Prelude Therapeutics Announces Exclusive Option Agreement with Incyte to Advance Mutant Selective JAK2V617F JH2 Inhibitors

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Incyte secures an exclusive option to acquire Prelude's mutant selective JAK2V617F JH2 inhibitor program

Mutant selective JAK2V617F JH2 inhibitors have disease-modifying potential in treating patients living with myeloproliferative neoplasms (MPNs)

Prelude to receive a $35 million upfront payment and $25 million strategic equity investment, $100 million if Incyte were to exercise the option to acquire the program, and up to $775 million in additional potential milestones plus royalties on net sales

Prelude will continue to develop all JAK2V617F program assets during the option period; if optioned, Incyte would lead development and commercialization globally

WILMINGTON, Del., Nov. 04, 2025 (GLOBE NEWSWIRE) -- Prelude Therapeutics Incorporated (Nasdaq:PRLD), a clinical-stage precision oncology company, today announced an exclusive option agreement with Incyte (Nasdaq:INCY) focused on Prelude's previously undisclosed mutant selective JAK2V617F JH2 inhibitor program in development for patients with myeloproliferative neoplasms (MPNs). Per the agreement, Incyte secures an exclusive option to acquire the JAK2V617F program in exchange for an upfront payment and a strategic equity investment in Prelude, plus potential downstream milestones and royalties.

Kris Vaddi, Ph.D., Chief Executive Officer of Prelude stated, "We're pleased to put this agreement in place with Incyte, recognized global leaders in the MPN field. Prelude and Incyte both aim to deliver transformational treatments to improve upon the standard of care established with first generation JAK2 JH1 inhibitors like Jakafi® (ruxolitinib). Our research team made significant progress discovering the first known inhibitors that bind into the JAK2 JH2 'deep pocket' where the V617F mutation resides. These potent and orally bioavailable compounds demonstrate mutant specific inhibition and the potential for disease modification in multiple preclinical models of MPNs. Today's agreement with Incyte provides us with the capital needed to advance further our JAK2V617F program, while also allowing us to advance the development of our other pipeline programs."

"The agreement with Prelude provides an opportunity to enhance our robust portfolio of clinical and preclinical JAK2V617F candidates for patients with MPNs," said Bill Meury, President and Chief Executive Officer of Incyte. "This transaction aligns with our strategy to develop new and innovative therapies poised to make a meaningful difference for patients."

Terms of the Agreement
Under the terms of the Transaction Agreement, Incyte secures an exclusive option to acquire Prelude's mutant selective JAK2V617F JH2 inhibitor program, including Prelude's library of preclinical candidates. Prelude will receive $60 million in capital, comprised of an upfront payment of $35 million, plus a $25 million equity investment by Incyte in Prelude. Incyte will purchase 6.25 million shares of Prelude non-voting common stock at a price of $4.00 per share at deal close. Prelude intends to apply the upfront payment and net proceeds from the sale of the purchased shares to advance the JAK2V617F program and other pipeline assets, and for working capital and general corporate purposes.

Prelude expects to advance the JAK2V617F program to pre-defined milestones. Incyte may elect to exercise its exclusive option during the option period to acquire the program and associated assets from Prelude for $100 million. As the JAK2V617F program candidates advance in the clinic, Prelude would be eligible to receive up to $775 million in additional clinical and regulatory milestones, and single digit royalties on global net sales. Combined, total potential cash payments from the transaction, excluding royalties, could reach up to $910 million.

If Incyte elects to not exercise its option to acquire the program, all JAK2V617F global program rights and interests would remain in the sole ownership and control of Prelude.

Prelude Therapeutics was advised on the transaction by Morgan Lewis & Bockius LLP as legal counsel.

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. If successful, this approach has potential to reduce mutant allele burden, modify disease progression, and transform treatment outcomes for MPN patients. 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. The first disclosure of program data was accepted for oral presentation at the American Society of Hematology (ASH) 67th Annual Meeting taking place in Orlando, FL December 6-9, 2025. The abstract can be found on the ASH 2025 website ASH Annual Meeting & Exposition - Hematology.org.

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 mutant selective JAK2V617F JH2 inhibitors - new approaches to clinically validated targets with transformative potential for patients. We are also 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.

Prelude 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.

Contacts:

Prelude:
Robert A. Doody, Jr.
Senior Vice President, Investor Relations
Prelude Therapeutics Incorporated
484.639.7235
rdoody@preludetx.com