Celldex Presents Promising Interim Data from Phase 1 Study of Differentiated CD40 Agonist CDX-1140 at the Society for Immunotherapy of Cancer's 33rd Annual Meeting

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--Well tolerated; dose dependent biological effects consistent with CD40-mediated immune cell activity--
--Program development expanded based on results observed to date--

HAMPTON, N.J., Nov. 09, 2018 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) presented interim data today from the Phase 1 dose-escalation study of CDX-1140, a fully human agonist anti-CD40 antibody. CD40, expressed on dendritic cells and other antigen presenting cells, has long been an important target for immunotherapy, as it plays a critical role in the activation of innate and adaptive immune responses. The data were presented in a poster session at the Society for Immunotherapy of Cancer's (SITC) 33rd Annual Meeting.

"CDX-1140 was specifically designed to balance systemic dosing and safety, which has proven elusive for CD40-targeted activating therapeutics," said Tibor Keler, Ph.D., Executive Vice President and Chief Scientific Officer of Celldex Therapeutics. "We have completed four of the potential eight monotherapy dose levels and, to date, CDX-1140 has been well tolerated. Importantly, we are observing dose-dependent biological effects consistent with CD40-mediated immune cell activity. Based on these positive findings, we have expanded development of the program and recently initiated a combination cohort with CDX-301, our dendritic cell growth factor, to increase the number of dendritic cells which are critical to initiating antitumor immunity and a key target for CDX-1140. We also expanded the study to include patients with non-Hodgkin's lymphoma as our preclinical work has demonstrated that CDX-1140 has direct killing effect on CD40-expressing NHL cells. We look forward to continued data updates from this study in the first half of 2019."

Potent CD40 agonist antibodies have shown encouraging results in early clinical studies; however, systemic toxicity associated with broad CD40 activation has limited their dosing. CDX-1140 has unique 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 synergistic, antigen-specific agonist activity; and the antibody promotes strong immune activation without significant adverse events in preclinical toxicology studies.

Study Highlights:
Seventeen patients with solid tumors were enrolled at the time of data analysis (n=13 monotherapy; n=4 combination). Four single-agent dosing cohorts have completed (0.01; 0.03, 0.09 and 0.18 mg/kg) and enrollment to the 0.36 mg/kg monotherapy cohort is ongoing. Enrollment to the first CDX-1140/CDX-301 combination cohort is ongoing (0.09 mg/kg and 75 ug/kg, respectively). Dose dependent biological effects consistent with CD40-mediated immune activation have been observed in the study and no maximum tolerated dose (MTD) has been identified to date. Continued enrollment is ongoing to define the MTD and select a dose for disease-specific expansion cohorts that will be monitored for clinical activity.

- CDX-1140 has been well tolerated to date. One patient experienced a grade 3 dose-limiting toxicity (DLT) (pneumonitis and hypoxia) at the single-agent 0.18 mg/kg dose. Per protocol, three additional patients were enrolled in the cohort and no additional DLTs have been observed in this or subsequent cohorts.

- There have been no significant drug-related changes observed to date in liver function tests or platelets, which have been observed with other CD40 agonists.

- Transient dose-dependent pharmacodynamic effects have been observed including activation of immune cells and increases in pro-inflammatory cytokines and chemokines in the blood, which are consistent with CD40-mediated immune activation and the hypothesis that CDX-1140 may achieve dose levels optimal for systemic exposure.

- A combination cohort with Celldex's dendritic cell growth factor CDX-301 has been added to the CDX-1140 study. Dendritic cells, which express CD40, are rarely present or completely absent within the tumor microenvironment and are critical for initiating anti-tumor immunity. CDX-301 is being utilized to increase the number of dendritic cells in blood and tissue available for CDX-1140 activation. CDX-1140 should, in turn, activate the dendritic cells, an important step for enhancing anti-tumor immune responses. While this combination cohort just recently opened to enrollment, preliminary evidence of enhanced immune activation has been observed. Patients continue to be monitored for toxicity with no DLT observed to date.

- The study has also been amended to allow for the inclusion of patients with CD40-expressing B cell lymphomas (subtypes

of non-Hodgkin lymphoma or NHL) in up to two single-agent cohorts. Both immune activation and direct killing of CD40-expressing NHL cells by CDX-1140 have been shown to contribute to antitumor activity. Several B cell lymphomas, including diffuse large B-cell lymphoma and follicular lymphoma, also express both CD40 and CD27. Celldex's varlilumab is a potent CD27 agonist and has been shown to synergize with CDX-1140 in NHL models and may be evaluated in combination with CDX-1140 in the future.

About CDX-1140
CDX-1140 is a fully human antibody targeted to CD40, a key activator of immune response that is found on dendritic cells, macrophages and B cells and is also expressed on many cancer cells. Potent CD40 agonist antibodies have shown encouraging results in early clinical studies; however, systemic toxicity associated with broad CD40 activation has limited their dosing. CDX-1140 has unique 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 synergistic, antigen-specific agonist activity; and the antibody promotes strong immune activation without significant adverse events in preclinical toxicology studies. CDX-1140 has also shown direct antitumor activity in preclinical lymphoma models. Celldex believes that the potential for CDX-1140 will be best defined in combination studies with other immunotherapies, including CDX-301, Celldex's dendritic cell growth factor, varlilumab, Celldex's potent CD27 agonist, checkpoint blockade, radiation and other conventional cancer treatments.

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 meet, and with respect to the minimum bid price requirement, to regain compliance with, Nasdaq listing requirements; our ability to realize the anticipated benefits from the acquisition of Kolltan and to operate the combined business efficiently; 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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