Prelude Therapeutics Reports Full Year 2022 Financial Results and Provides Corporate Update

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Four differentiated clinical compounds progressing through Phase 1 towards key data milestones

Eight abstracts accepted for presentation at the 2023 American Association for Cancer Research (AACR) Annual Meeting

Cash balance of $201.7 million as of December 31, 2022; runway remains unchanged through Q4 2024

WILMINGTON, Del., March 15, 2023 (GLOBE NEWSWIRE) -- Prelude Therapeutics Incorporated (Nasdaq: PRLD), a clinical-stage precision oncology company, today reported its financial results for the fiscal year ended December 31, 2022, and provided a corporate update.

“We made considerable progress in 2022, including the filing and acceptance of two new INDs for our next generation CDK4/6 inhibitor and our first-in-class, highly selective SMARCA2 degrader. Our current clinical pipeline consists of four differentiated and internally discovered molecules that effectively target and block key oncogenic pathways in both hematological malignancies and solid tumors. Prelude’s highly productive internal discovery engine continues to deliver novel molecules across multiple therapeutic classes, including significant advances in our research efforts focused on identifying an orally available SMARCA2 degrader,” **stated Kris Vaddi, Ph.D., Chief Executive Officer of Prelude**.

Jane Huang, M.D., President and Chief Medical Officer of Prelude stated, “Prelude's six preclinical and two clinical abstracts accepted for presentation at the upcoming AACR Annual Meeting reflect the productivity and success of our research and development efforts. Initial data from PRT2527 and PRT1419 demonstrate encouraging safety, favorable pharmacokinetic and pharmacodynamic profiles in solid tumors, and support continued advancement in hematological cancers. Looking ahead, our top priority for 2023 is to efficiently advance these compounds forward into proof-of-concept clinical studies and determine appropriate next steps for each program.”

“Our recently announced collaboration with BeiGene reflects our commitment to maximize the therapeutic value of combining our highly selective and potent CDK9 inhibitor, PRT2527, with BTK inhibitors in hematologic malignancies,” added Dr. Huang.

Program Updates and Upcoming Milestones

PRT2527- CDK9 Inhibitor Program
PRT2527 is a potent and selective small molecule that has the potential to avoid off target toxicity and achieve higher clinical activity than other CDK9 programs currently in development. The Company is currently advancing PRT2527 as monotherapy in both solid and hematological indications. The Company also intends to pursue the clinically validated approach of combining PRT2527 with approved BTK inhibitors, beginning with its recently announced clinical collaboration with BeiGene.

Key 2023 objectives for this program include:

- *Present solid tumor safety dose escalation data at AACR 2023*
- *Determine RP2D in hematological malignancies in 2H 2023*
- *Present initial clinical results for hematological malignancies at a medical conference in 2H 2023*

PRT1419- MCL1 Inhibitor Program
Based on the Phase 1 dose escalation study in solid tumors, and safety measured by troponin levels and changes in ejection fraction, the Company is now advancing PRT1419 in hematologic malignancies as monotherapy. The Company also plans to study PRT1419 in combination with venetoclax and in combination with azacytidine.

Key 2023 objectives for this program include:

- *Solid tumor safety data to be presented at AACR 2023*
- *RP2D expected in hematological malignancies in 2H 2023*
- *Hematological malignancy data expected to be presented in 2H 2023*

PRT3645-Next Generation CDK4/6 Inhibitor Program
PRT3645 is a highly selective and differentiated CDK4/6 inhibitor. PRT3645 is a CDK4 biased compound with tissue and brain penetration qualities, and has potential in multiple indications including gliomas, head and neck cancers and non-small cell lung cancer, in addition to HR+/HER2- and HR+/HER2+ breast cancers.

Key 2023 objective includes:

- *Present initial Phase 1 clinical results at a medical conference in 2H 2023*

SMARCA2 Targeted Protein Degrader Program
PRT3789 is an IV administered, potent and highly selective SMARCA2 degrader. It is designed to achieve the requisite high selectivity for SMARCA2 over the isoform, SMARCA4, through a targeted protein degrader approach. PRT3789 is a first-in-class SMARCA2 candidate and is currently in Phase 1 clinical development in biomarker selected SMARCA4 mutant patients.

Prelude's discovery team has also identified orally bioavailable SMARCA2 degraders.

