Prelude Therapeutics Announces Third Quarter 2022 Financial Results and Provides Business Update

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FDA clearance of two new INDs: PRT3789 (First-in-class Selective SMARCA2 degrader) and PRT3645 (next generation CDK4/6 inhibitor)

Company to reprioritize clinical pipeline and discontinue PRMT5 program for internal development

Strong cash, cash equivalents and marketable securities of $224.0 million as of September 30, 2022, expected to fund multiple data catalysts with a runway into the fourth quarter of 2024

WILMINGTON, Del., Nov. 14, 2022 (GLOBE NEWSWIRE) -- Prelude Therapeutics Incorporated (Prelude) (Nasdaq: PRLD), a clinical-stage precision oncology company, today reported financial results for the third quarter ended September 30, 2022 and provided an update on recent clinical and development pipeline progress.

“We made meaningful advancements in the third quarter and to date in the fourth quarter, including FDA clearance for two new INDs, one for PRT3645, a next generation, brain penetrant CDK4/6 inhibitor and one for PRT3789, a novel, first-in-class selective SMARCA2 degrader. We’ve also made good progress in the clinical development of our CDK9 inhibitor, PRT2527 and PRT1419, the MCL1 inhibitor,” stated Kris Vaddi, Ph.D., Chief Executive Officer of Prelude.

“We continue to expand our highly innovative clinical pipeline. In order to focus resources on bringing compounds with the highest likelihood of success forward, we have decided to discontinue the internal development of our PRMT5 program. While PRT811 demonstrated a best-in-class safety profile and evidence of clinical activity in biomarker-selected patients with glioma and splicing mutated uveal melanoma, our prioritization reflects the high benchmark we set for clinical and regulatory success,” Dr. Vaddi added. “We are committed to delivering impactful medicines to patients and building significant and sustainable value.”

“Since joining Prelude, I have had the opportunity to critically review and to assess each program and identify clear next steps for clinical development,” said Jane Huang, M.D., President and Chief Medical Officer of Prelude. “With this prioritization, we believe we can generate proof-of-concept clinical data in the next 12 to 24 months to guide our future regulatory pathways to approval. Our CDK9 and MCL1 inhibitors are selective and potent, with potentially superior safety profiles. PRT3645 was specifically designed to be a brain penetrant CDK4/6 inhibitor and our SMARCA2 molecule is a unique, first-in-class degrader, targeting specific patient populations. I believe these programs offer the best chance to improve patient outcomes and I share our investigators’ excitement in our highly differentiated molecules.”

Recent Highlights and Upcoming Objectives

- **CDK9 Inhibitor Program**: Given the compelling clinical activity recently reported with CDK9 inhibitors, PRT2527, as a more selective compound, has the potential to be best-in-class, with a favorable toxicity profile, allowing for rapid development in combinations. The PRT2527 Phase 1 dose escalation study in solid tumors has enrolled 11 patients to date. Dose dependent increases in exposure and target engagement were observed as evidenced by MYC and MCL1 depletion to levels associated with tumor regression in preclinical models. No adverse events leading to dose reduction or discontinuation have been reported. The Company remains on track to select a recommended Phase 2 dose by year-end. Prelude will use these safety data to continue cohort expansion in solid tumors, as well as to inform and rapidly progress the hematology trial.
  - *ASH 2022: oral preclinical presentation*
  - *Session Name: 605. Molecular Pharmacology and Drug Resistance: Lymphoid Neoplasms: Targeting BH3, BTK, and CDK: PRT2527, a Novel Highly Selective Cyclin-Dependent Kinase 9 (CDK9) Inhibitor, Has Potent Anti-Leukemic Activity in Preclinical Primary Models of Human B-ALL, T-ALL, and CLL*
    - *Session Date: Saturday, December 10, 2022*
    - *Session Time: 2:00 PM - 3:30 PM*
    - *Presentation Time: 3:15 PM*
    - *Room: Ernest N. Morial Convention Center, 388-390*
  - *Present solid tumor dose escalation data at a medical conference in 1H 2023*

