Celldex Presents Data from Oncology Portfolio at SITC 2020

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-- Agonist anti-CD40 mAb CDX-1140 demonstrates best-in-class potential; additional expansion cohorts initiated--
--Axl and CDX-527 programs highlighted--

HAMPTON, N.J., Nov. 09, 2020 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today announced data from multiple presentations at the Society for Immunotherapy of Cancer's (SITC) 35th Anniversary Annual Meeting & Pre-Conference Programs (SITC 2020). An interim update from the Company's ongoing Phase 1 study of its CD40 agonist antibody, CDX-1140, and preclinical data from its AXL discovery program were presented at the meeting. In addition, the Phase 1 study design for the Company's bispecific candidate, CDX-527, which couples CD27 co-stimulation with blockade of the PD-L1/PD-1 pathway, were also presented in a clinical trial in progress poster.

"CDX-1140 continues to emerge as a potential best in class CD40 agonist," said Diane C. Young, MD, Senior Vice President and Chief Medical Officer of Celldex Therapeutics. "At SITC, we reported data from the monotherapy and CDX-301 combination cohorts at the recommended 1.5 mg/kg CDX-1140 dose, which provided high systemic exposure that led to effective modulation of the tumor microenvironment to a more pro-inflammatory and less suppressive state. We believe this supports the clinical activity we continue to see in very difficult to treat, refractory tumor types, including tumor shrinkage and necrosis in a number of patients with squamous cell head and neck cancers and a durable complete response, or CR, in a patient with heavily pre-treated follicular lymphoma.

We are building on this strong foundation by exploring CDX-1140 in combination with other key mechanisms that could be complementary, including with the PD-1 inhibitor pembrolizumab. At SITC, we reported preliminary safety data from this cohort, demonstrating that the combination is well tolerated, and announced the initiation of expansion cohorts with pembrolizumab in both head and neck squamous cell carcinoma and non-small cell lung cancer. We also recently initiated an expansion cohort with chemotherapy in pancreatic cancer which is supported by strong preclinical studies and promising early clinical data with CD40 agonist antibodies.

In addition to the CDX-1140 data, we were pleased to present the trial design from our ongoing study of the first bispecific candidate from our platform, CDX-527, and emerging data from our preclinical program targeting Axl, which is also being developed as a potential bispecific antibody. We look forward to updating across these programs next year," concluded Dr. Young.

Presentation Highlights

CDX-1140 Presentation Highlights (Poster #405): 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 and expansion study. The study includes monotherapy and combination cohorts, including with CDX-301, Celldex's dendritic cell growth factor, with the PD-1 inhibitor pembrolizumab in patients who have progressed on checkpoint therapy and in combination with standard of care chemotherapy (gemcitabine and nab-paclitaxel) in first line metastatic pancreatic cancer.

Prior data presented at SITC 2019 established the maximum tolerated dose (MTD) and recommended dose for continued study at 1.5 mg/kg—one of the highest systemic dose levels in the CD40 agonist class. The update presented at SITC 2020 focused on patients treated at the MTD from both the monotherapy (n=25) and CDX-301 (n=16) combination cohorts. In addition, preliminary safety data from the combination cohort with pembrolizumab (n=9; 4 at 0.72 mg/kg and 5 at 1.5 mg/kg CDX-1140) were also presented.

- CDX-1140 monotherapy and in combination with CDX-301 or pembrolizumab was generally well tolerated with mostly grade 1 or grade 2 drug related adverse events.
- Clinical activity both as a monotherapy and in combination with CDX-301 has been previously reported for CDX-1140 at varying doses, including an unconfirmed partial response (uPR) and tumor cavitation. At SITC 2020, analysis was focused on patients treated at the MTD and recommended dose of 1.5 mg/kg. 41 patients had been treated at the 1.5 mg/kg dose at the time of data cutoff; 29 patients had post-treatment scans performed and five patients had not reached their first post-treatment response assessment.
- Activity at 1.5mg/kg dose of CDX-1140 to date included:
    - An ongoing (6+ months) complete response (CR) in a patient with follicular lymphoma treated with CDX-1140 in combination with CDX-301;

