Prelude Therapeutics Announces Second Quarter 2023 Financial Results and Provides Corporate Update

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Four lead programs on track to deliver clinical data and to inform future development plans

Recent equity financing extends cash runway into 2026, enabling advancement of Prelude's pipeline through critical milestones

WILMINGTON, Del., Aug. 03, 2023 (GLOBE NEWSWIRE) -- Prelude Therapeutics Incorporated (Nasdaq: PRLD), a clinical-stage precision oncology company, today reported financial results for the second quarter ended June 30, 2023, and provided a corporate update.

Kris Vaddi, Ph.D., Chief Executive Officer of Prelude stated, "With the recent financing that extended our cash runway into 2026, we are in a strong position to advance our diverse pipeline of potentially best and/or first-in-class compounds to address the needs of patients with certain underserved cancers. Our focus remains on generating critical data for each of our molecules to make key strategic decisions. As disclosed recently, and based on additional data generated in this quarter, PRT2527 (CDK9 inhibitor) and PRT1419 (MCL1 inhibitor) demonstrated differentiated clinical safety profiles and strong target inhibition and are continuing to enroll patients with hematological malignancies, which is where we see the best opportunities for these molecules."

"Our first-in-class selective SMARCA2 degrader, PRT3789, and next generation CDK4/6 inhibitor, PRT3645, are progressing well in Phase 1 and are on track to reach confirmation doses in the first half of 2024 and by year end 2023, respectively," added Dr. Vaddi. "Based on meaningful progress made in the first half of the year, we look forward to sharing updates and clarity around strategic prioritization of our pipeline in the coming months."

Pipeline Updates

PRT2527- CDK9 Inhibitor Program
The Company believes its highly selective CDK9 inhibitor, PRT2527, has the potential to avoid off-target toxicities, achieve substantial clinical activity and become the best-in-class CDK9 inhibitor, making it amenable for combination with other therapies.

PRT2527 has completed a Phase 1 multi-dose escalation study (NCT05159518) in patients with solid tumors. In this trial, PRT2527 was shown to achieve high levels of target inhibition and the potential to be better tolerated than existing CDK9 inhibitors, specifically, manageable neutropenia and an absence of meaningful gastrointestinal events or hepatotoxicity. *

*AACR2023 Poster Presentation

A Phase 1 multi-dose escalation study (NCT05665530) is currently ongoing in hematologic malignancies. Patient recruitment for hematological clinical trials in the US is highly competitive and this trial has recently been expanded to include global sites to support patient recruitment.

The Company's objective is to establish a biologically active confirmation dose by Q1 2024. As part of this Phase 1 multi-dose escalation trial, the Company intends to expand the Phase 1 clinical trial and evaluate PRT2527 in combination with zanubrutinib.

Potential indications for PRT2527 include aggressive B-cell lymphoma subtypes, mantle cell lymphoma (MCL), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) including Richter syndrome, and T-cell lymphoma subtypes.

The Company intends to provide a program update by year end on the CDK9 inhibitor program and present initial results at a future scientific meeting.

PRT1419- MCL1 Inhibitor Program
PRT1419 is a potent and selective MCL1 inhibitor. With its optimized PK/PD profile, the Company believes PRT1419 has the potential to achieve greater target engagement and provide patients with better clinical outcomes as well as improved safety and tolerability, as compared to other MCL1 inhibitors in development.

PRT1419 has completed a Phase 1 multi-dose escalation study (NCT04837677) in patients with solid tumors. In this study, PRT1419 demonstrated an acceptable safety and tolerability profile in patients with advanced and metastatic solid tumors. No cardiac toxicity was observed. Pharmacokinetics/pharmacodynamics and safety data in the 80 mg/m2 QW dose cohort support further evaluation of this dose in future studies.

A Phase 1 multi-dose escalation clinical trial of PRT1419 in patients with hematologic malignancies is ongoing (NCT05107856). In this trial, PRT1419 is being evaluated as monotherapy for myeloid malignancies and in combination with azacitidine or venetoclax for patients with relapsed/refractory myeloid or B-cell malignancies.

The Company will provide a clinical update on PRT1419 by year end.

PRT3645- Next Generation CDK4/6 Inhibitor Program
PRT3645 is a highly potent and selective next generation CDK4/6 inhibitor with the potential to provide improved safety and tolerability outcomes and higher, more effective brain and tissue penetration than current CDK4/6 inhibitors.

In preclinical models *in vivo*, PRT3645 has been shown to be efficacious in multiple cancers as monotherapy as well as when combined with KRAS inhibitors, MEK inhibitors and with a brain penetrant HER2 receptor kinase inhibitor. Additionally, oral administration of PRT3645 has been shown to induce tumor regressions in preclinical models that are resistant to currently approved CDK4/6 inhibitors. Together, these data suggest that PRT3645 may extend the benefit of CDK4/6 inhibition beyond HR+ breast cancer.

A Phase 1 multi-dose escalation clinical trial of PRT3645 (NCT05538572) is underway and the Company expects to reach a biologically active dose

confirmation in Q4 2023.

Potential indications for PRT3645 in combination with other therapies, in addition to breast cancer with or without brain metastases, include endometrial, sarcomas, glioblastomas, non-small cell lung cancer, head and neck cancers.

The Company intends to provide a program update by year end and present initial results at a future scientific meeting.

PRT3789- SMARCA2 Targeted Protein Degrader Program
PRT3789 is a first-in-class highly selective degrader of SMARCA2 protein, which along with SMARCA4 controls gene regulation through chromatin remodeling. Cancer cells with SMARCA4 mutations are dependent on SMARCA2 for their growth and survival and selectively degrading SMARCA2 induces cell death in cancer cells while sparing normal cells. PRT3789 is efficacious and well tolerated in preclinical models of SMARCA4 deleted/mutated cancers as monotherapy and in combination with standards of care. The Company believes a selective SMARCA2 degrader has the potential to be of benefit in up to 70,000 US/EU cancer patients with the SMARCA4 mutation.

