Celldex Therapeutics, Inc. Logo

Data from Multiple Celldex Programs Presented at American Association for Cancer Research (AACR) Annual Meeting 2018

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-- Early data from investigator-initiated pilot study of CDX-301/radiation therapy combination in patients with advanced NSCLC show promising effect on tumor burden even in non-irradiated tumors --

-- Additional four posters at AACR Annual Meeting support ongoing Phase 2 study of CDX-3379, Phase 1 study of CDX-1140 and preclinical bispecific antibody (CD27xPDL1) program --

HAMPTON, N.J., April 20, 2018 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today announced promising early data from an investigator-initiated pilot study evaluating the combination of CDX-301 and stereotactic body radiotherapy (SBRT) in patients with advanced non-small cell lung cancer (NSCLC). CDX-301 (recombinant human Flt3 ligand) is a potent hematopoietic cytokine that uniquely expands dendritic cells and hematopoietic stem cells. This translational study is the culmination of significant preclinical research into strategically combining radiation and immunotherapy to effectively treat aggressive tumors and is supported by a Small Business Innovation Research (SBIR) grant from the National Cancer Institute to Celldex in collaboration with Albert Einstein College of Medicine, part of Montefiore. The data were presented during a plenary session at the American Association for Cancer Research (AACR) Annual Meeting 2018 earlier this week by Nitin Ohri, M.D., Attending Physician, Montefiore and Assistant Professor, Department of Radiation Oncology, Einstein, and principal investigator on the study.

The concept that increasing the number of dendritic cells with Flt3 ligand combined with an ablative course of radiation to the primary tumor induces a systemic anti-tumor response, suppresses metastases and promotes survival and immune memory was demonstrated through preclinical studies led by Dr. Chandan Guha and colleagues at the Einstein College of Medicine.[1] Based on this seminal work, a Phase 2 pilot study of CDX-301 in combination with SBRT was initiated at the Montefiore Einstein Center for Cancer Care. The study is currently enrolling up to 29 patients, and the primary objective is progression-free survival at four months after treatment (PFS4). Key secondary objectives include evaluation of dose-limiting toxicities and response rate in non-irradiated tumors, where tumor shrinkage from radiation therapy or CDX-301 independently would not be expected. Responses were particularly impressive when classified by PERCIST (PET Response in Solid Tumors) criteria, in which a partial response is at least a 45% reduction of total glycolytic activity, a volumetric measure of disease burden. The presentation included data from nine patients, seven of whom were previously treated with anti-PD(L)1 checkpoint inhibitors. The one-week course of treatment included subcutaneous injections of CDX-301 and SBRT directed to a single lung tumor lesion.

Key Highlights

- PFS4 was achieved in 56% (5/9) of patients overall (n=9; enrollment ongoing) and in 100% (5/5) of patients who experienced partial responses (PRs) by PERCIST
- Notably, PRs were observed in non-irradiated tumors in 56% (5/9) of patients at two months; 3 PRs (3/9) were confirmed by immune-related response criteria (irRC)
- In the patients previously treated with immune checkpoint inhibitors, 71% (5/7) experienced PRs and PFS4 versus 0% (0/2) in patients not treated with an anti-PD(L)1 therapy
- SBRT in combination with CDX-301 induced and reactivated anti-tumor immune responses in patients who had progressive disease on checkpoint inhibitors
- No dose-limiting toxicities were observed

“The combination of CDX-301 and radiation produced a significant decrease in tumor burden after just one course of treatment, even in non-irradiated tumors. We saw a longer period of survival for several of our patients with advanced lung cancer,” said Dr. Ohri. “We are looking forward to completing enrollment in the study, determining an optimal dosing regimen and identifying additional immune modulating agents.”

“Of particular interest is the potential correlation of clinical benefit with those patients who previously were treated with PD-1 blockade therapy, suggesting SBRT and CDX-301 may be able to reboot the immune system for an effective anti-tumor response,” said Tibor Keler, Ph.D., Executive Vice President and Chief Scientific Officer of Celldex Therapeutics. “We believe that the activity of this combination may potentially be augmented by the addition of CDX-1140, our unique CD40 agonist antibody, which is designed to activate dendritic cells and is currently in a Phase 1 dose-escalation study.”

