Praxis Precision Medicines to Present at the American Epilepsy Society 2022 Annual Meeting

November 28, 2022

BOSTON, Nov. 28, 2022 (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 announced that it will deliver presentations on its epilepsy programs at the American Epilepsy Society (AES) 2022 Annual Meeting, held December 2-6, 2022 in Nashville, Tennessee.

“It’s an incredibly exciting time for Praxis and our epilepsy portfolio, with first-in-patient studies for PRAX-222 and PRAX-562 and a first-in-human study for PRAX-628 expected to start shortly,” said Steven Petrou, co-founder and chief scientific officer of Praxis. “We look forward to presenting data for PRAX-562 and PRAX-628 at AES, along with novel insights into DEEs and the patient populations we are seeking to serve. Our epilepsy programs have the potential to go beyond seizure control and disrupt the course of the diseases they target by addressing the underlying causes, and we are grateful for the opportunity to discuss these programs with the epilepsy community at this important meeting.”

Presentation Details:

PRAX-562 is a Well-tolerated, Novel Persistent Sodium Channel Blocker with Broad Anticonvulsant Activity in Multiple DEE Mouse Models

- Session Date/Time: Saturday, December 3, 12:00 p.m. - 2:00 p.m. CT
- Abstract number: 1.281
- Summary: In multiple preclinical models of non-Na_V developmental and epileptic encephalopathy (DEE), PRAX-562 exhibited robust anticonvulsant activity indicating broad protection regardless of the underlying genetic cause. Moreover, PRAX-562 exhibited markedly improved preclinical tolerability compared to standard of care Na_V blockers, which may translate into well-tolerated efficacy in epilepsy as well as other indications caused by neuronal hyperexcitability.

Disease Impact and Burden in Patients with SCN2A-Related Developmental and Epileptic Encephalopathy

- Session Date/Time: Sunday, December 4, 12:00 p.m. - 2:00 p.m. CT
- Abstract number: 2.092
- Summary: Using large, real-world clinical data sets and functional variant characterization, the study provides unprecedented insight into clinical phenotypes, disease burden and treatment patterns in SCN2A. Findings demonstrate that symptoms are diverse and extend beyond seizures, with patient burden compounded by comorbidities, high treatment use, procedural interventions, as well as profound developmental impairment extending through to early adulthood. This work provides novel insights into the broad, longitudinal impact of disease, with the potential to inform trial endpoints beyond seizure symptomatology.

A Novel Approach to Assess the Impact of Disease in Patients with SCN8A-Related Developmental and Epileptic Encephalopathy

- Session Date/Time: Sunday, December 4, 12:00 p.m. - 2:00 p.m. CT
- Abstract number: 2.096
- Summary: Using large, real-world clinical data sets, this natural history study provides the most robust, longitudinal real-world dataset to date on disease burden and progression in SCN8A-DEE. Our findings highlight the severity and burden of disease in SCN8A-DEE, particularly in the first year of life for patients with seizures presenting earlier in life (≤6 months); further compounded by multiple factors including high medication usage, hospital duration and comorbidities. Together with ongoing efforts to better understand underlying genotype-phenotype relationships, our findings will guide development of targeted, innovative therapies that can benefit patients and their caregivers.

A Phase 1 Trial Evaluating the Safety, Tolerability, Pharmacokinetics and Food Effect of PRAX-562 in Healthy Volunteers

- Session Date/Time: Sunday, December 4, 12:00 p.m. - 2:00 p.m. CT
- Abstract number: 2.24
- Summary: In a first-in-human study to evaluate safety, tolerability and pharmacokinetics, PRAX-562 was well tolerated in healthy participants at single doses up to 150 mg (fasted), at multiple doses of up to 120 mg once-daily (QD) for 14 days (fasted), and at a single dose of 90 mg in the fed and fasted states. These findings across 112 participants further suggest that PRAX-562 can be administered without regard for food and support the program's advancement into Phase 2 clinical investigation.

A Phase 1 Trial Evaluating the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of PRAX-562 in Healthy Volunteers

- Session Date/Time: Sunday, December 4, 12:00 p.m. - 2:00 p.m. CT
- Abstract number: 2.478
- Summary: In a two-part randomized, placebo-controlled Phase 1 study, PRAX-562 was evaluated at 90 mg QD for 28 days (Part A), and in combination with oxcarbazepine at 120 mg QD (Part B). PRAX-562 was well tolerated in Part A. In Part B, the majority of AEs including SAEs were considered to be due to coadministration of projected supratherapeutic doses of PRAX-562 with oxcarbazepine, and likely additive Na_V blocking effects. Together with pharmacokinetic findings demonstrating a 13-fold increase in concentrations compared to preclinical maximal electroshock seizure effects, our results are consistent with earlier work suggesting a wide therapeutic window for PRAX-562. Furthermore, pharmacodynamic findings indicate CNS modulation and expected target engagement for PRAX-562 across multiple EEG measures.

