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Celldex Therapeutics' CDX-1127 Well Tolerated and Demonstrates Anti-Tumor Activity in Phase 1 Dose-Escalation Study

Very favorable safety profile; no evidence of immune related toxicities

Three patients with significant tumor shrinkage, including an ongoing CR in Hodgkin disease

Eight patients with stable disease or better; PFS range of 3.0 to 14+ months

Immune monitoring data in patients confirms CDX-1127 mechanism of action

PHILLIPSBURG, N.J., Nov. 7, 2013 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (Nasdaq:CLDX) today reported data from its ongoing Phase 1 dose-escalation study of the fully human monoclonal antibody CDX-1127. The results suggest an excellent safety profile and demonstrate clear biologic activity and promising signs of clinical activity in an advanced, refractory patient population. No maximum tolerated dose has been reached to date. The data will be presented in two poster sessions (poster #144 and 146) at the 2013 Society for Immunotherapy of Cancer (SITC) Annual Meeting, November 7 — 10, 2013. In addition, a third poster (#85) will be presented on preclinical combination studies of CDX-1127 with chemotherapies and checkpoint inhibitors. The Company will host a webcast/conference call at 8:30 am ET today to discuss the results (details provided below).

"CDX-1127 has exceeded our expectations thus far in this ongoing Phase 1 dose-escalation study," said Thomas Davis, MD, Senior Vice President and Chief Medical Officer of Celldex Therapeutics. "Our primary goal was to establish a favorable safety profile, a challenge that other agonist antibodies in this class have not been able to meet. To date, CDX-1127 has demonstrated minimal toxicity and, importantly, no evidence of worrisome overlap with toxicities seen with other immunotherapies—a critical hurdle for combination therapy. We were also very pleased to see clear evidence of biologic and anti-cancer activity in a heavily pretreated patient population. While future data from the expansion cohorts will be important to understanding single-agent activity, we are confident based on the dose-escalation data we have seen to date that we are well positioned to initiate combination studies of CDX-1127, with a particular interest in immune modulators."

"We are encouraged by the initial safety and activity profile observed to date and believe CDX-1127 could play an important role in the field of cancer immunotherapy," said Howard A. "Skip" Burris, III, MD, Chief Medical Officer and Executive Director of the Drug Development Program at Sarah Cannon Research Institute and a lead investigator of the Phase 1 CDX-1127 study. "An agonist with this safety and biologic activity profile has potential, particularly in combination with checkpoint inhibitors, where the ability to mount an immune response could expand the effectiveness of these compounds for more patients."

CDX-1127 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 less toxicities due to its restricted expression and regulation. CDX-1127 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, CDX-1127 has an additional mechanism through a direct anti-tumor effect.

Study Overview:

The Phase 1 dose-escalation study of CDX-1127 includes two arms—solid tumors and lymphoid malignancies and is designed to evaluate five doses (0.1, 0.3, 1, 3, 10 mg/kg). Enrollment is complete in the solid tumor dose-escalation arm (n=25) and expansion cohorts are ongoing in metastatic melanoma and renal cell carcinoma. In the dose-escalation lymphoid malignancies arm (n=17), enrollment recently initiated in the 10 mg/kg cohort and expanded development is being planned. Currently, first response assessments are pending for four patients across the 1 and 3 mg/kg cohorts and all patients in the 10 mg/kg cohort in the lymphoid malignancies arm. Patients enrolled in the study across both arms had advanced disease and most were heavily pretreated. Patients progressed on previous therapies and had no remaining approved treatment options before study entry. The median number of prior therapies is 5 anti-cancer (3 cytotoxic) for solid tumors and 4 anti-cancer (3 cytotoxic) for lymphoid malignancies.

Safety and Immune Monitoring Overview:

In the solid tumor dose-escalation phase, CDX-1127 was associated with minimal toxicity including at the highest dose levels through multiple cycles. No maximum tolerated dose was reached. The most common treatment-related adverse events were decreased appetite (12%) and fatigue (12%). One patient experienced a dose limiting toxicity (DLT), a Grade 3 transient asymptomatic hyponatremia 14 days after a single 1.0 mg/kg dose of CDX-1127. Hyponatremia has not been attributed to CDX-1127 in any other patient. The safety data from the lymphoid malignancies arm also show that CDX-1127 has been well tolerated with no DLTs to date.

The preliminary assessment of pharmacokinetics demonstrates significant exposure to CDX-1127 throughout the duration of the study period. Immune monitoring assessments conducted in the solid tumor arm support the overall safety profile and also demonstrate that CDX-1127 induces immunologic activity in patients that is consistent with both its mechanism of action and preclinical models, including an increase in Natural Killer cells and in T cells that express the activation marker, HLA-DR. The study also identified the serum chemokine, interferon-gamma inducible protein 10 (IP-10) as a significant biomarker for CDX-1127 treatment. Of note, the study confirms that CDX-1127 does not induce major lymphocyte depletion, but does reduce the number of regulatory T cells, which are thought to have immune suppressive activity. Taken together, these markers demonstrate clear evidence of lymphocyte activation—the direct purpose of CDX-1127 therapy.

