Praxis Precision Medicines Reports PRAX-114 Perimenopausal Depression (PMD) Phase 2a Proof-of-Concept Trial Results and Announces Plans to Advance to Phase 2b Study in Women with Menopausal and Mood Symptoms

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PRAX-114 showed rapid and marked improvements in menopausal and mood symptoms in Phase 2a PMD study

PRAX-114 was well tolerated in Phase 2a PMD study with no change in overall safety profile

CAMBRIDGE, Mass., Aug. 16, 2021 (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 imbalance, today reported results from its PRAX-114 Phase 2a Part B proof-of-concept trial for treatment of perimenopausal depression (PMD) and announced plans to advance PRAX-114 to a Phase 2b study in women with menopausal and mood symptoms. Plans for the Phase 2b trial will be disclosed by the end of 2021.

In the Phase 2a trial for treatment of PMD, participants treated with a single daily dose of PRAX-114 60 mg suspension formulation (n=6) for 14 days in an outpatient setting showed improvements in menopausal and mood symptoms that were rapid, marked and maintained throughout the two-week treatment period. Results trended toward baseline following discontinuation of PRAX-114, suggesting the need for continued treatment. PRAX-114 was well tolerated in Part B of the three-part Phase 2a study, with no change in the overall PRAX-114 safety profile.

“The ability to impact both menopausal and mood symptoms in the PRAX-114 proof-of-concept study in PMD was our criteria to continue development of this program. The rapid and consistent improvement across distinct efficacy measures gives us confidence to advance to a Phase 2b trial,” said Marcio Souza, president and chief executive officer of Praxis. “A significant unmet need exists with an estimated 3 million women in the US living with PMD and limited treatment options for both menopausal and mood symptoms.”

Efficacy Results

Daily treatment of PRAX-114 in Part B of the Phase 2a study showed a rapid and marked decrease in menopausal symptoms throughout the 14-day treatment period. Treatment with PRAX-114 resulted in mean decreases from baseline at Day 15 of 60% in frequency of moderate-to-severe hot flashes and 68% in the total score of the Perimenopausal Depression Questionnaire (Meno-D)[1], a 12-item, self-reported questionnaire assessing the presence and severity of symptoms of PMD. Improvements were observed in each of the 12 items of the Meno-D, with the largest reductions observed in measures of low energy, sexual interest, sleep disturbance, irritability and anxiety. At Day 28, two weeks following discontinuation of treatment, frequency of moderate-to-severe hot flashes and Meno-D total score trended toward baseline.

Daily treatment of PRAX-114 in Part B of the Phase 2a study showed a rapid and marked decrease in mood symptoms throughout the 14-day treatment period. Treatment with PRAX-114 resulted in mean decreases from baseline at Day 15 of 47% in the HAM-D total score, 65% in the HAM-A total score and 40% in the total score of the Symptoms of Depression Questionnaire (SDQ)[2], a patient reported outcome of depression severity. At Day 28, two weeks following discontinuation of treatment, HAM-D, HAM-A and SDQ total scores trended toward baseline.

Figure 1: Rapid and marked decrease in menopausal and mood symptoms, as measured by frequency of moderate-to-severe hot flashes per day, the Meno-D total score, the Hamilton Depression Rating Scale (HAM-D) total score, the Hamilton Anxiety Rating Scale (HAM-A) total score and SDQ total score

	Baseline Mean (SD)	Day 15 CFB Mean (SD) [%]	Day 28* Follow-up CFB Mean (SD) [%]
Mod-Severe Hot Flashes	3.2 (0.43)	-1.9 (1.23) [-60%]	-0.9 (2.19) [-23%]
Meno-D	25.3 (5.85)	-18.4 (5.27) [-68%]	-10.2 (5.63) [-37%]
HAM-D	25.3 (2.16)	-12.0 (8.09) [-47%]	-8.2 (6.69) [-31%]
HAM-A	24.8 (4.31)	-16.2 (5.22) [-65%]	-8.4 (8.14) [-32%]
SDQ	166.2 (14.72)	-67.6 (25.64) [-40%]	-53.0 (32.58) [-31%]

Change from baseline (CFB) columns present mean, standard deviation (SD) and % change from baseline values

*Day 28 assessment performed two-weeks following discontinuation of treatment

Safety Results

Daily treatment with 60mg of PRAX-114 suspension formulation in Part B of the Phase 2a study was well tolerated, with no change in the overall safety profile. One Part B participant discontinued treatment due to adverse events (AEs) of moderate daytime sedation and mild feeling abnormal. There have been no prior reports of daytime sedation in the PRAX-114 Phase 1 and Phase 2 studies, which includes 185 participants. All AEs were mild to moderate in severity. There were no serious adverse events (SAEs).

