UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): November 1, 2023

Prelude Therapeutics Incorporated

(Exact Name of Registrant as Specified in its Charter)

Delaware	**001-39527**	**81-1384762**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

200 Powder Mill Road **Wilmington, Delaware** **(Address of principal executive offices)**	**19803** **(Zip Code)**

Registrant's telephone number, including area code: (302) 467-1280

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	PRLD	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition

On November 1, 2023, Prelude Therapeutics Incorporated (the "Company") issued a press release announcing its financial results for the three months ended September 30, 2023. A copy of the press release is attached as Exhibit 99.1 to this report.

The information in this Current Report on Form 8-K and in Exhibit 99.1 attached hereto is being furnished, but shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (“Exchange Act”), and is not incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press release issued by Prelude Therapeutics Incorporated regarding its financial results for the three months ended September 30, 2023, dated November 1, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL Document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

PRELUDE THERAPEUTICS INCORPORATED

Date: November 1, 2023

By: /s/ Laurent Chardonnet
Laurent Chardonnet
Chief Financial Officer

Exhibit 99.1

Prelude Announces Strategic Pipeline Progress and Updates, including its Partnership with AbCellera, and Reports Third Quarter Financial Results

Prioritization of its first-in-class SMARCA2 degrader and potentially best-in-class CDK9 inhibitor programs for continued clinical development

Enters partnership with AbCellera to develop a portfolio of precision ADCs with first program being a SMARCA degrader-antibody conjugate

Cash runway into 2026 with $230.5 million of cash, cash equivalents and marketable securities

WILMINGTON, Del. – November 1, 2023 – Prelude Therapeutics Incorporated (Prelude) (Nasdaq: PRLD), a clinical-stage precision oncology company, today provides strategic pipeline updates and reports third quarter financial results.

Recent clinical progress and strategic prioritization of the pipeline include:

- First-in-class SMARCA2 degrader (PRT3789): Encouraging initial clinical data including selective and dose-dependent SMARCA2 degradation, safety profile and robust enrollment of biomarker-selected patients provide increased confidence in the potential of PRT3789 to address a significant clinical need.

- Potentially best-in-class CDK9 inhibitor (PRT2527): Continued demonstration of a differentiated safety profile, desired target inhibition and the opportunity in multiple hematological cancers support advancement of PRT2527 in patients with select B-cell malignancies and AML.

- MCL-1 inhibitor (PRT1419): Phase 1 dose escalation in hematological malignancies was completed. Given the overlap with the CDK9 program, Prelude does not plan to advance PRT1419 further at this time.

- CDK4/6 inhibitor (PRT3645): Phase 1 dose escalation data demonstrated plasma drug exposure and target inhibition, reaching levels needed for efficacy in preclinical models, at generally well tolerated doses. Given the focus of the Company on SMARCA2 and CDK9, Prelude will not advance the program further and is actively pursuing further clinical development with external partners.

“We made significant progress in the third quarter with our four clinical stage molecules and, as planned, conducted a rigorous assessment of each program. Based on this assessment, we are prioritizing our resources on our first-in-class SMARCA2 degrader molecules, IV and oral, and our potential best-in-class CDK9 inhibitor program,” stated Kris Vaddi, Ph.D., Chief Executive Officer of Prelude. “We are confident that these two programs represent compelling opportunities for demonstrating clinical proof-of-concept in 2024, for advancing into potential Phase 2/3 registration studies, and for becoming important new medicines. This decision reflects our dual commitment to deliver differentiated treatments to patients and to build significant and sustainable value for our shareholders.”

Dr. Vaddi continued, “Regarding our recently announced partnership with AbCellera, this alliance combines our strengths in small molecule drug discovery and development with AbCellera’s powerful antibody discovery engine. We plan to build a portfolio of first-in-class precision ADCs that will utilize highly selective and potent small molecules and degraders as payloads targeting critical oncogenic pathways. We have already started work on our first program with a SMARCA payload on an antibody selected from a lead panel of antibodies previously discovered by AbCellera. We believe that this program further expands the potential of our SMARCA2 selective degraders.”