Key objectives include:

- *Provide Clinical update on PRT3789 2H 2023*
- *Advance an oral SMARCA2 degrader for investigational new drug (IND) submission in 1H 2024*

Upcoming presentations

The following clinical abstracts will be presented at AACR 2023:

1. **Title: A phase 1, open-label, dose-escalation study of PRT1419, a selective induced myeloid leukemia cell differentiation protein (MCL-1) inhibitor, in patients (pts) with advanced/metastatic solid tumors**.
   Presenter: Gerald Falchook
   - Session Title: First-in-Human Phase I Clinical Trials 2
   - Session Date and Time: Tuesday Apr 18, 2023, 9:00 AM - 12:30 PM
   - Location: Poster Section 45
   - Poster Board Number: 4
   - Abstract Presentation Number: CT172
2. **Title: A phase 1, open-label, multicenter, dose-escalation study of PRT2527, a cyclin-dependent kinase 9 (CDK9) inhibitor, in adult patients (pts) with advanced solid tumors**.
   Presenter: Jason Henry
   - Session Title: First-in-Human Phase I Clinical Trials 2
   - Session Date and Time: Tuesday Apr 18, 2023 9:00 AM - 12:30 PM
   - Location: Poster Section 45
   - Poster Board Number: 5
   - Abstract Presentation Number: CT173

The following preclinical abstracts will be presented at AACR 2023:

1. **Title: SMARCA2 (BRM) degraders promote differentiation and inhibit proliferation in AML models**
   Presenter: Anjana Agarwal
   - Session Category: Experimental and Molecular Therapeutics
   - Session Title: New Therapeutic Targeted Agents
   - Session Date and Time: Monday Apr 17, 2023 9:00 AM - 12:30 PM
   - Location: Section 16
   - Poster Board Number: 17
   - Abstract Presentation Number: 1594
2. **Title: Development of pharmacodynamic assays for quantifying SMARCA2 protein degradation and target gene expression in response to a SMARCA2 degrader (PRT3789)**
   Presenter: Andrew Moore
   - Session Category: Experimental and Molecular Therapeutics
   - Session Title: Pharmacokinetics, Pharmacodynamics, and Molecular Pharmacology
   - Session Date and Time: Monday Apr 17, 2023 1:30 PM - 5:00 PM
   - Location: Section 18

- Poster Board Number: 15
- Abstract Presentation Number: 2792

3. **Title: Combination therapy with selective SMARCA2 (BRM) degraders for treatment of SMARCA4 (BRG1)-deficient cancers**
   Presenter: Michael Hulse
   - Session Category: Experimental and Molecular Therapeutics
   - Session Title: Epigenetics
   - Session Date and Time: Wednesday Apr 19, 2023 9:00 AM - 12:30 PM
   - Location: Section 20
   - Poster Board Number: 8
   - Abstract Presentation Number: 6270
4. **Title: The brain penetrant CDK4/6 Inhibitor, PRT3645, is highly effective in combination with other targeted therapies in preclinical models of NSCLC and HER2-positive breast cancer**
   Presenter: Yue Zou
   - Session Category: Molecular/Cellular Biology and Genetics
   - Session Title: Cyclin-dependent Kinases and Cyclin-dependent Kinase Inhibitors
   - Session Date and Time: Wednesday Apr 19, 2023 9:00 AM - 12:30 PM
   - Location: Section 9
   - Poster Board Number: 2
   - Abstract Presentation Number: 5973
5. **Title: MCL1 inhibitor PRT1419 demonstrates anti-tumor activity in PBRM1-altered clear cell renal cancer and synergizes with standard of care agents**
   Presenter: Norman Fultang
   - Session Category: Experimental and Molecular Therapeutics
   - Session Title: Cell Death Pathways and Treatment / Molecular Classification of Tumors for Diagnostics, Prognostics, and Therapeutic Outcomes
   - Session Date and Time: Wednesday Apr 19, 2023 9:00 AM - 12:30 PM
   - Location: Section 16
   - Poster Board Number: 9
   - Abstract Presentation Number: 6147
6. **Title: Selective and orally bioavailable SMARCA2 targeted degraders induce synthetic lethality in SMARCA4- deficient solid tumor**
   Presenter: Koichi Ito
   - Session Category**:** Experimental and Molecular Therapeutics
   - Session Title: Epigenetics
   - Session Date and Time: Wednesday Apr 19, 2023 9:00 AM - 12:30 PM
   - Location: Section 20
   - Poster Board Number: 15
   - Abstract Presentation Number: 6277

Corporate Update

On February 20, 2023, Bryant D. Lim, Esq., joined Prelude Therapeutics as Chief Legal Officer and Corporate Secretary. He has more than 20 years of experience in pharma and biotech, with expertise in business development, regulatory matters, fundraising and SEC reporting. Kris Vaddi, Ph.D. commented, “We are excited to welcome Bryant to Prelude and expand our leadership team to include his relevant expertise. Bryant is an excellent addition, helping us to move forward in our growth as a Company.”