    - Notable tumor shrinkage and/or necrosis in 6 patients with squamous cell head and neck cancer (SCCHN), including extensive tumor cavitation/necrosis of a large baseline protruding neck mass associated with decreased tumor pain in a patient; and,
    - Stable disease (n=10) for 11 to 32 weeks.
- CDX-1140 at the recommended dose of 1.5 mg/kg provided good systemic exposure that enhanced the distribution into tissues and tumor and resulted in marked changes in the tumor microenvironment (TME) consistent with a more inflammatory and less immunosuppressive state as demonstrated by gene expression analysis.
- Interferon signaling and cytotoxicity pathways were most highly upregulated, while immunosuppression via TGFb signaling and metastatic pathways were downregulated, marking the first clear demonstration in patients of biological activity within the TME for a systemically administered agonist anti-CD40 mAb.
- Pre-treatment of patients with CDX-301 greatly increased the number of circulating dendritic cells prior to CDX-1140 administration and peripheral blood mononuclear cells (PBMCs) isolated from CDX-301 pretreated patients were more responsive to CDX-1140 than PBMCs from non-pretreated patients.

Ongoing cohorts:

- The combination of CDX-1140 with pembrolizumab has completed the safety run-in and expansion cohorts in patients with checkpoint-refractory squamous cell head and neck cancer and non-small cell lung cancer have initiated.
- The combination of CDX-1140 with gemcitabine/nab-paclitaxel recently opened to enrollment to patients with previously untreated metastatic pancreatic adenocarcinoma.
- Data updates from these cohorts are expected in the first half of 2021.

Axl Preclinical Program (Poster: #550): Axl is a member of the TAM (Tyro3/Axl/MerTK) family of receptor tyrosine kinases and a negative regulator of innate immunity. Activation of Axl through its ligand, Gas6, leads to suppression of myeloid cell activity, while its activation in tumor cells drives tumor growth and metastasis, and is associated with acquired resistance to targeted therapies, including radiotherapy and chemotherapy. The presentation described a Celldex-created humanized IgG1 Axl-targeting monoclonal antibody (mAb) that potently inhibits Gas6 binding and activation of Axl in tumor cell lines. The preclinical candidate elicited a robust inflammatory response in human primary myeloid cells via an FcR-dependent mechanism, leading to T cell activation in mixed lymphocyte reactions. Administration of the Axl-targeting mAb to tumor cells co-cultured with human PBMCs led to dose-dependent killing of Axl-expressing tumor cells *in vitro* and *in vivo*. The pleiotropic effects of Axl activation in cancer support combination of Axl-targeting agents with other targeted agents, either as drug combinations or as part of the same molecule. To this end, Celldex has developed a prototype tetravalent bispecific antibody combining PD-L1 and Axl targeting that retains all the properties of the parental antibodies and demonstrates enhanced activity in immune activation assays. Other combinations are also under consideration and future efforts will focus on the development of a multispecific molecule co-targeting Axl with a second immune modulator.

CDX-527 Presentation Highlights (Poster #406): CDX-527 is the first candidate from Celldex's bispecific antibody platform. It uses the Company's proprietary highly active anti-PD-L1 and CD27 human antibodies to couple CD27 costimulation with blockade of the PD-L1/PD-1 pathway to help prime and activate anti-tumor T cell responses through CD27 costimulation, while preventing PD-1 inhibitory signals that subvert the immune response. In August 2020, Celldex initiated a multi-center Phase 1 dose-escalation study in up to ~90 patients with advanced or metastatic solid tumors that have progressed during or after standard of care therapy to be followed by tumor-specific expansion cohorts. The study is designed to determine the MTD during a dose-escalation phase and to recommend a dose level for further study in the subsequent expansion phase. The expansion is designed to further evaluate the tolerability, and biologic and anti-tumor effects of selected dose level(s) of CDX-527 in specific tumor types. Enrollment is ongoing and initial data from the Phase 1 study are anticipated in the first half of 2021.

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About Celldex Therapeutics, Inc.
Celldex is a clinical stage biotechnology company dedicated to developing monoclonal and bispecific antibodies that address devastating diseases for which available treatments are inadequate. Our pipeline includes antibody-based therapeutics which have the ability to engage the human immune system and/or directly affect critical pathways to improve the lives of patients with inflammatory diseases and many forms of cancer. 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; the effects of the outbreak of COVID-19 on our business and results of operations; 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 cost of paying development, regulatory approval and sales-based milestones under

our merger agreement with Kolltan, including the cost, timing, and outcome of our declaratory judgment action against the Kolltan stockholder representative with respect to certain of those milestones; 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; our ability to continue to obtain 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; 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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