Jane Huang, MD, President and Chief Medical Officer, said, “Our SMARCA2 program continues to receive strong interest and support from investigators as patients with deleterious SMARCA4 mutations do not have effective treatment options. Based on our ability to select patients using a readily available biomarker, we have been able to enroll efficiently our ongoing Phase 1 clinical trial for PRT3789. We are encouraged not only by the pace of enrollment but also by early clinical data demonstrating selective degradation of SMARCA2, and by the compound’s safety profile to date. Our top priority is to generate initial clinical proof-of-concept data in 2024. Provided these results are as we expect, we anticipate advancing the compound into a registrational Phase 2/3 trial thereafter.”

“For our CDK9 inhibitor PRT2527, we are also encouraged by the emerging data in both solid and hematological cancers. These data demonstrate that our highly targeted compound has been generally safe and well-tolerated with a strong inhibition of the pathway required for efficacy in preclinical models and is well-differentiated from other CDK9 inhibitors. These results strengthen our confidence in its potential best-in-class profile and position us to be the most advanced CDK9 inhibitor for patients with B-cell malignancies and AML. Our key objective is to establish clinical proof-of concept data in both the monotherapy setting and in combinations in 2024.”

SMARCA Programs

PRT3789- SMARCA2 Targeted IV Protein Degrader
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 standard of care. Prelude 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.

A Phase 1 multi-dose escalation clinical trial of PRT3789 is ongoing (NCT05639751) in biomarker-selected SMARCA4 mutated cancers. Prelude intends to evaluate PRT3789 as monotherapy as well as in combination and plans to share initial Phase 1 data in mid-2024.

SMARCA2 - Oral Program
Prelude recently nominated a potent, orally bioavailable and highly selective SMARCA2 degrader candidate. This compound is >1000x selective for SMARCA2 over SMARCA4 and is currently in IND-enabling studies. Prelude expects to file an IND in the first half of 2024.

SMARCA - Precision ADC
Prelude and its partner AbCellera began work on an early-stage discovery program involving potent degraders of the SMARCA family of proteins as payloads for novel antibodies targeting tumor specific antigens. Given the potent anti-tumor activity of these molecules in pre-clinical models of cancers beyond those targeted by our SMARCA2 selective degraders, we believe that these precision ADCs have the potential to extend the therapeutic utility of this class.

CDK9 Inhibitor Program
Prelude 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.

PRT2527 has completed a Phase 1 dose escalation study (NCT05159518) in patients with solid tumors. In this trial, PRT2527 was shown to achieve high levels of target inhibition and to potentially be better tolerated than existing CDK9 inhibitors, specifically manageable neutropenia and an absence of meaningful gastrointestinal events or hepatotoxicity.
The observed dose-dependent downregulation of MYC and MCL1 mRNA expression, CDK9 transcriptional targets, was consistent with the degree of target engagement required for preclinical efficacy. As predicted by the preclinical models, 12 mg/m2 QW dosing showed optimal target inhibition and has been selected as the optimal dose. The overall safety profile observed in this study supports further development of PRT2527 in hematologic malignancies (NCT05665530) and this study is currently ongoing with initial clinical data expected in mid 2024.

MCL1 Inhibitor Program

Prelude has concluded Phase 1 development of PRT1419 and established a confirmation dose in hematological cancers. Based on the potential to address the intended patient populations with the CDK9 inhibitor which potently inhibits MCL-1, Prelude has made a decision to prioritize its CDK9 inhibitor, PRT2527, over PRT1419.

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 to achieve higher, more effective brain and tissue penetration than current CDK4/6 inhibitors.

