April 18, 2016

Celldex Therapeutics Presents Favorable Safety Profile and Immune Response Data from Phase 1/2 Study of Varlilumab and Nivolumab at the AACR Annual Meeting 2016

-- All varlilumab dose levels showed acceptable tolerability/safety in combination regimen; Phase 2 portion of study now open to enrollment --

-- Celldex and collaborating investigators presenting seven posters on pipeline programs at AACR 2016 --

HAMPTON, N.J., April 18, 2016 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) announced today new safety and immune response data from the Phase 1 portion of a Phase 1/2 dose escalation and cohort expansion study examining the investigational combination of varlilumab, Celldex's CD27 targeting investigational immune-activating antibody, and Bristol-Myers Squibb's anti-PD-1 immunotherapy Opdivo® (nivolumab). The data were presented today in a poster at the American Association for Cancer Research (AACR) Annual Meeting 2016 in New Orleans. The Phase 1 portion of the study, conducted in patients with solid tumors, has completed enrollment (n=36) and primarily enrolled patients with colorectal (n=20) and ovarian cancer (n=8). The primary objective of the Phase 1 portion of the study was to evaluate the safety and tolerability of the combination. The Phase 2 portion of the study is open to enrollment.

Key Highlights:

- Combining the potent immune activator, varlilumab, with the PD-1 inhibitor, nivolumab, showed acceptable tolerability and safety across all dose levels without any evidence of increased autoimmunity or inappropriate immune activation.
- Combination therapy led to marked changes in the tumor microenvironment including increased infiltrating CD8+ T cells and increased PD-L1 expression, which have been shown to correlate with a greater magnitude of treatment effect from checkpoint inhibitors in other clinical studies.
  - Additional favorable immune biomarkers, such as increase in inflammatory chemokines and decrease in T regulatory cells, were also noted.
- In a subset of patients (n=17) on study who had both pre- and post-tumor biopsies available, preliminary evidence suggest a correlation between biomarker data and stable disease or better in seven of these patients (4 ovarian cancer, 2 colorectal cancer, 1 squamous cell carcinoma of the head and neck).

"The combination of varlilumab and nivolumab demonstrated acceptable tolerability across all dose levels of varlilumab, showing that immune stimulation through CD27 was safely combined with PD-1 blockade," said Tibor Keler, Ph.D., Executive Vice President and Chief Scientific Officer of Celldex Therapeutics. "In addition, we observed favorable changes in intratumoral immune biomarkers, most notably an increase in tumor infiltrating lymphocytes, which is recognized to correlate with improved clinical outcome. Based on the strong preclinical data, scientific rationale and these recent results, we are very excited for the Phase 2 portion of the trial, which is now open to enrollment across six different indications."

The Phase 2 portion of the study includes cohorts in advanced non-small cell lung cancer (n=35), colorectal cancer (n=18), ovarian cancer (n=18), head and neck squamous cell carcinoma (n=18), renal cell carcinoma (n=25) and glioblastoma (n=20). The primary objective of the Phase 2 study is overall response rate for all cohorts except glioblastoma, where the primary objective is the rate of 12-month overall survival. Secondary objectives include pharmacokinetics assessments, determining the immunogenicity of varlilumab when given in combination with nivolumab and further assessing the anti-tumor activity of combination treatment, including duration of response, time to response, progression-free survival and overall survival. The study is being conducted by Celldex under a clinical trial collaboration with Bristol-Myers Squibb Company. The companies are sharing development costs.

Celldex and its collaborating investigators are presenting seven posters at the AACR Annual Meeting. As of Monday, April 18, four of these posters have been presented and summaries of these, including the Phase 1/2 varlilumab/nivolumab combination study, can be found below.

Title: Phase 1 results from the combination of an immune activating anti-CD27 antibody (varlilumab) in combination with PD-1 blockade (nivolumab): activation across multiple immune pathways without untoward immune-related adverse events

The Phase 1, dose-escalation portion of the study assessed the safety and tolerability of varlilumab at doses ranging from 0.1 to 10 mg/kg when administered with nivolumab (3 mg/kg). Enrollment to the Phase 1 study portion is complete with a total of 36 patients treated. Data for 35 patients are included in the poster: colorectal cancer (n=20), ovarian cancer (n=8), metastatic melanoma (n=4) and head and neck squamous cell carcinoma (n=3). 69% of patients had three or more prior therapies.

All dose levels of the combination therapy showed acceptable tolerability and safety, without identification of a maximum tolerated dose. In the Phase 2 portion of the study, varlilumab will be administered at 3 mg/kg, which is based upon cumulative data across multiple studies.

The safety profile of the varlilumab and nivolumab combination has been consistent with that of each agent individually, and no unexpected toxicities have been observed. The most frequent treatment related adverse events, occurring in more than 10% of patients, were fatigue (25.7%), lymphopenia (20%), nausea (20%), chills (17.1%), arthralgia (14.3%), pruritus (14.3%) and rash (11.4%), the majority of which were grade 1 or 2. Two patients experienced drug-related serious adverse events. In the 10 mg/kg cohort, grade 4 hepatitis and grade 3 renal insufficiency was observed in a patient with ovarian cancer. Also in the 10 mg/kg cohort, grade 2 paresthesia (tingling/numbness) was observed in a patient with colorectal cancer.

