Celldex Therapeutics, Inc. Logo

Celldex's KIT Inhibitor CDX-0159 Demonstrates Profound, Sustained Dose-dependent Reductions in Plasma Tryptase—an Indicator of Mast Cell Burden—and a Favorable Safety Profil

June 6, 2020

--Data strongly support expanding development into mast cell driven diseases--
--Data presented in a late-breaking session at EAACI Annual Congress 2020--

HAMPTON, N.J., June 06, 2020 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today announced results from the Company's Phase 1 randomized, double-blind, placebo-controlled, dose escalation study of KIT inhibitor CDX-0159 in healthy subjects. Data (presentation #1829) were featured in a late breaking presentation today at the European Academy of Allergy and Clinical Immunology (EAACI) Annual Congress 2020.

CDX-0159 demonstrated a favorable safety profile as well as profound and durable reductions of plasma tryptase, consistent with systemic mast cell suppression. A single dose of CDX-0159 induced dose-dependent tryptase reduction below the level of assay detection within days at doses as low as 1.0 mg/kg and maintained suppression for over two months at 3.0 mg/kg and above. Tryptase is an enzyme synthesized and secreted almost exclusively by mast cells and decreases in plasma tryptase levels are believed to reflect a systemic reduction in mast cell burden in both healthy volunteers and in disease, providing important proof of concept for the program. The data also support expansion of the program into mast cell driven diseases, including initially studies in forms of chronic urticaria (CU) given the central role mast cells are known to play in the etiology of CU.

The data were presented by Dr. Marcus Maurer, Professor of Dermatology and Allergy and Director of Research at the Department of Dermatology and Allergy at the Allergie-Centrum-Charité of the Charité - Universitätsmedizin in Berlin. Dr. Maurer is also head of the Specialty Clinics for Urticaria, Mastocytosis, Pruritus and Angioedema and the Dermatological Allergology, and is a leading medical expert in urticaria whose research focuses on the physiological and pathological functions of mast cells.

"The profound decreases in plasma tryptase coupled with the favorable safety profile observed in this study suggest that CDX-0159 has significant potential as a disease-modifying therapeutic for mast cell disorders driven by wild-type KIT," said Dr. Maurer. "Chronic urticarias can have significant impact on quality of life, especially for patients with severe disease, where the intense itching can lead to insomnia, lack of energy, social withdrawal and depression. Currently approved therapies address the symptoms of the disease but not the root cause – the mast cells themselves. With continued positive data, CDX-0159 could be an important new drug for patients as it directly targets and inhibits mast cells. I look forward to results from future studies."

"These results support the rapid advancement of CDX-0159 into clinical studies in our target patient populations," said Diane C. Young, M.D., Senior Vice President and Chief Medical Officer, Celldex Therapeutics. "We look forward to initiating studies in chronic spontaneous urticaria and chronic inducible urticaria—both mast cell driven diseases—later this year. Importantly, these indications will provide data read outs along the way with ful data expected in chronic inducible urticaria early next year and in chronic spontaneous urticaria in the second half of 2021."

Presentation Summary

The Phase 1 study is a randomized, double-blind, placebo-controlled, single ascending dose escalation study of CDX-0159 in healthy subjects (n=32; 8 subjects per cohort, 6 CDX-0159; 2 placebo). Subjects received a single intravenous infusion of CDX-0159 at 0.3, 1.0, 3.0, or 9.0 mg/kg or placebo. The objectives of the study included safety and tolerability, pharmacokinetics (PK) and pharmacodynamics (tryptase and stem cell factor) and immunogenicity. CDX-0159 demonstrated a favorable safety profile and profound tryptase suppression, indicative of systemic mast cell ablation.

- Most common adverse events were mild infusion-related reactions, all of which spontaneously resolved without intervention. Mild and asymptomatic decreases in neutrophil and white blood cell count were observed in laboratory testing.
- A single dose of CDX-0159 suppressed plasma tryptase levels in a dose-dependent manner, indicative of systemic mast cell suppression. Tryptase suppression below the level of detection was observed after a single 1.0 mg/kg dose and was maintained for more than 2 months at single doses of both 3.0 and 9.0 mg/kg of CDX-0159.
- Dose dependent increases in plasma stem cell factor mirror decreases in tryptase, consistent with allosteric blockade of stem cell factor to KIT and demonstrate complete target engagement *in vivo*.
- Long serum half-life and non-immunogenic profile support a convenient dosing schedule.
- Enhanced PK profile and durable tryptase suppression at low doses support re-formulation for sub-cutaneous administration.
- Data support clinical studies with repeat dosing in patients with mast cell driven disorders.

Next Steps

Celldex plans to initiate Phase 1b studies of CDX-0159 in patients with chronic spontaneous urticaria (CSU) and chronic inducible urticaria (CINDU), diseases where mast cell degranulation plays a central role in the onset and progression of the disease, by year end. The prevalence of CSU and CINDU is approximately 0.5-1% of the total population or up to 1 to 3 million patients in the United States alone (Weller et al. 2010. Hautarzt. 61(8), Bartlett et al. 2018. DermNet. Org). CSU presents as itchy hives, angioedema or both for at least six weeks without a specific trigger; multiple episodes can play out over years or even decades. About 50% of patients with CSU achieve symptomatic control with antihistamines or leukotriene receptor antagonists. Omalizumab, an IgE inhibitor, provides relief for roughly half of the remaining antihistamine/leukotriene refractory patients. Consequently,

there is a need for more effective later line therapies. CINDUs are forms of urticaria that have an attributable cause or trigger associated with them, typically resulting in hives or wheals. Celldex is exploring cold-induced and dermographism (scratch-induced) urticarias. Full results from the CINDU and CSU studies as currently planned would be available in Q1 2021 and 2H 2021, respectively. Celldex is also exploring additional mast cell driven diseases for future development, including mast cell activation, auto-immune, inflammatory, allergic and fibrotic disorders.

About CDX-0159

CDX-0159 is a monoclonal antibody that binds the KIT receptor with high specificity and potently inhibits its activity. The KIT receptor tyrosine kinase is expressed in a variety of cells, including mast cells, which mediate inflammatory responses such as hypersensitivity and allergic reactions. KIT signaling controls the differentiation, tissue recruitment, survival and activity of mast cells. Currently approved therapies for chronic urticarias do not inhibit mast cells and provide symptomatic relief only. Celldex believes that CDX-0159 has significant potential to interfere with mast cells at multiple steps upstream of current treatments, which, in turn, could be disease modifying for patients. In addition, Celldex is also evaluating additional opportunities in other mast cell driven diseases where CDX-0159's potency and high specificity for KIT could be important.

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; the effects of the outbreak of COVID-19 on our business and results of operations; 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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Source: Celldex Therapeutics, Inc.