Praxis Precision Medicines Provides Corporate Update and Reports Second Quarter 2022 Financial Results

August 8, 2022

PRAX-944 Phase 2b Essential1 Study topline results expected in 4Q22; primary endpoint updated to efficacy

PRAX-562 Phase 1 study completed, confirming biomarker change and potential for wide therapeutic window

Cash and investments of $165.4 million as of June 30, 2022 supports runway into 1Q24

BOSTON, Aug. 08, 2022 (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 provided a corporate update and reported financial results for the second quarter of 2022.

"Through the lens of epilepsy genetics, we have efficiently built a broad portfolio of clinical stage and preclinical CNS programs with uncorrelated risk," said Marcio Souza, president and chief executive officer of Praxis. "In our clinical stage programs, recent data for PRAX-944 in essential tremor and for PRAX-562 have been encouraging and give us greater confidence as we trend toward key milestones later this year. Reflecting this increased confidence, we updated the primary endpoint in the ongoing Essential1 Study to Modified Activities of Daily Living, the FDA-suggested efficacy endpoint for ET. The results from the PRAX-562 Phase 1 study deepen our conviction that we have a well-tolerated and differentiated sodium channel blocker with potential for a higher therapeutic index than existing therapies."

Recent Business Highlights and Upcoming Milestones:

Movement Disorders

- In May 2022, Praxis reported positive topline results from Part B of its Phase 2a study evaluating the safety and efficacy of PRAX-944 for the treatment of essential tremor (ET). In the study, treatment with PRAX-944 resulted in clinically meaningful improvements in function, which were supported by improvements in tremor amplitude.
    - During the open-label period of the trial, patients treated with PRAX-944 demonstrated mean improvement from baseline of 42% in the Modified Activities of Daily Living (ADL) score (N=11, nominal $p<0.05$). In the placebo-controlled, randomized withdrawal period of the study, the difference between patients who remained on treatment (N=6) and those randomized to placebo (N=5) was clinically and statistically significant.
    - PRAX-944 was generally well tolerated in the study, with no new safety findings.

- The Company expects topline results from the ongoing PRAX-944 Essential1 Study in the fourth quarter of 2022. Essential1 is a randomized, double-blinded, placebo-controlled, dose-range-finding Phase 2b trial evaluating the efficacy, safety and tolerability of once-daily daytime treatment of 60 mg or 100 mg of PRAX-944 compared to placebo after 56 days, for the treatment of moderate to severe ET. Following the positive topline results of Part B of the Phase 2a study of PRAX-944 for the treatment of ET, the Essential1 study design was revised, including changing the primary endpoint to efficacy from safety. Key study design updates include:
    - The primary endpoint is now the change from baseline to Day 56 on the modified ADL.
    - An extension was added, offering continuation of treatment to those participants randomized to PRAX-944 and new treatment to those randomized to placebo.
    - Approximately 130 participants are now planned to be randomized.

- Praxis plans to initiate a Phase 2 placebo-controlled trial to evaluate the safety, pharmacokinetics (PK) and efficacy of PRAX-944 as a non-dopaminergic treatment for the motor symptoms of Parkinson's disease in the second half of 2022. Topline results are expected in 2023.

- In June 2022, following the PRAX-114 Aria Study results, the Company discontinued the PRAX-114 Phase 2 study for the treatment of ET.

Epilepsy

- Praxis has completed the PRAX-562 Phase 1, two-part, placebo-controlled study evaluating the safety, tolerability, PK and pharmacodynamics of 90 mg of PRAX-562 over 28 days (Part A, N=12) and of 600 mg BID of oxcarbazepine (a sodium channel blocker, or SCB) in combination with 120 mg of PRAX-562 as compared to oxcarbazepine alone in adult healthy volunteers (Part B, N=18). PRAX-562 was well-tolerated as a stand-alone therapy and led to the expected changes in quantitative electroencephalogram (qEEG) biomarkers; additive effect was shown when combined with oxcarbazepine at supra-therapeutic doses. A summary of the findings is included below:

- PRAX-562 was well-tolerated in Part A of the study, with no clinically significant safety findings. The majority of Treatment Emergent Adverse Events (TEAEs) were considered mild to moderate in both Part A and Part B of the study.
- Part B evaluated the combination of oxcarbazepine and PRAX-562 as compared with oxcarbazepine alone. The co-administration of supra-therapeutic doses of PRAX-562 and oxcarbazepine led to additive sodium blocking effects, providing information about optimal target exposures for concomitant use of PRAX-562 and oxcarbazepine, and additional supportive evidence of PRAX-562 sodium channel blocking effects. Participants in Part B who received PRAX-562 in combination with oxcarbazepine developed TEAEs consistent with sodium channel blocking effects, leading to study withdrawal for five participants. One participant in Part B experienced drug-related Serious Adverse Events (SAEs) that required hospitalization and resolved that day. No similar SAEs have been previously reported for PRAX-562.
- In Part A, dosing with 90 mg of PRAX-562 over 28 days resulted in concentrations that exceeded the EC50 in the maximal electroshock seizure (MES) model by 13-fold (based on mean concentration at Day 28), indicating the potential for a wider therapeutic index than other SCBs.
- In Part A, statistically significant changes were observed between placebo and 90 mg of PRAX-562 on qEEG and on auditory steady state response (ASSR), a pharmacosensitive biomarker for assessing neuronal sensory function.

- Praxis plans to initiate a PRAX-562 Phase 2, placebo-controlled trial for treatment of developmental epileptic encephalopathies (DEEs) in pediatric patients in the second half of 2022, including initial cohorts of patients with SCN2A-DEE and SCN8A-DEE. The Company has completed the juvenile toxicology studies and pediatric formulation development necessary to initiate the study. Topline results are expected in mid-2023.

- In June 2022, Praxis received an email communication from the FDA regarding the clinical hold for the Company's Investigational New Drug (IND) application for the first-in-patient study of PRAX-222, an antisense oligonucleotide (ASO) for the treatment of patients with SCN2A gain-of-function mutations, which indicated that the IND could be cleared upon submission of additional documentation related to the completed 13-week non-human primate toxicology study supporting the starting dose proposed by the Company. The Company submitted the required data in July 2022 and expects to start its first-in-patient study with PRAX-222 in the second half of 2022.

- Praxis expects to initiate a PRAX-628 Phase 1 study in the fourth quarter of 2022 and subsequently initiate a Phase 2 study in focal epilepsy in 2023.

Psychiatry

- In June 2022, Praxis reported that the PRAX-114 Phase 2/3, placebo-controlled Aria Study for monotherapy treatment of Major Depressive Disorder (MDD) did not achieve statistical significance on the primary endpoint or on any secondary endpoints. As a result, the Company closed screening and enrollment in the Phase 2 Acapella Study evaluating the presence of a dose response signal for PRAX-114 in MDD at doses up to 60 mg and intends to read out results from approximately 110 patients in the third quarter of 2022. The Company also stopped enrollment in the Phase 2 study evaluating PRAX-114 for the treatment of post-traumatic stress disorder.

General Corporate Updates

- In May 2022, Praxis announced the appointment of Jill DeSimone to its board of directors. Most recently, Ms. DeSimone served as president of U.S. Oncology at Merck & Co., Inc. from 2014 to May 2022. During her time at Merck, Ms. DeSimone also temporarily served as interim president of U.S. Pharma to help navigate the business through the COVID-19 pandemic.

- In June 2022, following the Aria Study topline results, Praxis announced a strategic realignment to focus resources on its Movement Disorders and Epilepsy franchises, which resulted in a reduction of the Company's workforce and future operating expenses and extended cash runway into the first quarter of 2024.

- In July 2022, the Company announced that Bernard Ravina, M.D., former chief medical officer of Praxis, transitioned to a part-time role as strategic advisor as of August 1, 2022.

