Prelude Therapeutics Reports Full Year 2024 Financial Results and Provides Program Outlook for 2025

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PRT3789 has demonstrated clinical proof-of-concept that selectively degrading SMARCA2 is generally safe and has monotherapy anti-tumor activity in patients with SMARCA4-deficient, non-small cell lung (NSCLC), gastric and esophageal cancer

PRT3789 monotherapy dose escalation enrollment is nearing completion and dose escalation in combination with docetaxel continues with plans to present additional results from both cohorts in the second half of 2025

Enrollment into the Phase 1 study of Prelude's once daily, oral SMARCA2 degrader, PRT7732 is on track and an interim data update is anticipated in the second half of 2025

Current cash runway into second quarter of 2026 with $133.6 million in cash, cash equivalents and marketable securities as of December 31, 2024

WILMINGTON, Del., March 10, 2025 (GLOBE NEWSWIRE) -- Prelude Therapeutics Incorporated (Nasdaq: PRLD), a clinical-stage precision oncology company, today reported its financial results for the full year and fourth quarter ended December 31, 2024 and provided an update on its clinical development pipeline and other corporate developments.

"2024 was a productive year for Prelude highlighted by our efforts to advance the first ever highly selective SMARCA2 degraders to treat cancer patients who harbor SMARCA4 deleterious mutations," stated Kris Vaddi, Ph.D., Chief Executive Officer of Prelude. "These patients have a very poor clinical prognosis and are faced with limited treatment options. Through our development efforts to date with both monotherapy and combination approaches with PRT3789, we were the first to establish that selectively targeting SMARCA2 in patients with SMARCA4-deficient cancers could represent an important new class of therapy. Our SMARCA2 degraders appear generally safe and well-tolerated in clinical trials and have anti-tumor activity in several types of SMARCA4-deficient cancers."

Continued Vaddi, "We look forward to sharing data throughout the year both from our ongoing dose escalation and combination studies with PRT3789, and the first clinical data from our ongoing clinical trial of our once-daily oral SMARCA2 degrader, PRT7732. Lastly, our research and development organization was incredibly productive throughout 2024 continuing our mission to deliver new precision oncology medicines for patients with significant unmet need. We anticipate providing an update on our emerging discovery pipeline in the first half of 2025."

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, a particularly aggressive form of the disease, have a very poor clinical prognosis. For example, fewer than 10% of patients with advanced stage, SMARCA4-mutated NSCLC are expected to respond to standard of care chemotherapy and are not eligible for other targeted therapies. We believe that this represents an area of high unmet medical need.

PRT3789 is in Phase 1 clinical development in patients with biomarker selected SMARCA4-mutated cancers. The Company is nearing conclusion of monotherapy dose escalation which is now at the 665 mg once weekly IV dose and identifying dose(s) for advancement to any potential future trials. In addition, enrollment of patients in dose escalation in the combination of PRT3789 with docetaxel is ongoing.

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 the 2025 Japanese Society of Medical Oncology Annual Meeting
The Company presented an encore oral presentation titled: PRT3789, a First-in-Class Intravenous SMARCA2 Degrader, in Advanced Solid Tumors with a SMARCA4 Mutation: Phase 1 Trial at the 2025 Japanese Society of Medical Oncology Annual Meeting on March 8, 2025. The presentation 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 32 advanced NSCLC or esophageal patients with Class 1 (loss of function) mutations who were treated with monotherapy (all doses) and evaluable for efficacy as of the November 30, 2024 data cutoff, RECIST confirmed partial responses (PRs) were observed in 5 patients (2 esophageal, 2 NSCLC, 1 gastric).

Of the 13 patients with Class 1 mutations treated at doses of 283 mg or higher, 3 had RECIST confirmed partial responses (2 NSCLC, 1 gastric). 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 on study for more than a year.

Initial observations of safety from evaluable patients in the PRT3789 plus docetaxel combination dose escalation arm of the trial through the first three cohorts (500 mg + docetaxel) were also presented. To date, PRT3789 in combination with docetaxel has demonstrated an acceptable safety profile.

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. The Company expects to provide an interim data update in the second half of 2025.

Precision ADCs 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 as payloads for precision ADCs. 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 SMARCA2/4 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 (MMAF) 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 presented interim phase 1 results of the dose-escalation study as part of a poster session at the 66th American Society of Hematology Annual Meeting (ASH) in the fourth quarter of 2024. PRT2527 demonstrated activity across a range of relapsed/refractory lymphoid malignancies, including patients who received prior CAR-T therapy. The presentation can be found at Publications - Prelude Therapeutics.

The Company also announced that it intends to seek a partner for any future continued advancement of PRT2527, as a result of the Company's strategic focus on the SMARCA2 degrader development program.

