Prelude Therapeutics Reports Third Quarter 2024 Financial Results and Provides Corporate Update

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Presented interim data from the ongoing Phase 1 dose escalation study of PRT3789, its first-in-class IV SMARCA2 degrader, demonstrating clinical proof of concept

Initiated a Phase 1 trial for PRT7732, its first-in-class oral SMARCA2 degrader in patients with SMARCA4-mutated cancers

Presented first preclinical data from its next generation degrader antibody conjugate (Precision ADC) platform

Interim phase 1 clinical data with potentially best-in-class CDK9 inhibitor, PRT2527, in hematological malignancies to be presented at the American Society of Hematology Annual Meeting in December 2024

Current cash runway into 2026 with $153.6 million in cash, cash equivalents and marketable securities as of September 30, 2024

WILMINGTON, Del., Nov. 06, 2024 (GLOBE NEWSWIRE) -- Prelude Therapeutics Incorporated (Nasdaq: PRLD), a clinical-stage precision oncology company, today reported its financial results for the third quarter ended September 30, 2024 and provided an update on its clinical development pipeline and other corporate developments.

“Our third quarter was marked by dedicated execution and the achievement of essential milestones for our lead clinical programs targeting SMARCA2,” stated Kris Vaddi, Ph.D., Chief Executive Officer of Prelude. “We have demonstrated the first-ever clinical proof of concept with our first-in-class, highly selective IV SMARCA2 degrader, PRT3789, in patients with aggressive SMARCA4 mutated cancers including non-small cell lung cancer (NSCLC) and esophageal cancers as monotherapy. We also demonstrated an encouraging early safety profile with no overlapping toxicities in our ongoing PRT3789 combination study with docetaxel. We are focused on completing monotherapy dose escalation and rapidly enrolling combination arms to support advancement of PRT3789 into next phase of development, initially in these two cancer types.”

Dr. Vaddi continued, “Additional accomplishments for the quarter include the commencement of patient enrollment for our first-in-class, highly selective oral SMARCA2 degrader, PRT7732 in a biomarker selected phase 1 trial. With two highly differentiated SMARCA2 degraders in the clinic, we are well-positioned to build on our leadership in this novel and important therapeutic class and provide optionality for patients. We look forward to reporting our progress on both of these programs beginning early 2025.”

Dr. Vaddi also added, “Other milestones for the quarter included presentation of first preclinical data from our Precision ADC program demonstrating the potential of SMARCA2/4 degrader as a potent and effective payload on multiple antibodies, as well as acceptance of interim clinical data in hematological malignancies of our potential best-in-class CDK9 inhibitor, PRT2527 at the American Society of Hematology Meeting in December.”

Clinical Program Updates and Upcoming Milestones

PRT3789 – A first-in-class, highly selective, intravenous SMARCA2 Degrader
PRT3789 is designed to treat patients with a SMARCA4 mutation. Patients with SMARCA4-mutated cancer have a poor prognosis. This represents an area of high unmet medical need.

PRT3789 is in Phase 1 clinical development in patients with biomarker selected SMARCA4-mutated cancers. Enrollment remains on track, and the Company expects to conclude monotherapy dose escalation by year-end 2024 and identify a dose for advancement to registrational trials. In addition, enrollment of patients into back-fill cohorts enriched for NSCLC and SMARCA4 loss-of-function mutations is ongoing, as is enrollment of the combination with docetaxel cohort. The Company also initiated a Phase 2 clinical trial evaluating PRT3789 in combination with KEYTRUDA® (pembrolizumab) in patients with SMARCA4-mutated cancers, per the previously announced collaboration with Merck (known as MSD outside of the US and Canada).

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Interim Phase 1 data presented at medical congresses in Q3 2024
The Company presented the first interim clinical data updates of the Phase 1 dose escalation study of PRT3789 in SMARCA4 mutated cancers at ESMO Congress 2024 and the 36th EORTC-NCI-AACR Symposium. The presentations can be found at Publications - Prelude Therapeutics.

As reported by investigators, PRT3789 was generally safe and well-tolerated at doses tested to date. Of the 26 advanced NSCLC or esophageal patients with Class 1 (loss of function) mutations who were evaluable for efficacy, RECIST confirmed partial responses (PRs) were observed in 4 patients (2 esophageal, 2 NSCLC). Of the 9 patients with Class 1 mutations treated at doses of 283 mg or higher, two had RECIST confirmed partial responses and both were NSCLC patients. Tumor shrinkage was observed in patients with both Class 1 and Class 2 SMARCA4 mutations. Additional patients on-study demonstrated clinical benefit as measured by prolonged SD, including one advanced NSCLC patient who remains stable and on study having been treated for more than a year.