In the Phase 2a study overall, PRAX-114 suspension formulation was well tolerated in 52 participants with major depressive disorder (MDD) or PMD.

The most common AEs were headache, somnolence, dizziness, fatigue and feeling abnormal. The majority of AEs were mild, and there were no SAEs.

Figure 2: Treatment emergent adverse events reported in ≥10% of participants across all parts of the PRAX-114 Phase 2a study (Parts A, B and C)

Preferred Term	45 mg* (N=13)	60 mg (N=32)	80 mg* (N=7)	Overall (N=52)
Any TEAE	9 (69.2%)	31 (96.9%)	7 (100.0%)	47 (90.4%)
Headache	7 (53.8%)	12 (37.5%)	3 (42.9%)	22 (42.3%)
Somnolence	2 (15.4%)	12 (37.5%)	3 (42.9%)	17 (32.7%)
Dizziness	0 (0.0%)	5 (15.6%)	4 (57.1%)	9 (17.3%)
Fatigue	3 (23.1%)	2 (6.3%)	1 (14.3%)	6 (11.5%)
Feeling abnormal	1 (7.7%)	4 (12.5%)	1 (14.3%)	6 (11.5%)
Nausea	0 (0.0%)	5 (15.6%)	1 (14.3%)	6 (11.5%)

*Includes participants from Part A only
In Part A, PRAX-114 was administered at daytime of Day 1, nighttime of Days 2-14

About the PRAX-114 Phase 2a Study for Depression

The PRAX-114 Phase 2a study for depression included three open-label parts to assess the safety and efficacy of PRAX-114 suspension formulation in patients with moderate to severe MDD or PMD. Part A of the open-label trial included 14-days of treatment and was designed to evaluate the timing and magnitude of the antidepressant effects of PRAX-114 across a range of doses (45 mg, 60 mg, 80 mg) in patients with MDD. Part B of the Phase 2a study was an open-label, proof-of-concept assessment of a single daily dose of PRAX-114 60 mg suspension formulation administered for 14-days in an outpatient setting to women with PMD. The objectives of the study were to examine safety and efficacy of PRAX-114 in PMD, a population of women with symptoms of menopause, including vasomotor symptoms (hot flashes), insomnia and sexual dysfunction, and mood symptoms, including depression and anxiety. Part C was intended to evaluate the safety of 28-day outpatient dosing of PRAX-114 and the efficacy profile from Day 15 to Day 28 in patients with MDD.

About PRAX-114

PRAX-114 is an extrasynaptic $GABA_A$ receptor preferring positive allosteric modulator (PAM) under development for the potential treatment of patients suffering from MDD and PMD, with planned studies upcoming in post-traumatic stress disorder (PTSD) and essential tremor (ET). As an extrasynaptic $GABA_A$ receptor preferring PAM, PRAX-114 may have several advantages relative to currently available therapies and other product candidates in the $GABA_A$ PAM therapeutic class, including a wider therapeutic window, improved tolerability, and the ability to administer for a sustained period with or without food. PRAX-114 is currently being investigated as a monotherapy treatment for MDD in adults in the Phase 2/3 Aria Study and as an adjunctive treatment for MDD in adults in the Phase 2 Acapella Study, with topline results from both trials expected in the first half of 2022.

About Praxis
Praxis Precision Medicines is a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for central nervous system disorders (CNS) characterized by neuronal imbalance. Praxis is applying insights from genetic epilepsies to broader neurological and psychiatric disorders, using our understanding of shared biological targets and circuits in the brain. Praxis has established a broad portfolio, including multiple disclosed programs across CNS disorders including depression, epilepsy, movement disorders and pain syndromes, with three clinical-stage product candidates. For more information, please visit https://praxismedicines.com/ and follow us on LinkedIn and Twitter.

Forward-Looking Statements
This press release may contain 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 planned clinical trials and regulatory filings, interim trial results, our goals to develop and commercialize 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 and in the availability and timing of data from ongoing clinical trials; whether interim results from a clinical trial will be predictive of the final results of the trial; whether results from earlier clinical studies will be predictive of the results of future trials; the expected timing of submissions for regulatory approval or review by governmental authorities; regulatory approvals to conduct trials or to market products; risks, uncertainties and assumptions regarding the impact of the continuing COVID-19 pandemic on Praxis' business, operations, strategy, goals and anticipated timelines, Praxis' ability to initiate, enroll, conduct or complete ongoing and planned clinical trials and Praxis' timelines for regulatory submissions; and other risks concerning Praxis' programs and operations are described in additional detail in its Annual Report on Form 10-K for the year ended December 31, 2020, its Quarterly Reports on Form 10-Q and other subsequent filings made with the Securities and Exchange Commission from time to time. Although Praxis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts 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.

[1] https://www.nature.com/articles/s41398-018-0172-0
[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4524555/

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