Prelude Therapeutics Receives FDA Clearance of IND for PRT3789, a Potent and Selective First-in-Class SMARCA2 Protein Degrader

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Phase 1 Study Will Include Biomarker Selected Patients with Advanced Solid Tumors

WILMINGTON, Del., Oct. 18, 2022 (GLOBE NEWSWIRE) -- Prelude Therapeutics Incorporated (Prelude) (Nasdaq: PRLD), a clinical-stage precision oncology company, today announced that the U.S. Food and Drug Administration, (FDA) cleared the company to proceed with a Phase 1 study under its Investigational New Drug Application (IND) for PRT3789, a first-in-class potent and selective SMARCA2 (BRM) protein degrader. The company anticipates dosing the first patient in Q1 of 2023.

“Preclinical models with SMARCA4 deletions demonstrated that selective degradation of SMARCA2 with our potent and highly selective molecule PRT3789, resulted in significant anti-tumor activity at well tolerated doses,” said Dr. Peggy Scherle, Chief Scientific Officer of Prelude. “Historically, structural similarities between members of the SMARCA family have made it challenging to selectively inhibit SMARCA2. Based on the breadth and depth of Prelude’s discovery engine expertise however, we have found an innovative solution by leveraging the emerging technology of targeted protein degradation to achieve exceptional selectivity for SMARCA2 over SMARCA4.”

“Clearance of the IND for PRT3789 represents a major milestone for Prelude Therapeutics, as we advance our first-in-class SMARCA2 protein degrader from discovery to the clinic. There is a significant need for treatment options for patients with cancers carrying genetic alterations in SMARCA4 (BRG1) because these patients do not generally present with other targetable oncogenic drivers. While the field is evolving around SMARCA mutations, early observations indicate that patients with SMARCA mutations have aggressive disease with an urgent need for more therapies. Patients with specific SMARCA4 loss of function mutations can be easily identified with standard next generation sequencing panels and understanding how to best identify the patients who will benefit the most from PRT3789 will be investigated in the Phase 1 study,” said Dr. Jane Huang, President and Chief Medical Officer of Prelude.

The Phase 1 study of PRT3789 will enroll patients with advanced solid tumors in a biomarker selected SMARCA4 mutated population. The trial will be enriched for patients with non-small cell lung cancer, where these mutations are frequently present. The primary endpoints of the study include safety, tolerability and establishment of a recommended phase two dose with additional evaluation of pharmacokinetics and pharmacodynamic parameters, and evidence of clinical activity.

About SMARCA2

SMARCA2 (BRM) and SMARCA4 (BRG1) are involved in multiple oncogenic processes, including the process that allows DNA to be transcribed to RNA. SMARCA4 mutations enable cells to become cancerous and can be found in 10-20% of select cancers, including non-small cell lung cancer (NSCLC). Because the activity of either SMARCA2 or SMARCA4 is required for the tumor cells to grow, SMARCA4-deficient (mutated) cancer cells become highly dependent on SMARCA2 for their survival. Degrading the SMARCA2 protein in SMARCA4-deficient cancers is believed to produce a strong synthetic lethality, resulting in cell death, while sparing normal cells that do not have SMARCA4 deficiencies.

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 five candidates currently in clinical development: PRT811, a highly selective, potent, orally bioavailable PRMT5 inhibitor; PRT1419, a potent, selective inhibitor of MCL1; PRT2527, a potent and highly selective CDK9 inhibitor, PRT3645, a brain penetrant CDK4/6 inhibitor, and PRT3789, a 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 PRT811, PRT1419, PRT 2527, PRT3645 and PRT3789, the timing and results from the Phase 1 clinical trial for PRT3789, and the potential benefits of Prelude’s product candidates and platform. 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.

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