Praxis Precision Medicines Provides Corporate Update and Reports First Quarter 2021 Financial Results

May 11, 2021

Expands pipeline with new indications for PRAX-114 and PRAX-944

PRAX-114 Phase 2 trial for treatment of post-traumatic stress disorder to initiate in 2H21

PRAX-114 Phase 2 trial for treatment of essential tremor to initiate in 2H21

PRAX-944 Phase 2 trial for treatment of Parkinson's disease to initiate in 1H22

Cash balance of $270.8M as of March 31, 2021 supports cash runway into 4Q22

CAMBRIDGE, Mass., May 11, 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 provided a corporate update and reported financial results for the first quarter ended March 31, 2021.

"I'm inspired by our team's continued execution and the progress throughout our pipeline during the first quarter, with key milestones achieved across each of our programs. As the pipeline advances, our conviction in our programs continues to grow," said Marcio Souza, president and chief executive officer of Praxis. "In addition to the ongoing enrollment in our PRAX-114 Phase 2/3 Aria study for monotherapy MDD, we are excited to announce the expansion of PRAX-114 into post-traumatic stress disorder and essential tremor, as well as the expansion of PRAX-944 into Parkinson's disease. These disorders all have significant unmet need, as well as both genetic and mechanistic linkage to the respective targets and programs. We believe that Praxis' foundational approach to identifying targets through human genetics, the extensive use of translational tools to inform development and always keeping patient needs top of mind have been instrumental in developing a deep pipeline of CNS programs with considerable optionality."

Recent Business Highlights and Upcoming Milestones:

Psychiatry

- Praxis plans to initiate a PRAX-114 Phase 2 trial for treatment of post-traumatic stress disorder (PTSD) in the second half of 2021. Topline results are expected in the second half of 2022.
- Praxis expects topline results from the ongoing PRAX-114 Phase 2/3 Aria Study (Study 213) for monotherapy treatment of Major Depressive Disorder (MDD) in the first half of 2022. If positive, the Aria Study is intended to serve as one of two trials required by the U.S. Food and Drug Administration (FDA) to demonstrate clinical efficacy to support registration of PRAX-114 for monotherapy treatment of MDD.
- Praxis plans to initiate a PRAX-114 Phase 2 Study (Study 214) for adjunctive treatment of MDD in the third quarter of 2021. Topline results from Study 214 are expected in the first half of 2022.
    - Study 214 is designed to include patients with moderate to severe MDD (HAM-D>23) with insufficient response to standard of care antidepressant treatment in the current episode and will evaluate efficacy and safety of PRAX-114 at doses of 10mg, 20mg, 40mg and 60mg.
    - Study 214 will provide controlled data to support advancing a Phase 3 adjunctive MDD trial and will increase the understanding of the dose range for expected Phase 3 monotherapy and adjunctive treatment trials.
- Praxis has completed the Part A (N=33) and Part C (N=13) MDD cohorts of the PRAX-114 Phase 2a trial for treatment of patients with MDD and perimenopausal depression (PMD). Praxis expects to announce topline results from the ongoing Part B cohort for treatment of patients with PMD in the second half of 2021.
    - Across both MDD cohorts (N=46), PRAX-114 led to a rapid and marked improvement in the HAM-D score of participants, with mean improvements of 16.4 points, or 65%, at Day 15 for monotherapy treatment (N=11) and 12.7 points, or 51%, at Day 15 for adjunctive treatment (N=35).
    - Anxiety symptoms, as assessed by the HAM-A, demonstrated an improvement of 11 points, or 50%, at Day 15 across both MDD cohorts.

- Insomnia symptoms, as assessed by the total of 3 HAM-D insomnia items, demonstrated an improvement of 3.1 points, or 76%, at Day 15 across both MDD cohorts.

- PRAX-114 demonstrated a generally well-tolerated safety profile throughout the 14-day treatment period in Part A and the 28-day treatment period in Part C. Treatment emergent adverse events were generally mild to moderate. Rates of somnolence, which is characterized by sleepiness or drowsiness, increased with exposure, demonstrating a pharmacological effect which was substantially mitigated by dosing at night versus daytime dosing.

- In May 2021, Praxis published a white paper, "*Best Practices in Clinical Trials of Antidepressants: Overcoming Challenges to Optimize Success*," highlighting essential learnings and best practices to improve the chances of success in MDD clinical trials through appropriate study design and conduct.

