Celldex Therapeutics Presents Positive Topline Results from Barzolvolimab Phase 2 Study in Chronic Inducible Urticaria

July 29, 2024

- *Met primary endpoint demonstrating clinically meaningful and statistically significant complete response rate across both dose groups*
- *First large, randomized, placebo-controlled study to demonstrate success in CIndU*
- *Favorable safety and tolerability consistent with prior studies*
- *Plans to advance CIndU into Phase 3 registration development*
- *Company to host webcast call today at 4:30 pm ET*

HAMPTON, N.J., July 29, 2024 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) announced today positive topline 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.

"Barzolvolimab is the first drug in development to demonstrate statistically significant and clinically meaningful results in a large, randomized, placebo-controlled study in chronic inducible urticaria. These data are unprecedented and clearly demonstrate that barzolvolimab has the potential to become a critically needed new treatment option for patients suffering from this disease," said Anthony S. Marucci, President and Chief Executive Officer of Celldex Therapeutics. "Inducible urticaria is a disease of misery for patients who despite their best efforts 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. We look forward to advancing barzolvolimab into registrational studies in inducible urticaria and moving towards our goal of bringing this potential new medicine to patients. We would like to thank the patients and investigators who participated in this study and look forward to presenting the full 12 week data from this study at an upcoming medical meeting in the fourth quarter of this year."

Data from the 196 patients randomized in the study showed that barzolvolimab achieved the primary efficacy endpoint, 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. Importantly, barzolvolimab demonstrated rapid, durable and clinically meaningful responses in patients with CIndU refractory to antihistamines. Demographics and baseline disease characteristics were well balanced across treatment groups.

Summary of Clinical Assessments at Week 12						
	Cold Urticaria			**Symptomatic Dermographism**		
	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)
% of patients with negative provocation test at Week 12 (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%

Barzolvolimab was well tolerated with a favorable safety profile consistent with prior studies. Most adverse events were mild to moderate in severity; through 12 weeks, the most common treatment emergent adverse events in barzolvolimab treated patients were hair color changes (13%) and neutropenia (11%). The rate of infections was similar between barzolvolimab-treated patients and placebo with no association between neutropenia and infections.

The Phase 2 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 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-NRS (worst itch numeric rating scale).

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
To access the live and archived 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 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 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 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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