Celldex Therapeutics, Inc. Logo

CDX-1140 Demonstrates Clinical and Biological Activity in Patients with Advanced Solid Tumors in Phase 1 Dose Escalation Study

November 8, 2019

-Recommended and maximum tolerated dose defined as 1.5 mg/kg for further study-
-Expansion cohort in head and neck squamous cell carcinoma added based on observed clinical activity-
-Clinical trial collaboration with Merck announced to evaluate CDX-1140 with KEYTRUDA®-

HAMPTON, N.J., Nov. 08, 2019 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) presented data from the Company's ongoing CD40 agonist program today at the Society for Immunotherapy of Cancer's (SITC) 34th Annual Meeting. 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 for systemic therapy.

CDX-1140 is currently in a Phase 1 dose escalation study. The study includes both monotherapy and combination cohorts with CDX-301, Celldex's dendritic cell growth factor, designed to increase the number of dendritic cells which are critical to initiating antitumor immunity and are a key target for CDX-1140. Celldex intends to add additional combination cohorts with mechanisms that the Company believes could be complementary or synergistic with CDX-1140 and has prioritized a combination with KEYTRUDA® (pembrolizumab).

"CDX-1140 has exceeded the hurdles we defined for Phase 1 monotherapy development and has potential to be a best in class CD40 agonist," said Diane C. Young, MD, Senior Vice President and Chief Medical Officer. "Based on the clinical activity observed in patients with head and neck squamous cell carcinoma in the monotherapy arm of the study, we have added an expansion cohort of 15 patients to further explore this potential. Dose escalation in the combination arm with CDX-301 is ongoing, but data observed to date suggest that CDX-301 is capable of further enhancing this effect and support our plans to explore CDX-1140's potential in combination with other mechanisms of action that could be complementary or synergistic. We are particularly excited about the newly added combination cohort of CDX-1140 with pembrolizumab as it joins two key immune mechanisms—the enhancement of the immune system with CDX-1140 and the releasing of the brake on the immune system with pembrolizumab," concluded Dr. Young.

"At 1.5 mg/kg, CDX-1140 has achieved one of the highest systemic dose levels in the CD40 agonist class and is associated with manageable immune-related adverse events that are consistent with approved, effective therapies like checkpoint inhibitors," said Rachel Sanborn, MD, Co-director of the Thoracic Oncology Program and Director of the Phase 1 Trials Program at Providence Cancer Institute and a lead investigator in this study. "Reaching higher dose levels increases the likelihood of effectively activating dendritic cells and macrophages within the tumor, which may be an important contributing factor in driving meaningful clinical activity, such as we are observing in these checkpoint refractory patients. I am very enthusiastic about CDX-1140's potential and look forward to future data updates from the study," concluded Dr. Sanborn.

Study Highlights

Promising clinical activity emerging with CDX-1140 monotherapy and combination with CDX-301 (n=38 patients with pre- and post-scans; n=7 patients awaiting assessment; enrollment ongoing). Patients were heavily pretreated (median of 4 prior therapies) and per protocol were required to have received all standard of care treatments prior to study entry.

- Two patients with radiographic evidence of tumor necrosis among 5 patients with recurrent/refractory HNSCC, including prior checkpoint inhibition therapy, treated with CDX-1140 monotherapy doses of 0.72mg/kg or higher
  - Patient one: dramatic shrinkage of a large, protruding neck mass on physical exam after two doses of CDX-1140 at 1.5 mg/kg, evidence of tumor necrosis/cavitation on CT scan, patient reported decreased tumor pain
  - Patient two: cavitation of greater than 50% of lung metastases on CT scan after one dose of CDX-1140 at 3 mg/kg
- A patient with gastroesophageal carcinoma with RECIST response after two cycles of CDX-1140 at 0.36 mg/kg plus CDX-301
  - 41% shrinkage of liver and lymph node target lesions, including near complete resolution of the liver lesion
  - Response duration of four months
- Six patients with stable disease: n=4 CDX-1140 monotherapy; n=2 CDX-1140/CDX-301 combination; duration 1.8 months to 5.4 months; one patient with immune unconfirmed progressive disease (iUPD) noted on first scan who has since continued treatment without confirmation of progressive disease for 10+ months at CDX-1140 at 0.09 mg/kg plus CDX-301

CDX-1140 monotherapy and combination with CDX-301 has been generally well tolerated to date

- CDX-1140 monotherapy dose escalation completed to 3.0 mg/kg, with maximum tolerated dose and recommended Phase 2 dose determined to be 1.5 mg/kg
- Mostly grade 1 or grade 2 drug related adverse events
- Mostly low grade, transient changes in serum liver transaminases
- 2 of 6 patients with pneumonitis at CDX-1140 3.0 mg/kg exceeding MTD
- No dose limiting toxicities to date in the CDX-301 combination cohorts up to 0.72 mg/kg CDX-1140; CDX-1140 at 1.5 mg/kg plus CDX-301 cohort currently ongoing

Potent pharmacological effects associated with immune activation observed

- Transient induction of inflammatory cytokines and chemokines associated with dendritic cell and T cell activation at higher dose levels
    - Similar activation observed with each cycle of therapy
- Peripheral blood immune cells have upregulated immune activation markers
- CDX-301 markedly increases the number of dendritic cells and is associated with higher IL-12p40 induction; IL-12 is a key molecule for inducing anti-tumor T cell responses

Future development:
Based on the clinical activity observed in HNSCC, Celldex is actively enrolling up to an additional 15 patients with HNSCC at 1.5 mg/kg CDX-1140 monotherapy. Dose escalation of CDX-1140 in combination with CDX-301 is nearing completion with patients currently enrolling to the 1.5 mg/kg CDX-1140 cohort. In addition, Celldex has amended the ongoing Phase 1 study to evaluate CDX-1140 in combination with KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 therapy under a clinical trial collaboration agreement with Merck (known as MSD outside of the U.S. and Canada). The cohort is designed to characterize the safety, pharmacodynamics and activity of CDX-1140 in combination with pembrolizumab in patients refractory to PD1/PDL1 treatment. Celldex expects this cohort will open to enrollment in Q1 2020.

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ USA.

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 maintain compliance with Nasdaq listing requirements; our ability to realize the cost benefits of consolidating our office and laboratory space and to retain key personnel after that consolidation; our ability to realize the anticipated benefits from the acquisition of Kolltan; 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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