Full Year 2022 Financial Results

- **Cash and Cash Equivalents:** Cash and cash equivalents as of December 31, 2022 were $201.7 million. Following Prelude’s recently announced program prioritization initiatives, the Company has extended its cash guidance and anticipates that its existing cash, cash

equivalents and marketable securities will fund Prelude's operations through the fourth quarter of 2024.

- **Research and Development (R&D) Expenses**: R&D expenses for the year ended December 31, 2022 increased $6.1 million to $92.9 million compared to $86.8 million for the year ended December 31, 2021. Included in research and development expenses for the year ended December 31, 2022, was $11.5 million of non-cash expense related to stock-based compensation expense, including employee stock options, compared to $9.5 million for the year ended December 31, 2021. The increase in research and development expense was primarily due to an increase in discovery-stage program expenses and from the growth and advancement of our clinical pipeline and an increase in non-cash stock-based compensation expense.
- **General and Administrative (G&A) Expenses**: G&A expenses for the year ended December 31, 2022 increased by $3.7 million to $30.7 million compared to $27.0 million for the year ended December 31, 2021. Included in the general and administrative expenses for the year ended December 31, 2022, was $13.6 million of non-cash expense related to stock-based compensation expense, including employee stock options, as compared to $11.5 million for the same period in 2021. The increase in general and administrative expense was primarily due to an increase in non-cash stock-based compensation expense.
- **Net Loss:** Net loss for the year ended December 31, 2022 was $115.4 million or $2.44 per share, compared with a net loss of $111.7 million, or $2.43 per share for the year ended December 31, 2021.

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**,** and PRT3789 an IV administered, potent and highly selective SMARCA2 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 PRT2527 and PRT1419, the timing of reporting expected findings related to PRT1419, PRT2527, PRT3645 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 through 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

	Year ended December 31,	
(in thousands, except share and per share data)	**2022**	**2021**
Operating expenses:		
Research and development	$ 92,889	$ 86,778
General and administrative	30,651	26,957
Total operating expenses	123,540	113,735
Loss from operations	(123,540)	(113,735)
Other income, net	8,102	2,041
Net loss	$ (115,438)	$ (111,694)
Per share information:		

Net loss per share of common stock, basic and diluted	$ (2.44)	$ (2.43)
Weighted average common shares outstanding, basic and diluted	47,371,589	46,049,763
Comprehensive loss		
Net loss	$ (115,438)	$ (111,694)
Unrealized gain (loss) on marketable securities, net of tax	(981)	(711)
Comprehensive loss	$ (116,419)	$ (112,405)

PRELUDE THERAPEUTICS INCORPORATED
BALANCE SHEETS

	December 31,	
(in thousands, except share and per share data)	**2022**	**2021**
Assets		
Current assets:		
Cash and cash equivalents	$ 30,605	$ 31,828
Marketable securities	171,123	259,405
Prepaid expenses and other current assets	2,652	3,882
Total current assets	204,380	295,115
Restricted cash	4,044	4,044
Property and equipment, net	4,908	3,929
Right-of-use asset	1,792	1,707
Other assets	5,376	303
Total assets	$ 220,500	$ 305,098
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 6,777	$ 7,840
Accrued expenses and other current liabilities	13,093	9,621
Operating lease liability	1,832	1,740
Total current liabilities	21,702	19,201
Other liabilities	3,361	-
Total liabilities	25,063	19,201
Commitments		
Stockholders' equity:		
Voting common stock, $0.0001 par value: 487,149,741 shares authorized; 36,496,994 and 36,200,299 shares issued and outstanding at December 31, 2022 and 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 December 31, 2022 and 2021, respectively	1	1
Additional paid-in capital	531,682	505,723
Accumulated other comprehensive income (loss)	(1,692)	(711)
Accumulated deficit	(334,558)	(219,120)
Total stockholders' equity	195,437	285,897
Total liabilities and stockholders' equity	$ 220,500	$ 305,098

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