Prelude Therapeutics Announces Presentation of Encouraging Data from Multiple Programs at the AACR-NCI-EORTC Virtual International Conference on Molecular Targets and Cancer Therapeutics

October 7, 2021 1:01 PM EDT

– Lead oral PRMT5 inhibitors PRT543 and PRT811 demonstrate favorable safety profile, evidence of preliminary clinical activity including durable responses and high levels of target inhibition of PRMT5 in Phase 1 dose escalation in unselected patients –

– CDK9 inhibitor PRT2527 demonstrates strong efficacy in hematological malignancies and solid tumor models with MYC dysregulation in preclinical studies –

WILMINGTON, Del., Oct. 07, 2021 (GLOBE NEWSWIRE) -- Prelude Therapeutics Inc. (Nasdaq: PRLD), a clinical-stage precision oncology company, today announced the presentation of data from multiple pipeline programs, including the dose escalation portions of the Company's ongoing Phase 1 trials of lead oral protein arginine methyltransferase 5 (PRMT5) inhibitors PRT543 and PRT811. These data will be featured at the AACR-NCI-EORTC Virtual International Conference on Molecular Targets and Cancer Therapeutics being held October 7-10, 2021.

"We are encouraged by the Phase 1 dose escalation data for our lead oral PRMT5 inhibitors, PRT543 and PRT811, both of which demonstrated favorable safety profiles, dose-dependent increases in pharmacokinetic parameters, target engagement, and achieved degrees of PRMT5 inhibition required for efficacy in preclinical models at well tolerated doses. We are also encouraged by the preliminary clinical activity observed with both molecules in multiple tumor types, including durable responses in cancers with high unmet need. Importantly, our brain penetrant molecule, PRT811, demonstrated a very high level of systemic PRMT5 inhibition at well tolerated doses and without central nervous system adverse events, which expands the potential clinical utility of this molecule," said Kris Vaddi, Ph.D., Chief Executive Officer. "We are leveraging insights from these data as we move forward through the expansion cohorts in selected patient populations, and we anticipate a cadence of data from these cohorts throughout 2022."

Dr. Vaddi added, "With respect to PRT2527, our potent and selective CDK9 inhibitor, we are encouraged by preclinical findings which support its potential in solid tumors and hematological malignancies demonstrating dysregulation of *MYC* gene expression. We remain on track to submit an IND application and initiate a Phase 1 clinical trial by year-end."

Summary of Data Presented

A copy of each poster will be available in the Publications section of the Prelude Therapeutics website.

PRT543

Title: A phase 1 dose-escalation study of protein arginine methyltransferase 5 (PRMT5) inhibitor PRT543 in patients with advanced solid tumors and lymphoma
Presenter: Meredith McKean, M.D., MPH, Sarah Cannon Research Institute, Tennessee Oncology
Poster: P039

- As of an August 6, 2021 data cutoff date, the dose escalation portion of the ongoing Phase 1 trial of PRT543, which is designed to be a potent and selective inhibitor of PRMT5, enrolled a total of 49 patients across 18 unselected advanced solid tumors and lymphoma. Patients enrolled received an average of three prior lines of therapy. PRT543 demonstrated target engagement and inhibition of PRMT5 functional activity as evidenced by a 69% reduction in serum symmetric dimethylarginine (sDMA) at a dose of 45 mg/5x per week. In addition, PRT543 demonstrated signs of preliminary clinical activity, including a durable complete response (CR) maintained for over 18 months in a patient with HRD+ ovarian cancer who remains on treatment, and prolonged stable disease (SD) persisting for over six months in five patients, including four patients with adenoid cystic carcinoma (ACC) and one patient with uveal melanoma. PRT543 was generally well tolerated: the most common grade 3 or higher treatment-related adverse events (AE) occurring in at least 5% of patients were thrombocytopenia (27%) and anemia (12%), both of which were reversible upon treatment interruption. Patients were largely able to remain on therapy with few AE-related dose interruptions (27%), reductions (22%), or discontinuations (4%).

  Patient enrollment is ongoing in specific biomarker-selected solid tumor and hematologic

malignancy expansion cohorts. The Company expects to present data from the expansion cohorts at medical meetings throughout 2022.

"Preliminary findings support that PRT543 could represent a much-needed treatment option across multiple malignancies," said Dr. McKean. "Of note, preliminary clinical activity observed in heavily pre-treated patients with historically difficult to treat disease, including a durable CR in a patient with HRD+ ovarian cancer, offers support for the continued assessment of this promising agent."

