Celldex Therapeutics Presents Positive Data from Barzolvolimab Chronic Urticaria Program at EAACI 2023

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- Data updates at EAACI 2023 continue to position barzolvolimab as a potential best-in-class addition to a historically limited treatment landscape -
- At week 24, 55% of all patients with CSU in the 1.5 mg/kg, 3.0 mg/kg and 4.5 mg/kg dose groups had complete response (UAS7) and 69% had well-controlled disease (UCT) -
- Patients in the CSU study with angioedema treated at these doses had profound and durable angioedema symptom improvement -
- Single 3.0 mg/kg dose of barzolvolimab was well tolerated and demonstrated impressive clinical activity in difficult to treat cholinergic urticaria with a 56% complete response rate and patients reporting clinically significant improvement in quality of life -
- Phase 2 CSU study nearing enrollment completion with topline data by year-end; Phase 2 CindU study enrolling as planned -

HAMPTON, N.J., June 10, 2023 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) announced today that updated data from the Company's Phase 1b multi-dose clinical trial in chronic spontaneous urticaria (CSU) and new data from the Phase 1b single-dose cholinergic cohort included in the chronic inducible urticaria (CIndU) trial were presented at the European Academy of Allergy and Clinical Immunology (EAACI) Annual Congress 2023. 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 the function and survival of mast cells. Data continue to support that mast cell depletion by barzolvolimab, as demonstrated by tryptase suppression, parallels symptom improvement.

The CSU data were presented by Dr. Marcus Maurer, Professor of Dermatology and Allergy at Charité – Universitätsmedizin in Berlin, in a late breaking oral presentation (#000401) and the cholingeric data were presented by Dr. Eva Grekowitz, Clinical Investigator, Department of Dermatology, Venerology and Allergy at Charité – Universitätsmedizin in Berlin in an oral presentation (#000393).

"As we expand development into more patients and new disease settings, the data repeatedly support that barzolvolimab's mast cell depleting mechanism holds great potential to offer patients a much needed rapid, profound and durable treatment option for chronic urticarias— including patients who are not seeing meaningful benefits from the current standard of care," said Marcus Maurer, M.D. "In the CSU study, we also observed very significant improvements in angioedema which can be a devastating manifestation of urticaria for many patients. In cholinergic urticaria, barzolvolimab again demonstrated remarkable response rates and impressive improvements in quality of life in this tough to treat form of inducible urticaria."

"We are extremely pleased with these further results which once again demonstrated strong clinical activity, rapid onset and sustained durability with a well-tolerated safety profile, including in patients who had previously taken omalizumab," commented Anthony S. Marucci, President and Chief Executive Officer of Celldex Therapeutics. "These strong results support our ongoing Phase 2 studies in urticaria. We look forward completing accrual ahead of schedule in the Phase 2 CSU study later this month and reporting topline data by the end of this year."

Summary of Barzolvolimab Phase 1b Chronic Spontaneous Urticaria (CSU) Data Update

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 do not respond to omalizumab. Celldex's 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. Approximately 40% of patients with CSU report accompanying episodes of angioedema, which typically presents as swelling in the lips, cheeks, around the eyes, arms, legs, or genitals[1]; patients with CSU and angioedema typically experience significant negative impacts on health-related quality of life, daily activities and productivity in work compared to patients with CSU who do not have angioedema[2].

Clinical Activity Data
Celldex previously presented interim Phase 1b CSU data at the American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting 2023. The 0.5 mg/kg, 1.5 mg/kg and 3.0 mg/kg cohorts had completed study participation through 24 weeks; 6 of 9 patients in the 4.5 mg/kg cohort had completed through the week 20 visit (last barzolvolimab dose administered at 8 weeks). The study is now complete. At EAACI 2023, Celldex presented data on the complete 24 week experience for the 4.5 mg/kg cohort and data on angioedema impact across all study cohorts. 45 patients with moderate to severe CSU refractory to antihistamines were enrolled and treated [35 barzolvolimab (n=9 in 0.5 mg/kg; n=8 in 1.5 mg/kg; n=9 in 3.0 mg/kg; n=9 in 4.5 mg/kg) and 10 placebo]. Data for the 0.5 mg/kg and placebo group are only outlined below through week 12 because, as expected, most patients from these groups had significant symptoms ahead of week 24 and discontinued follow up. Two patients did not receive all doses of study treatment [4.5 mg/kg (1), placebo (1)].

- These data show that multiple doses of barzolvolimab resulted in rapid dose-dependent decreases in itch and hives with durable and prolonged symptom control in patients with moderate to severe CSU refractory to antihistamines, including patients with prior omalizumab treatment.
- Mean reduction from baseline in urticaria activity (UAS7) at week 24 was 80% in the 1.5 mg/kg dose group (n=7), 70% in the 3.0 mg/kg dose group (n=6) and 77% in the 4.5 mg/kg dose group (n=7).
- Complete response (UAS7=0) at week 24 was 57% in the 1.5 mg/kg dose group, 67% in the 3.0 mg/kg dose group and 43% in the 4.5 mg/kg dose group.

- Well-controlled disease (UCT≥ 12) at week 24 was 75% in the 1.5 mg/kg dose group, 67% in the 3.0 mg/kg dose group and 67% in the 4.5 mg/kg dose group.
- During post-treatment follow up, 71% (10 of 14) of patients who had been treated with doses greater than or equal to 1.5 mg/kg and had a complete response (UAS7=0) at week 12, remained urticaria free at week 24.
- Profound and durable improvement in angioedema symptoms as measured through the angioedema activity score over 7 days (AAS7) was achieved across all dose levels evaluated with sustained activity observed with the 1.5 mg/kg and greater dose levels.
    - 31 patients on study (n=26 barzolvolimab; 5=placebo) reported angioedema activity at baseline when enrolling in the study. 86% of the barzolvolimab treated patients at 1.5 mg/kg or greater were angioedema free at week 12 and 83% were angioedema free at week 24.