- *RP2D in hematological malignancies in 2H 2023*
- *Present initial clinical results for hematological malignancies at a medical conference in 2H 2023*

- **MCL1 Inhibitor Program:** To date, 26 patients have been enrolled in the PRT1419 Phase 1 solid tumor dose escalation and confirmation cohorts, including 15 patients at the recommended expansion dose of 80 mg/m^2. PRT1419 has demonstrated a differentiated profile with no cardiotoxicity observed in patients to date. Cardiovascular parameters including troponin levels and ejection fraction changes were evaluated, in addition to standard safety, pharmacokinetics and target engagement metrics. The clinical pharmacodynamic profile of PRT1419 demonstrates the desired level of target engagement, as measured by caspase activation in peripheral mononuclear cells and reduction of CD14+ monocytes to levels associated with tumor regressions in preclinical models of hematological cancers. Advancement in hematological cancers will include monotherapy expansions in CLL and NHL based on a strong rationale for MCL1 inhibition and the need for novel treatments in second line.
  - *Solid tumor data is expected to be presented at a medical conference 1H 2023*
  - *RP2D expected in hematological malignancies in 2H 2023*
  - *Hematological malignancy data expected to be presented in 2H 2023*

- **Brain Penetrant CDK4/6:** Phase 1 clinical trial is being initiated for PRT3645 in biomarker enriched patients with select tumor types including sarcomas, mesothelioma, gliomas, head and neck cancers and non-small cell lung cancer, in addition to breast cancer with or without brain metastases.
  - *Present initial clinical results at a medical conference in 2H 2023*
  - *RP2D in solid tumors in 2H 2024*

- **SMARCA2/BRM Protein Degrader Program**: Prelude received IND clearance in October for PRT3879. Prelude plans to dose the first patient in Q1 2023. SMARCA2 inhibition has the greatest potential in patients with SMARCA4 deficient cancers, including up to 10% of all non-small cell lung cancers.
  - *Provide Clinical update 2H 2023*

- **PRMT5 Programs:** In the Phase 1 trials for PRT543 and PRT811, both molecules were generally well tolerated. In the PRT811 clinical trial, a total of 82 patients across multiple tumor types were enrolled in dose escalation and expansion, of whom 57 had glioma or uveal melanoma. Out of 38 glioma patients (16 IDH+ and 22 IDH-), two complete responses were observed in IDH+ glioma. These responses remain ongoing for 62 and 21 weeks, respectively. In addition, out of 19 uveal melanoma patients (8 SPLC+ and 11 SPLC-), one confirmed PR (duration of response of 42 weeks) and a second ongoing unconfirmed PR were observed, both in patients who were SPLC+. The most common adverse events of any grade, with an incidence of >20% were nausea (57.3%), vomiting (41.5%) fatigue (31.7%), constipation (25.6%), and thrombocytopenia (24.4%), and were predominantly grade 1-2. The most common adverse events (grade ≥3), occurring >5% were thrombocytopenia (9.76%), anemia (7.32%), and fatigue (7.32%). Full results from the two clinical trials will be shared in the first half of 2023.

Third Quarter 2022 Financial Results

Cash, Cash Equivalents and Marketable Securities: Cash, cash equivalents, and marketable securities as of September 30, 2022, were $224.0 million. Prelude anticipates that its existing cash, cash equivalents and marketable securities will be sufficient to fund Prelude's operations into the fourth quarter of 2024.

