Prelude Therapeutics Announces Strategic Business Update

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Prelude to prioritize development of mutant selective JAK2V617F JH2 inhibitor and KAT6A selective degrader programs

Pausing further clinical development of SMARCA2 selective degrader programs

JAK2V617F option agreement with Incyte, as previously announced, includes upfront payment of $35 million, a $25 million equity investment and $100 million if option is exercised

Cumulative capital expected to fund planned operations into 2027 based on the Company's preliminary estimates, and potentially into the third quarter of 2028 if Incyte exercises option on JAK2 program

Company to release third quarter 2025 financial results and conduct an investor conference call on November 12, 2025

WILMINGTON, Del., Nov. 04, 2025 (GLOBE NEWSWIRE) -- Prelude Therapeutics Incorporated (Nasdaq: PRLD), a precision oncology company, today is providing a number of strategic updates, including its recently executed option agreement with Incyte Corporation centered on its previously undisclosed JAK2V617F mutant selective inhibitor program, prioritizing development of its first-in-class KAT6A selective degrader program and pausing of its SMARCA2 programs.

Earlier today, Prelude announced an exclusive option agreement with Incyte to advance its mutant selective JAK2V617F JH2 inhibitor program for patients with myeloproliferative neoplasms (MPNs). With this transaction, Incyte secures an exclusive option to acquire the JAK2V617F program in exchange for an upfront payment and an equity investment in Prelude, plus downstream milestones and royalties. Prelude will continue to own and develop all JAK2V617F program assets until point of option exercise, after which Incyte will lead development and commercialization globally.

Prelude is prioritizing the development of its highly selective KAT6A degrader for ER+ breast cancer. Selectively degrading KAT6A is a novel approach to a clinically validated target with transformative potential for patients. The Company expects to advance the program into clinical development in 2026 and generate initial proof-of-concept clinical data, including a potentially differentiated efficacy and safety profile compared to non-selective KAT6A/B inhibitors currently in clinical development.

Prelude also announced it has decided to pause the clinical development of its SMARCA2 degrader program. The decision to pause was based on a comprehensive review of clinical data generated to date and the Company's assessment of the capital and resource allocation required to advance the SMARCA2 program, versus the JAK2 and KAT6A programs, to key points of value inflection.

Based on these announcements, the Company's cash runway is now expected to extend into 2027 based on the Company's preliminary estimates. The cash runway could potentially be expected to extend into the third quarter of 2028 if Incyte exercises its option on the JAK2 program subject to customary closing conditions and based on the Company's preliminary estimates. As of October 31, 2025, the Company had approximately $52 million of cash, cash equivalents and marketable securities and will receive $60 million following the closing of the option and securities purchase from Incyte's upfront payment and equity investment.

"This morning, we announced important strategic decisions that we believe provide the most compelling set of opportunities to address important unmet needs for patients and value creation for our investors," stated Kris Vaddi, Ph.D. Chief Executive Officer of Prelude. "Our research team made significant breakthroughs in discovering highly differentiated molecules targeting clinically validated mechanisms that are positioned to enter the clinic in 2026. These molecules present potential proof of concept and differentiation opportunities early in clinical development with well understood development paths."

Vaddi continued, "Having actively pursued the clinical development of our SMARCA2 selective degraders, we determined that complex biology and aggressiveness of disease in patients with SMARCA4 deletions will likely require early intervention and combination strategies to make a meaningful impact for patients. We are not resourced to explore the mechanism fully in the timeframe needed to deliver a concrete and viable path forward. In addition, we believe that optimally resourcing the JAK2V617F mutant selective inhibitor and KAT6A degrader programs are of paramount importance and as noted in this morning's previous announcement, the agreement with Incyte brings in significant capital enabling us to advance both programs."

Prelude also announced the departure of President and Chief Medical Officer Jane Huang, M.D. to pursue other opportunities. Victor Sandor, M.D.C.M., former Chief Medical Officer of Array BioPharma and current Prelude board member and chair of the Science and Technology Committee, will provide strategic and operational oversight of clinical development as the Company advances KAT6A towards first-in-human studies, and its JAK2 program. Dr. Sandor brings extensive oncology development leadership experience, notably through his successful tenures at Incyte Corporation, Biogen Idec and AstraZeneca. The Company will seek to augment the clinical development leadership in a timeframe that fits with the maturation of the programs.

Added Vaddi, "Lastly, we would like to thank Dr. Huang for her many contributions to Prelude and wish her continued success in her future endeavors. We are honored and gratified that Dr. Sandor is stepping in to provide strategic leadership and oversight of our clinical development programs, as we prepare for IND filing and first in human studies for the mutant selective JAK2V617F and KAT6A programs."

Key Pipeline Programs

Highly selective KAT6A oral degrader program

KAT6 is an emerging and recently validated target in the treatment of ER+ breast cancer. Prelude discovered and is developing first-in-class, highly potent, highly selective and orally bioavailable KAT6A selective degraders. The Company has selected a development candidate and remains on track to file an IND in mid-2026. Prelude believes that selectively degrading KAT6A has the potential for improved efficacy, tolerability and combinability with other agents relative to non-selective inhibitors of KAT6A/B. The Company recently presented preclinical data supporting this hypothesis at the AACR Annual Meeting 2025. The presentation can be found at Publications - Prelude Therapeutics.

Mutant selective JAK2V617F JH2 inhibitor program
JAK2V617F is the primary driver mutation responsible for disease progression in the majority of patients living with myeloproliferative neoplasms (MPNs). The mutation impacts approximately 95% of patients with polycythemia vera (PV), 60% of patients with essential thrombocythemia (ET) and 55% of patients with myelofibrosis (MF). Identifying JAK2 JH2 inhibitors that selectively target V617F+ cells has long been a shared goal and challenge for industry. Prelude has discovered novel allosteric inhibitors that bind into the JAK2 JH2 “deep pocket” where the V617F mutation resides. These candidates demonstrate mutant specific inhibition in multiple preclinical models of MPNs. Prelude believes this approach may have the potential to reduce mutant allele burden, slow or even reverse disease progression, and transform treatment outcomes for MPN patients.

Mutated Calreticulin (mCALR) degrader antibody conjugates (DACs)
Mutant CALR is a neoantigen presented on the cell surface of malignant myeloid cells but not normal cells and is found in approximately 25-35% of patients with myelofibrosis (MF) and essential thrombocythemia (ET). Recently, a mCALR-targeted monoclonal antibody demonstrated robust clinical activity in high-risk ET patients. Prelude is seeking to further optimize this modality by developing mCALR-targeted DACs using the Company’s proprietary degrader payloads. The Company presented the first preclinical data from this discovery effort at the European Hematology Association 2025 Congress in June. The presentation can be found at Publications - Prelude Therapeutics.

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. These data demonstrated that SMARCA2/4 degrader antibody conjugates have potential for significantly better *in vivo* efficacy and tolerability when compared to traditional cytotoxic ADCs when tested head-to-head in xenograft models. The presentation can be found at Publications - Prelude Therapeutics.

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 features highly selective KAT6A degraders and JAK2V617F mutant selective inhibitors -- new approaches to clinically validated targets with transformative potential for patients. We are leveraging our expertise in targeted protein degradation to discover and develop next generation degrader antibody conjugates (DACs) with novel payloads. 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. 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, 2024, 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.

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