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Celldex's Varlilumab Demonstrates Synergistic Anti-Tumor Activity with PD-1 Signaling Blockade in Preclinical Studies

Data presented at 2015 AACR Annual Meeting

HAMPTON, N.J., April 20, 2015 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (Nasdaq:CLDX) announced today preclinical results that further support varlilumab's expansion into combination studies with PD-1 inhibitors. The data were presented in a poster session entitled "Synergistic anti-tumor activity of PD-1 signaling blockade and CD27 costimulation correlates with enhanced ratio of effector to regulatory T cells at the tumor site" at the 2015 American Association for Cancer Research Annual Meeting.

Varlilumab is a fully human immunoglobulin (Ig)G1 agonist antibody that binds to and activates CD27, a critical T-cell co-stimulatory molecule in the immune-activation cascade. Specific and controlled activation of CD27 in the presence of T-cell receptor (TCR) signaling by varlilumab results in enhanced immune responses with a favorable safety profile. Varlilumab is in clinical development for a range of cancers in combination with other therapies that target potentially synergistic points of immune-regulation, including with Opdivo®, BMS's PD-1 blocking antibody and with MPDL3280A, Roche's anti-PDL1 investigational cancer immunotherapy.

"These latest studies demonstrate that the combination of varlilumab and anti-PD-L1 induces a potent immune-mediated effect that results in important changes in the tumor microenvironment," said Tibor Keler, PhD, Co-founder, Executive Vice President and Chief Scientific Officer of Celldex Therapeutics. "Most notably, we observed that the combination strategy improved the ratio of effector T cells to regulatory T cells, which was accompanied by a reduction in the expression of PD-1 on both effector and regulatory T cells. Overall these studies, along with our clinical data where varlilumab has demonstrated anti-tumor activity with minimal toxicity in advanced, refractory disease, provide strong rationale for us to broadly explore varlilumab in combination with a number of complementary investigational and approved oncology drugs, including agents that work through the PD-1 signaling blockade."

Key findings:

The combination of varlilumab and anti-PD-L1 resulted in a significant improvement in survival over monotherapy in multiple preclinical tumor models, including a CT-26 colon model, an E.G7 thymoma model and a BCL1 disseminated lymphoma model. The properties of the BCL1 lymphoma model allowed for further analysis into the mechanism of synergy between varlilumab and anti-PD-L1. Importantly, mice cured by the combination therapy were shown to have developed protective immunity against the BCL1 tumor, demonstrating that a long lasting and potent memory response was generated during treatment. Additional key observations were made by analyzing the spleens (the primary site of tumor growth) following treatment. The major changes associated with the combination therapy included:

- A greater reduction in tumor cells (as measured by % decrease in CD19+ cells)
- Increased numbers of functional CD4+ and CD8+ T cells (as measured by IFNγ production)
- An increase in the ratio of CD8+ T cells (effector T cells) to regulatory T cells or Tregs
- A notable increase in myeloid cells, particularly neutrophils

These changes at the site of tumor growth, particularly the balance between effector T cells and regulatory T cells, are consistent with an immune-mediated effect resulting in the destruction of tumor cells. The increase in myeloid cells merits further investigation into their role in the combination therapy effect. Other changes including increases in natural killer cells and decreased PD-1 expression on T cells were noted, but these were similar in magnitude to the monotherapy treatments.

About Varlilumab

Varlilumab is a fully human monoclonal antibody that targets CD27, a critical molecule in the activation pathway of lymphocytes. 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 sustained 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. Varlilumab is currently being studied in three Phase 1/2 combination studies and several additional combination studies will be initiated in 2015.

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.

Celldex 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; 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 our 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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