Research and Development (R&D) Expenses: For the third quarter of 2022, R&D expenses increased to $22.9 million for the three months ended September 30, 2022, from $22.7 million for the three months ended September 30, 2021. Included in research and development expenses for the quarter ending September 30, 2022, was $3.2 million of non-cash expense related to stock-based compensation expense, including employee stock options, compared to $3.3 million for the three months ended September 30, 2021. Research and development expenses remain steady as our clinical pipeline advances into clinical trials. We expect our research and development 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 2022, G&A expenses decreased to $7.5 million for the three months ended September 30, 2022, from $8.1 million for the three months ended September 30, 2021. Included in the general and administrative expenses for the quarter ended September 30, 2022, was $3.2 million of non-cash expense related to stock-based compensation expense, including employee stock options, as compared to $3.8 million for the same period in 2021. The decrease in general and administrative expenses was primarily due to non-cash stock-based compensation expense and prudent management of expenses.

Net Loss: For the three months ended September 30, 2022, net loss was $30.0 million, or $0.63 per share of common stock, basic and diluted compared to $30.7 million, or $0.66 per share, respectively, for the prior year period. Included in the net loss for the quarter ended September 30, 2022, was $6.4 million of non-cash expense related to the impact of expensing share-based payments, including employee stock options, as compared to $7.1 million for the prior year period.

About Prelude

Prelude is a clinical-stage precision oncology company developing innovative drug candidates targeting critical cancer cell pathways. Prelude'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 brain penetrant CDK4/6 inhibitor, and PRT3879 a first-in-class SMARCA2/BRM protein degrader.

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, timing of availability and announcements of clinical results for PRT1419 and PRT3645, the timing of reporting expected findings related to PRT1419, PRT2527, PRT2645 and PRT3789, 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 the fourth quarter of 2024. 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, the impact of the COVID-19 pandemic on Prelude's business, clinical trial sites, 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)

	Three Months Ended September 30,	
(in thousands, except share and per share data)	**2022**	**2021**
Operating expenses:		
Research and development	$ 22,889	$ 22,721
General and administrative	7,517	8,115
Total operating expenses	30,406	30,836
Loss from operations	(30,406)	(30,836)
Other income, net	448	149
Net loss	$ (29,958)	$ (30,687)
Per share information:		
Net loss per share of common stock, basic and diluted	$ (0.63)	$ (0.66)
Weighted average common shares outstanding, basic and diluted	47,449,811	46,330,794
Comprehensive loss		
Net loss	$ (29,958)	$ (30,687)
Unrealized gain (loss) on marketable securities, net of tax	(69)	(176)
Comprehensive loss	$ (30,027)	$ (30,863)

PRELUDE THERAPEUTICS INCORPORATED
BALANCE SHEETS
(UNAUDITED)

(in thousands, except share data)	**September 30,**	**December 31,**

	2022	2021
Assets		
Current assets:		
Cash and cash equivalents	$ 52,022	$ 31,828
Marketable securities	172,021	259,405
Prepaid expenses and other current assets	2,850	3,882
Total current assets	226,893	295,115
Restricted cash	4,044	4,044
Property and equipment, net	5,110	3,929
Right-of-use asset	1,354	1,707
Other assets	4,926	303
Total assets	$ 242,327	$ 305,098
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 10,250	$ 7,840
Accrued expenses and other current liabilities	9,922	9,621
Operating lease liability	1,388	1,740
Total current liabilities	21,560	19,201
Other liabilities	3,360	—
Total liabilities	24,920	19,201
Commitments		
Stockholders' equity:		
Voting common stock, $0.0001 par value: 487,149,741 shares authorized; 36,444,776 and 36,200,299 shares issued and outstanding at September 30, 2022 and December 31, 2021, respectively	4	4
Non-voting common stock, $0.0001 par value; 12,850,259 shares authorized; 11,402,037 and 11,402,037 shares issued and outstanding at September 30, 2022 and December 31, 2021, respectively	1	1
Additional paid-in capital	525,682	505,723
Accumulated other comprehensive income (loss)	(2,363)	(711)
Accumulated deficit	(305,917)	(219,120)
Total stockholders' equity	217,407	285,897
Total liabilities and stockholders' equity	$ 242,327	$ 305,098

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