Praxis announces accelerated development path for relutrigine in SCN2A and SCN8A DEE patients following positive FDA feedback

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Comprehensive meeting with FDA conducted in Q3 in conjunction with Breakthrough Therapy Designation

Key aspects of a potential NDA application discussed and aligned with the Agency

Praxis plans to perform an interim analysis of the EMBOLD cohort 2 pivotal trial in Q4 2025, which if positive should serve as the basis of an NDA in early 2026

BOSTON, Nov. 04, 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 announced that, following a comprehensive Type B meeting and recent meeting minutes and written advice on the protocol and SAP, it has reached alignment with the FDA on several aspects of the relutrigine program in SCN2A and SCN8A developmental and epileptic encephalopathies (DEEs), including the use of the ongoing EMBOLD study to serve as the basis of substantial evidence of effectiveness for the NDA submission. The FDA agreed that Praxis' proposed interim analysis, if positive, may serve as the basis of the NDA submission in early 2026. The interim analysis is planned to be conducted in the fourth quarter of 2025.

"We are appreciative of the recent collaborative discussion with the FDA about opportunities to bring relutrigine to SCN2A and 8A patients sooner, which came as a result of our breakthrough therapy designation (BTD)," commented Steven Petrou, chief scientific officer. "We reached alignment on key elements of the NDA with FDA, and upon a successful result from the upcoming interim analysis, we would quickly submit the NDA for relutrigine. This could be our second NDA under review, pending acceptance of the ulixacaltamide NDA."

SCN2A- and SCN8A-DEEs are ultra-rare, life-threatening pediatric epilepsies characterized by early-onset, pharmacoresistant seizures, rapid neurodevelopmental decline, and high premature mortality. There are no FDA approved therapies. Off-label polytherapy with ASMs remains the only therapeutic option but is largely ineffective, carries substantial toxicity risks, and imposes a significant burden for the approximately 5,000 patients living with the condition in the US.

In the current cohort of the EMBOLD study, patients were randomized (1:1) to receive relutrigine QD for 16 weeks, or relutrigine QD for 12 weeks and matching placebo QD for 4 weeks, administered orally or via gastrostomy/jejunostomy tube (G/J-tube). The primary endpoint is the change in monthly (28-day) seizure frequency. The primary endpoint will be analyzed using an ANCOVA on log-transformed data. The ANCOVA model will include fixed effect for treatment group (relutrigine and placebo).

The interim analysis will be based off approximately 70% of patients enrolled in the 16-week study and will be controlled at the 4% alpha level. If the study is not declared positive at interim, the final analysis will be conducted at the 1% alpha level (n~80).

In the first cohort of EMBOLD, shared in September 2024, the results using the agreed upon endpoint and analysis methods with the FDA are summarized below:

	Placebo (n = 7)	PRAX-562 (relutrigine) (n = 15)
Log-transformed change from baseline in seizure frequency during double-blind period, LSmean (SE)	-0.102 (0.223)	-0.688 (0.207)
Log Difference in LSMean (SE))		-0.585 (0.259)
ANCOVA p-value		0.0354

Relutrigine is also being investigated in patients across all DEEs in the EMERALD trial. EMERALD is a registrational, 16-week, placebo-controlled study evaluating seizure reduction in patients diagnosed with developmental epilepsies evaluating relutrigine. Enrollment for the EMERALD study began in the third quarter of 2025 and is expected to be complete in the second half of 2026, receiving strong interest in the geographies where it is planned. Assuming successful conclusion of the EMBOLD study and subsequent NDA approval, if positive, the EMERALD study would serve as the basis for an sNDA by 2027.

About Relutrigine (PRAX-562)
Relutrigine is a first-in-class small molecule in development for the treatment of developmental and epileptic encephalopathies (DEEs) as a preferential inhibitor of persistent sodium current, shown to be a key driver of seizure symptoms in severe DEEs. Relutrigine's mechanism of precision sodium channel (NaV) modulation is consistent with superior selectivity for disease-state 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 modulation. Data from cohort 1 of the Phase 2 EMBOLD study demonstrated a well-tolerated, robust, short- and long-term improvement in motor

seizures in a heavily pre-treated population, alongside maintained seizure freedom in some patients with SCN2A- and SCN8A-DEE. Relutrigine has received Orphan Drug Designation (ODD) and Rare Pediatric Disease Designation from the FDA for the treatment of SCN2A-DEE, SCN8A-DEE and Dravet syndrome; as well as Breakthrough Therapy Designation (BTD), and ODD from the European Medicines Agency for the treatment of SCN2A-DEE and SCN8A-DEE. To learn more about the EMERALD and EMBOLD studies, please visit ResilienceStudies.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 the anticipated timing of regulatory submissions and interactions, 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 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, its Quarterly Report on Form 10-Q for the quarter ended June 30, 2025 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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