Initial observations of safety from evaluable patients in the PRT3789 plus docetaxel combination dose escalation arm of the trial were also presented. To date, PRT3789 in combination with docetaxel demonstrated an acceptable safety profile, with no dose limiting toxicities or study drug serious adverse events reported.

PRT7732 – A potent, highly selective and orally bioavailable SMARCA2 Degrader
PRT7732 is a highly selective and orally bioavailable SMARCA2 degrader. The Company initiated and enrolled our first patients in a phase 1 multi-dose escalation trial of PRT7732 (NCT06560645) in biomarker selected SMARCA4 mutated cancers.

Pfizer Ignite Collaboration
Prelude has entered into a collaboration agreement with Pfizer Ignite enabling streamlined access to Ignite services in support of Prelude's SMARCA2 degrader development programs. Per Pfizer, Ignite is a service offering providing partners access to Pfizer's significant resources, scale and expertise in developing potentially breakthrough medicines. Under the terms of the collaboration agreement, Prelude retains full ownership and global license rights to all of its programs.

Precision ADC with SMARCA2/4 dual degrader payload
Prelude is developing potent SMARCA2/4 dual degraders that robustly inhibit cancer cell growth and induce cell death across multiple cancer types.

The Company presented the first preclinical data from its Precision ADC platform at the 36th EORTC-NCI-AACR Symposium in October. The data demonstrated potent activity of a SMARCA 2/4 degrader payload when conjugated to a range of commercially available antibodies, including PSMA, TROP2, C-MET, CEACAM5, and CD33. The SMARCA2/4 degrader payload conjugated to an anti-PSMA antibody demonstrated tumor regressions and significantly better *in vivo* efficacy compared to a traditional PSMA-targeted cytotoxic ADC in xenograft models of prostate cancer at well tolerated doses. The presentation can be found at Publications - Prelude Therapeutics.

PRT2527 – A potent and highly selective CDK9 Inhibitor
PRT2527 is a potent and highly selective CDK9 inhibitor that has the potential to avoid off-target toxicities observed with other less selective CDK9 inhibitors. The Company is currently advancing PRT2527 as monotherapy in both lymphoid and myeloid hematological malignancies, and in combination with zanubrutinib in B-cell malignancies.

PRT2527 is expected to complete monotherapy dose escalation in B-cell malignancies this year. Initiation of dose escalation in myeloid malignancies occurred in the first half of 2024. Interim phase 1 clinical data with potentially best-in-class CDK9 inhibitor, PRT2527 in hematological malignancies will be presented at the American Society of Hematology Annual Meeting in December 2024.

Third Quarter 2024 Financial Results

Cash, Cash Equivalents, and Marketable securities:
Cash, cash equivalents and marketable securities as of September 30, 2024 were $153.6 million. The Company anticipates that its existing cash, cash equivalents and marketable securities will fund Prelude's operations into 2026.

Research and Development (R&D) Expenses:
For the third quarter of 2024, R&D expense increased to $29.5 million from $26.3 million for the prior year period. Included in the R&D expense for the three months ended September 30, 2024 was $3.4 million of non-cash expense related to stock-based compensation expense, including employee stock options, compared to $3.3 million for three months ended September 30, 2023. Research and development expenses increased primarily due to an increase in our chemistry, manufacturing, and controls (CMC) costs supporting our pre-clinical and clinical programs. We expect our R&D expenses to vary from quarter to quarter, primarily due to the timing of our clinical development activities.

General and Administrative (G&A) Expenses:
For the third quarter of 2024, G&A expenses increased to $7.9 million from $7.1 million for the prior year period. Included in general and administrative expenses for the three months ended September 30, 2024, was $2.5 million of non-cash expense related to stock-based compensation expense, including employee stock options, compared to $3.4 million for three months ended September 30, 2023. General and administrative expenses increased primarily due to an increase in professional fees incurred to support our research and development efforts.

Net Loss:
For the three months ended September 30, 2024, net loss was $32.3 million, or $0.43 per share compared to $30.6 million, or $0.45 per share, for the prior year period. Included in the net loss for the quarter ended September 30, 2024, was $5.9 million of non-cash expenses related to the impact of expensing share-based payments, including employee stock options, as compared to $6.7 million for the same period in 2023.