Prelude intends to complete the dose escalation portion of the Phase 1 clinical trial of PRT3645 this year. Prelude is actively exploring continued clinical development with external partners.
At the recent AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, Prelude presented data showing that treatment with PRT3645 was associated with substantial decreases in both pRb and Ki67 expression, indicating a dose-dependent target engagement at the doses evaluated. Also, PRT3645 treatment was generally well tolerated in the initial three dose cohorts of patients with no clinically meaningful gastrointestinal, hematologic or neurological events reported to date, reflecting its enhanced selectivity profile.

Third Quarter Financial Results

Cash, Cash Equivalents and Marketable Securities: Cash, cash equivalents, and marketable securities as of September 30, 2023, were $230.5 million. Prelude 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 2023, R&D expenses increased to $26.3 million from $22.9 million for the prior year period. R&D 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 third quarter of 2023, G&A expenses decreased to $7.1 million from $7.5 million for the prior year period. G&A expenses decreased reflecting Prelude's continued careful management of its G&A expenses.

Net Loss: For the three months ended September 30, 2023, net loss was $30.6 million, or $0.45 per share compared to $30.0 million, or $0.63 per share, for the prior year period. Included in the net loss for the quarter ended September 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 $6.4 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 three candidates currently in clinical development: PRT3789 an IV administered, potent and highly selective SMARCA2 degrader, PRT2527, a potent and highly selective CDK9 inhibitor, PRT3645 a next generation CDK4/6 inhibitor, and a preclinical oral candidate targeting SMARCA2. For more information, visit our website and follow us on LinkedIn.

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 proof-of-concept data and clinical trial results for Prelude's product candidates, the sufficiency of Prelude's cash runway into 2026, and Prelude's planned prioritization of its SMARCA2 degrader molecule and CDK9 inhibitor programs in the near-term. 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 Prelude's Annual Report on Form 10-K for the year ended December 31, 2022, 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.

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PRELUDE THERAPEUTICS INCORPORATED

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(UNAUDITED)

(in thousands, except share and per share data)	Three Months Ended September 30, 2023	2022
Operating expenses:		
Research and development	$ 26,261	$ 22,889
General and administrative	7,124	7,517
Total operating expenses	33,385	30,406
Loss from operations	(33,385)	(30,406)
Other income, net	2,777	448
Net loss	$ (30,608)	$ (29,958)
Per share information:		
Net loss per share of common stock, basic and diluted	$ (0.45)	$ (0.63)
Weighted average common shares outstanding, basic and diluted	67,639,993	47,449,811
Comprehensive loss:		
Net loss	$ (30,608)	$ (29,958)
Unrealized (loss) gain on marketable securities, net of tax	106	(69)
Comprehensive loss	$ (30,502)	$ (30,027)

PRELUDE THERAPEUTICS INCORPORATED

BALANCE SHEETS
(UNAUDITED)

(in thousands, except share data)	September 30, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 15,896	$ 30,605
Marketable securities	214,610	171,123
Prepaid expenses and other current assets	4,410	2,652
Total current assets	234,916	204,380
Restricted cash	4,044	4,044
Property and equipment, net	6,618	4,908
Right-of-use asset	464	1,792
Prepaid expenses and other non-current assets	12,469	5,376
Total assets	$ 258,511	$ 220,500
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 5,170	$ 6,777
Accrued expenses and other current liabilities	11,248	13,093
Operating lease liability	475	1,832
Total current liabilities	16,893	21,702
Other liabilities	3,361	3,361
Total liabilities	20,254	25,063
Commitments		
Stockholders' equity:		
Voting common stock, $0.0001 par value: 487,149,741 shares authorized; 41,965,472 and 36,496,994 shares issued and outstanding at September 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 September 30, 2023 and December 31, 2022, respectively	1	1
Additional paid-in capital	662,172	531,682
Accumulated other comprehensive loss	(605)	(1,692)
Accumulated deficit	(423,315)	(334,558)
Total stockholders' equity	238,257	195,437
Total liabilities and stockholders' equity	$ 258,511	$ 220,500