Praxis Precision Medicines Announces Topline Results from the Essential1 Study of Ulixacaltamide for the Treatment of Essential Tremor and Continued Advancement of Program to Phase 3

March 3, 2023 at 7:30 AM EST

Based upon observed efficacy and safety profile, Praxis intends to engage with the FDA in an end of Phase 2 meeting and initiate a ulixacaltamide Phase 3 study for the treatment of essential tremor in 2H23

Ulixacaltamide demonstrated improvement in modified Activities of Daily Living (mADL) primary efficacy endpoint relative to placebo that did not reach statistical significance (p=0.126), and achieved nominal statistical significance in TETRAS-ADL secondary endpoint (p=0.026)

Nominal statistically significant improvements observed in Clinical Global Impression-Severity (CGI-S) and in Patient Global Impression-Change (PGI-C)

Ulixacaltamide was well tolerated in the Essential1 study, with no new safety findings

Company to host conference call to discuss the results at 8:00 a.m. ET

BOSTON, March 03, 2023 (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 topline results from the Essential1 study evaluating the efficacy, safety and tolerability of ulixacaltamide (PRAX-944) for the treatment of essential tremor (ET).

In Essential1, ulixacaltamide treated participants demonstrated improvement relative to placebo participants in the primary endpoint, change from baseline to Day 56 in the modified Activities of Daily Living (mADL[1]) score, that did not reach statistical significance. Nominal statistically significant improvement was observed in the TETRAS-ADL score secondary endpoint. Additional secondary endpoints were supportive of the ulixacaltamide efficacy profile, including nominal statistically significant improvements in the Clinical Global Impression-Severity (CGI-S) and Patient Global Impression-Change (PGI-C) scores. Praxis intends to engage with the FDA in an end of Phase 2 meeting and initiate a Phase 3 study for the treatment of essential tremor in the second half of 2023 based upon the observed efficacy and safety profile.

“The impact of essential tremor transcends the action tremor that is the hallmark of the disease. Essential tremor can be debilitating, causing significant disruption of everyday activities. There is significant unmet need for an effective and tolerable precision medicine that can improve patient functioning, and to date there exists no medicine specifically developed for tremor,” said William G. Ondo, M.D., Professor of Neurology at the Houston Methodist Hospital and Weill Cornell Medical College. “The results from Essential1 give hope to the essential tremor community that a targeted therapy is within reach, and we eagerly anticipate additional data from the ulixacaltamide program.”

“The results from Essential1 illustrate the clear potential of ulixacaltamide as an effective and well tolerated treatment for people with essential tremor,” said Marcio Souza, president and chief executive officer of Praxis. “The study showed meaningful improvement in patient’s daily functioning, while also providing insights to guide the program’s advancement to Phase 3, including a deeper understanding of endpoints and trial design. It’s clear to us based on these results and prior clinical experience, that ADLs are the preferred endpoint for a registrational study for essential tremor. We look forward to meeting with the FDA to discuss the data and our Phase 3 plans.”

Essential1 Efficacy Results

Essential1 is a randomized, double-blind, placebo-controlled, dose-range-finding Phase 2b trial evaluating the efficacy, safety and tolerability of once-daily daytime treatment of 60 or 100 mg of ulixacaltamide compared to placebo after 56 days. The primary endpoint for the study was the change from baseline to day 56 in the mADL score. A total of 132 patients with essential tremor were randomized and treated in the study.

The primary analysis population was the modified intention to treat (mITT[2]). In the mITT analysis (n=116), ulixacaltamide (n=78) showed numerical difference versus placebo (n=38) at day 56 in the mADL score (-3.01 points for ulixacaltamide treated participants, -1.44 for placebo participants [LS mean difference 1.58; 95% CI: -3.60, 0.45; p=0.126]) and nominal statistical significance versus placebo at day 56 in the TETRAS-ADL secondary endpoint (-3.60 points for ulixacaltamide treated participants, -1.07 for placebo participants [LS mean difference 2.53; 95% CI: -4.75, -0.31; p=0.026]). Consistent effect was observed across both the 60 mg and 100 mg dosing regimens. Observed changes across 10 of the 12 ADL scored items in the mITT favored ulixacaltamide treated participants relative to placebo and there were no items that favored placebo.

Patients and clinicians reported higher overall impression of improvement with ulixacaltamide relative to placebo. In the PGI-C, 47% of ulixacaltamide treated patients reported improvement, while 30% of placebo participants reported improvement ($p<0.05$, rank analysis). In the CGI-S, investigators reported that 42% of ulixacaltamide treated patients improved and 26% of placebo participants improved ($p<0.05$, rank ANCOVA).

Essential1 Safety and Tolerability Results

Ulixacaltamide was well-tolerated. No dose response relationship was observed between participants assigned to the 60 mg or the 100 mg dose regimens in effect or safety. Adverse events (AEs) were generally consistent with the safety profile of ulixacaltamide seen to date, with no new safety findings.

The most commonly reported treatment emergent adverse events (TEAEs) in ≥5% of all participants treated with ulixacaltamide (n=91) were dizziness (13, 14.3%), constipation (9, 9.9%), headache (8, 8.8%), fatigue (8, 8.8%), anxiety (6, 6.6%), feeling abnormal (6, 6.6%) and paraesthesia (6, 6.6%). There were no drug related serious adverse events (SAEs)[3]. The rate of discontinuations due to AEs in the mITT was 12% in ulixacaltamide treated participants and 3% in placebo participants.

Conference Call and Webcast
Praxis will host a conference call and webcast to review the Essential1 study topline results today, March 3, 2023, at 8:00 a.m. ET. The live audio webcast with slides may be accessed through the Events & Presentations page of the Investors + Media section of the company's website. To access the live conference call by phone please click this link. After registering, an email will be sent including dial-in details and a unique conference call pin required to join the call. To avoid delays, participants are encouraged to dial into the conference call 15 minutes ahead of the scheduled start time. A replay of the webcast will be available on Praxis' website approximately two hours following completion of the event and will be archived for 90 days following the event.

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 development for the treatment of essential tremor and as a non-dopaminergic treatment for the motor symptoms of Parkinson's disease.

About Essential Tremor
Essential Tremor (ET) is the most common movement disorder, affecting roughly seven million people in the United States alone, including approximately two million diagnosed patients. 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. There is only one approved pharmacotherapy for ET, propranolol, a beta blocker approved by the FDA in 1967, that offers limited efficacy and poor tolerability and is 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. For these reasons, approximately 40% of patients who seek pharmacotherapy treatment discontinue within two years.

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 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 our clinical trials and regulatory interactions and the development of our product candidates, including the treatment potential of our 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; regulatory approvals to conduct trials; Praxis' ability to continue as a going concern; and other risks concerning Praxis' programs and operations as described in its Annual Report on Form 10-K for the year ended December 31, 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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[1]mADL is a composite sum of items 1 to 11 of the TETRAS-ADL subscale and items 6 (bilateral) and 7 of the TETRAS-PS; mADL score is calculated as the sum of all 13 items (item 6 of TETRAS-PS x2) and ranges from 0 to 42

[2] mITT analysis defined as all patients enrolled under Version 4 of protocol (or enrolled in prior version and eligible for Version 4), who were randomized to treatment, and received at least 1 dose of study drug

[3] 3 SAEs in 2 subjects, all deemed unrelated to treatment (exacerbation of COPD in 1 patient; esophageal obstruction & gastric adenocarcinoma in 1 patient)

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