About Prelude Therapeutics

Prelude Therapeutics is a leading precision oncology company developing innovative medicines in areas of high unmet need for cancer patients. Our pipeline is comprised of several novel drug candidates including first-in-class, highly selective IV and oral SMARCA2 degraders, and a potentially best-in-class CDK9 inhibitor. We are also leveraging our expertise in targeted protein degradation to discover, develop and commercialize next generation degrader antibody conjugates (Precision ADCs) with partners. We are on a mission to extend the promise of precision medicine to every cancer patient in need. Our corporate presentation can be found at Events & Presentations - Prelude Therapeutics. For more information, visit preludetx.com.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to, anticipated discovery, preclinical and clinical development activities for Prelude's product candidates, the potential safety, efficacy, benefits and addressable market for Prelude's product candidates, the expected timeline for initial proof-of-concept data and clinical trial results for Prelude's product candidates, and the sufficiency of Prelude's cash runway into 2026. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. The words "believes," "anticipates," "estimates," "plans," "expects," "intends," "may," "could," "should," "potential," "likely," "projects," "continue," "will," "schedule," and "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are predictions based on the Company's current expectations and projections about future events and various assumptions. Although Prelude believes that the expectations reflected in such forward-looking statements are reasonable, Prelude cannot guarantee future events, results, actions, levels of activity, performance or achievements, and the timing and results of biotechnology development and potential regulatory approval is inherently uncertain. Forward-looking statements are subject to risks and uncertainties that may cause Prelude's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties related to Prelude's ability to advance its product candidates, the receipt and timing of potential regulatory designations, approvals and commercialization of product candidates, clinical trial sites and our ability to enroll eligible patients, supply chain and manufacturing facilities, Prelude's ability to maintain and recognize the benefits of certain designations received by product candidates, the timing and results of preclinical and clinical trials, Prelude's ability to fund development activities and achieve development goals, Prelude's ability to protect intellectual property, and other risks and uncertainties described under the heading "Risk Factors" in Prelude's Annual Report on Form 10-K for the year ended December 31, 2023, its Quarterly Reports on Form 10-Q and other documents that Prelude files from time to time with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this press release, and Prelude undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof, except as may be required by law.

PRELUDE THERAPEUTICS INCORPORATED

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(UNAUDITED)

(in thousands, except share and per share data)	Three Months Ended September 30, 2024	2023
Revenue from license agreement	$ 3,000	$ —
Operating expenses		
Research and development	29,457	26,261
General and administrative	7,919	7,124
Total operating expenses	37,376	33,385
Loss from operations	(34,376)	(33,385)
Other income, net	2,105	2,777
Net loss	$ (32,271)	$ (30,608)
Per share information:		
Net loss per share of common stock, basic and diluted	$ (0.43)	$ (0.45)
Weighted average common shares outstanding, basic and diluted	75,855,949	67,639,993
Comprehensive loss:		
Net loss	$ (32,271)	$ (30,608)
Unrealized gain (loss) on marketable securities, net of tax	457	106
Comprehensive loss	$ (31,814)	$ (30,502)

PRELUDE THERAPEUTICS INCORPORATED

BALANCE SHEETS

(in thousands, except share data)	September 30, 2024	December 31, 2023
Assets	(unaudited)	
Current assets:		
Cash and cash equivalents	$ 11,134	$ 25,291
Marketable securities	142,492	207,644
Prepaid expenses and other current assets	2,761	2,654
Total current assets	156,387	235,589
Restricted cash	4,044	4,044
Property and equipment, net	7,202	7,325
Operating lease right-of-use asset	29,182	30,412
Other assets	405	295
Total assets	$ 197,220	$ 277,665
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 5,921	$ 4,580
Accrued expenses and other current liabilities	13,579	15,768
Operating lease liability	2,365	1,481
Finance lease liability	359	—
Total current liabilities	22,224	21,829
Other liabilities	3,153	3,339
Operating lease liability	15,412	15,407
Total liabilities	40,789	40,575
Commitments		
Stockholders' equity:		
Voting common stock, $0.0001 par value: 487,149,741 shares authorized; 42,178,012 and 42,063,995 shares issued and outstanding at September 30, 2024 and December 31, 2023, respectively	4	4
Non-voting common stock, $0.0001 par value: 12,850,259 shares authorized; 12,850,259 shares issued and outstanding at both September 30, 2024 and December 31, 2023	1	1
Additional paid-in capital	711,091	693,252
Accumulated other comprehensive income	167	223
Accumulated deficit	(554,832)	(456,390)
Total stockholders' equity	156,431	237,090
Total liabilities and stockholders' equity	$ 197,220	$ 277,665

Investor Contact:
Robert A. Doody, Jr.
Senior Vice President, Investor Relations
Prelude Therapeutics Incorporated
484.639.7235
rdoody@preludetx.com