Patients with SMARCA4 mutations or deletions may have poor clinical outcomes and limited treatment options. Therefore, mutated, or deleted SMARCA4 cancers provides a potential biomarker to select those patients most likely to respond to treatment with a highly selective SMARCA2 degrader.

A Phase 1 multi-dose escalation clinical trial of PRT3789 is ongoing (NCT05639751) in biomarker selected SMARCA4 mutated cancers. The Company intends to evaluate PRT3789 as monotherapy as well as in combination.

The Company intends to provide a program update by year end and expects to reach confirmation dose in the first half of 2024.

SMARCA2- Oral Program
The Company has also recently nominated a new chemical entity as a potent, orally bioavailable and highly selective SMARCA2 degrader candidate (>1000x over SMARCA4) and intends to file an IND early in 2024.

Second Quarter 2023 Financial Results

Cash, Cash Equivalents and Marketable Securities: In May 2023, the Company completed a public offering of common stock, raising gross proceeds of $113.0 million before deducting underwriting discounts, commissions and offering expenses. Net proceeds received, $110.4 million, will be focused on the continued development and expansion of the Company's product pipeline.

Cash, cash equivalents, and marketable securities as of June 30, 2023, were $255.0 million. Prelude anticipates that its existing cash, cash equivalents and marketable securities will fund the Company's operations into 2026.

Research and Development (R&D) Expenses: For the second quarter of 2023, R&D expense increased to $25.0 million from $21.3 million for the prior year period. Research and development expenses increased primarily due to the timing of our clinical research 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 second quarter of 2023, G&A expenses decreased to $7.4 million from $8.2 million for the prior year period. General and administrative expenses decreased reflecting the Company's careful management of its G&A expenses.

Net Loss: For the three months ended June 30, 2023, net loss was $30.4 million, or $0.54 per share compared to $27.4 million, or $0.58 per share, for the prior year period. Included in the net loss for the quarter ended June 30, 2023, was $6.7 million of non-cash expense related to the impact of expensing share-based payments, including employee stock options, as compared to $6.0 million for the same period in 2022.

About Prelude Therapeutics

Prelude Therapeutics is a clinical-stage precision oncology company developing innovative drug candidates targeting critical cancer cell pathways. The Company's diverse pipeline is comprised of highly differentiated, potentially best-in-class proprietary small molecule compounds aimed at addressing clinically validated pathways for cancers with selectable underserved patients. Prelude's pipeline includes four candidates currently in clinical development: PRT1419, a potent, selective inhibitor of MCL1, PRT2527, a potent and highly selective CDK9 inhibitor, PRT3645 a next generation CDK4/6 inhibitor**,** PRT3789 an IV administered, potent and highly selective SMARCA2 degrader, and a preclinical oral candidate targeting SMARCA2.

For more information, visit our website and follow us on LinkedIn and Twitter.

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, the timing and/or announcements relating to the reporting of expected findings for PRT1419, PRT2527, PRT3645, PRT3789, and its preclinical oral SMARCA2 degrader, the potential benefits of Prelude's product candidates and platform, and the sufficiency of cash and cash equivalents to fund operating expenses and capital expenditures into 2026. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. 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 documents 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.

PRELUDE THERAPEUTICS INCORPORATED

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(UNAUDITED)

(in thousands, except share and per share data)	Three Months Ended June 30, 2023	2022
Operating expenses:		
Research and development	$ 24,966	$ 21,310
General and administrative	7,432	8,151
Total operating expenses	32,398	29,461
Loss from operations	(32,398)	(29,461)
Other income, net	1,967	2,087
Net loss	$ (30,431)	$ (27,374)
Per share information:		
Net loss per share of common stock, basic and diluted	$ (0.54)	$ (0.58)
Weighted average common shares outstanding, basic and diluted	56,240,491	47,276,684
Comprehensive loss		
Net loss	$ (30,431)	$ (27,374)
Unrealized (loss) gain on marketable securities, net of tax	(313)	19
Comprehensive loss	$ (30,744)	$ (27,355)

PRELUDE THERAPEUTICS INCORPORATED

BALANCE SHEETS
(UNAUDITED)

(in thousands, except share data)	June 30, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 26,446	$ 30,605
Marketable securities	228,543	171,123
Prepaid expenses and other current assets	5,221	2,652
Total current assets	260,210	204,380
Restricted cash	4,044	4,044
Property and equipment, net	6,082	4,908
Right-of-use asset	918	1,792
Prepaid expenses and other non-current assets	9,357	5,376
Total assets	$ 280,611	$ 220,500
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 5,585	$ 6,777
Accrued expenses and other current liabilities	8,667	13,093
Operating lease liability	938	1,832
Total current liabilities	15,190	21,702
Other liabilities	3,361	3,361
Total liabilities	18,551	25,063
Commitments (Note 8)		
Stockholders' equity:		
Voting common stock, $0.0001 par value: 487,149,741 shares authorized; 41,958,456 and 36,496,994 shares issued and outstanding at June 30, 2023 and December 31, 2022, respectively	4	4
Non-voting common stock, $0.0001 par value: 12,850,259 shares authorized; 12,850,259 and 11,402,037 shares issued and outstanding at June 30, 2023 and December 31, 2022, respectively	1	1
Additional paid-in capital	655,473	531,682
Accumulated other comprehensive loss	(711)	(1,692)
Accumulated deficit	(392,707)	(334,558)
Total stockholders' equity	262,060	195,437
Total liabilities and stockholders' equity	$ 280,611	$ 220,500

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