Celldex Initiates Global Registrational Phase 3 Program of Barzolvolimab in Cold Urticaria and Symptomatic Dermographism

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- *No advanced therapies approved to treat ColdU and SD—diseases of misery that dramatically impact all aspects of patient life*
- *Barzolvolimab is the only drug in development to demonstrate clinical benefit in patients in ColdU and SD in a large, randomized, placebo-controlled study--all primary and secondary endpoints met with high statistical significance at 12 weeks and sustained through end of treatment period (20 weeks) in Phase 2 study*
- *Initiation of EMBARQ-ColdU and SD marks second barzolvolimab Phase 3 program; Phase 3 in CSU ongoing*

HAMPTON, N.J., Dec. 09, 2025 (GLOBE NEWSWIRE) -- Celldex (NASDAQ:CLDX) announced today the initiation of its global Phase 3 trial (EMBARQ-ColdU and SD) designed to establish the efficacy and safety of barzolvolimab in adult patients with cold urticaria (ColdU) and symptomatic dermographism (SD) who remain symptomatic despite H1 antihistamine treatment. ColdU and SD are characterized by the occurrence of hives or wheals that have an attributable trigger associated with them—exposure to cold temperatures in ColdU and scratching/rubbing of the skin in SD. Mast cell activation is known to be a critical driver in ColdU and SD. Barzolvolimab is a humanized monoclonal antibody that specifically binds the receptor tyrosine kinase KIT with high specificity and potently inhibits its activity, which is required for mast cell function and survival.

“Across studies in cold urticaria and symptomatic dermographism, barzolvolimab has demonstrated a unique and profound ability to offer rapid, sustained, complete disease response, providing hope for patients who are impacted by severe itching and hives that dramatically impact all aspects of their lives despite constant vigilance to avoid disease triggers,” said Diane C. Young, MD, Senior Vice President and Chief Medical Officer of Celldex. “Advancing a promising agent that addresses the root driver of the disease—the mast cell—into a registrational study is a significant step forward for patients and physicians who desperately neec better treatment options.”

EMBARQ-ColdU and SD is designed to establish the efficacy and safety of barzolvolimab in adult participants with ColdU and SD who remain symptomatic despite H1 antihistamine treatment. Participants who remain symptomatic after treatment with biologics are also eligible for the study. The randomized, double-blind, placebo-controlled, parallel group Phase 3 study will recruit participants from approximately 75 clinical trial sites across 7 countries. Approximately 240 participants will be enrolled to 2 separate cohorts (differentiated by subtype) to include approximately 120 participants with ColdU and 120 participants with SD. Participants in each cohort will be randomized in a 1:1 ratio to one of two treatment arms: cohort 1: barzolvolimab 150 mg every 4 weeks (Q4W) following a loading dose of 450 mg on Day 1 or cohort 2: matching placebo for 24 weeks. The primary endpoint of the study will evaluate the percent of patients with complete response (negative provocation test) at Week 12 as assessed by the TempTest® in ColdU and the FricTest® in SD. After completing the treatment period, participants will continue to be followed for 16 weeks.

“Barzolvolimab is now advancing across five indications demonstrating its significant potential to treat a broad array of mast cell driven diseases with Phase 3 studies ongoing in chronic spontaneous urticaria, cold urticaria and symptomatic dermographism and Phase 2 studies in prurigo nodularis and atopic dermatitis,” said Anthony Marucci, Co-founder, President and Chief Executive Officer of Celldex. “We remain focused on executing these trials seamlessly and achieving our goal of making barzolvolimab available to meet the needs of patients.”

There are no advanced therapies approved to treat the more than 533K patients impacted by ColdU and SD across the United States and Europe. Patients are typically treated with up to four times the labeled dose of antihistamines, but more than 80% continue to report inadequate disease control. ColdU and SD are diseases of misery and despite best efforts, patients often find it impossible to avoid disease triggers and are impacted by severe itching and burning hives that dramatically impact all aspects of their lives. More than 60% of patients report moderate to severe impact on their mental/emotional well-being, daily activities, and social/intimate relationships, suffering from social stigma, including being asked if they are contagious, being stared at in public, and people refusing to shake hands or touch them.[1] Not surprisingly, patients with ColdU and SD also report high rates of anxiety and depression.[2]

Results from a placebo controlled Phase 2 study in ColdU and SD demonstrated that barzolvolimab met the primary endpoint of the study, a statistically significant difference between the percent of participants with a negative provocation test compared to placebo at Week 12 as assessed by the TempTest® in ColdU and the FricTest® in SD. Importantly, barzolvolimab demonstrated rapid, durable and clinically meaningful responses with up to 75% of patients with ColdU and 67% of patients with SD obtaining a partial or complete response. Secondary endpoints in the study were also achieved at week 12 and strongly supported the primary endpoint results, including responder analyses, improvements in Critical Temperature and Critical Friction Thresholds (CFT and CFT), changes in WI-NRSprovo (itch associated with provocation test) and Urticaria Control Test. These effects were sustained

through the end of the treatment period (20 weeks) with up to 78% of patients with ColdU and 58% of patients with SD obtaining a partial or complete response. Barzolvolimab demonstrated a well-tolerated safety profile over the course of the study. Patients were followed for up to 24 weeks after treatment completion and patients with returning or continuing symptoms were given the option to enter an open label extension (OLE) during this follow up period. Consistent with the clinical endpoint results at Week 20, placebo-treated patients entered the OLE at a faster rate compared to barzolvolimab-treated patients. Data from the OLE are expected to be presented in Q1 2026.

For additional information on *EMBARQ-ColdU and SD* (NCT07266402), please visit www.clinicaltrials.gov.

[1]Winders et al. Impact of chronic inducible urticaria (CIndU) on patients' health-related quality of life: Results from Urticaria Voices study; presented at EAACI Congress 2025.
[2]EADV poster: Prevalence, clinical profile and burden of chronic inducible urticaria in EU5, US and Japan, Sep 2022.

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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), two forms of chronic inducible urticaria (CIndU) – cold urticaria (ColdU) and symptomatic dermographism (SD), prurigo nodularis (PN) and atopic dermatitis (AD), with additional indications planned for the future.

About Chronic Inducible Urticaria (CIndU), Cold Urticaria (ColdU) and Symptomatic Dermographism (SD):
Cold Urticaria (ColdU) and Symptomatic Dermographism (SD) are forms of Chronic Inducible Urticaria (CIndU), characterized by the occurrence of hives or wheals that have an attributable trigger associated with them. ColdU symptoms include itching, burning wheals/hives and angioedema when skin is exposed to cold temperatures. SD symptoms include the development of wheals in response to stroking, scratching or rubbing of the skin. Approximately 0.5% of the total population suffers from chronic inducible urticarias. For these diseases, mast cell activation leading to release of soluble mediators is thought to be the driving mechanism leading to the wheals and other symptoms. There are currently no approved therapies for ColdU and SD other than antihistamines and patients attempt to manage symptoms associated with their disease through avoidance of triggers.

About Celldex
Celldex is pioneering new horizons in immunology to deliver life-changing therapies. We are relentless in our pursuit of novel antibody-based treatments that engage the human immune system and directly affect critical pathways to improve the lives of patients with allergic, inflammatory and autoimmune disorders.
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) and CDX-622, 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.

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