Praxis Precision Medicines Highlights 2025 Corporate Strategy and Business Priorities

January 12, 2025 at 9:00 PM EST

Three blockbuster-potential assets in late-stage clinical trials and four pivotal readouts expected in 2025; anticipate four commercial assets by 2028

Study 1 of Essential3 program for ulixacaltamide in essential tremor (ET) on track for Q1 2025 interim analysis; NDA filing for ulixacaltamide expected in 2025

Enrollment in EMBOLD study of relutrigine cohort 2 is on track; targeting NDA filing in 2026

Vormatrigine ENERGY program advancing with read-outs of RADIANT in first half of 2025 and POWER1 by year-end 2025

UCB has exercised its option to license KCNT1 small molecule candidate for global development and commercialization

Cash and investments ~ $470 million at the end of 2024 support runway into 2028

BOSTON, Jan. 12, 2025 (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 highlighted its portfolio progress and provided its business priorities for 2025.

“2024 was a landmark year for Praxis with positive topline results from the Phase 2 photoparoxysmal response (PPR) trial of vormatrigine that led to initiating our ENERGY program in common epilepsies. Additional highlights this year were the unprecedented efficacy in cohort 1 of the EMBOLD study of relutrigine in developmental and epileptic encephalopathies (DEEs), followed by the initiation of the registrational cohort 2, and the continued overwhelming interest in the Essential3 program. Together, this progress has led to three blockbuster programs in late stage, with the potential for four product launches between 2026 and 2028,” said Marcio Souza, president and chief executive officer.

Mr. Souza continued, “We are now well positioned for a readout-rich 2025, with results anticipated for ulixacaltamide in the Essential3 program in ET followed by our first NDA filing, as well as topline results for vormatrigine from the RADIANT study in focal onset seizures (FOS) and generalized epilepsy, and the POWER1 study in FOS. We are also thrilled to have received a third rare pediatric drug designation (RPDD) for relutrigine in Dravet Syndrome, and with strong interest in cohort 2 of the EMBOLD study, we expect to file the NDA in 2026. With regulatory feedback on the elsunersen program, we expect to initiate the pivotal trial in the first half of 2025. We are sufficiently funded to advance all programs through their topline readouts, with runway into 2028. We look forward to providing a thorough update across our portfolio at the planned Investor R&D Day in the second quarter of 2025.”

Portfolio updates and anticipated milestones

Cerebrum™ Small Molecule Platform
Ulixacaltamide for Essential Tremor
ET is an inadequately managed, undertreated and high burden disease with a prevalence of seven million patients in the U.S. The Essential3 program includes two Phase 3, registrational studies: Study 1 is a parallel design, placebo-controlled study (N=400) and Study 2 is a randomized withdrawal study (N=200). Since beginning recruitment in November 2023, over 100,000 patients have demonstrated interest in participating in the study.

- A pre-planned interim analysis of Study 1 is anticipated in the first quarter of 2025.
- At the time of the interim analysis update, Praxis will provide further detail on timing for the full readouts of Study 1 and Study 2.
- Praxis anticipates filing the NDA for ulixacaltamide in 2025.
- Following positive results from Essential3, the Company plans to re-initiate a study of ulixacaltamide in Parkinson’s disease, where there is significant and unmet need for non-dopaminergic treatment options.

Vormatrigine (PRAX-628) for Common Epilepsies (Focal Onset Seizures and Generalized Epilepsy)
An estimated 3.5 million people in the U.S. suffer from common epilepsies. Sodium channel therapy is the cornerstone of treatment for patients with epilepsy yet currently approved drugs have significant safety and efficacy limitations. Vormatrigine is the most potent sodium-channel modulator ever designed to precisely target the hyperexcitable state of sodium-channels in adult common epilepsies.

- In recently completed Phase 1 studies, vormatrigine continued to demonstrate an ideal profile with strong competitive differentiation. Full results will be shared at an upcoming medical conference and highlights include:
  - Results from an additional 45 mg multiple ascending dose (MAD) cohort showed a dose proportional increase in exposure with excellent tolerability, similar to the 20 and 30 mg MAD cohorts completed previously.

- A Phase 1 food effect study demonstrated that food intake does not affect vormatrigine absorption and therefore there is no need to take vormatrigine with food, which increases flexibility in dosing and ease of use.

- Praxis continues to make progress on the ENERGY program to advance vormatrigine through efficacy and registrational trials.
  - The EMPOWER observational study, in partnership with the Epilepsy Study Consortium, is aiming to better characterize seizure burden started enrolling patients in 2024 and has enrolled over 2,000 patients. Early results were shared during the Praxis scientific exhibit at the December 2024 American Epilepsy Society (AES) Annual Meeting. The RADIANT Phase 2 study for FOS and generalized epilepsy is currently enrolling patients, with topline results expected in the first half of 2025. RADIANT is an open-label study recruiting up to 50 patients with FOS or generalized epilepsy, who will be treated with a 30 mg dose over an 8-week period to evaluate the impact of vormatrigine on seizure burden.
  - Enrollment for the POWER1 Phase 2/3 registrational study in patients with treatment resistant FOS is progressing as planned, with topline results anticipated in the second half of 2025. POWER1 is assessing adjunctive treatment, allowing dosing of vormatrigine on top of 1 to 3 antiseizure medications (ASMs), and aims to enroll approximately 250 patients in a parallel-arm study, comparing a treatment arm of 20 mg for 6 weeks followed by 30 mg for 6 weeks versus a placebo arm for 12 weeks.
  - POWER2 will be the second registrational study for vormatrigine and is expected to begin enrollment in the second half of 2025 as a three-arm, 12-week study.