Biomarker data from all varlilumab dose levels indicate increases in inflammatory chemokines and decreases in circulating T regulatory cells, which is generally consistent with varlilumab monotherapy. Importantly, in tissue biopsies from patients, the authors noted, where pre-treatment and on-study specimens were available (n=17), a marked increase of tumor infiltrating lymphocytes and an increase in PD-L1 expression. Although the Phase 1 portion of the study was focused on immune response and safety, a correlation between this biomarker readout and stable disease or better (n=7) was observed in this preliminary dataset.

The poster is available on the "Publications" page of the "Science" section of the Celldex website.

Title: *In situ* Vaccine for Low-Grade Lymphoma: Combination of Intratumoral Flt3L and Poly-ICLC With Low-Dose Radiotherapy

The potential activity of CDX-301 (recombinant human Flt3 ligand) is being explored in an investigator-sponsored, Phase 1/2 study of CDX-301 and poly-ICLC in combination with low-dose radiotherapy in patients with low-grade B-cell lymphomas conducted by the Icahn School of Medicine at Mount Sinai. CDX-301 is a potent hematopoietic cytokine that uniquely expands dendritic cells and hematopoietic stem cells. To date, the study has enrolled 12 patients with indolent non-Hodgkin lymphoma. The authors presented flow cytometry and mass cytometry data from selected patients, which demonstrate the ability of CDX-301 to induce dendritic cell mobilization.

The poster is available on the "Publications" page of the "Science" section of the Celldex website.

Title: IHC and RT-PCR Assays for Detection of Cancer Antigen NY-ESO-1 in Human Tissues

The Company presented data from the development of diagnostic assays for NY-ESO-1, the target of CDX-1401, an antibody-based NY-ESO-1-specific therapeutic vaccine for multiple solid tumors. Samples from 75 solid tumor types and 38 normal adjacent tissue samples were analyzed by immunohistochemistry (IHC) and quantitative RT-PCR assays, which were developed to determine NY-ESO-1 expression. The validated diagnostic tests for use in the clinical development of CDX-1401 and preliminary screening suggest that several cancers, including non-small cell lung cancer (NSCLC), melanoma and ovarian cancer, express NY-ESO-1, which is consistent with published literature.

The poster is available on the "Publications" page of the "Science" section of the Celldex website.

Title: Targeting the melanosome: overcoming MAPK-inhibitor resistance in melanoma
Abstract: 296

Research collaborators examined the role of MiTF-regulated melanosomal differentiation antigens (MDAs), such as gpNMB, as potential therapeutic targets that could potentially overcome MAPK inhibitor resistance in melanoma. MiTF is a transcription factor that has been identified as an indicator of melanoma resistance, and through the interrogation of the TCGA melanoma database, the authors found it to be strongly correlated with MDAs, including gpNMB. In a preclinical study investigating resistance mechanisms in melanoma, glembatumumab vedotin, an antibody-drug conjugate that targets gpNMB, demonstrated synergies with therapies for BRAF mutated melanoma and overcame phenotypes associated with resistance, suggesting use of glembatumumab vedotin may be particularly effective as a single-agent or in combination in this refractory patient population.

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. Varlilumab has completed a single-agent Phase 1 dose-escalation study, demonstrating 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.

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. 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-1401
CDX-1401 is a next-generation, off-the-shelf cancer vaccine designed to activate the patient's immune system against cancers that express the tumor marker, NY-ESO-1. CDX-1401 consists of a fully human monoclonal antibody with specificity for the dendritic cell receptor DEC-205 genetically linked to the NY-ESO-1 tumor antigen. Celldex has accessed NY-ESO-1 through a licensing agreement with the Ludwig Institute for Cancer Research. By selectively delivering the NY-ESO-1 antigen to dendritic cells in the body, CDX-1401 is intended to induce robust immune responses against the antigen-expressing cancer cells.

About Glembatumumab Vedotin
Glembatumumab vedotin is a fully-human monoclonal antibody-drug conjugate (ADC) that targets glycoprotein NMB (gpNMB). gpNMB is a protein overexpressed by multiple tumor types, including breast cancer, melanoma, lung cancer, uveal melanoma and osteosarcoma. gpNMB has been shown to be associated with the ability of the cancer cell to invade and metastasize and to correlate with reduced time to progression and survival in breast cancer. The gpNMB-targeting antibody, CR011, is linked to a potent cytotoxic, monomethyl auristatin E (MMAE), using Seattle Genetics' proprietary technology. Glembatumumab vedotin is designed to be stable in the bloodstream but to release MMAE upon internalization into gpNMB-expressing tumor cells, resulting in a targeted cell-killing effect. Glembatumumab vedotin is in development for the treatment of locally advanced or metastatic breast cancer with an initial focus in triple negative disease, stage III and IV melanoma, uveal melanoma and osteosarcoma.

Opdivo® is a registered trademark of Bristol-Myers Squibb Company.

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 glembatumumab vedotin ("glemba"; CDX-011), varlilumab, and other products and our goals for 2016. 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 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 Fast Track designation for glembatumumab vedotin 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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