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# Celldex Presents Positive Interim Results from Phase 1 Study of CD40 Agonist CDX-1140 at American Association for Cancer Research (AACR) Annual Meeting 2019

April 2, 2019

*--CDX-1140 has achieved good systemic exposure without reaching a maximum tolerated dose to date--*
*--Addition of dendritic cell growth factor CDX-301 enhances cytokine response without additive toxicity at dose levels tested to date--*
*--Tumor specific expansion cohorts planned--*

HAMPTON, N.J., April 02, 2019 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) presented interim data from the Company's CD40 agonist program in a late-breaking poster session today at the American Association for Cancer Research (AACR) Annual Meeting 2019. CD40, expressed on dendritic cells and other antigen presenting cells, is an important target for immunotherapy, as it plays a critical role in the activation of innate and adaptive immune responses.CDX-1140 is a fully human agonist anti-CD40 monoclonal antibody that was specifically designed to balance good systemic exposure and safety with potent biological activity, a profile which differentiates CDX-1140 from other CD40-activating antibodies.

CDX-1140 is currently in a Phase 1 dose escalation study. The study includes both monotherapy and combination cohorts with CDX-301, Celldex's dendritic cell growth factor, designed to increase the number of dendritic cells which are critical to initiating antitumor immunity and are a key target for CDX-1140.

"Preclinical data support that CD40 activation could play an extremely important role in cancer immunotherapy by activating anti-tumor immunity and overcoming resistance to PD-1 blockade," said Rachel Sanborn, MD, Co-director of the Thoracic Oncology Program and Leader of the Phase 1 Trials Program at Providence Cancer Institute and a lead investigator in this study. "The interim results presented today have demonstrated that CDX-1140 is a potent activator of CD40 and can be safely administered at doses that we believe will support good tissue and tumor penetration. We are now reaching dose levels that have the potential for meaningful clinical benefit, especially in combination with drugs that target other key immune pathways, and look forward to initiating tumor specific expansion cohorts to test potential clinical activity."

CDX-1140 has a unique combination of properties relative to other CD40 agonist antibodies: potent agonist activity resulting in dendritic cell and B cell activation is independent of Fc receptor interaction, contributing to more consistent, controlled immune activation; CD40 ligand (CD154) binding is not blocked, allowing potential synergy with the natural CD40 activation pathway; and the antibody promotes strong immune activation without significant adverse events in preclinical toxicology studies.

**Presentation Highlights:**

Abstract #: LB-194: First in human Phase 1 study of the CD40 agonist monoclonal antibody (mAb) CDX-1140 alone and in combination with CDX-301 (rhFLT3L) in patients with advanced cancers: interim results (Sanborn, et. al)

- Overview: 30 patients were enrolled in the study at the time of data analysis (n=22 monotherapy; n=8 combination. Six monotherapy dosing cohorts in both solid tumors and non-Hodgkin lymphoma (NHL) (0.01, 0.03, 0.09, 0.18, 0.36 and 0.72 mg/kg) have been completed. The seventh monotherapy cohort at 1.5 mg/kg is currently being enrolled. Two combination cohorts in solid tumors (0.09 and 0.18 mg/kg) with CDX-301 have been completed and the third cohort at 0.36 mg/kg is currently being enrolled. In general, patients have advanced disease and are heavily pretreated (median number of prior therapies: 4 monotherapy arm; 3.5 combination arm).

- Safety: CDX-1140 has been generally well tolerated. A maximum tolerated dose (MTD) has not been reached to date and only three patients have experienced serious treatment related adverse events (pneumonitis and hypoxia; possible cytokine release, fatigue and fever; and, fatigue and nausea). High grade, drug-related (Grade 3 and above) changes in liver function tests or platelet count have not been observed to date, including at CDX-1140 dose levels which exceed the MTDs reported with other CD40 agonists. The addition of CDX-301 has not affected the tolerability of CDX-1140 at dose levels tested to date in the combination cohorts.

- Systemic Dosing and Biomarker Analysis: Higher dose levels have achieved circulating antibody concentrations in the range of 20 to 30 micrograms CDX-1140 per milliliter. Transient dose-dependent pharmacodynamic effects have been observed including activation of dendritic cells and B cells, along with increases in pro-inflammatory cytokines and chemokines in the blood, all of which are consistent with CD40-mediated immune activation and the hypothesis that CDX-1140 is achieving dose levels optimal for systemic exposure. The addition of CDX-301 has further enhanced cytokine responses.

- Early Clinical Activity: While not anticipated at these lower CDX-1140 dose levels, stable disease has been observed in this heavily pretreated population who have received, at a minimum, all standard of care therapies for their tumor type. Recently enrolled dose levels are still under evaluation.

- Future development: Additional patient enrollment (backfill) has been initiated at the 0.72 mg/kg CDX-1140 dose level to characterize the effects of CDX-1140 in the tumor microenvironment and tumor specific expansion cohorts are planned. Future combination opportunities are being considered, including with PD-1 or PD-L1 inhibitors, radiation therapy and

Celldex's potent CD27 agonist monoclonal antibody varlilumab. Several B cell lymphomas (subtypes of NHL) express both CD40 and CD27 and varlilumab has been shown to synergize with CDX-1140 in NHL models.

**About Celldex Therapeutics, Inc.**
Celldex is developing targeted therapeutics to address devastating diseases for which available treatments are inadequate. Our pipeline includes immunotherapies and other targeted biologics derived from a broad set of complementary technologies which have the ability to engage the human immune system and/or directly inhibit tumors to treat specific types of cancer or other diseases. 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. These statements are typically preceded by words such as "believes," "expects," "anticipates," "intends," "will," "may," "should," or similar expressions. These 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 or that those goals will be achieved, 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 Company 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; our ability to maintain compliance with Nasdaq listing requirements; our ability to realize the anticipated benefits from the acquisition of Kolltan; 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 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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