Celldex Therapeutics Presents Positive Interim Data from Barzolvolimab Phase 1b Study in Chronic Spontaneous Urticaria at EAACI 2022

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-Rapid, profound and durable responses across multiple dosing groups with favorable safety profile-
-Mean reduction from baseline in urticaria activity (UAS7) of 66.6% in 1.5 mg/kg dose group at week 12 and 75.1% at week 8 in the 3 mg/kg dose group (reflects one dose; ongoing)-
-Complete response (UAS7=0) of 57.1% in 1.5 mg/kg dose group at week 12 and 44.4% at 8 weeks in 3 mg/kg dose group (reflects one dose; ongoing)-
-42% of patients treated with barzolvolimab had prior omalizumab and had similar symptom improvement as overall population-
-Company to host webcast conference call on Thursday, June 30 at 6:30 p.m. ET-

HAMPTON, N.J., June 30, 2022 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today announced interim data from the Company's ongoing Phase 1b clinical trial of barzolvolimab in patients with moderate to severe chronic spontaneous urticaria (CSU) refractory to 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. CSU is characterized by the occurrence of hives or wheals for 6 weeks or longer without identifiable specific triggers or causes.

Data show that multiple doses of barzolvolimab resulted in dose-dependent decreases in itch and hives, as measured through the urticaria activity score over 7 days (UAS7), with a mean UAS7 reduction of 66.6% in all patients in the 1.5 mg/kg dose group (n=8) at week 12 and 75.1% in all patients in the ongoing 3.0 mg/kg dose group (n=9) at week 8 (reflects one dose), demonstrating meaningful symptom improvements for patients. Complete response as measured by UAS7=0 was 57.1% for patients in the 1.5 mg/kg dose group at week 12 and 44.4% for the patients in the 3.0 mg/kg dose group at week 8 (reflects one dose; ongoing).

Importantly, administering multiple doses of barzolvolimab demonstrated a favorable safety profile, supporting Phase 2 clinical development. These data were presented by Dr. Marcus Maurer, Professor of Dermatology and Allergy at Charité – Universitätsmedizin in Berlin, as a late-breaking electronic poster presentation (#100097) as part of the European Academy of Allergy and Clinical Immunology (EAACI) Annual Congress 2022.

"We are excited by these interim multiple dose data which demonstrate strong clinical activity, rapid onset and sustained durability with a well-tolerated safety profile, including in patients with prior omalizumab experience," commented Anthony S. Marucci, President and Chief Executive Officer of Celldex Therapeutics. "We believe these impressive early data further demonstrate barzolvolimab's unique mechanism and its potential to provide meaningful symptom relief to patients suffering from diseases driven by mast cells. These data support the continued development of barzolvolimab, including our recently initiated Phase 2 chronic urticaria studies."

"These remarkable early results confirm that chronic urticaria is driven by mast cells and barzolvolimab has again demonstrated its ability to bring meaningful improvements to patients suffering from these often very severe and debilitating diseases," said Marcus Maurer, M.D., Professor of Dermatology and Allergy at Charité – Universitätsmedizin in Berlin and a lead investigator on the study. "There are extensive numbers of patients globally with CSU who cannot be helped at all with the current standard of care, so barzolvolimab would represent a considerable advance in the treatment landscape for these patients and potentially other diseases with mast cell involvement."

Summary of Data from Ongoing Phase 1b CSU Trial of Barzolvolimab

As of the data cut-off on May 23, 2022, 34 patients with CSU were enrolled and treated [26 barzolvolimab (n=9 in 0.5 mg/kg; n=8 in 1.5 mg/kg; n=9 in 3.0 mg/kg) and 8 placebo]. The 0.5 mg/kg and 1.5 mg/kg cohorts had completed study participation through 24 weeks; 7 of 12 patients in the 3.0 mg/kg cohort had completed week 12; enrollment in the 4.5 mg/kg cohort was ongoing. Adverse events through data cutoff and hematology data through week 12 were included for all dose groups; clinical activity and tryptase data were included through week 12 for 0.5 mg/kg and 1.5 mg/kg, and through week 8 for 3 mg/kg (ongoing; reflecting the administration of only one dose).

Interim Clinical Activity Results

- Barzolvolimab results in rapid, marked and durable responses in patients with moderate to severe CSU refractory to antihistamines, including patients with prior omalizumab treatment.
- Mean reduction from baseline in urticaria activity (UAS7) of 66.6% in all patients in the 1.5 mg/kg dose group (n=8) at week 12 and 75.1% in all patients in the 3.0 mg/kg dose group (n=9) at week 8 (reflects one dose; ongoing),

demonstrating clinically meaningful symptom improvements for patients.

