Celldex Therapeutics Presents Positive 12 Week Results from Barzolvolimab Phase 2 Study in Chronic Spontaneous Urticaria

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- Primary and secondary endpoints met with clinically meaningful and statistically significant decreases in urticaria disease activity across multiple dose groups -
- Sustained activity with rapid onset within 2 weeks -
- Similar improvement in omalizumab-experienced/refractory and omalizumab-naïve disease consistent with unique mechanism of action -
- Favorable safety profile -
- 52 week results and Phase 3 CSU trial initiations anticipated in 2024 -
- Company to host webcast February 25th at 9:45 am ET-

HAMPTON, N.J., Feb. 24, 2024 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) announced today positive 12 week results from the Company's Phase 2 clinical trial of barzolvolimab in patients with moderate to severe chronic spontaneous urticaria (CSU) refractory to antihistamines, including patients with biologic-refractory disease. The studies will continue dosing patients until week 52. 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. CSU is characterized by the occurrence of hives or wheals for 6 weeks or longer without identifiable specific triggers or causes. Treatment options for patients with CSU are limited and there are no approved therapies for patients who are not adequately controlled by omalizumab. The data were presented by Dr. Marcus Maurer, Professor of Dermatology and Allergy at Charité – Universitätsmedizin in Berlin, in a late breaking oral presentation (L18) as part of the American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting 2024.

"These data continue to support barzolvolimab's potential to bring meaningful improvements to patients suffering from this often very severe and debilitating disease," said Marcus Maurer, M.D. "The novel mast cell depleting mechanism of barzolvolimab addresses the root driver of chronic spontaneous urticaria providing early, durable and, most importantly, the opportunity for complete disease control for patients who are not seeing meaningful benefits from the current standard of care, including patients with omalizumab refractory disease."

"We are thrilled to share these positive results, which we believe further establish barzolvolimab as a potential transformative treatment option for patients suffering with CSU, and are actively planning for the initiation of our Phase 3 program in CSU this summer," commented Anthony S. Marucci, President and Chief Executive Officer of Celldex Therapeutics. "We also thank the patients and investigators for their participation in this study and look forward to reporting 52 week data later this year."

Data from the 208 patients randomized in the study showed that barzolvolimab achieved the primary efficacy endpoint, with a statistically significant mean change from baseline to week 12 in UAS7 (weekly urticaria activity score) compared to placebo at all dose levels. Secondary and exploratory endpoints in the study were also achieved at week 12 and strongly support the primary endpoint results, including changes in ISS7 (weekly itch severity score) and HSS7 (weekly hives severity score) and responder analyses. Importantly, barzolvolimab demonstrated rapid, durable and clinically meaningful responses in patients with moderate to severe CSU refractory to antihistamines, including patients with prior omalizumab treatment. Demographics and baseline disease characteristics were well balanced across treatment groups. The majority of patients on study had severe disease (UAS7≥28).

Summary of Clinical Activity Assessments at Week 12				
	300 mg Q8W (n=51)	150 mg Q4W (n=52)	75 mg Q4W (n=53)	Placebo (n=51)
UAS7 Changes				
Baseline UAS7 (mean)	31.33	30.75	30.30	30.09
LS Mean change at Week 12	-23.87	-23.02	-17.06	-10.47
LS Mean difference from placebo (Confidence Interval, p value)	-13.41 (CI: -17.47, -9.34) **p<0.0001**	-12.55 (CI:-16.56, -8.55) **p<0.0001**	-6.60 (CI:-10.71, -2.49) p=0.0017	
HSS7 Changes				
Baseline HSS7 (mean)	14.92	15.05	14.86	14.47
LS Mean change at Week 12	-12.19	-11.19	-8.25	-4.95
LS Mean difference from placebo (Confidence Interval, p value)	-7.24 (CI:-9.36, -5.12) **p<0.0001**	-6.24 (CI:-8.33, -4.16), **p<0.0001**	-3.31 (CI:-5.40, -1.22), p=0.0020	
ISS7 Changes				
Baseline ISS7 (mean)	16.42	15.70	15.44	15.61
LS Mean change at Week 12	-11.79	-11.68	-8.62	-5.47

LS Mean difference from placebo (Confidence Interval, p value)	-6.32 (CI: -8.50, -4.13), **p<0.0001**	-6.21 (CI: -8.38, -4.04), **p<0.0001**	-3.16 (CI: -5.41, -0.91), p=0.0061	
Responder Analyses/Clinical Responses				
UAS7=0 (Complete Control)	37.5%	51.1%	22.9%	6.4%
UAS7≤6 (Well-controlled)	62.5%	59.6%	41.7%	12.8%

UAS7, HSS7 and ISS7 data were analyzed using ANCOVA model and multiple imputation.

Barzolvolimab demonstrated strong improvement in UAS7 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.

Barzolvolimab was well tolerated with a favorable safety profile. Most adverse events were mild to moderate in severity; through 12 weeks, the most common treatment emergent adverse events in barzolvolimab treated patients were urticaria/CSU (10%), hair color changes (9%), and neutropenia/ANC decrease (8%). The rate of infections was similar between barzolvolimab treated patients and placebo with no association between neutropenia and infections.

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

Webcast
The Company will host a conference call/webcast tomorrow to discuss the results at 9:45 a.m. ET. Management will be joined by Dr. Marcus Maurer and by Dr. Allen Kaplan, both broadly recognized as preeminent experts in the field of allergy and, specifically in chronic urticaria. The event will be webcast live and can be accessed by going to the "Events & Presentations" page under the "Investors & Media" section of the Celldex Therapeutics website at www.celldex.com.

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 effects of the outbreak of COVID-19 on our business and results of operations; 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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