Clinical Activity Overview:

Across both arms, eight patients experienced stable disease or better with a PFS range of 3.0 to 14+ months. In addition, three patients experienced significant tumor shrinkage, including a complete response as outlined below.

- A 28 year old female with Stage IV Hodgkin lymphoma achieved a complete response, including complete resolution of B symptoms (drenching sweats, pruritus and weight loss)—an important marker of disease activity in Hodgkin disease, after three cycles of CDX-1127 (0.3 mg/kg). The patient remains in remission at 8.6+ months. During treatment, the area of measurable lesions first increased and then regressed. This pattern is consistent with the current perception of an immune mediated response. The patient was heavily pretreated, including high dose chemotherapy with autologous marrow transplantation, and most recently had progressed after less than one month on Adcetris™ plus chemotherapy.

- A 69 year old male with Stage IV colorectal cancer metastatic to the liver, lung and peritoneum was treated with CDX-1127 (1 mg/kg) and had a 33% unidimensional shrinkage of measurable disease and a PFS of 5.7 months. The shrinkage was associated with small, new lesions representing a mixed response. The patient had previously received multiple agents, including Avastin® and most recently had progressed through Xeloda®/radiation at two weeks.

- A 67 year old male with Stage III marginal zone B-cell lymphoma who received CDX-1127 (0.3 mg/kg) experienced a 36% shrinkage of measurable disease, including complete disappearance of disease in the inguinal and iliac regions and had a PFS of 5.6 months. The patient was very heavily pretreated with 10 prior regimens of cytotoxic, radiation and Rituxan® therapy.

Two patients received all five cycles of treatment and were on trial for greater than a year, including:

- An 83 year old male with Stage IV renal cell carcinoma metastatic to liver and lung who remains progression-free at 14+ months after study entry, and

- A 52 year old male with Stage IV follicular lymphoma who had a PFS of 14 months.

The Company also reported very early data from the solid tumor expansion cohorts, where CDX-1127 has been well-tolerated to date. The melanoma cohort has accrued 14 patients at 3 mg/kg with eight patients continuing treatment, seven who have not yet been seen for the first assessment of response. One patient with uveal melanoma who is entering the third round of treatment has experienced a 12% shrinkage of measurable disease by RECIST and stable disease is ongoing at 5.7 months. The renal cell carcinoma arm has accrued eight patients at 3 mg/kg with seven continuing treatment, all of whom have not yet been seen for the first assessment of response.

In a separate poster, the Company reported new data of CDX-1127 in combination therapy using mouse tumor models. Agents that induce tumor killing to provide a source of antigen and agents that block T cell inhibitory molecules were chosen for their potentially complementary mechanisms of action. Employing challenging treatment settings where single agent activity is limited, a clear survival benefit was observed with CDX-1127 combinations of cyclophosphamide or checkpoint blockade. These studies, together with the favorable safety profile and activity data from the Phase 1 trial with CDX-1127, support the initiation of combination trials with conventional and immune-based therapies.

Webcast/Conference Call Information:

Celldex management will host a conference call/webcast at 8:30 am ET today to discuss the CDX-1127 program. Mario Sznol, MD, Professor, Internal Medicine, Vice-Chief, Section of Medical Oncology, Co-director, Yale Spore in Skin Cancer and Translational Research Leader, Melanoma Program at Yale Cancer Center and Dr. Madhav Dhodapkar, MBBS, Professor of Medicine and Chief, Section of Hematology at Yale Cancer Center will join the call.

The conference call and presentation will be webcast live over the Internet and can be accessed by logging on to the Events & Presentations section under "Investors and Media" of the Celldex Therapeutics website at www.celldex.com. The call can also be accessed by dialing (866) 743-9666 (within the United States) or (760) 298-5103 (outside the United States). The passcode is 93902541.

A replay of the call will be available approximately one week after the live call concludes through November 14, 2013. To access the replay, dial 855-859-2056 (within the United States) or 404-537-3406 (outside the United States). The passcode is 93902541. The webcast will also be archived on the Company's website.

Adcetris is a registered trademark of Seattle Genetics; Avastin and Xeloda are registered trademarks of Roche; Rituxan is a registered trademark of Biogen.

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.

Safe Harbor Statement Under the Private Securities Litigation Reform Act of 1995: *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 rindopepimut (CDX-110), Glembatumumab vedotin ("glemba"; CDX-011), CDX-1135, CDX-1401, CDX-1127, CDX-301, Belinostat and other products. 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 rindopepimut, glemba 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; our ability to adapt our APC Targeting Technology™ to develop new, safe and effective vaccines against oncology and infectious disease indications; our ability to successfully complete product research and further development of our programs; the uncertainties inherent in clinical testing; our limited experience in bringing programs through Phase 3 clinical trials; our ability to manage research and development efforts for multiple products at varying stages of development; 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.*

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.

CONTACT: Sarah Cavanaugh

Vice President of Investor Relations &

Corp Communications

Celldex Therapeutics, Inc.

(781) 433-3161

scavanaugh@celldex.com

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