Praxis Precision Medicines Provides Update on Essential3 and Corporate Update

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BOSTON, Feb. 28, 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 provided an update on the interim analysis for Study 1 of the Essential3 program of ulixacaltamide in essential tremor (ET), an update on other therapies in development and a financial update.

Results of the Planned Interim Analysis and Update on Topline Read-out for the Essential3 Program:

The Independent Data Monitoring Committee (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 Praxis 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, Praxis has 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.

“We are disappointed with and surprised by the outcome of the interim analysis for Study 1. Following the advice of the committee, we will explore different analysis methods for the final dataset, which is expected in the third quarter of 2025,” said Marcio Souza, president and chief executive officer of Praxis. “We remain focused on delivering on major near-term milestones in our other development programs, including the topline results from the RADIANT and POWER1 studies in focal onset seizures (FOS) and generalized epilepsy with vormatrigine, and the initiation of our EMERALD registrational study of relutrigine in developmental epilepsies and encephalopathies (DEEs) by mid-year 2025. We maintain a robust financial position that supports our continued investment in this exciting pipeline.”

Corporate Updates, Recent Highlights and Anticipated Milestones:

Cerebrum™ Small Molecule Platform

- **Vormatrigine (PRAX-628) for Focal Onset Seizures and Generalized Epilepsy:** The ENERGY program continues to progress, with multiple topline readouts expected in 2025.
  - The EMPOWER observational study, in partnership with the Epilepsy Study Consortium, characterizing seizure burden, is ongoing with over 3,000 patients consented. Early results were shared during the Praxis scientific exhibit at the December 2024 American Epilepsy Society (AES) Annual Meeting, demonstrating significant disease burden compounded by persistent, uncontrolled, often untracked seizures alongside profound psychosocial impact.
  - Praxis has initiated the RADIANT Phase 2, open-label, single-arm study for FOS and generalized epilepsy assessing seizure burden with vormatrigine treatment, with topline results expected by mid-year 2025.
  - Praxis has also initiated the POWER1 Phase 2/3 registrational study of vormatrigine for treatment resistant FOS, with topline results anticipated in the second half of 2025.
  - POWER2, the second registrational study for FOS, is on track to begin enrollment in the second half of 2025.

- **Relutrigine (PRAX-562) for Developmental and Epileptic Epilepsies (DEEs):**
  - EMBOLD is currently enrolling patients with SCN2A and SCN8A DEEs in the registrational cohort 2, with topline results anticipated in the first half of 2026, followed by a potential NDA filing in 2026.
  - In December 2024, Praxis received Rare Pediatric Disease Designation (RPDD) from the U.S. Food and Drug Administration (FDA) for relutrigine for Dravet Syndrome. This is the third RPDD for relutrigine, in addition to SCN2A and SCN8A DEEs.
  - Following recent regulatory interactions, Praxis anticipates initiating the EMERALD study for DEEs by mid-year 2025.

Solidus™ Antisense Oligonucleotide (ASO) Platform

- **Elsunersen (PRAX-222) for early-seizure-onset SCN2A-DEE:**
  - Following discussions with global regulatory agencies, Praxis has finalized the registrational trial design. EMBRAVE3 will be a global, 24-week, double-blind, sham-procedure controlled study, with approximately 40

early-onset SCN2A-DEE patients, and is anticipated to start enrolling patients by mid-year 2025.
    - The second cohort of the EMBRAVE study evaluating safety and efficacy of elsunersen versus sham procedure continues enrolling patients in Brazil, with topline readout anticipated in the first half of 2026.

Additional Pipeline Updates:

- UCB exercised its option to in-license global development and commercialization rights for a KCNT1 small molecule development candidate. 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).

Fourth Quarter and Full-Year 2024 Financial Results:

As of December 31, 2024, Praxis had $469.5 million in cash, cash equivalents and marketable securities, compared to $81.3 million in cash and cash equivalents as of December 31, 2023. This increase of $388.2 million was primarily due to net proceeds from Praxis' January 2024 and April 2024 follow-on public offerings and net proceeds from at-the-market sales of common stock, offset by cash used in operating activities. The Company's cash, cash equivalents and marketable securities as of December 31, 2024 are expected to fund operations into 2028.

Praxis recognized $7.5 million and $8.6 million in collaboration revenue during the three months and year ended December 31, 2024, respectively, related to its Option and License Agreement with UCB which was entered into in December 2022.

Research and development expenses were $56.3 million for the fourth quarter of 2024, compared to $18.4 million for the fourth quarter of 2023. Research and development expenses were $152.4 million for the year ended December 31, 2024, compared to $86.8 million for the year ended December 31, 2023. The increase in research and development expenses for full year 2024 of $65.6 million was primarily attributable to a $61.9 million increase in expense related to Praxis' Cerebrum™ platform, a $14.5 million increase in personnel-related costs and a $2.5 million increase in indirect expenses, partially offset by a $13.3 million decrease in expense related to Praxis' Solidus™ platform.

General and administrative expenses were $15.1 million for the fourth quarter of 2024, compared to $9.9 million for the fourth quarter of 2023. General and administrative expenses were $56.3 million for the year ended December 31, 2024, compared to $42.1 million for the year ended December 31, 2023. The increase in general and administrative expenses for full year 2024 of $14.2 million was primarily attributable to an $11.7 million increase in personnel-related costs, a $1.7 million increase in professional fees and a $0.9 million increase in other expenses.

Praxis incurred a net loss of $58.7 million for the fourth quarter of 2024, including $8.6 million of stock-based compensation expense, compared to $26.9 million for the fourth quarter of 2023, including $5.7 million of stock-based compensation expense. Praxis reported a net loss of $182.8 million for the year ended December 31, 2024, including $41.4 million of stock-based compensation expense, compared to a net loss of $123.3 million for the year ended December 31, 2023, including $24.9 million of stock-based compensation expense.

As of December 31, 2024, Praxis had 19.4 million shares of common stock outstanding.

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., 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 epilepsy and movement disorders, 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, 2024 to be filed 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.

PRAXIS PRECISION MEDICINES, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(Amounts in thousands)
(Unaudited)

	December 31, 2024	December 31, 2023
Assets		
Cash and cash equivalents	$ 215,372	$ 81,300
Marketable securities	254,156	—
Prepaid expenses and other current assets	11,805	3,580
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		
Accounts payable	$ 12,528	$ 5,815
Accrued expenses	23,763	7,416
Operating lease liabilities	1,369	2,495
Deferred revenue	—	2,553
Common stock	14	13
Additional paid-in capital	1,281,522	723,577
Accumulated other comprehensive loss	654	—
Accumulated deficit	(836,740)	(653,921)
Total liabilities and stockholders' equity	$ 483,110	$ 87,948

PRAXIS PRECISION MEDICINES, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(Amounts in thousands, except share and per share amounts)
(Unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2024	**2023**	**2024**	**2023**
Collaboration revenue	$ 7,463	$ 515	$ 8,553	$ 2,447
Operating expenses:				
Research and development	56,288	18,388	152,413	86,766
General and administrative	15,131	9,933	56,305	42,054
Total operating expenses	71,419	28,321	208,718	128,820
Loss from operations	(63,956)	(27,806)	(200,165)	(126,373)
Other income:				
Other income, net	5,277	928	17,346	3,096
Total other income	5,277	928	17,346	3,096
Net loss	$ (58,679)	$ (26,878)	$ (182,819)	$ (123,277)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.94)	$ (2.97)	$ (10.21)	$ (18.69)
Weighted average common shares outstanding, basic and diluted	19,980,179	9,060,813	17,906,794	6,594,316

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