Celldex Therapeutics, Inc. Logo

Celldex Announces Data from CDX-3379 Clinical Program Presented at ASCO 2019; Promising Biomarker Strategy Identified for Head and Neck Squamous Cell Carcinoma

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--Evaluation of biomarkers for patient selection to be incorporated into expanded development program--

HAMPTON, N.J., June 01, 2019 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today presented results from the CDX-3379 clinical program at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago. To date, three studies of CDX-3379 have enrolled patients with head and neck squamous cell carcinoma (HNSCC), including the ongoing Phase 2 exploratory study of CDX-3379 in combination with Erbitux® (cetuximab) in patients with cetuximab-resistant, advanced human papillomavirus (HPV) negative HNSCC who have previously been treated with an anti-PD1 checkpoint inhibitor.

Emerging data from the Phase 2 study and earlier studies of CDX-3379 suggest that antitumor activity may be associated with somatic mutations in certain genes. Based on these observations, Celldex conducted an exploratory biomarker analysis in 18 HNSCC patients across the CDX-3379 clinical development program. These results support the further development of CDX-3379 in biomarker-selected patient populations and were highlighted during a presentation at ASCO by Julie E. Bauman, MD, MPH, Professor of Medicine, Chief, Division of Hematology and Oncology, Associate Director, Translational Research, University of Arizona Cancer Center, lead author for the poster and an investigator in the Phase 2 study.

“We have observed intriguing clinical activity across a number of patients with similar gene mutation patterns in a disease that has extremely limited treatment options and a particularly poor prognosis,” said Dr. Bauman. “While the data are early, they are provocative and suggest the potential for a biomarker enrichment strategy that could change the standard of care for these patients. I look forward to the opportunity to obtain additional data on CDX-3379 in biomarker selected patient populations.”

CDX-3379 is a human monoclonal antibody that uniquely blocks the activity of ErbB3 (HER3). ErbB3 is expressed in many cancers, including head and neck squamous cell cancer (HNSCC) and is believed to be an important receptor regulating cancer cell growth and survival as well as resistance to targeted therapies.

Biomarker analysis

Next-generation sequencing was performed on tumor samples from 18 patients with HNSCC treated with CDX-3379 across the three clinical studies. This data set included four patients with clinical responses, including two durable complete responses (11+ months and 8.3 months), an exceptional partial response (greater than 92% tumor shrinkage) and an unconfirmed partial response; eight patients with stable disease and/or tumor shrinkage; and, six patients with progressive disease.

- Across the CDX-3379 program, FAT1 and NOTCH1, NOTCH2, or NOTCH3 mutations and primary tumor site of oral cavity were associated with clinical activity (clinical response, tumor shrinkage and stable disease) in HNSCC
  - All four clinical responses occurred in patients with FAT1 mutations
  - All four clinical responses occurred in patients with a primary tumor site of oral cavity
  - Three of the four clinical responses occurred in patients who also had NOTCH1, NOTCH2 or NOTCH3 mutations
  - Also, of note, all patients (n=7 of 18) who experienced clinical benefit (objective response or stable disease greater than or equal to 12 weeks) had FAT1 and/or NOTCH1-3 mutations.
- Current literature suggests that loss of FAT1 function results in activation of the transcriptional cofactor YAP1[1]; YAP1 has been shown to upregulate components of ErbB signaling pathways[2,3], including the ErbB3 ligand NRG1[4]
- Inactivating mutations in the FAT1 and NOTCH genes have been identified in 32% and 26% of HPV(-) HNSCC tumors, respectively[5]
- Preclinical studies investigating the association of CDX-3379 sensitivity and inactivating mutations of FAT1 and other genes are ongoing

Phase 2 CDX-3379 Study Results and Next Steps

This multicenter, open-label, Phase 2 study of CDX-3379 in combination with cetuximab is designed to enroll approximately 30 patients with cetuximab-resistant, advanced, HPV negative HNSCC who have previously been treated with an anti-PD1 checkpoint inhibitor, a population with limited options and a particularly poor prognosis. Cetuximab is dosed weekly (initial dose at 400 mg/m^2 IV, then 250 mg/m^2 IV); CDX-3379 (12 mg/kg IV) is administered once every three weeks. Treatment continues until disease progression or intolerance, and assessments occur every six weeks. Using a Simon two-stage design, the first stage of study was designed to enroll 13 patients, and if at least one patient achieved a partial response or complete response, enrollment could progress to the second stage; this objective was met.

Fifteen patients were enrolled in stage 1 of the study. Patients had a median of 3 (range of 2-6) prior cancer therapy treatments. All patients had received prior checkpoint inhibitor treatment and 14 of 15 patients were cetuximab refractory. Notable clinical activity was observed in this refractory patient population where treatment options are limited.

- A durable confirmed complete response (11+ months) was observed; this response remains ongoing and the patient continues to receive treatment.
- An unconfirmed partial response (uPR) in a patient that had not received cetuximab was also observed.
- 7 patients experienced stable disease (47%; includes uPR).

- A clinical benefit rate of 29% was achieved (objective response or stable disease greater than or equal to 12 weeks).
- Dose reductions and/or delays to the combination therapy in the majority of patients may have impacted the magnitude of anti-tumor activity; dose modifications are being considered for future studies.
- CDX-3379 in combination with cetuximab was generally associated with the expected target-mediated adverse events of diarrhea and rash.

Celldex intends to incorporate evaluation of biomarkers for patient selection into the CDX-3379 development program, either through amending the existing study or concluding the study and initiating a new clinical trial. The Company, working together with investigators and key opinion leaders in the treatment of HNSCC, anticipates finalizing these plans in the coming weeks.

Erbitux® is a registered trademark of Eli Lilly & Co.
[1]Martin D, Nat Commun 2018. [2]Zhang J, Nat Cell Biol 2009. [3]Wang C, Cancer Res 2017. [4]He C, Oncogene 2015. [5]Cancer Genome Atlas Network, Nature 2015.

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 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 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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