Praxis Precision Medicines Provides Portfolio Update at 2023 R&D Day

October 2, 2023 at 1:17 PM EDT

Positive results from preliminary analysis of PRAX-222 Part 1 showed 44% median reduction in seizures after three doses for SCN2A-gain-of-function pediatric patients

Phase 3 (Essential3) program for ulixacaltamide initiating this quarter with mADL11 as primary endpoint; nearly 600 patients have already expressed interest in participating

BOSTON, Oct. 02, 2023 (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 clinical portfolio at the company's R&D Day. Praxis' leaders were joined by two esteemed key opinion leaders in movement disorders and epilepsy, respectively: Alberto J. Espay, M.D., MSc, FAAN, FANA, Professor and Endowed Chair of the James J. and Joan A. Gardner Center for Parkinson's Disease at the University of Cincinnati, as well as Jacqueline French, M.D., Professor of Neurology at NYU Grossman School of Medicine and President, Director and Founder of the Epilepsy Study Consortium.

"We were thrilled to be able to share important updates from our portfolio. Especially exciting is the early efficacy data we have seen with our PRAX-222 program in SCN2A gain-of-function developmental epilepsies and encephalopathies (DEEs). Additionally, we are well on our way to initiate our Essential3 program in essential tremor this quarter and have been very encouraged by the early response from the community about participating in these trials," said Marcio Souza, president and chief executive officer of Praxis.

A replay of the R&D day webcast will be available through the Events & Presentations page of the Investors + Media section of the company's website at www.praxismedicines.com for the next 90 days.

Event Highlights:
Ulixacaltamide

- Additional analysis from the Essential1 data set continues to support the design of the Phase 3 program for ulixacaltamide (Essential3)
    - Data from Essential1 showed a meaningful difference in a minimum 3-point improvement in the modified Activities of Daily Living 11-point scale (mADL11) between patients on ulixacaltamide v. placebo (55% v. 31%, p=0.023)
    - In the extension period of Essential1, which continued after Week 8 through Week 14, 64% of patients in the ulixacaltamide arm showed at least a 3-point improvement in mADL11 versus baseline. For patients transitioning from placebo at Week 8 onto ulixacaltamide, 69% achieved at least a 3-point improvement to baseline at Week 14
    - Ulixacaltamide also demonstrated incremental benefit to patients on propranolol. 48% of patients on propranolol and ulixacaltamide in the Essential1 study achieved at least a 3-point improvement in mADL11 compared to 25% for patients on propranolol and placebo
- mADL11 confirmed to serve as primary endpoint in both Phase 3 studies of Essential3 based on protocol feedback received from the U.S. Food and Drug Administration (FDA)
- In a pre-recruitment observational study launched in September 2023, nearly 600 essential tremor patients have already expressed interest in joining a Phase 3 trial sponsored by Praxis
- Praxis expects to submit a New Drug Application (NDA) for ulixacaltamide in 2025

PRAX-222

- Dosing for Part 1 of the EMBRAVE study is nearing completion, with patients receiving 1 mg doses once a month for four months at Le Bonheur Children's Hospital in Memphis, Tennessee
- No treatment related adverse events (AEs) or serious adverse events (SAEs) were observed in preliminary safety analysis as of the cutoff date of September 26, 2023
- As of the cutoff date, data was evaluable for three of four dosing periods showing:
    - Patients achieved a 44% median reduction in seizures versus baseline, on top of best available standard of care

- Patients observed an increased number of days without seizures, achieving a median of 35% seizure free days over the dosing period compared to a baseline of 21% seizure free days
- All patients achieved significant seizure reduction after one dose

- Praxis intends to request a meeting in the fourth quarter of 2023 with the FDA to align on next steps for the program

PRAX-628

- Additional data from the Phase 1 single ascending dose (SAD) and multiple ascending dose (MAD) study continue to reinforce the potential of PRAX-628 as a next generation precision anti-seizure medication (ASM)
- Electroencephalogram (EEG) data showed rapid and sustained activity in the brain when dosing PRAX-628 as compared to placebo
- PRAX-628 achieved and sustained target therapeutic concentrations in excess of the equivalent Maximal Electroshock Seizure Model (MES) EC_{50} after first administration
- Praxis expects to read out the results from the Phase 2 Photoparoxysmal Response (PPR) study in the fourth quarter of 2023

PRAX-562

- Praxis is utilizing a decentralized recruiting and enrollment approach for its Phase 2 EMBOLD study for the treatment of pediatric patients with DEEs, with sites in both the U.S. and Europe
- Praxis expects topline results from the EMBOLD study in the first half of 2024

About the EMBRAVE Study
Part 1 of the EMBRAVE study is a 21-week open label cohort, in which participating pediatric patients (aged 2-18 years) with early-onset SCN2A developmental and epileptic encephalopathy (SCN2A-DEE) receive PRAX-222 for up to 13 weeks, designed to determine the safety and tolerability of intrathecal delivery of PRAX-222. Praxis expects topline results in the fourth quarter of 2023. To learn more about the EMBRAVE study, please visit https://www.embravestudy.com/.

About PRAX-222
PRAX-222 (elsunersen) 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 from the European Medicines Agency (EMA) for the treatment of SCN2A-DEE. The PRAX-222 program is ongoing under a collaboration with Ionis Pharmaceutics, Inc. (NASDAQ: IONS), and RogCon, Inc.

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 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 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 tremorwww.praxisessentialtremor.com.

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; reported interim data from ongoing studies and trials 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.

Investor Contact: Praxis Precision Medicines investors@praxismedicines.com 857-702-9452 Media Contact: Ian Stone Evoke Canale Ian.stone@evokecanale.com 619-849-5388