Celldex Therapeutics Presents Data Demonstrating Profound Improvements in Angioedema in Barzolvolimab Phase 2 Study in Chronic Spontaneous Urticaria at EAACI 2024

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- Clinically meaningful and statistically significant improvements across multiple angioedema measurements and barzolvolimab dose groups -
- Sustained activity with rapid onset within 2 weeks -
- Data further support barzolvolimab clinical benefit to patients with CSU -

HAMPTON, N.J., June 02, 2024 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today announced data demonstrating that barzolvolimab profoundly improves angioedema at 12 weeks in the Company's Phase 2 clinical trial in chronic spontaneous urticaria (CSU). Angioedema, characterized by swelling of the deeper dermal layers of the skin and mucous membranes, is a painful, debilitating symptom of CSU that has significant impact on quality of life. It commonly affects the face (lips and eyelids), hands, feet, and genitalia but can also involve the tongue, uvula, soft palate, and pharynx[1].

The data were presented today by Dr. Marcus Maurer, Professor of Dermatology and Allergy at Charité – Universitätsmedizin in Berlin, in an oral presentation at the European Academy of Allergy and Clinical Immunology (EAACI) Congress 2024. Celldex previously announced that the Phase 2 study in CSU met its primary and secondary endpoints at 12 weeks with clinically meaningful and statistically significant decreases in UAS7 (weekly urticaria activity score) compared to placebo across multiple dose groups and demonstrated a favorable safety profile. The data presented today further support these results by demonstrating improvements in AAS7 (weekly angioedema activity score) and additional measures of angioedema control.

"The majority of patients with severe CSU suffer with angioedema, which is often extremely painful and causes disfigurement, dramatically impacting quality of life," said Diane C. Young, MD, Senior Vice President and Chief Medical Officer of Celldex Therapeutics. "Consistent with previously reported clinical outcomes, we observed rapid, durable and significant angioedema relief, including in omalizumab refractory disease. These data continue to support barzolvolimab's potential to become a transformative treatment option for CSU and we look forward to moving closer to this goal with the initiation of our Phase 3 studies this summer."

Phase 2 Barzolvolimab Study in CSU (n=208) ***Summary of Angioedema Clinical Activity Assessments at Week 12***				
	300 mg Q8W (n=51)	150 mg Q4W (n=52)	75 mg Q4W (n=53)	Placebo (n=51)
Angioedema at baseline, n (%)	42 (82%)	35 (67%)	40 (75%)	32 (63%)
AAS7 Changes				
Baseline AAS7 (mean)	53.15	54.60	54.05	56.30
LS Mean difference from placebo (Confidence Interval, p value)	-25.32 (CI:-36.32, -14.32) p<0.0001	-23.56 (CI:-35.08, -12.04) p<0.0001	-17.52 (CI:-29.35, -5.69) p=0.0039	
>8 point improvement in AAS7 (%)	85.0 P<0.05	87.1 P<0.05	82.9 P<0.05	57.1
Angioedema Free Days (mean)	65.1 P<0.05	54.5 P<0.05	43.3	36.2

AAS7 data were analyzed using ANCOVA model and multiple imputation. Data are presented for patients with angioedema at baseline.

- Barzolvolimab demonstrated significant improvements in AAS7 in patients with angioedema across all doses at Week 12. This improvement was rapid (within 2 weeks) and durable (continued through 12 weeks).
- Barzolvolimab demonstrated strong improvement in AAS7 independent of omalizumab status at Week 12. Approximately 20% (n=41) of enrolled patients received prior treatment with omalizumab and more than half of these patients had omalizumab-refractory disease. These patients experienced a similar clinical benefit as the overall treated population within their individual dosing groups consistent with the barzolvolimab mechanism of action.
- Patients on barzolvolimab experienced a > 8 point improvement in AAS7 (considered a clinically meaningful result) across all doses compared to placebo (p<0.05).

- Barzolvolimab increased angioedema free days compared to placebo through 12 weeks. Patients in the 300 mg cohort were angioedema free 77% of the time over the 12 week period.

Phase 2 Study Design
The randomized, double-blind, placebo-controlled, parallel group Phase 2 study is evaluating the efficacy and safety profile of multiple dose regimens of barzolvolimab in patients with CSU who remain symptomatic despite antihistamine therapy, to determine the optimal dosing strategy. 208 patients were randomly assigned on a 1:1:1:1 ratio to receive subcutaneous injections of barzolvolimab at 75 mg every 4 weeks, 150 mg every 4 weeks, 300 mg every 8 weeks or placebo during a 16-week placebo-controlled treatment period. After 16 weeks, patients then enter a 36-week active treatment period, in which patients receiving placebo or the 75 mg dose are randomized to receive barzolvolimab 150 mg every 4 weeks or 300 mg every 8 weeks; patients already randomized to the 150 mg and 300 mg treatment arms remain on the same regimen as during the placebo-controlled treatment period. After 52 weeks, patients then enter a follow-up period for an additional 24 weeks. The primary endpoint of the study is mean change in baseline to Week 12 in UAS7 (weekly activity score). Secondary endpoints include other assessments of safety and clinical activity including ISS7 (weekly itch severity score), HSS7 (weekly hives severity score) and AAS7 (weekly angioedema activity score).

For additional information on this trial (NCT05368285), please visit www.clinicaltrials.gov

[1]DermNet.

About Chronic Spontaneous Urticaria (CSU)
CSU is characterized by the occurrence of hives or wheals for 6 weeks or longer without identifiable specific triggers or causes. The activation of the mast cells in the skin (release of histamines, leukotrienes, chemokines) results in episodes of itchy hives, swelling and inflammation of the skin that can go on for years or even decades. Current therapies provide symptomatic relief only in some patients.

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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