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Celldex Presents Varlilumab Mechanism Data at SITC Annual Meeting 2015

-- Preclinical data suggest cancers vary in sensitivity to mechanisms of CD27 immune modulation --

-- Clinical experience with varlilumab is consistent with immune co-stimulation and regulatory T cell depletion mechanisms, a potential unique benefit for varlilumab --

-- Multiple Phase 1/2 varlilumab combination studies currently ongoing --

HAMPTON, N.J., Nov. 6, 2015 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today presented new preclinical data on varlilumab, a fully human monoclonal agonist antibody that binds and activates CD27, a critical co-stimulatory molecule in the immune activation cascade. Results suggest that cancers may respond to CD27 immune modulation by independent mechanisms, such as immune co-stimulation and regulatory T cell (Treg) depletion. Varlilumab has the unique ability to act through both of these mechanisms. The new data were presented in a poster entitled "[The mechanism of anti-tumor immunity induced by varlilumab, a CD27 agonist mAb, is model dependent](#)" at the Society for the Immunotherapy of Cancer (SITC) Annual Meeting.

"Our data show that CD27 modulation through varlilumab results in immune activation and suppression of Treg activity, either of which can be independently responsible for a therapeutic effect, depending on the cancer model," said Tibor Keler, Ph.D., Executive Vice President and Chief Scientific Officer of Celldex Therapeutics. "Because individual human cancers are also likely to have different sensitivities to these anti-tumor activities, varlilumab's ability to act through both mechanisms provides the broadest potential for therapeutic benefit. Our collection of preclinical and clinical results to date support Celldex's broad clinical development program across tumor types and in combinations with other anti-tumor agents."

To better understand each mechanism separately, scientists engineered varlilumab to possess either strong co-stimulatory activity (varli-mG1) or strong Treg suppression activity (varli-mG2a) and analyzed their efficacy in several preclinical tumor models. The data indicated that potent co-stimulation activity was required for therapeutic activity in a BCL1 lymphoma model, whereas control of Tregs was required for activity in several other models, such as E.G7 thymoma, CT26 colorectal and colon 26. Importantly, varlilumab has a combination of immune co-stimulation and Treg depleting activity and demonstrated potent anti-tumor activity in all the models.

The immune stimulating and Treg depleting effects of varlilumab were also observed in Celldex's Phase 1, single-agent clinical trial of varlilumab in patients with refractory, advanced cancers. Specifically, varlilumab administration was associated with a rapid and transient induction of pro-inflammatory cytokines, activation of T cells as assessed by increased HLA-DR expression and a significant decrease in circulating Tregs. The study also demonstrated promising clinical activity. Two patients experienced durable objective responses including a complete response in Hodgkin lymphoma (18.9+ months) and a partial response in renal cell carcinoma (13.6+ months). Thirteen patients experienced stable disease (3-36.2+ months). Varlilumab was very well tolerated and demonstrated minimal toxicity, even in elderly patients. There was no indication of immune-mediated adverse events often seen with other immunotherapies. Varlilumab is currently being studied in multiple ongoing Phase 1/2 clinical trials with several anti-tumor agents, including nivolumab (Opdivo®), ipilimumab (Yervoy®) and sunitinib (Sutent®) in advanced-stage cancers. Efforts are underway for additional Phase 2 studies with varlilumab, including a combination with atezolizumab (Roche's anti-PDL1 antibody), and the Company will provide updates on these studies as they are initiated.

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. Data from a Phase 1 dose-escalation study of varlilumab demonstrated 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.

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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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