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Celldex Therapeutics Initiates Phase 1/2 Study of Varlilumab in Combination with Atezolizumab in Renal Cell Carcinoma

HAMPTON, N.J., Dec. 8, 2015 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today announced the initiation of an open-label, Phase 1/2 safety and tolerability study examining the investigational combination of varlilumab and Roche's atezolizumab (MPDL3280A) in patients with unresectable stage III or IV renal cell carcinoma (RCC). Celldex previously announced the collaboration with Roche to evaluate the novel immunotherapy combination in March 2015. Under the terms of the agreement, Roche will provide atezolizumab, and Celldex will be responsible for conducting and funding the study. Varlilumab is currently being studied in five Phase 1/2 combination studies.

Varlilumab is Celldex's fully human monoclonal agonist antibody that binds and activates CD27, a critical co-stimulatory molecule in the immune activation cascade. Atezolizumab is designed to target PD-L1 expressed on tumor cells and tumor-infiltrating immune cells, preventing PD-L1 from binding to PD-1 and B7.1 on anti-tumor T cells. By inhibiting PD-L1, atezolizumab may enable the activation of anti-tumor T cells. These two antibodies are part of a new class of investigational medicines known as cancer immunotherapies. They are designed to harness the body's own immune system to fight cancer through separate yet complementary mechanisms of action that may enable the activation of T cells, restoring their ability to effectively detect and attack tumor cells.

Data from multiple preclinical tumor models suggest the combination of these two mechanisms are synergistic and enhance anti-tumor immune response compared to either agent alone. Also, in a Phase 1 study of varlilumab in multiple solid tumors, promising signs of clinical activity in patients with refractory RCC were observed, including a durable partial response (duration of response = 13.6+ months) that continued to decrease in tumor volume over time and prolonged stable disease (four patients with a range of 5.3 to 36.2+ months).

"Together, preclinical and clinical data suggest that combining varlilumab and atezolizumab may enhance anti-tumor immune responses compared to monotherapy," said Thomas Davis, M.D., Executive Vice President and Chief Medical Officer of Celldex Therapeutics. "Varlilumab is an attractive candidate for combination immunotherapy across a variety of cancers due to its target's restricted expression and strong activity in a variety of tumor models, as well as positive data and a favorable safety profile from our Phase 1 study."

Study Design

Phase 1 study portion

The Phase 1, dose-escalation portion of the study will assess the safety and tolerability of varlilumab at 0.3, 1.0 and 3.0 mg/kg combined with atezolizumab at 1200 mg in order to identify a recommended dose for the Phase 2 portion of the study. The Phase 1 portion will enroll patients with unresectable stage III or IV melanoma, RCC, triple negative breast cancer, bladder cancer, head and neck cancer or non-small cell lung cancer (NSCLC).

Phase 2 study portion

The Phase 2 portion of the study will enroll patients with RCC. The primary objective of this portion of the study is to assess the preliminary anti-tumor efficacy of the varlilumab/atezolizumab combination measured by objective response rate (ORR). Secondary objectives include safety and tolerability, pharmacokinetics, immunogenicity and further assessment of anti-tumor activity across a broad range of endpoints.

In total, the Phase 1/2 study is anticipated to include up to 10 sites in the United States and enroll approximately 60 patients. In each 12-week cycle for both phases of the trial, varlilumab and atezolizumab will be administered once every three weeks (four doses). Patients will be treated with varlilumab until intolerance, disease progression or completion of up to 4 cycles. There is no limit on the duration of treatment with atezolizumab.

About Varlilumab

Varlilumab is a fully human monoclonal agonist antibody that binds and activates CD27, a critical co-stimulatory molecule in

the immune activation cascade. CD27 can be effectively manipulated with activating antibodies to induce potent anti-tumor responses and may result in fewer toxicities due to its restricted expression and regulation. Varlilumab is a potent anti-CD27 agonist that induces activation and proliferation of human T cells when combined with T cell receptor stimulation. In lymphoid malignancies that express CD27 at high levels, varlilumab may have an additional mechanism of action through a direct anti-tumor effect. Varlilumab has completed a Phase 1 dose-escalation study, demonstrating potent immunologic activity consistent with its mechanism of action and anti-tumor activity in patients with advanced, refractory disease. No maximum tolerated dose was reached and minimal toxicities were observed. Celldex has initiated a broad development program for varlilumab to explore its role as an immune activator in combination with a number of complementary investigational and approved oncology drugs.

About Celldex Therapeutics, Inc.

Celldex is developing targeted therapeutics to address devastating diseases for which available treatments are inadequate. Our pipeline is built from a proprietary portfolio of antibodies and immunomodulators used alone and in strategic combinations to create novel, disease-specific therapies that induce, enhance or suppress the body's immune response. Visit www.celldex.com.

Forward Looking Statement

This release contains "forward-looking statements" made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including those related to the Company's strategic focus and the future development and commercialization (by Celldex and others) of RINTEGA® ("rindopepimut"; "rindo"; CDX-110), glembatumumab vedotin ("glemba"; CDX-011), varlilumab ("varli"; CDX-1127), CDX-1401, CDX-301 and other products and our goals for 2015. Forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events. Although management believes that the expectations reflected in such statements are reasonable, they give no assurance that such expectations will prove to be correct and you should be aware that actual results could differ materially from those contained in the forward-looking statements. Forward-looking statements are subject to a number of risks and uncertainties, including, but not limited to, our ability to successfully complete research and further development and commercialization of RINTEGA, glembatumumab vedotin and other drug candidates; our ability to obtain additional capital to meet our long-term liquidity needs on acceptable terms, or at all, including the additional capital which will be necessary to complete the clinical trials that we have initiated or plan to initiate; the uncertainties inherent in clinical testing and accruing patients for clinical trials; our limited experience in bringing programs through Phase 3 clinical trials; our ability to manage and successfully complete multiple clinical trials and the research and development efforts for our multiple products at varying stages of development; the availability, cost, delivery and quality of clinical and commercial grade materials produced by our own manufacturing facility or supplied by contract manufacturers, who may be our sole source of supply; the timing, cost and uncertainty of obtaining regulatory approvals; our ability to maintain and derive benefit from the Breakthrough Therapy Designation for RINTEGA, which does not change the standards for regulatory approval or guarantee regulatory approval on an expedited basis, or at all; the failure of the market for the Company's programs to continue to develop; our ability to protect the Company's intellectual property; the loss of any executive officers or key personnel or consultants; competition; changes in the regulatory landscape or the imposition of regulations that affect the Company's products; and other factors listed under "Risk Factors" in our annual report on Form 10-K and quarterly reports on Form 10-Q.

All forward-looking statements are expressly qualified in their entirety by this cautionary notice. You are cautioned not to place undue reliance on any forward-looking statements, which speak only as of the date of this release. We have no obligation, and expressly disclaim any obligation, to update, revise or correct any of the forward-looking statements, whether as a result of new information, future events or otherwise.

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