Prelude Therapeutics Presents Preliminary Results of Phase 1 Dose-escalation Study of PRT2527 as Monotherapy and in Combination with Zanubrutinib in Patients with Relapsed/Refractory Lymphoid Malignancies

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• PRT2527 demonstrated activity across a range of relapsed/refractory lymphoid malignancies, including patients who received prior CAR-T therapy

• Prelude plans to seek a partner for future development of PRT2527 in hematologic malignancies

WILMINGTON, Del., Dec. 11, 2024 (GLOBE NEWSWIRE) -- Prelude Therapeutics Incorporated (Nasdaq: PRLD) (“Prelude” or the “Company”), a clinical-stage precision oncology company, today announced the presentation of the first interim clinical data from its ongoing open-label, dose-escalation trial of PRT2527, a potent and highly selective CDK9 inhibitor, as monotherapy and in combination with zanubrutinib in patients with relapsed/refractory lymphoid malignancies. The data were presented at a poster session of the 66th American Society of Hematology Annual Meeting in San Diego, California.

The study investigators reported on the 46 patients that were enrolled, treated, and safety evaluable as of September 17, 2024. PRT2527 was generally well-tolerated through 4 dosing cohorts as monotherapy and 3 dosing cohorts in combination with zanubrutinib. PRT2527 monotherapy and in combination with zanubrutinib demonstrated an acceptable safety profile with evidence of preliminary activity in patients with relapsed/refractory lymphoid malignancies, including patients who received prior CAR-T therapy.

“CDK9 has long been considered a potential therapeutic approach for treating hematologic malignancies and a highly selective CDK9 inhibitor was sought to minimize off target toxicity,” stated Jane Huang, M.D., President and Chief Medical Officer of Prelude. “We are encouraged by the results demonstrated to date by PRT2527 both as a monotherapy and particularly in combination with zanubrutinib resulting in an overall response rate of 38.5% including two patients with aggressive lymphomas who had received prior CAR-T therapy. These results represent a positive step for CDK9 inhibition as a possible future therapeutic approach for patients with aggressive hematologic cancers with limited treatment options.”

PRT2527 Interim Phase 1 Results
PRT2527 is an investigational, potent and highly selective CDK9 inhibitor being evaluated in select relapsed/refractory (R/R) hematologic malignancies as monotherapy and in combination with zanubrutinib.

As of the cutoff date, 46 patients with relapsed/refractory lymphoid malignancies were treated with PRT2527. 29 patients were treated once weekly via intravenous infusion at four dose levels of PRT2527 monotherapy (9 mg/m^2, 15 mg/m^2, 18 mg/m^2, 24 mg/m^2) and 17 patients were treated once weekly at three dose levels of PRT2527 (9 mg/m^2, 15 mg/m^2, 18 mg/m^2) in combination with zanubrutinib administered orally starting on C1D1 at 320 mg daily or 160 mg BID.

Initial Safety Data
The most frequent treatment emergent adverse events (TEAEs) observed in ≥20% of patients were neutropenia (48%) and nausea (33%), and the most frequent grade ≥3 TEAEs (≥10% of patients) were neutropenia (46%) and anemia (11%). Five patients discontinued treatment due to TEAEs in the monotherapy cohort; 3 TEAEs in 1 patient were treatment related: grade 3 hypotension, grade 3 diarrhea, and grade 4 neutropenia (n=1 each). No TEAEs led to treatment discontinuation in the combination therapy cohort.

PRT2527 dose interruptions due to TEAEs occurred in 17 patients (11 monotherapy; 6 combination therapy). Most dose interruptions were due to neutropenia and were managed with growth factor support. One DLT of grade 3 tumor lysis syndrome (TLS) occurred in a patient with primary cutaneous peripheral T cell lymphoma who had extensive disease at the 24 mg/m^2 monotherapy dose level and did not receive ramp-up dosing. TLS was managed with rasburicase and IV fluids and resolved. The patient was able to resume study treatment as planned. No DLTs were observed in the combination therapy cohort.

Dose level 3 (18 mg/m^2) was selected for dose confirmation for monotherapy and in combination with zanubrutinib due to higher rates of grade 3/4 neutropenia and of dose interruptions and reductions in the 24 mg/m^2 dose level.

Analysis of Initial Clinical Activity
Of the 23 efficacy evaluable patients in the monotherapy cohort, complete responses (CRs) were observed in 1 patient (DLBCL) and 3 partial responses observed (TCL), with an overall response rate (ORR) of 17.4% (4 of 23). Of the 13 patients in the combination cohort who were evaluable for efficacy, complete responses (CRs) were observed in 3 patients (2 DLBCL, 1 MCL) and 2 partial responses (PRs) observed (DLBCL and CLL) with an overall response rate (ORR) of 38.5% (5 of 13).

The above-noted presentation can be found at Publications - Prelude Therapeutics (preludetx.com).

“We believe the clinical data presented today with PRT2527 confirm our hypothesis that a highly selective and potent inhibitor of CDK9 has the potential to offer meaningful clinical activity for patients with hematologic malignancies, while avoiding the off-target toxicities observed with less selective agents,” stated Kris Vaddi, Ph.D., Chief Executive Officer of Prelude. “However, given the significant progress and potential of our SMARCA degrader programs that are currently advancing in the clinic, along with our productive discovery organization, we plan to focus our resources towards the continued advancement of those programs. As a result, we will only advance the CDK9 program with a partner beyond completion of the current ongoing Phase 1 study.”

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 is comprised of several novel drug candidates including first-in-class, highly selective IV and oral SMARCA2 degraders, and a potentially best-in-class CDK9 inhibitor. We are also leveraging our expertise in targeted protein degradation to discover, develop and commercialize next generation degrader antibody conjugates (Precision ADCs) with partners. We are on a mission to extend the promise of precision medicine to every cancer patient in need. 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, 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, 2023, 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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