PRT811

Title: A phase 1 dose-escalation study of protein arginine methyltransferase 5 (PRMT5) brain-penetrant inhibitor PRT811 in patients with advanced solid tumors, including recurrent high-grade gliomas
Presenter: Gerald S. Falchook, M.D., Sarah Cannon Research Institute at HealthONE
Poster: P044

- As of an August 13, 2021 data cutoff date, the dose escalation portion of the ongoing Phase 1 trial of PRT811, which is designed to be a potent, selective, and brain penetrant PRMT5 inhibitor, enrolled a total of 45 patients, including 27 patients across 16 unselected advanced solid tumors and 18 patients with high-grade gliomas, including 17 patients with glioblastoma multiforme (GBM). PRT811 demonstrated dose dependent inhibition of PRMT5 activity as evidenced by an 83% reduction in serum sDMA at a dose of 600 mg daily (QD). In addition, PRT811 demonstrated signs of preliminary clinical activity, including an IDH1 mutated GBM patient who experienced a partial response (PR) that evolved into a durable CR for more than 13 months and remains on treatment. In addition, a patient with splicing-mutant (SF3B1) uveal melanoma demonstrated SD for more than six months with a 25% tumor regression and remains on treatment. At a post data-cutoff on September 20, 2021, one additional patient (800 mg QD) with SF3B1 uveal melanoma had an unconfirmed PR and 47% decrease in target lesion, and a patient with triple negative breast cancer (800 mg QD) who demonstrated a 27% decrease in target lesions. Both patients continue treatment. PRT811 was generally well-tolerated; the most common grade 3 or higher treatment-related AE was thrombocytopenia (7%), which was reversible upon treatment interruption. Patients were largely able to remain on therapy with few AE-related dose interruptions (13%), reductions (4%), or discontinuations (3%).

The study remains ongoing, and the Company expects to commence enrollment in the expansion portion of the trial in the fourth quarter. Data from the expansion cohorts are expected to be presented at medical meetings throughout 2022.

"Patients with high-grade gliomas and uveal melanoma have limited treatment options and face a particularly poor prognosis," said Dr. Falchook. "I am encouraged by the initial data from the dose escalation portion of the study, which include a patient with recurrent GBM harboring an IDH1 mutation whose durable initial PR subsequently evolved into a CR, as well as a patient with splicing-mutant uveal melanoma and a patient with triple negative breast cancer who both experienced decreases in their target lesions and remain on therapy. Given the role of PRMT5 in DNA damage response, the results thus far provide impetus for the continued evaluation of PRT811 within this patient population."

Preclinical Data

Title: PRT2527 is a potent and selective CDK9 inhibitor that demonstrates anti-cancer activity in preclinical models of hematological malignancies and solid tumors with MYC amplification
Presenter: Yang Zhang, Ph.D., Prelude Therapeutics
Poster: P237

- This study sought to assess PRT2527, which is designed to be a potent and selective CDK9 inhibitor, in preclinical models of multiple hematological malignancies and solid tumors. Treatment with PRT2527 was shown to deplete oncogenic drivers with short half-lives such as MYC and MCL1 and induce apoptosis. Intermittent intravenous administration of PRT2527 demonstrated strong efficacy in hematological malignancies and solid tumor models with *MYC* dysregulation. The Company remains on track to submit an Investigational New Drug (IND) application for PRT2527 and initiate a Phase 1 clinical trial by the end of the year.

Prelude Therapeutics

Prelude Therapeutics is a clinical-stage precision oncology company developing innovative drug candidates targeting critical cancer cell pathways. The Company's lead product candidates are designed to be oral, potent, and selective inhibitors of PRMT5. Prelude's first clinical candidate, PRT543, is in Phase 1 development for advanced solid tumors and select myeloid malignancies. Prelude is also advancing PRT811, a second PRMT5 inhibitor optimized for high brain exposure, in a Phase 1 clinical trial including glioblastoma multiforme (GBM). The Company's pipeline also includes its third

clinical candidate, PRT1419, an orally available MCL1 inhibitor in Phase 1 development for patients with relapsed/refractory hematologic malignancies, and its two most advanced preclinical candidates, PRT2527, a CDK9 inhibitor, and PRT-SCA2, a SMARCA2 protein degrader.

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, the timing of the expansion portion for its Phase 1 clinical trial for PRT543 and PRT811, the timing of IND-related activities for PRT2527 and the potential benefits of the Company's product candidates and platform. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. Although the Company believes that the expectations reflected in such forward-looking statements are reasonable, the Company 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 the Company's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties related to the Company'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 the Company's business, clinical trial sites, supply chain and manufacturing facilities, the Company's ability to maintain and recognize the benefits of certain designations received by product candidates, the timing and results of preclinical and clinical trials, the Company's ability to fund development activities and achieve development goals, the Company's ability to protect intellectual property, and other risks and uncertainties described under the heading "Risk Factors" in documents the Company 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 the Company undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

Investor Contacts:
Stacey Jurchison
Executive Director, Corporate Affairs
sjurchison@preludetx.com

Melissa Forst
Argot Partners
212.600.1902
prelude@argotpartners.com

Media Contact:
Paige Donnelly
Argot Partners
212.600.1902
prelude@argotpartners.com