Praxis Precision Medicines Provides Update on Advancing Clinical Stage Portfolio

January 8, 2024

Positive preliminary analysis of 15 mg cohort in the PRAX-628 study in epilepsy patients with Photo-Paroxysmal Response (PPR) exceeds expectations; topline results expected in 1Q 2024 after completion of *45 mg cohort*

Enrollment for both ulixacaltamide Phase 3 Studies in the Essential3 program on track to be completed in 1H 2024 with topline results in 2H 2024

Recently announced licensing partnership with Tenacia Biotechnology to develop and commercialize ulixacaltamide in Greater China with total consideration over $275 million

BOSTON, Jan. 08, 2024 (GLOBE NEWSWIRE) -- Praxis Precision Medicines, Inc. (NASDAQ: PRAX), a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for central nervous system (CNS) disorders characterized by neuronal excitation-inhibition imbalance, today provided an update on its portfolio and planned key milestones in 2024:

- Topline results of PRAX-628 in Phase 2a PPR study in the first quarter of 2024, followed by the expected initiation of the Phase 2b study in focal epilepsy in 2024
- Topline results for both Phase 3 studies evaluating ulixacaltamide in essential tremor in the second half of 2024
- Complete regulatory interactions to advance elsunersen (PRAX-222) towards a pivotal study for the treatment of SCN2A gain-of-function (GOF) developmental epilepsies
- Topline results of the Phase 2 EMBOLD study of PRAX-562 in SCN2A and SCN8A developmental epilepsies in the first half of 2024

“We are thrilled to continue building on the momentum of an exciting 2023 and start the year with four assets in the clinic, including our lead program, ulixacaltamide, and PRAX-628, which continues to show its potential as a best-in-class drug in epilepsy. The recently announced partnership with Tenacia extends ulixacaltamide’s reach to Greater China, underscoring our commitment to realize the global value of our programs,” said Marcio Souza, president and chief executive officer.

PRAX-628 for Focal Epilepsy

- Praxis made strong progress in developing PRAX-628 for focal epilepsy, which affects over 1 million Americans. Initial data from PRAX-628 show it has a good tolerability profile, a potentially wide therapeutic index and reaching efficacious concentrations within 24 hours. (**poster**)
- Praxis is conducting a Phase 2a PPR study to evaluate the efficacy of PRAX-628 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. This approach has been validated with several approved and new therapies.
- A preliminary analysis of the 15 mg cohort showed that this cohort exceeds the expectations in terms of drug activity. The full data set will be disclosed after completion of the ongoing 45 mg cohort and full analysis of the Study.
- In 2023, Praxis disclosed results from a Phase 1 dose escalation study of PRAX-628 in healthy volunteers:
    - PRAX-628 was generally well-tolerated at all tested doses. Pharmacokinetic data demonstrated dose-dependent exposure supporting once-daily dosing without titration to achieve potentially therapeutically effective drug concentration levels. (**press release**)
    - Further analysis of patients in the Phase 1 study using qEEG data showed a pharmacodynamic effect at all dose levels and was significantly different from placebo. (**poster**)

Ulixacaltamide for Essential Tremor

Essential tremor affects up to seven million people in the United States with action tremors that impact daily living, and there are currently no drugs specifically designed for essential tremor.

- Enrollment in Essential3 remains on track, with plans to complete in the first half of 2024 and topline results expected in the second half of 2024, supporting a planned New Drug Application (NDA) submission in 2025.
- Key elements of the Essential3 registrational program are:
    - Two simultaneous Phase 3 trials, including a 12-week, parallel design study and a 12-week randomized withdrawal study for stable responders
    - Using the modified Activities of Daily Living 11 (mADL11) as a primary endpoint
        - In the Phase 2 Essential1 study, mADL11 produced a consistent and meaningful response in ulixacaltamide when compared to placebo after 8 weeks of treatment (p=0.042, nominal)

    - Using a single 60 mg dose in the Phase 3 trials
    - Safety database for a NDA by ICH guidelines requiring 300 patients with six-months of exposure and 100 patients with one-year of exposure
- On January 5, 2024, Praxis announced a partnership with Tenacia Biotechnology to develop and commercialize ulixacaltamide in Greater China (**press release**)

Elsunersen (PRAX-222) for SCN2A Gain-of-Function Developmental Epilepsies
SCN2A developmental and epileptic encephalopathy (SCN2A-DEE) is a debilitating and fatal monogenic epilepsy disorder caused by variants in the SCN2A gene. More than 70% of early-onset SCN2A-DEE patients live with uncontrolled seizures, and approximately 75% live with severe intellectual disability with patients rarely surviving beyond their teenage years.

- In December 2023 at the American Epilepsy Society annual conference, Praxis shared data from Part 1 of the EMBRAVE study, where four patients were dosed once a month for a four-month period (**poster**)
    - Patients showed a 43% median reduction in seizures from baseline
    - Patients showed a 48% increase in seizure-free days from baseline
    - There were no drug-related treatment-emergent adverse events or serious adverse events
- Praxis has an upcoming meeting with the FDA to discuss next steps in developing elsunersen

PRAX-562 for SCN2A and SCN8A Developmental Epilepsies
Praxis continues to progress PRAX-562 as a unique sodium channel modulator targeting developmental and epileptic encephalopathies (DEEs).

- Praxis expects topline results from the EMBOLD study in pediatric patients with SCN2A-DEE and SCN8A-DEE in the first half of 2024

About Ulixacaltamide
Ulixacaltamide is a differentiated and highly selective small molecule inhibitor of T-type calcium channels designed to block abnormal neuronal burst firing in the Cerebello-Thalamo-Cortical (CTC) circuit correlated with tremor activity. Ulixacaltamide, the most advanced program within Praxis' Cerebrum™ small molecule platform, is currently in development for the treatment of essential tremor. www.praxisessentialtremor.com.

