Prelude Therapeutics Announces Publication of Abstracts for Presentation at the American Society of Hematology 67th Annual Meeting

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WILMINGTON, Del., Nov. 03, 2025 (GLOBE NEWSWIRE) -- Prelude Therapeutics Incorporated (Nasdaq: PRLD) ("Prelude" or the "Company"), a clinical-stage precision oncology company, today announced the publication of two abstracts with preclinical data on the Company's JAK2V617F mutant selective inhibitors and CALR-targeted degrader antibody conjugates (DACs) discovery program, both accepted for oral presentation at the American Society of Hematology (ASH) 67th Annual Meeting taking place in Orlando, FL December 6-9, 2025. The abstracts can be found on the ASH 2025 website ASH Annual Meeting & Exposition - Hematology.org.

"We are excited for the opportunity to share the first-time disclosure of our novel JAK2V617F mutant selective inhibitor program as well as the discovery of first-in-class CALR-targeted precision DACs delivering CDK9 degrader payloads," stated Peggy Scherle, Ph.D., Chief Scientific Officer of Prelude. "For JAK2, our research team made a breakthrough in the discovery of the first known molecules that bind into the JH2 'deep pocket' where the V617F mutation resides. These compounds demonstrate mutant specific inhibition in multiple preclinical models of myeloproliferative neoplasms (MPNs). In our mCALR DAC discovery program, we engineered a novel CDK9 degrader conjugated to a CALR antibody leveraging our expertise in both CDK9 chemistry and MPN biology, which gives an additional payload option to our previously disclosed SMARCA2/4 mCALR DAC. We believe both of these programs represent novel disease modifying treatment options in significant areas of unmet need for patients living with MPNs."

Details on the oral presentations are as follows:

Title: Discovery and preclinical characterization of orally bioavailable JAK2V617F mutant selective JH2 inhibitors with disease modification potential in myeloproliferative neoplasms
Presenter: Dr. Neha Bhagwat

Session Name: 631. Myeloproliferative Syndromes and Chronic Myeloid Leukemia: Basic and Translational: Precision targeting in MPN
Session Date and Time: December 6, 2025; 9:30 AM – 11:00 AM
Presentation Time: 10:15 AM – 10:30 AM
Location: OCCC-W414AB
Publication Number: 70

Utilizing structure-based drug design, we created a series of highly potent, allosteric mutant JAK2 selective inhibitors that bind into the deep pocket where the JAK2V617F mutation resides. These compounds demonstrate a potent and selective reduction in JAK2VF cells *in vitro* and *in vivo* compared to WT cells. In JAK2VF-dependent mouse models, inhibitor treatment led to normalization of white blood cells, platelets and spleen size without causing cytopenias or other adverse effects. Most importantly, analysis of progenitor populations revealed *a selective decrease* in proliferation of JAK2VF stem cells, key contributors to MPN pathogenesis, without an impact on WT cells. These data establish our JAK2VF selective inhibitors as highly differentiated agents with disease-modifying potential.

Title: Discovery of first-in-class CALR-targeted precision ADCs delivering a CDK9 degrader payload for the treatment of CALR-mutated MPNs
Presenter: Dr. Norman Fultang
Session Name: 631. Myeloproliferative Syndromes and Chronic Myeloid Leukemia: Basic and Translational: Precision targeting in MPN
Session Date and Time: December 6, 2025; 9:30 AM – 11:00 AM
Presentation Time: 10:45 AM – 11:00 AM
Location: OCCC-W414AB
Publication Number: 72

Calreticulin (CALR) mutations are found in 20–30% of MPN patients and lead to the surface expression of CALR only in mutant cells, thereby making mutant CALR a promising target for DACs. We report the development of a novel DAC designed to selectively bind mutant CALR and deliver a highly potent CDK9 degrader payload. CDK9 plays a critical role in maintaining cell survival in hematologic malignancies, including MPN. The resulting CALR x CDK9 DAC selectively bound and internalized in CALR mutant cells, selectively eliminating CALR-mutant MPN progenitors while sparing CD34+ stem cells from healthy donors. These results support further development of mCALR x CDK9 DAC as a potential disease-modifying therapeutic for CALR-mutant MPN.

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 SMARCA2 and KAT6A degraders as well as JAK2V617F mutant selective inhibitors. We are leveraging our expertise in targeted protein degradation to discover and develop next generation degrader antibody conjugates (DACs) with novel payloads available for partnering. 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.

Mutant selective JAK2V617F JH2 inhibitor program
JAK2V617F is the primary driver mutation responsible for disease progression in the majority of patients living with 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 abstract can be found on the ASH 2025 website ASH Annual Meeting & Exposition - Hematology.org

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 CDK9 and SMARCA2/4 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. The latest abstract can be found on the ASH 2025 website ASH Annual Meeting & Exposition - Hematology.org

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, and clinical trial results for Prelude's product candidates. 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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