Second Quarter 2022 Financial Results:

As of June 30, 2022, Praxis had $165.4 million in cash, cash equivalents and marketable securities, compared to $275.9 million in cash, cash equivalents and marketable securities as of December 31, 2021. This decrease of $110.5 million primarily reflects cash used in operations of $111.3 million during the six months ended June 30, 2022. The Company's cash, cash equivalents and marketable securities as of June 30, 2022 are expected to fund operations into the first quarter of 2024.

Research and development expenses were $43.6 million for the three months ended June 30, 2022, compared to $25.7 million for the three months ended June 30, 2021. The increase in research and development expenses of $17.9 million was primarily attributable to $14.1 million in increased expenses related primarily to clinical-related spend for the Company's franchises and $4.0 million in increased personnel-related costs due to increased headcount.

General and administrative expenses were $16.8 million for the three months ended June 30, 2022, compared to $10.8 million for the three months ended June 30, 2021. The increase in general and administrative expenses of $6.0 million was primarily

attributable to $3.4 million in increased personnel-related costs due to increased headcount and $2.6 million in increased other general and administrative expenses, none of which were individually material.

Praxis reported a net loss of $60.2 million for the three months ended June 30, 2022, including $7.6 million of stock-based compensation expense, compared to $36.4 million for the three months ended June 30, 2021, including $5.4 million of stock-based compensation expense.

As of June 30, 2022, Praxis had 45.6 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 CNS disorders characterized by neuronal excitation-inhibition imbalance. Praxis is applying insights from genetic epilepsies to both rare and more prevalent neurological disorders, using our understanding of shared biological targets and circuits in the brain. Praxis has established a broad portfolio with multiple programs, including product candidates across movement disorders, epilepsy and psychiatric disorders, with three 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 expectations, plans and timing for our clinical data, the anticipated timing of our clinical trials and regulatory filings, the development of our product candidates, including the design of our clinical trials and the treatment potential of our product candidates, and the sufficiency of our cash, cash equivalents and marketable securities, and 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; 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 and Praxis' timelines for regulatory submissions; and other risks concerning Praxis' programs and operations as described in its Annual Report on Form 10-K for the year ended December 31, 2021, its Quarterly Reports on Form 10-Q 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.

PRAXIS PRECISION MEDICINES, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(Amounts in thousands)
(Unaudited)

	June 30, 2022	December 31, 2021
Assets		
Cash and cash equivalents	$ 56,039	$ 138,704
Marketable securities	109,365	137,207
Prepaid expenses and other current assets	10,176	11,498
Property and equipment, net	1,134	1,213
Operating lease right-of-use assets	3,287	3,653
Other non-current assets	416	472
Total assets	$ 180,417	$ 292,747
Liabilities and stockholders' equity		
Accounts payable	$ 11,821	$ 10,780
Accrued expenses	25,768	26,844
Operating lease liabilities	3,959	4,311
Common stock	5	5
Additional paid-in capital	585,070	567,598
Accumulated other comprehensive loss	(680)	(176)

Accumulated deficit	(445,526)	(316,615)
Total liabilities and stockholders' equity	$ 180,417	$ 292,747

PRAXIS PRECISION MEDICINES, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(Amounts in thousands, except share and per share amounts)
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	**2021**	**2022**	**2021**
Operating expenses:				
Research and development	$ 43,620	$ 25,678	$ 96,272	$ 43,607
General and administrative	16,774	10,805	32,971	20,295
Total operating expenses	60,394	36,483	129,243	63,902
Loss from operations	(60,394)	(36,483)	(129,243)	(63,902)
Other income:				
Other income, net	200	82	332	128
Total other income	200	82	332	128
Net loss	$ (60,194)	$ (36,401)	$ (128,911)	$ (63,774)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.32)	$ (0.88)	$ (2.83)	$ (1.59)
Weighted average common shares outstanding, basic and diluted	45,542,600	41,569,782	45,499,131	40,028,807

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