About PRAX-628
PRAX-628 is a next-generation, functionally selective small molecule targeting the hyperexcitable state of sodium-channels in the brain that is currently being developed as a once daily, oral treatment for adult focal onset epilepsy. Preclinical data demonstrates PRAX-628 is differentiated from standard of care, with the potential to be best-in-class for focal epilepsy. In vitro, PRAX-628 has demonstrated superior selectivity for disease-state NaV channel hyperexcitability. In vivo studies of PRAX-628 have demonstrated unprecedented potency in the maximal electroshock seizure (MES) model, a highly predictive translational model for efficacy in focal epilepsy. Data from the PRAX-628-101 study demonstrated that PRAX-628 can be safely dosed in healthy subjects to greater than 15 times the predicted human equivalent of the rodent MES EC50.

About Elsunersen (PRAX-222)
Elsunersen (PRAX-222) is an antisense oligonucleotide (ASO) designed to selectively decrease SCN2A gene expression, directly targeting the underlying cause of early-seizure-onset SCN2A-DEE to treat seizures and other symptoms in patients with gain-of-function SCN2A mutations. In vitro studies of PRAX-222 have demonstrated reduction in both SCN2A gene expression and protein levels. In vivo, PRAX-222 has demonstrated significant, dose-dependent reduction in seizures, improvement in behavioral and locomotor activity and increased survival in SCN2A mouse models, with potential to be the first disease-modifying treatment for SCN2A-DEE. PRAX-222 has received Orphan Drug Designation (ODD) and Rare Pediatric Disease Designation (RPD) from the FDA, and ODD and PRIME designations from the European Medicines Agency (EMA) for the treatment of SCN2A-DEE. The PRAX-222 program is ongoing under a collaboration with Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), and RogCon, Inc. To learn more about the EMBRAVE study, please visit https://www.embravestudy.com/.

About SCN2A-DEE
SCN2A developmental and epileptic encephalopathy (SCN2A-DEE) is a debilitating and fatal monogenic epilepsy disorder caused by a variant in the SCN2A gene. The SCN2A gene is critical in the formation of sodium channel proteins in the brain, which control 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. SCN2A-DEE presents with a wide range of phenotypes. Early-onset SCN2A-DEE presents before three months 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 gastrointestinal or ocular. 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 to manage co-morbidities. Despite these interventions, more than 70% of early-onset SCN2A-DEE patients live with uncontrolled seizures, and approximately 75% live with severe intellectual disability with patients rarely surviving beyond their teenage years.

About PRAX-562
PRAX-562 is a first-in-class small molecule in development for the treatment of developmental and epileptic encephalopathy

(DEE) as a preferential inhibitor of persistent sodium current, shown to be a key driver of seizure symptoms in early onset SCN2A-DEE and SCN8A-DEE. PRAX-562's mechanism of sodium channel block is consistent with superior selectivity for disease state sodium channel (NaV) channel hyperexcitability. In vivo studies of PRAX-562 have demonstrated dose-dependent inhibition of seizures up to complete control of seizure activity in SCN2A, SCN8A and other DEE mouse models. PRAX-562 has been generally well-tolerated in three Phase 1 studies and has demonstrated biomarker changes indicative of NaV channel blocking effects. PRAX-562 has received ODD and RPD from the FDA, and ODD from the European Medicines Agency for the treatment of SCN2A-DEE and SCN8A-DEE. To learn more about the EMBOLD study, please visit https://www.emboldstudy.org/.

About Praxis

Praxis Precision Medicines is a clinical-stage biopharmaceutical company translating insights from genetic epilepsies into the development of therapies for CNS disorders characterized by neuronal excitation-inhibition imbalance. Praxis is applying genetic insights to the discovery and development of therapies for rare and more prevalent neurological disorders through our proprietary small molecule platform, Cerebrum™, and antisense oligonucleotide (ASO) platform, Solidus™, using our understanding of shared biological targets and circuits in the brain. Praxis has established a diversified, multimodal CNS portfolio including multiple programs across movement disorders and epilepsy, with four clinical-stage product candidates. For more information, please visit www.praxismedicines.com and follow us on Facebook, LinkedIn and Twitter/X.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 and other federal securities laws, including express or implied statements regarding Praxis' future expectations, plans and prospects, including, without limitation, statements regarding the anticipated timing of our clinical trials and the development of our product candidates, as well as other statements containing the words "anticipate," "believe," "continue," "could," "endeavor," "estimate," "expect," "anticipate," "intend," "may," "might," "plan," "potential," "predict," "project," "seek," "should," "target," "will" or "would" and similar expressions that constitute forward-looking statements under the Private Securities Litigation Reform Act of 1995.

The express or implied forward-looking statements included in this press release are only predictions and are subject to a number of risks, uncertainties and assumptions, including, without limitation: uncertainties inherent in clinical trials; preliminary analyses from ongoing studies differing materially from final data from preclinical studies and completed clinical trials; the expected timing of clinical trials, data readouts and the results thereof, and submissions for regulatory approval or review by governmental authorities; regulatory approvals to conduct trials; and other risks concerning Praxis' programs and operations as described in its Annual Report on Form 10-K for the year ended December 31, 2022, its Quarterly Reports on Form 10-Q and other filings made with the Securities and Exchange Commission. Although Praxis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on information and factors currently known by Praxis. As a result, you are cautioned not to rely on these forward-looking statements. Any forward-looking statement made in this press release speaks only as of the date on which it is made. Praxis undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future developments or otherwise.

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