Summary of Clinical Activity Assessments

All Patients	0.5 mg/kg Q4W at Week 12	1.5 mg/kg Q4W at Week 12/24	3.0 mg/kg Q8W at Week 12/24	4.5 mg/kg Q8W at Week 12/24	Placebo at Week 12
Baseline UAS7 (mean, range)	31 (20 -39)	30 (20 - 41)	29 (16 - 42)	28 (22 - 38)	36 (19 - 42)
UAS7 Changes					
Mean Score Change in UAS7 From Baseline	-11	-18 / -23	-21 / -23	-24 / -24	-14
Mean % Change in UAS7 From Baseline	-40%	-67% / -80%	-67% / -70%	-82% / -77%	-37%
Clinical Responses**					
UAS7=0 (Complete Response)	11%	57% / 57%	44% / 67%	67% / 43%	13%
UAS7 ≤ 6 (Well-controlled)	22%	57% / 57%	67% / 67%	67% / 57%	13%
UCT ≥ 12 (Well-controlled)	11%	75% / 75%	63% / 67%	89% / 67%	33%

**24 week data not shown for 0.5 mg/kg and placebo dose levels as most patients had significant symptoms ahead of week 24 and discontinued follow up.*

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.

*** Clinical responses shown are the proportion of patients with the defined response at the specific timepoint. Patients with missing data at the timepont are excluded.*

Safety Data
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.

Summary of Barzolvolimab Phase 1b Cholinergic (CIndU) Data Results

Chronic inducible urticarias are forms of urticaria that have an attributable trigger associated with them, typically resulting in wheals (hives) or angioedema. Cholinergic urticaria, a form of CindU, is triggered by physical exercise or passive warming and characterized by itchy hives/wheals that appear upon sweating. 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.

Clinical Activity Data
In this open-label, Phase 1 trial, a cohort of patients with antihistamine refractory cholinergic urticaria (n=9) received a single intravenous 3.0 mg/kg barzolvolimab dose with a 12-week follow-up. Assessments included provocation testing using pulse-controlled ergometry (PCE; complete response, CR=no whealing within 40 min of test initiation), urticaria control test (UCT), quality of life assessments, and measurement of circulating tryptase and stem cell factor and skin mast cell numbers. Safety assessments included adverse events and clinical laboratory monitoring. Data reported at EAACI 2023 include treatment and safety data through 12 weeks.

- 56% (5/9) patients achieved a complete response (negative test) with PCE provocation testing with just one dose of barzolvolimab and most responses remained durable through to week 12. PCE testing included controlled exercise on a stationary bicycle with monitoring for development of itch and wheals.
- 63% (5/8) patients reported well controlled disease (UCT ≥12) at week 8 and 50% (4/8) at week 12, respectively.
- 100% (6/6) patients who reported on quality of life (QoL) measurements at week 8 had clinically significant improvements in QoL. These improvements in QoL were sustained through week 12 for the majority (5/7, 71%) of patients.
- The kinetics of tryptase and mast cell reduction mirrored clinical activity

Safety Data

Barzolvolimab was generally well tolerated in patients with CholU, with a similar safety profile to that reported previously. The most common AEs were mainly mild; hair color changes (78%), nasopharyngitis (67%), taste disorders (44%), and infusion related reactions (33%). Hematology parameters were consistent with previous observation and generally remained within the normal ranges. Mild, transient, and asymptomatic decreases in hemoglobin and WBC parameters were noted.

[1]JAllergy Clin Immunol Pract. 2018 Jul-Aug; 6(4): 1097–1106; [2]Allergy 2018 Aug;73(8):1724-1734. doi: 10.1111/all.13430.

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.

About the Phase 1b CSU Study Design
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 enrolled 45 patients with CSU across four cohorts. Barzolvolimab was administered intravenously at 0.5 mg/kg every 4 weeks (3 doses), 1.5 mg/kg every 4 weeks (3 doses), 3 mg/kg every 8 weeks (2 doses), 4.5 mg/kg every 8 weeks (2 doses), as add-on treatment to H1-antihistamines, either alone or in combination with H2-antihistamines and/or leukotriene receptor agonists. Following completion of the 12 week treatment period, patients were followed for an additional 12 weeks or until resumption of symptoms, whichever was sooner. For additional information on this trial (NCT04538794), please visit www.clinicaltrials.gov.

About the Phase 1b CindU Study Design
The Phase 1b study is an open label clinical trial designed to evaluate the safety of a single dose of barzolvolimab in patients with cold urticaria, symptomatic dermographism and cholinergic urticaria who are refractory to antihistamines. Patients' symptoms are induced via provocation testing that resembles real life triggering situations. Secondary and exploratory objectives include pharmacokinetic and pharmacodynamic assessments, including changes from baseline provocation thresholds, measurement of tryptase and stem cell factor levels, clinical activity outcomes (impact on urticaria symptoms, disease control, clinical response), quality of life assessments and measurement of tissue mast cells through skin biopsies. The study enrolled 40 patients with inducible urticaria across four cohorts (cold urticaria, symptomatic dermagraphism and cholinergic urticaria at 3.0 mg/kg each and cold urticaria at 1.5 mg/kg). Barzolvolimab was administered intravenously as add on treatment to H1-antihistamines and patients were followed for 12 weeks after dosing, with an optional longer term follow up period. For additional information on this trial (NCT04548869), please visit www.clinicaltrials.gov.

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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