PRAX-628: A Novel Sodium Channel Blocker with Greater Potency and Activity Dependence Compared to Standard of Care

- Session Date/Time: Monday, December 5, 12:00 p.m. - 1:45 p.m. CT
- Abstract number: 3.311
- Summary: In a study evaluating the in vitro effects of PRAX-628 on sodium current (I_{Na}), the next generation sodium channel (Na_V) blocker showed increased potency and activity dependence for peak I_{Na} as well as greater potency for persistent I_{Na}. The preferential targeting of neuronal hyperexcitability by PRAX-628 may represent a differentiated therapeutic option for diseases of hyperexcitability, where standard of care Na_V blockers have demonstrated efficacy but poor tolerability.

PRAX-628 is a Novel, Well-tolerated, Activity Dependent Sodium Channel Blocker with Potent Anticonvulsant Activity

- Session Date/Time: Monday, December 5, 12:00 p.m. - 1:45 p.m. CT
- Abstract number: 3.28
- Summary: In in vivo studies, PRAX-628 exhibited markedly improved preclinical tolerability compared to standard of care Na_V blockers, potentially due to its improved activity dependent inhibition of peak I_{Na}. The demonstrated profile of PRAX-628 may translate into well-tolerated efficacy in epilepsy as well as other indications caused by neuronal hyperexcitability.

About PRAX-562
PRAX-562 is a first-in-class small molecule in development for the treatment of DEEs 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. In vitro, PRAX-562 has demonstrated superior selectivity for disease-state Na_V channel hyperexcitability and a wider therapeutic window compared to other anti-seizure medicines, with potential for enhanced efficacy and improved tolerability. In vivo studies of PRAX-562 have demonstrated dose-dependent block of seizures up to complete inhibition 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 Na_V channel blocking effects. PRAX-562 has received Orphan Drug Designation (ODD) and Rare Pediatric Disease Designation from the FDA, and ODD from the European Medicines Agency for the treatment of SCN2A-DEE and SCN8A-DEE respectively.

About PRAX-628
PRAX-628 is a novel activity-dependent inhibitor of peak sodium current (I_{Na}) and persistent I_{Na} 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 sodium channel (Na_V) blockers, with the potential to be a best-in-class Na_V blocker for focal epilepsy. In vitro, PRAX-628 has demonstrated superior selectivity for disease-state Na_V channel hyperexcitability. In vivo studies of PRAX-628 have demonstrated an unprecedented therapeutic window which may translate to superior safety and efficacy.

About SCN2A-DEE
SCN2A-DEE is a 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 for 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.

About SCN8A-DEE
SCN8A-DEE is a rare developmental and epileptic encephalopathy caused by a variant in the SCN8A gene. The SCN8A gene is critical in the formation of sodium channel proteins in the brain, which control the follow 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. Patients 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 movement disorders, such as dystonia or ataxia; and problems in other body systems such as gastrointestinal or ocular. SCN8A-DEE patients also may experience autonomic features such as increases or decreases in heart rate, abnormal breathing and cyanosis.

About Praxis
Praxis Precision Medicines is a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for CNS disorders characterized by neuronal excitation-inhibition imbalance. Praxis is applying insights from genetic epilepsies to both rare and more prevalent neurological disorders, using our understanding of shared biological targets and circuits in the brain. Praxis has established a broad 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 LinkedIn and Twitter.

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 Praxis' clinical trials, our expectations, plans and timing for Praxis' clinical data and the development of Praxis' product candidates, including the design of clinical trials and the treatment potential of Praxis' 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; the expected timing of submissions for regulatory approval or review by governmental authorities; risks, uncertainties and assumptions regarding the impact of the continuing COVID-19 pandemic on Praxis' business, operations, strategy, goals and anticipated timelines, Praxis' ability to initiate, enroll, conduct or complete ongoing and planned clinical trials and Praxis' timelines for regulatory submissions; and other risks concerning Praxis' programs and operations as described in its Quarterly Report on Form 10-Q for the quarter ended June 30, 2022 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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