- Complete response (UAS7=0) of 57.1% in the 1.5 mg/kg dose group at week 12 and 44.4% at week 8 (reflects one dose; ongoing) in the 3 mg/kg dose group which is a key therapeutic goal.
- 75% well-controlled disease by Urticaria Control Test (UCT) in the 1.5 mg/kg dose group at week 12 and 83.3% in the 3 mg/kg dose group at week 8 (reflects one dose; ongoing).
- Patients with prior omalizumab therapy had similar symptom improvement as all patients.
- All three doses of barzolvolimab markedly improved urticaria symptoms and disease control, with rapid improvement in itch and hives. As predicted, the lowest dose of 0.5 mg/kg resulted in suboptimal clinical activity compared to the higher doses.
- Rapid onset of responses after initial dosing and sustained durability were observed; onset as early as 1 week after the first dose.
- Tryptase suppression, indicative of mast cell depletion, paralleled symptom improvement, demonstrating the impact of mast cell depletion on CSU disease activity.

Summary of Clinical Activity Assessments at week 12 for 0.5 mg/kg and 1.5 mg/kg dose groups and week 8 for 3.0 mg/kg dose group (ongoing, clinical activity reflects one dose):

All Patients	0.5 mg/kg Q4W at Week 12	1.5 mg/kg Q4W at Week 12	3.0 mg/kg Q8W at Week 8 (ongoing)	Placebo at Week 12/8
UAS7 Changes				
Mean Score Change in UAS7 From Baseline	-11.1	-18.1	-22.7	-14.3 / -12.4
Mean % Change in UAS7 From Baseline	-39.7%	-66.6%	-75.1%	-35.9% / -31.1%
Clinical Responses				
UAS7=0 (Complete Response)	11.1%	57.1%	44.4%	16.7% / 0%
UAS7 ≤ 6 (Well-controlled)	22.2%	57.1%	55.6%	16.7% / 0%
UCT ≥ 12 (Well-controlled)	12.5%	75.0%	83.3%	16.7% / 0%

The UAS7 score is calculated as the sum over 7 days of the daily intensity of itch (ISS7 itch severity score) and number of hives (HSS7 hives severity score). UAS7 values range from 0 to 42, with higher values reflecting higher disease activity. UCT has 4 items with 5 answer options (scored with 0-4 points); recall period of 4 weeks. Low points indicate high disease activity and low disease control. The minimum and maximum UCT scores are 0 and 16, with 16 points indicating complete disease control and ≥12 indicating well controlled disease.

Safety Results

- Barzolvolimab was well tolerated with a favorable safety profile; effects of multiple dose administration were consistent with observations in single dose studies.
- Most AEs were mild or moderate in severity and resolved while on study, with none leading to treatment discontinuation. The most common treatment emergent adverse events were urinary tract infections, headache, neutropenia and back pain. UTIs, headache and backpain were all reported as unrelated to treatment. There was one severe adverse event of salmonella gastroenteritis which was also not related to study therapy.
- Changes in hematologic parameters were consistent with observations in single dose studies, with no pattern of further decreases with multiple doses; hematologic values generally remained within the normal range. Four patients with screening and baseline neutrophil counts at the lower end of the normal range on study initiation had decreases in neutrophil counts reported as AEs. The pattern observed in the neutrophil changes for these patients was similar to the pattern seen in patients across the barzolvolimab program to date—generally transient, asymptomatic, and mild.

The Phase 1b study is a randomized, double-blind, placebo-controlled clinical trial designed to assess the safety of multiple ascending doses of barzolvolimab in patients with moderate to severe CSU who remain symptomatic despite treatment with antihistamines. Secondary and exploratory objectives include pharmacokinetic and pharmacodynamic assessments, including measurement of tryptase and stem cell factor levels and clinical activity outcomes (impact on urticaria symptoms, disease control, clinical response) as well as quality of life assessments. The study is expected to enroll approximately 40 patients with CSU across four cohorts (8 barzolvolimab; 2 placebo). Barzolvolimab is administered intravenously at 0.5 mg/kg mg every 4 weeks, 1.5 mg/kg every 4 weeks, 3 mg/kg every 8 weeks, 4.5 mg/kg every 8 weeks, as add-on treatment to H1-antihistamines, either alone or in combination with H2-antihistamines and/or leukotriene receptor agonists. For additional information on this trial (NCT04538794), please visit www.clinicaltrials.gov.

Webcast and Conference Call

The Company will host a conference call/webcast along with Dr. Marcus Maurer to discuss the results at 6:30 p.m. ET on Thursday, June 30. 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. The call can also be accessed by dialing

(866) 743-9666 (within the United States) or (760) 298-5103 (outside the United States). The conference ID is 6130457. A replay of the call will be archived on the Company's website or can be accessed by dialing (855) 859-2056 (within the United States) or (404) 537-3406 (outside the United States). The conference ID is 6130457.

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 (also referred to as CDX-0159) is a humanized monoclonal antibody that specifically 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.

About Celldex Therapeutics, Inc.
Celldex is a clinical stage biotechnology company dedicated to developing monoclonal and bispecific antibodies that address devastating diseases for which available treatments are inadequate. 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 inflammatory diseases and many forms of cancer. 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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Celldex therapeutics

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