- Praxis continues to evaluate the potential for expansion of one of its highly functionally selective compounds into pain indications. The program will be discussed at Praxis' planned R&D Day in the second quarter of 2025.

Relutrigine (PRAX-562) for Developmental and Epileptic Encephalopathies
DEEs cover a wide range of genetically and phenotypically defined epileptic conditions that are often characterized by onset of seizures at or shortly after birth and occur in approximately 200,000 patients in the U.S. Relutrigine is a sodium channel modulator with therapeutic potential across developmental epilepsies. Relutrigine is currently being evaluated in the EMBOLD study in SCN2A and SCN8A DEEs, with future plans for the EMERALD study in a broader, pan-DEE patient population.

- In cohort 1 of the EMBOLD study assessing relutrigine versus placebo in SCN2A gain-of-function (GoF) and SCN8A patients, relutrigine showed unparalleled results, with an update on the open-label extension (OLE) shared at the 2024 AES Annual Meeting . Key results included:
  - 46% placebo-adjusted reduction in monthly motor seizures from baseline over a 16-week period.
  - 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 while on relutrigine.
  - Patients achieving seizure freedom had a median of 46 days of seizure freedom, inclusive of OLE period, compared to 3 days at baseline.
  - Meaningful gains observed in alertness, communication and seizure severity suggest relutrigine has a disease modifying effect.
  - Relutrigine was generally well-tolerated with no drug-related serious adverse events or dose reductions required.
- EMBOLD is currently enrolling 80 patients with SCN2A and SCN8A DEEs in registrational cohort 2, with topline results anticipated in the first half of 2026, to be followed by an NDA filing later in 2026.
- In December 2024, Praxis received RPDD for relutrigine for Dravet Syndrome. This is the third RPDD for relutrigine, in addition to SCN2A and SCN8A DEEs.
- Praxis remains on track to initiate the EMERALD registrational study in the first half of 2025.
- At the 2024 AES Annual Meeting, Praxis shared an update for an emergency use patient with extended benefit achieved after receiving relutrigine

Solidus™ Antisense Oligonucleotide (ASO) Platform
Elsunersen (PRAX-222) for early-seizure-onset SCN2A-DEE

SCN2A GoF-DEE is a rare, genetic epilepsy characterized by early-onset and severe impact on development. The disease, as with all DEEs, affects not only the patient but also the entire caregiver ecosystem. In a Part 1 analysis of the EMBRAVE study, four patients receiving elsunersen over a four-month period achieved a 43% reduction in seizure burden compared to baseline.

- Praxis has completed discussions with global regulatory agencies to harmonize a registrational study design for elsunersen

and will share the trial design and expected timelines in the first quarter of 2025.

- The second cohort of the EMBRAVE study continues to enroll patients in Brazil, evaluating safety and efficacy of elsunersen versus sham procedure.
- At the 2024 AES Annual Meeting, Praxis shared an update on four emergency access patients, including updates from the first-in-patient case who has received elsunersen for over 15 months.

Additional Pipeline Updates

- In December 2024, UCB exercised its option to in-license global development and commercialization rights for a KCNT1 small molecule development candidate as part of the strategic research collaboration established in December 2022. Praxis has earned an option exercise fee and is eligible to receive future success-based development and commercialization milestone payments, for a total of up to approximately $100 million, in addition to tiered royalties on net sales of any resulting products from the collaboration.
- Praxis remains on track to nominate a development candidate for each of its early stage ASO therapeutic initiatives in 2025
  - PRAX-080: Focused on targeting PCDH19 mosaic expression which represents a pioneering approach to treating PCDH19-related epilepsy, a rare but devastating genetic disorder characterized by early-onset seizures and cognitive impairment, disproportionately affecting females.
  - PRAX-090: Designed to address SYNGAP1 loss-of-function (LoF) mutations, a leading cause of severe intellectual disability and epilepsy in DEEs.
  - PRAX-100: Targeting SCN2A LoF mutations, the predominant genetic link to de novo autism spectrum disorders (ASD).

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 late-stage development for the treatment of essential tremorEssential3 study.

About Vormatrigine (PRAX-628)
Vormatrigine 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 seizures and generalized 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 Na_V channel hyperexcitability. In vivo studies of vormatrigine have demonstrated unprecedented potency in the maximal electroshock seizure (MES) model, a highly predictive translational model for efficacy in focal epilepsy. Data from the study demonstrated that vormatrigine can be safely dosed in healthy subjects to greater than 15 times the predicted human equivalent of the rodent MES EC_{50}. To learn more about the POWER1 study please visit POWER1 study.

About Relutrigine (PRAX-562)
Relutrigine 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. Relutrigine's mechanism of sodium channel blocking is consistent with superior selectivity for disease state sodium channel (NaV) channel hyperexcitability. In vivo studies of relutrigine have demonstrated dose-dependent inhibition of seizures up to complete control 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 NaV channel blocking effects. Relutrigine has received ODD and RPDD from the FDA, and ODD from the European Medicines Agency for the treatment of SCN2A-DEE and SCN8A-DEE and RPDD for Dravet Syndrome from the FDA. To learn more about the EMBOLD study, please visit EMBOLD study.

About Elsunersen (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 elsunersen have demonstrated reduction in both SCN2A gene expression and protein levels. In vivo, elsunersen 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. Elsunersen has received ODD and RPD from the FDA, and ODD and PRIME designations from the European Medicines Agency for the treatment of SCN2A-DEE. The Elsunersen 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 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, the development of our product candidates and plans to initiate new clinical programs, the anticipated timing of regulatory submissions and interactions and our projected cash runway, 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, 2023 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: Dan Ferry Life Science Advisors Daniel@lifesciadvisors.com 617-430-7576