- Preclinical and clinical data for PRAX-114 was presented at the Society of Biological Psychiatry Meeting (SOBP) from April 29 - May 1, 2021. One abstract included preclinical data demonstrating PRAX-114's extrasynaptic GABAA receptor preference, robust β-EEG link to preclinical anxiety and depression models, and wide therapeutic window with exposures associated with efficacy separating from those associated with sedation by 11-fold. A second abstract included clinical data demonstrating that PRAX-114's robust CNS pharmacodynamic effect and translational β-EEG and tolerability data generated in preclinical experiments was replicated in a clinical study in healthy participants.

Movement Disorders

- Praxis expects to initiate a PRAX-114 Phase 2 trial for treatment of essential tremor (ET) in the second half of 2021. Topline results are expected in the second half of 2022.

- Praxis expects to initiate a PRAX-944 Phase 2 trial for treatment of Parkinson's disease in the first half of 2022.

- Praxis is currently in the second of two cohorts in its PRAX-944 Phase 2a trial for ET, assessing up to twelve patients titrated up to 120 mg/day of PRAX-944. Preliminary topline open-label safety, tolerability and efficacy data is expected in mid-2021.

- To inform dose selection for PRAX-944 for tremor studies, population PK-PD analyses were performed to predict the effect of PRAX-944 exposure on selected EEG endpoints including the sigma band absolute power during non-rapid eye movement (NREM) sleep, which is believed to be a relevant biomarker for the T-type calcium channel in the thalamus, a key part of the tremor network. PRAX-944 had a significant pharmacodynamic (PD) effect on sigma band EEG power during NREM sleep across the 5 to 120 mg dose range evaluated. The results of the analysis suggest that doses as low as 5 mg/day may show effect while doses of up to ~120 mg/day may drive additional PD effect relative to the doses explored in ET patients to date (up to 40mg/day).

- Praxis plans to initiate a Phase 2 randomized, double-blind, placebo-controlled trial of PRAX-944 for treatment of ET in the fourth quarter of 2021. In addition, a Phase 1 study to explore faster titration schemes for PRAX-944 for treatment of ET is expected to initiate in mid-2021.

- Praxis recently interacted with the FDA to discuss the development of PRAX-944 for treatment of ET and received feedback pertaining to clinical endpoints necessary to support PRAX-944's potential approval. The FDA indicated that primary clinical endpoints to support approval for treatment of ET should adequately measure clinically meaningful benefit for patients such as assessment of activities of daily living or performance-based functional tests.

Rare Disease

- Praxis has completed the single ascending dose (SAD) and the multiple ascending dose (MAD) cohorts in its Phase 1 trial of PRAX-562 in healthy volunteers up to the highest planned dose. The highest planned dose in the MAD cohort was well tolerated with concentrations that exceed EC_{75} in the MES mouse model, a model with demonstrated predictive validity. Praxis will be escalating the dose further to explore tolerability at higher dose levels. Safety, tolerability and PK data from the ongoing Phase 1 trial of PRAX-562 is expected in mid-2021.

- Praxis expects to initiate an exploratory Phase 2 trial of PRAX-562 in the second half of 2021 for treatment of patients with rare adult cephalgias, including a cohort of participants with Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing (SUNCT) and Short-lasting Unilateral Neuralgiform headache with Autonomic symptoms (SUNA), and a cohort of participants with Trigeminal Neuralgia (TN).

- Praxis plans to initiate a Phase 2 trial of PRAX-562 for treatment of developmental epileptic encephalopathies (DEEs), including SCN8A-DEE and SCN2A-DEE, in the first half of 2022.

- In April 2021, Praxis announced that the FDA granted orphan drug designation to PRAX-562 for treatment of SCN8A-DEE and for treatment of SCN2A-DEE. Data from preclinical studies demonstrated that PRAX-562 dose-dependently inhibits seizures in SCN8A and SCN2A animal models, completely extinguishing seizures at the highest dose level tested in each model.

- Praxis plans to complete the ongoing IND-enabling toxicology study by the end of 2021 for its lead antisense oligonucleotide (ASO) candidate, PRAX-222, and to initiate a Phase 1/2 trial of PRAX-222 for treatment of SCN2A-DEE in the first half of 2022. PRAX-222 is a precision medicine candidate designed to down-regulate SCN2A mRNA in epilepsy patients with SCN2A gain-of-function mutations.

General Corporate Updates

- In April 2021, Praxis announced the appointment of Jeffrey Chodakewitz, M.D., to its board of directors. Dr. Chodakewitz has more than 30 years of management experience in the biopharmaceutical industry. Most recently he served as the chief medical officer and executive vice president, global medicines development & medical affairs at Vertex Pharmaceuticals.