Corporate Updates
In February 2025, the Company named Bryant D. Lim as the Company's permanent Chief Financial Officer. Mr. Lim has been serving as interim Chief Financial Officer since April of 2024 in addition to his role as Chief Legal Officer and Corporate Secretary.

Upcoming Investor Conference
The Company will participate in the Barclays 27th Annual Global Healthcare Conference taking place in Miami, FL. On Tuesday, March 11, 2025 at 12:30 PM ET, Kris Vaddi, Ph.D., Chief Executive Officer, and Jane Huang, M.D., President and Chief Medical Officer, and Bryant Lim, Chief Financial Officer will participate in a fireside chat.

A live webcast of the fireside chat can be accessed here and on the Company's website under Events and Presentations. The recording will be archived and available on the Company's website for 90 days.

Full Year 2024 Financial Results

Cash, Cash Equivalents, and Marketable securities:
Cash, cash equivalents and marketable securities as of December 31, 2024 were $133.6 million. The Company anticipates that its existing cash, cash equivalents and marketable securities will fund Prelude's operations into the second quarter of 2026.

Research and Development (R&D) Expenses:
For the year ended December 31, 2024, R&D expense increased to $118.0 million from $103.4 million for the prior year period. Included in the R&D expense for the year ended December 31, 2024 was $12.1 million of non-cash expense related to stock-based compensation expense, including employee stock options, compared to $12.6 million for year ended December 31, 2023. Research and development expenses increased due to a higher number of patients enrolled in clinical trials during 2024 driving an increase in related costs, such as chemistry, manufacturing and controls ("CMC") expenses, to support the trials. Research and development expenses may fluctuate from period to period depending upon the stage of certain projects and the level of preclinical and clinical trial-related activities.

General and Administrative (G&A) Expenses:
For the year ended December 31, 2024, G&A expenses decreased to $28.7 million from $28.9 million for the prior year period. Included in general and administrative expenses for the year ended December 31, 2024, was $9.2 million of non-cash expense related to stock-based compensation expense, including employee stock options, compared to $13.0 million for year ended December 31, 2023. The decrease in general and administrative expenses was primarily due to a decrease in stock-based compensation, offset by an increase in professional fees incurred to support our research and development efforts.

Net Loss:
For the year ended December 31, 2024, net loss was $127.2 million, or $1.68 per share compared to $121.8 million, or $2.02 per share, for the prior year period. Included in the net loss for the year ended December 31, 2024, was $21.3 million of non-cash expenses related to the impact of expensing share-based payments, including employee stock options, as compared to $25.6 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 ongoing research into other precision oncology targets. 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 clinical trial results for Prelude's product candidates, and the sufficiency of Prelude's cash runway into the second quarter of 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

	Year ended December 31,	
(in thousands, except share and per share data)	**2024**	**2023**
Revenue from license agreement	$ 7,000	$ —
Operating expenses:		
Research and development	117,995	103,393
General and administrative	28,719	28,884
Total operating expenses	$ 146,714	$ 132,277
Loss from operations	(139,714)	(132,277)
Other income, net	12,541	10,445
Net loss	$ (127,173)	$ (121,832)
Per share information:		
Net loss per share of common stock, basic and diluted	$ (1.68)	$ (2.02)
Weighted average common shares outstanding, basic and diluted	75,805,840	60,357,052
Comprehensive loss		
Net loss	$ (127,173)	$ (121,832)
Unrealized (loss) gain on marketable securities, net of tax	(188)	1,915
Comprehensive loss	$ (127,361)	$ (119,917)

PRELUDE THERAPEUTICS INCORPORATED
BALANCE SHEETS

	December 31,	
(in thousands, except share and per share data)	**2024**	**2023**
Assets		
Current assets:		
Cash and cash equivalents	$ 12,474	$ 25,291
Marketable securities	121,140	207,644
Prepaid expenses and other current assets	2,281	2,654
Total current assets	135,895	235,589
Restricted cash	4,044	4,044
Property and equipment, net	6,767	7,325
Right-of-use asset	28,699	30,412
Prepaid expenses and other non-current assets	110	295
Total assets	$ 175,515	$ 277,665
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 7,732	$ 4,580
Accrued expenses and other current liabilities	15,209	15,768
Operating lease liability	2,492	1,481
Finance lease liability	208	—
Total current liabilities	25,641	21,829
Other liabilities	3,090	3,339
Operating lease liability	15,325	15,407
Total liabilities	44,056	40,575
Commitments		
Stockholders' equity:		
Voting common stock, $0.0001 par value: 487,149,741 shares authorized; 42,298,859 and 42,063,995 shares issued and outstanding at December 31, 2024 and 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 December 31, 2024 and 2023	1	1
Additional paid-in capital	714,982	693,252
Accumulated other comprehensive income	35	223
Accumulated deficit	(583,563)	(456,390)
Total stockholders' equity	131,459	237,090
Total liabilities and stockholders' equity	$ 175,515	$ 277,665

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