Praxis Precision Medicines Announces Positive Topline Results from Two Pivotal Phase 3 Studies of Ulixacaltamide HCl in the Essential3 Program for Essential Tremor

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Patients treated with ulixacaltamide in the parallel-group study (Study 1) showed a mean improvement from baseline in the Modified Activities of Daily Living 11 at Week 8, the pre-specified primary endpoint, of 4.3 points (p<0.0001)

All key secondary endpoints in Study 1 - rate of disease improvement over 12 weeks, PGI-C and CGI-S - were also statistically significant (p<0.001)

Study 2 met its pre-specified primary endpoint, with patients showing superior maintenance of effect while on ulixacaltamide versus placebo during the randomized-withdrawal phase (p=0.0369)

The first key secondary endpoint in Study 2 - rate of disease improvement during the randomized-withdrawal phase - also demonstrated superior effect in ulixacaltamide treated patients versus placebo (p=0.0042)

Ulixacaltamide was generally well tolerated with a safety profile consistent with previous trials and no drug-related serious adverse events

Praxis has submitted a pre-NDA meeting request to the FDA

*Praxis to host an investor call today, Thursday, October 16 at 8am EST **link***

BOSTON, Oct. 16, 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 positive topline results for the Phase 3 Essential3 program of ulixacaltamide in essential tremor (ET).

“To all the patients living with ET, I am thrilled with the results of the Essential3 Program. All of us at Praxis will be forever indebted to the bravery you have demonstrated participating in the program, in the face of such a debilitating condition,” said Marcio Souza, president and chief executive officer. “Patients in Essential3 had been living with essential tremor for an average of 30 years, with worsening symptoms and no effective treatment options. In just 15 months of recruitment, we had over 200,000 people interested in participating in this study, which is a powerful reflection of the large unmet need for a therapy like ulixacaltamide. We look forward to the opportunity to have a pre-NDA meeting with the FDA soon to discuss the potential NDA.”

“This is incredibly exciting news, for the first time we have a medication designed specifically for our ET patients. As a clinical researcher and movement disorder specialist, it is very rewarding to see such positive results with the potential to truly change lives. Ulixacaltamide represents more than data on a chart - it is a real opportunity to help people regain their independence and improve their daily functioning in meaningful ways,” said Salima Brillman, MD, Founder, Parkinson's Disease and Movement Disorders Center of Silicon Valley, co-lead investigator of the E3 program.

“The trial’s innovative home-based design, with participants across all 50 states completing visits from their homes, brings real-world results to the ET community. The ulixacaltamide Phase 3 studies allowed us to engage a broad and representative ET population that truly reflects the diversity of those living with this condition, including people who might not have participated in clinical research otherwise. These positive results truly reflect the patient experience and highlight what is most meaningful to those living with essential tremor,” said Jill Farmer, DO, MPH, FCPP, DipABLM, BoroNeuro, co-lead investigator of the E3 program.

“As a lead investigator in the Essential3 program, I am extremely encouraged by these results, showing clinically meaningful improvements in tremor control and daily function for adults with ET. These results give hope that ulixacaltamide could be widely used in people suffering from this condition. These findings represent important progress for the ET community and underscore the value of modern, patient-centered trial execution for advancement of neurological science,” said Alexander Shtilbans, MD, PhD, FAAN, Hospital for Special Surgery, Department of Neurology, Weill Cornell Medicine, and co-lead investigator of the E3 program.

“For years, our community has waited for hope grounded in data. The positive results of Essential3 mark an extraordinary step forward bringing ulixacaltamide, a much-needed therapy to the under-served ET community. We are deeply grateful to Praxis, the investigators and the trial patients for their dedication to advancing science,” said Patrick McCartney, Executive Director, International Essential Tremor Foundation.

About the Essential3 Program Trial Design

The Essential3 Phase 3 program (NCT06087276) included two simultaneously enrolled studies utilizing a decentralized design conducted within the United States, where participants were allocated to the studies in a 2:1 blinded randomization (Study 1:Study 2).

Study 1 was a double-blind, parallel design, placebo-controlled study that enrolled 473 patients randomized 1:1 to receive either ulixacaltamide or placebo for 12 weeks. The primary endpoint was the change from baseline in mADL11 at Week 8.

Study 2 was a stable-responder randomized withdrawal study that enrolled 238 patients to receive ulixacaltamide for 8 weeks. Patients who improved by 3 points in the mADL11 from baseline were then randomized to receive either placebo or to continue receiving ulixacaltamide for an additional 4 weeks. The primary endpoint evaluated the proportion of patients who maintained response receiving ulixacaltamide versus placebo.

There were two additional pre-specified hypotheses evaluating combinations of arms in Study 1 and Study 2 using the change in mADL11 at Week 8. Hypothesis 3 compared the ulixacaltamide arms of Study 1 and Study 2 with the placebo arm of Study 1, and Hypothesis 4 compared the ulixacaltamide arm of Study 2 with the placebo arm of Study 1.

Key secondary endpoints in Studies 1 and 2 assessed the rate of disease improvement (slope of mADL11 change), the Patient Global Impression of change (PGI-C) and Clinical Global Impression of severity (CGI-S).

Summary of Essential3 Program Results

Study 1: Placebo-controlled Parallel Group Study Topline Efficacy Results
In Study 1, there was a statistically significant and clinically meaningful 4.3 point mean improvement in the mADL11 score at Week 8 (p<0.0001). The effect was sustained from Week 2 throughout the 12-week dosing period. All key secondary endpoints achieved statistical significance.