- In April 2021, Praxis announced the appointment of Merit Cudkowicz, M.D., to its board of directors. Dr. Cudkowicz is the chief of neurology at Mass General Hospital, director of the Sean M. Healey & AMG Center for ALS, and director and the Julieanne Dorn professor of neurology at Harvard Medical School. She has brought innovations to accelerate the development of treatments for people with neurological disorders such as ALS, including a leadership role in the first antisense oligonucleotide treatment for a neurological disorder.

First Quarter 2021 Financial Results:

As of March 31, 2021, Praxis had $270.8 million in cash, cash equivalents and marketable securities, compared to $296.6 million in cash and cash equivalents as of December 31, 2020. This decrease of $25.8 million primarily reflects cash used in operations. The company's cash, cash equivalents and marketable securities as of March 31, 2021 are expected to fund operations into the fourth quarter of 2022.

Research and development expenses were $17.9 million for the first quarter of 2021, compared to $6.9 million for the first quarter of 2020. The increase in R&D expenses of $11.1 million was primarily attributable to $4.5 million in increased personnel-related costs due to increased headcount, $2.7 million in increased expenses related to our discovery-stage programs, $1.8 million in increased expenses related to our PRAX-562 program, $1.3 million in increased expenses related to our PRAX-114 program and $0.6 million in increased expenses related to our PRAX-944 program.

General and administrative expenses were $9.5 million for the first quarter of 2021, compared to $1.6 million for the first quarter of 2020. The increase in general and administrative expenses of $7.9 million was primarily attributable to $3.8 million in increased personnel-related costs due to increased headcount, $2.3 million in increased professional fees and $1.8 million increase in other general and administrative expenses, including $1.1 million in increased insurance and other costs related to becoming a public company.

Praxis reported net loss of $27.4 million for the first quarter of 2021, including $4.7 million of stock-based compensation expense, compared to $8.3 million for the first quarter of 2020, including $0.1 million of stock-based compensation expense.

As of March 31, 2021, Praxis had 38.6 million shares of common stock outstanding.

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 expectations and plans for presenting pre-clinical and clinical data, projections regarding future revenues and financing performance, our long-term growth, cash, cash equivalents and marketable securities, the anticipated timing of our clinical trials and regulatory filings, the development of our product candidates and advancement of our preclinical programs, the timing, progress and success of our collaborations, 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 preclinical studies or 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; whether Praxis' cash resources will be sufficient to fund Praxis' foreseeable and unforeseeable operating expenses and capital expenditure requirements; risks, uncertainties and assumptions regarding the impact of the continuing COVID-19 pandemic on Praxis' business, operations, strategy, goals and anticipated timelines, Praxis' ongoing and planned preclinical activities, Praxis' ability to initiate, enroll, conduct or complete ongoing and planned clinical trials, Praxis' timelines for regulatory submissions and Praxis' financial position; 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 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.

PRAXIS PRECISION MEDICINES, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS

(Amounts in thousands)

(Unaudited)

	March 31, 2021	December 31, 2020
Assets		
Cash and cash equivalents	$ 131,152	$ 296,608
Marketable securities	139,659	—
Prepaid expenses and other current assets	7,753	5,718
Property and equipment, net	109	82
Operating lease right-of-use assets	571	754
Other non-current assets	9	15
Total assets	$ 279,253	$ 303,177
Liabilities and stockholders' equity		
Accounts payable	$ 5,774	$ 4,088
Accrued expenses	7,386	10,869
Operating lease liabilities	578	763
Common stock	4	4
Additional paid-in capital	442,524	437,007
Accumulated other comprehensive loss	(86)	—
Accumulated deficit	(176,927)	(149,554)
Total liabilities and stockholders' equity	$ 279,253	$ 303,177

PRAXIS PRECISION MEDICINES, INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS

(Amounts in thousands, except share and per share amounts)

(Unaudited)

	Three Months Ended March 31,	
	2021	2020
Operating expenses:		
Research and development	$ 17,929	$ 6,868
General and administrative	9,490	1,601
Total operating expenses	27,419	8,469
Loss from operations	(27,419)	(8,469)
Other income:		
Interest income, net	46	128
Total other income	46	128
Loss before benefit from income taxes	(27,373)	(8,341)

Benefit from income taxes	—	11
Net loss	$ (27,373)	$ (8,330)
Accretion and cumulative dividends on redeemable convertible preferred stock	—	(2,064)
Gain on repurchase of redeemable convertible preferred stock	—	493
Net loss attributable to common stockholders	$ (27,373)	$ (9,901)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.71)	$ (6.08)
Weighted average common shares outstanding, basic and diluted	38,470,710	1,629,340

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