Additionally, Celldex and its collaborating investigators presented four posters at the AACR Annual Meeting 2018:

- **Poster CT058: Molecular and clinical activity of CDX-3379, an anti-ErbB3 monoclonal antibody, in head and neck squamous cell carcinoma: A preoperative "window of opportunity" study (Duvvuri, *et al*)**

  A “window-of-opportunity” study enrolled 12 patients to evaluate the effect of CDX-3379 on phosphorylated ErbB3 (pErbB3) and other potential biomarkers in patients with head and neck squamous cell carcinoma (HNSCC). Patients with newly diagnosed HNSCC received two doses of CDX-3379, at a two-week interval prior to tumor resection. CDX-3379 reduced pErbB3 levels in 83% (10/12) of patient samples, with greater than or equal to 50% decreases in 58% of patients (7/12), which met the primary study objective. Stable disease was observed in 92% (11/12) of patients prior to surgery, and a patient with HPV-negative disease experienced significant tumor shrinkage (92% in primary tumor; 26% in metastatic lesion). CDX-3379 was well-tolerated, and no treatment-related adverse events were observed.

- **Poster 876: Effective reduction of PD-L1 expression by simultaneous blockade of EGFR and HER3 (ErbB3) in head and neck cancer (Chen, *et al*)**

  Investigators examined the effects of combining CDX-3379, a monoclonal antibody targeting ErbB3, and cetuximab, a monoclonal antibody targeting EGFR, in xenograft models of head and neck squamous cell carcinoma. Combining CDX-3379 and cetuximab inhibited tumor growth more potently than cetuximab alone. Mechanistic studies demonstrated a reduction of PD-L1 expression from the combination.

- **Poster 3816: Efficacy of CDX-1140, an agonist CD40 antibody, in preclinical tumor models (Thomas, *et al*)**

  Building off previously presented preclinical work, CDX-1140 was further characterized showing tumor shrinkage and prolonged survival in several xenograft models. These preclinical studies support the potential of CDX-1140 having direct anti-tumor effects on CD40-positive tumors that may supplement its activity as an immune activating agent.

- **Poster 5624: Development of novel bispecific immune modulating antibodies (Vitale, *et al*)**

  Celldex's initial bispecific antibody (BsAb) couples CD27 co-stimulation with blockade of the PD-L1/PD-1 pathway, using novel highly active anti-PD-L1 antibodies. The BsAb was more potent in human T cell activation and anti-tumor activity, compared to the combined CD27 and PD-L1 antibodies. Enhanced efficacy has been attributed to more efficient cross-linking of the BsAb/CD27 receptor, resulting in stronger T cell activation.

The CDX-301 presentation and all posters are available on the "Publications" page of the "Science" section of the Celldex website.

About CDX-301
CDX-301 (Flt3L) is a potent hematopoietic cytokine that has demonstrated a unique capacity to increase the number of circulating dendritic cells in both laboratory and clinical studies, including CD141+ dendritic cells critical for cross-presenting tumor antigens to cytotoxic T cells. In addition, CDX-301 has shown impressive results in models of cancer, infectious diseases and inflammatory/autoimmune diseases. Celldex believes this ligand may hold significant opportunity for synergistic development in combination with other proprietary molecules in the Company's portfolio.

About CDX-3379
CDX-3379 is a human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody that selectively binds and inhibits ErbB3 activity. ErbB3 may be an important receptor regulating cancer cell growth and survival as well as resistance to targeted therapies, and it is expressed in many cancers, including head and neck, thyroid, breast, lung and gastric cancers, as well as melanoma. The proposed mechanism of action for CDX-3379 sets it apart from other drugs in development in this class due to its ability to block both ligand-independent and ligand-dependent ErbB3 signaling by binding to a unique epitope. It has a favorable pharmacologic profile, including a longer half-life and slower clearance relative to other drug candidates in this class. CDX-3379 also has potential to enhance anti-tumor activity and/or overcome resistance in combination with other targeted and cytotoxic therapies to directly kill tumor cells.

About CDX-1140
CDX-1140 is a fully human monoclonal 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 is independent of Fc receptor interaction, contributing to more consistent, controlled immune activation; CD40L binding is not blocked, leading to potential synergistic effects of agonist activity with activated T cells in lymph nodes and tumors; and the antibody does not promote cytokine production in whole blood assays. CDX-1140 activates dendritic cells and other CD40 expressing cells and has also shown direct anti-tumor activity in preclinical models of lymphoma. The Company believes that the potential for CDX-1140 will be best defined in combination studies with other immunotherapies or conventional cancer treatments.

References
1. Chakravarty, *et al. Cancer Res.* 1999. 59(24):6028-32.

About Celldex Therapeutics, Inc.
Celldex is developing targeted therapeutics to address devastating diseases for which available treatments are inadequate. Our pipeline includes antibodies, antibody-drug conjugates and other protein-based therapeutics 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 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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