Results Summary

mITT population	Ulixacaltamide (n=199)	Placebo (n=233)	p-value
Primary Endpoint			
Day 56 CFB mADL11	-4.3	-1.7	<0.0001
Key Secondary Endpoints			
Rate of Disease Improvement, Baseline to Day 56 mADL11	-4.0	-1.7	<0.0001
PGI-C Day 56	3.3	3.9	<0.0001
CGI-S CFB to Day 56	-0.41	-0.12	0.0007
Select Sensitivity Analyses			
Imputation of missing data for primary analysis*	-3.3	-1.6	0.0026
Day 84 CFB mADL11**	-3.4	-1.9	0.0049

* Results from a pre-specified delta-adjusted tipping-point analysis remained statistically significant at the maximum tested shift (Δ = 2.5; p = 0.0026), exceeding the ~½ SD robustness criterion of Ratitch et al. (2013) and confirming strong resilience of the primary endpoint to non-MAR assumptions.

**Primary endpoint at the time of interim analysis (assessed as the average of Day 77 and Day 84)

Study 2: Randomized Withdrawal Study Topline Efficacy Results
In Study 2, after blinded exposure for 8 weeks with ulixacaltamide, patients meeting the responder criteria (n=80) were then randomized to continue receiving ulixacaltamide or switch to placebo for an additional 4 weeks. 55% of patients in the ulixacaltamide arm maintained response vs 33% in the placebo group (p=0.0369, OR=2.7 CI (1.06-6.92)). The first key secondary endpoint – rate of disease improvement – achieved statistical significance, and other secondary endpoints (PGI-C, CGI-S) were numerically in favor of ulixacaltamide, but not statistically significant.

Results Summary

mITT population	Ulixacaltamide (n=40)	Placebo (n=40)	p-value
Primary Endpoint			
Maintenance of Response	55%	33%	0.037
Key Secondary Endpoints			
Rate of Disease Improvement, RW Baseline to Day 84	2.8	5.2	0.004
PGI-C Day 84	3.24	3.67	0.087
CGI-S Day 56 to Day 84	0.39	0.73	0.055
Select Exploratory Endpoint			
PGI-S Day 56 to Day 84	0.24	0.59	0.027

Combined Study 1 and Study 2 Hypotheses
Hypothesis 3 and 4 further supported the precision of the effect of ulixacaltamide versus placebo.

- For Hypothesis 3, there was a 4.3 point improvement in mADL11 at Week 8 for the combined Studies 1 and 2 ulixacaltamide groups vs Study 1 placebo (p<0.0001)
- For Hypothesis 4, there was a 4.2 point improvement in mADL11 at Week 8 for the Study 2 ulixacaltamide group vs Study 1 placebo (p<0.0001), respectively.

Safety

Ulixacaltamide was generally well tolerated over 12 weeks of treatment. The most common (≥10% patients) treatment emergent adverse events (TEAs) were constipation, dizziness, euphoric mood, brain fog, headache, paraesthesia and insomnia. There were no deaths and no drug-related serious adverse events. Discontinuations were primarily due to TEAEs, with the most common being dizziness and brain fog.

Overview of Adverse Events

	Study 1		Study 2
Category	Ulixacaltamide (n = 233)	Placebo (n = 234)	Ulixacaltamide (n = 231)

Participants with any TEAE	221 (94.9%)	177 (75.6%)	209 (90.5%)
Participants with:			
Mild TEAEs	98 (42.0%)	89 (38.0%)	87 (37.7%)
Moderate TEAEs	109 (46.8%)	78 (33.3%)	105 (45.5%)
Severe TEAEs	14 (6.0%)	10 (4.3%)	17 (7.4%)
Participants with any SAE*	2 (0.86%)	8 (3.4%)	4 (1.73%)
Participants with drug-related TEAEs leading to discontinuation	63 (27.0%)	4 (1.7%)	65 (28.1%)
Discontinued from the study	83 (35.6%)	13 (5.6%)	88 (38.1%)

*not related to study drug

Corporate updates

Praxis has submitted a pre-NDA meeting request to the FDA with plans to submit the NDA by early 2026, upon agreement with the agency.

Praxis intends to share additional data from these studies at upcoming medical conferences and peer reviewed publications.

Praxis to hold an investor call to discuss the Essential3 Study results today, Thursday October 16, at 8:00am EST. Interested participants can register using this **link** or on the Praxis Medicines investor website **link**.

About Essential Tremor (ET)
Essential Tremor is the most common movement disorder, affecting roughly seven million people in the United States alone, representing a multi-billion dollar commercial opportunity. ET is characterized by involuntary rhythmic movement in the upper limbs, with or without tremor in other body locations such as the head, vocal cords, or legs. These tremors significantly disrupt daily living and are progressive in nature, with increases in tremor severity and amplitude commonly observed over the course of the disease. Propranolol, a beta-blocker, is the only approved pharmacotherapy for ET, offering limited efficacy and poor tolerability and is also contraindicated for comorbidities that affect a significant share of the ET population. Other beta blockers and anti-convulsants are used off-label, though similarly are characterized by limited efficacy and tolerability. The vast majority of patients are left without a treatment option, with estimated minimum of 2 million patients seeking treatment. In a patient survey, up to 77% of patients felt their ET is inadequately controlled and up to 50% of patients aren't receiving treatment. Indeed, U.S. neurologists surveyed indicated that 85% of their visits are for patients seeking treatment, and 40% of their patients are not receiving any treatment. These findings underscore the need for more effective treatments for ET.

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 is the most advanced program within Praxis' Cerebrum™ small molecule platform.

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, Instagram, 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 clinical development of ulixacaltamide 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 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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