Celldex Announces Barzolvolimab Met All Primary and Secondary Endpoints with High Statistical Significance in Positive Phase 2 Study in Chronic Inducible Urticaria

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- *First to demonstrate clinical benefit in patients with chronic inducible urticaria (CIndU) in large, randomized, placebo-controlled study*
- *Favorable safety and tolerability*
- *Plan to advance CIndU into Phase 3 development*
- *Company to host webcast call Monday at 8:00 am ET*

HAMPTON, N.J., Oct. 26, 2024 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) announced today positive results from the Company's Phase 2 clinical trial of barzolvolimab in two of the most common forms of chronic inducible urticaria (CIndU)—cold urticaria (ColdU) and symptomatic dermographism (SD). The study includes patients who remain symptomatic despite treatment with antihistamines. 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. CIndU is 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.

The data were presented in a late breaking oral presentation at the American College of Allergy, Asthma & Immunology's Annual Scientific Meeting in Boston by Dr. Jonathan Bernstein, Professor of Clinical Medicine, Department of Internal Medicine, Division of Rheumatology, Allergy and Immunology, University of Cincinnati Medical Center and Partner, Bernstein Allergy Group and Clinical Research Center.

"Chronic inducible urticaria is a devastating disease for patients who despite constant vigilance often find it impossible to avoid their disease triggers and are impacted by severe itching and burning hives that dramatically impact all aspects of their lives," said Diane C. Young, MD, Senior Vice President and Chief Medical Officer of Celldex Therapeutics. "Barzolvolimab is the first drug to achieve success in a large, randomized, placebo-controlled study in chronic inducible urticaria and we are excited to report that all primary and secondary endpoints across the study were highly statistically significant and clinically meaningful. We believe these study results achieve the goal of treatment for patients by dramatically improving their trigger thresholds and enabling them to regain control of their lives. We are actively working towards bringing this potential new medicine to patients and look forward to initiating Phase 3 development in inducible urticaria in 2025."

Celldex previously reported that barzolvolimab achieved the primary efficacy endpoint of the study, a statistically significant difference between the percent of patients with a negative provocation test compared to placebo at Week 12 as assessed by the TempTest® in ColdU and the FricTest® in SD. Today the Company reported that all secondary endpoints in the study were also achieved at Week 12 and strongly support 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.

196 patients with CIndU refractory to antihistamines were randomized to the study and 193 patients were included in the full analysis (mITT) and safety set (3 patients randomized to the study were not treated). 90% (n=173) of patients on study completed the study through 12 weeks (discontinuation rate of 8% barzolvolimab compared to 14% placebo). Demographics and baseline disease characteristics were well balanced across treatment groups. In cold urticaria, patients presented with a mean baseline critical temperature threshold of approximately 19°C or 66°F on the TempTest on initial provocation testing. In patients with symptomatic dermographism baseline FricTest thresholds were an average of 3.6 out of 4 pins. UCT scores at baseline reflect poorly controlled disease.

Summary of Clinical Assessments at Week 12						
	Cold Urticaria			**Symptomatic Dermographism**		
All measurements at Week 12	150 mg q4w (n=32)	300 mg q8w (n=32)	Placebo (n=32)	150 mg q4w (n=33)	300 mg q8w (n=33)	Placebo (n=31)
Primary endpoint: % of patients with negative provocation test (complete response)	46.9% **p=0.0023**	53.1% **p=0.0011**	12.5%	57.6% **p<0.0001**	42.4% **p=0.0003**	3.2%
% of patients with complete or partial response per provocation test	62.5% **p=0.0118**	75% **p=0.0006**	31.3%	66.6% **p<0.0001**	57.5% **p=0.0002**	12.9%
Improvement in Critical Temperature (CTT) and Critical Friction (CFT) Thresholds	-8.82°C **p<0.0001**	-9.61°C **p<0.0001**	-0.30°C	-2.46 pins **p<0.0001**	-2.27 pins **p=0.0002**	-0.82 pins
% of patients with Urticaria Control Test >12	58.6% **p=0.0048**	68.8% **p<0.0001**	31.0%	54.8% **p=0.0015**	65.5% **p<0.0001**	32.0%

Patients experienced rapid disease improvement as early as two weeks (the first assessment) after receiving the initial dose of barzolvolimab as demonstrated by reductions in critical temperature and friction thresholds resulting in hives and rapid reduction in itch at the time of provocation testing (WI-NRSprovo).

Barzolvolimab was well tolerated with a favorable safety profile consistent with prior studies. Most adverse events were grade 1 (mild). Through 12 weeks, the most common treatment emergent adverse events in barzolvolimab treated patients were hair color changes (13%; Grade 1, n=15 / Grade 2, n=2) and neutropenia (10%; Grade 1, n=7 / Grade 2, n=6), which are mechanism related (KIT) and expected to be reversible. The rate of infections was similar between barzolvolimab-treated patients and placebo with no association between neutropenia and infections.

For additional information on this trial (NCT05405660), please visit www.clinicaltrials.gov.

TempTest® and FricTest® are registered trademarks of Moxie GmbH.

Webcast and Conference Call

The Company will host a conference call/webcast on Monday, October 28th to discuss the results at 8:00 am ET. To access the webcast, please visit the Investor Relations page of Celldex's website at https://ir.celldex.com/events-presentations. Parties interested in participating via telephone may register here to receive the dial-in numbers and unique PIN to seamlessly access the call. Otherwise please access the listen-only webcast link. The archived webcast will be available for a limited time on the Company's website.

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) and eosinophilic esophagitis (EOE) with additional indications planned for the future, including atopic dermatitis (AD).

About the Phase 2 CIndU Study: This study is a randomized, double-blind, placebo-controlled, parallel group study evaluating the efficacy and safety profile of two dose regimens of barzolvolimab in patients with CIndU who remain symptomatic despite antihistamine therapy. 196 patients in 2 cohorts (differentiated by CIndU subtype) including 97 patients with ColdU and 99 patients with SD were randomly assigned on a 1:1:1 ratio to receive subcutaneous injections of barzolvolimab at 150 mg every 4 weeks, 300 mg every 8 weeks or placebo during a 20-week treatment phase. Patients then enter a follow-up phase for an additional 24 weeks. The study also includes an Open Label Extension that allows patients with symptoms during the follow-up phase (including patients who were on placebo during the 20-week treatment phase) to receive active study drug for an additional 20 weeks. The primary endpoint of the study is the percentage of patients with a negative provocation test at Week 12 (using TempTest® for ColdU and FricTest® for SD). Secondary endpoints include safety and other assessments of clinical activity including CTT (critical temperature threshold), CFT (critical friction threshold) and WI-NRSprovo (worst itch numeric rating scale associated with provocation testing).

About Chronic Inducible Urticaria (CIndU)

CIndU is 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 chronic inducible urticarias other than antihistamines and patients attempt to manage symptoms associated with their disease through avoidance of triggers.

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.

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