspend trades or terminate if legal, regulatory, or contractual restrictions are imposed on the insider, or other events occur that would prohibit sales under such a plan (*e.g.*, change in control transactions or public offerings). |
| **Company Not Party to the Plan** | The Plan may not have the Company as party to the Plan, although it can have a representation by the participant to the effect that the Company has reviewed the Plan and that the Plan is in compliance with Company policy. |

**SUBSIDIARIES OF PRAXIS PRECISION MEDICINES, INC.**

| **Name** | **Jurisdiction of Formation / Incorporation** |
| --- | --- |
| Praxis Security Corporation | Massachusetts |

**Exhibit 23.1**

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement and related prospectus (Form S-3 No. 333-284016) of Praxis Precision Medicines, Inc.,

(2) Registration Statement (Form S-8 No. 333-276786) pertaining to the Praxis Precision Medicines, Inc. 2024 Inducement Plan, as amended by Post-Effective Amendment No. 1 to Form S-8 Registration Statement to include the Praxis Precision Medicines, Inc. 2020 Stock Option and Incentive Plan, as Amended and Restated,

(3) Registration Statement (Form S-8 Nos. 333-277652, 333-269615, 333-263081 and 333-254410) pertaining to the Praxis Precision Medicines, Inc. 2020 Stock Option and Incentive Plan and the Praxis Precision Medicines, Inc. 2020 Employee Stock Purchase Plan, and

(4) Registration Statement (Form S-8 No. 333-249522) pertaining to the Praxis Precision Medicines, Inc. 2017 Stock Incentive Plan, the Praxis Precision Medicines, Inc. 2020 Stock Option and Incentive Plan and the Praxis Precision Medicines, Inc. 2020 Employee Stock Purchase Plan;

of our reports dated February 28, 2025, with respect to the consolidated financial statements of Praxis Precision Medicines, Inc. and the effectiveness of internal control over financial reporting of Praxis Precision Medicines, Inc. included in this Annual Report (Form 10-K) of Praxis Precision Medicines, Inc. for the year ended December 31, 2024.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 28, 2025

**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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (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: February 28, 2025

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, Timothy Kelly, 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)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (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: February 28, 2025

By: /s/ TIMOTHY KELLY

Timothy Kelly
Chief Financial Officer
(Principal Financial Officer)

**Exhibit 32.1**

**CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND 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, 2024 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: February 28, 2025 By: /s/ MARCIO SOUZA

Marcio Souza
Chief Executive Officer
(Principal Executive Officer)

Date: February 28, 2025 By: /s/ TIMOTHY KELLY

Timothy Kelly
Chief Financial Officer
(Principal Financial Officer)