Celldex Presents Histology Data from Phase 2 Study of Barzolvolimab in EoE Supporting Potential of Mast Depleting Agent in this Difficult to Treat Disease

May 5, 2025

Phase 2 study fully enrolled; data expected in 2H 2025

HAMPTON, N.J., May 05, 2025 (GLOBE NEWSWIRE) -- Celldex announced today the presentation of histology data from the Company's ongoing Phase 2 study of barzolvolimab in eosinophilic esophagitis (EoE). Biopsies taken during screening demonstrate the presence of high numbers of intraepithelial mast cells in participants with active EoE and correlate with eosinophil counts, supporting the hypothesis that treating EoE with barzolvolimab—a mast cell depleting agent—could provide promising therapeutic benefit. The data were discussed in a poster presentation at the Digestive Disease Week (DDW) 2025 conference in San Diego today. Celldex announced in February 2025 that enrollment to the Phase 2 study is complete and that clinical results are expected in the second half of 2025.

"These data continue to add to a growing body of literature suggesting that eosinophilic esophagitis involves more than just eosinophils and that mast cells play an important role in the disease process," said Evan S. Dellon, MD, MPH, Professor of Medicine and Director of the Center for Esophageal Diseases and Swallowing at the University of North Carolina School of Medicine and the lead author of the poster. "This is further supported by previous findings that mast cells are present in the biopsy tissue of some patients who continue to suffer from EoE even after eosinophils have been depleted. Barzolvolimab has been shown to deplete cutaneous mast cells and we believe it will likely also deplete esophageal mast cells, which could lead to clinical improvement in EoE—an indication that sorely needs additional effective treatment options. I look forward to seeing the clinical data from the study later this year."

EoE is the most common type of eosinophilic gastrointestinal disease, a chronic inflammatory disease of the esophagus characterized by the infiltration of eosinophils. Chronic inflammation can result in trouble swallowing, chest pain, vomiting and impaction of food in the esophagus – a medical emergency. Several studies have suggested that mast cells may be an important driver in the disease. Mast cells are present and activated in the esophageal epithelium of EoE biopsy specimens[1-11], are important sources of inflammatory cytokines[2,9] and are associated with disease features of EoE including histological abnormalities and pain[5,7,12,13,14]. Mast cells persist in patients who are refractory to topical corticosteroid therapy, even when eosinophils regress[13]. The Phase 2 "EvolvE" study is designed to test the hypothesis that barzolvolimab, a monoclonal antibody (mAb) against c-KIT previously shown to deplete cutaneous mast cells[15], will deplete esophageal mast cells and lead to clinical improvement in EoE.

Phase 2 EvolvE presentation details: "Intraepithelial Mast Cells are Elevated in Active Eosinophilic Esophagitis and Correlate with Eosinophils: Baseline Data from a Randomized Controlled Trial of Barzolvolimab"; poster #Mo1345

- Ongoing 28-week, randomized, double-blind, placebo controlled study evaluating 300 mg of barzolvolimab or placebo administered every 4 weeks in participants with known EoE. Eligible participants have at least 15 eosinophils per high power field (hpf) in 2 of 3 segments of the esophagus and at least 4 dysphagia days in the 2 weeks prior to baseline (dysphagia symptom questionnaire [DSQ] score ≥ 8). Primary endpoint is reduction in peak esophageal epithelial mast cell count (PMC) cell at 12 weeks, with key secondary endpoints of reduction in peak eosinophil count (PEC) and reduction in DSQ at 12 weeks.

- Pinch biopsies from 151 screened participants were obtained at screening from three different esophageal segments (proximal, middle, distal). Screening histology data from this trial demonstrate that high numbers of intraepithelial mast cells are present in participants with active EoE and correlate with eosinophil counts:

    - Intraepithelial mast cells (Tryptase and CD117 positive) and eosinophil counts per hpf from screening biopsies were enumerated by IHC and H&E staining. Similar numbers of cells were observed across the three biopsy sites, with a trend towards greater numbers in the distal esophagus. Participants who failed screening due to low eosinophil counts also tended to have lower tryptase+ and CD117+ mast cell counts.

    - Pearson correlations show a strong association between both CD117+ or tryptase+ total and peak mast cells and eosinophils, as well as between CD117+ and tryptase+ total and peak mast cells.

- Patients are currently completing treatment and the follow up phase on study; clinical data from the study is expected to be presented in the second half of 2025.

References: [1]Tappata et al. Allergy 2018; [2]Aceves et al. JACI 2010; [3]Abonia et al. JACI 2010; [4]Colombo et al. WJGPT 2013; [5]Dellon et al. AJG 2011; [6]Lomazi et al. Arq Gast 2017; [7]Zhang et al. JACI 2024; [8]Kleuskens et al. Muc Imm 2023; [9]Ben-Baruch Morgenstern et al. JACI 2022; [10]Dunn et al. JACI 2020; [11]Kirsch et al. JPGN 2007;[12]Alvarado et al. Allergy 2023;[13]Bolton et al. AMJ 2020; [14]Zhang et al. Allergy 2022;[15]Terhorst-Molawi et al. Allergy 2023.

About Eosinophilic Esophagitis (EOE):
EoE, the most common type of eosinophilic gastrointestinal disease, is a chronic inflammatory disease of the esophagus characterized by the infiltration of eosinophils. This chronic inflammation can result in trouble swallowing, chest pain, vomiting and impaction of food in the esophagus – a medical emergency. Currently, there are limited treatment options for EoE. Several studies have suggested that mast cells may be an important driver in the disease. Given the lack of effective therapies for EoE and barzolvolimab's potential as a mast cell depleting agent, Celldex believes EoE is an important indication for study. For additional information on the Phase 2 EvolvE study of barzolvolimab in EOE (NCT05774184), please visit clinicaltrials.gov.

About Barzolvolimab
Barzolvolimab is a humanized monoclonal antibody that binds the receptor tyrosine kinase KIT with high specificity and potently inhibits its activity. KIT 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. In certain inflammatory diseases, such as chronic urticaria, mast cell activation plays a central role in the onset and progression of the disease. Barzolvolimab is currently being studied in chronic spontaneous urticaria (CSU), chronic inducible urticaria (CIndU), prurigo nodularis (PN), eosinophilic esophagitis (EOE) and atopic dermatitis (AD), with additional indications planned for the future.

About Celldex Therapeutics, Inc.
Celldex is a clinical stage biotechnology company leading the science at the intersection of mast cell biology and the development of transformative therapeutics for patients. 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 severe inflammatory, allergic, autoimmune and other devastating 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, including barzolvolimab (also referred to as CDX-0159), in current or future indications; 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 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.

Company Contact
Sarah Cavanaugh
Senior Vice President, Corporate Affairs & Administration
(508) 864-8337
scavanaugh@celldex.com

Patrick Till
Meru Advisors
(484) 788-8560
ptill@meruadvisors.com

Source: Celldex Therapeutics, Inc.