Celldex Therapeutics Presents Positive Data from Barzolvolimab Phase 1b Study in Chronic Inducible Urticaria at Global Urticaria Forum 2022

Dec 6, 2022

- 100% complete response rate in cold urticaria after single dose of barzolvolimab at 1.5 mg/kg, including in omalizumab refractory patients -
- Long term follow up of patients with chronic inducible urticaria treated at 3.0 mg/kg confirm that barzolvolimab-induced responses and mast cell suppression are durable and linked -
- Company to host webcast conference call on Tuesday, December 6 at 8:00 a.m. ET -

HAMPTON, N.J., Dec. 06, 2022 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today announced new data from the Company's open label Phase 1b clinical trial of barzolvolimab in patients with antihistamine refractory chronic inducible urticarias are being presented at the GA²LEN Global Urticaria Forum (GUF) held in Berlin, Germany. These diseases, which are often severe and debilitating, can significantly impact patients' lives. Barzolvolimab is a humanized monoclonal antibody that binds the receptor tyrosine kinase KIT with high specificity and potently inhibits its activity.

All 9 of 9 (100%) cold urticaria patients who received a 1.5 mg/kg single full dose of barzolvolimab experienced a complete response as assessed by provocation testing, including 4 of 4 patients with omalizumab refractory disease. This cohort was added to the Phase 1b trial in patients with chronic inducible urticaria after Celldex previously reported a 95% complete response rate in July 2021 in patients with antihistamine-refractory cold urticaria and symptomatic dermographism who received a single 3.0 mg/kg dose of barzolvolimab.

The Company also added an optional long term follow up evaluation for the initial cohorts of patients treated at 3.0 mg/kg beyond the original 12 week follow up period out to 36 weeks and confirmed that barzolvolimab-induced response and mast cell suppression are durable and linked.

"These impressive data continue to demonstrate the potential of barzolvolimab to be an important therapy for patients with chronic urticaria and other severe mast cell driven diseases," said Diane C. Young, M.D., Senior Vice President and Chief Medical Officer. "Once again, and with a lower dose, every patient with cold urticaria, including those with very limited treatment options who are refractory to omalizumab, experienced a complete response to treatment, further validating barzolvolimab's unique mechanism of action. These clinical results and the supportive data from our long term follow up of other patient cohorts add to our enthusiasm for barzolvolimab, and we are excited to continue advancing our clinical program, including the ongoing Phase 2 trials."

Celldex Presentations at GA²LEN Global Urticaria Forum (GUF) 2022
Presentations at GUF include data from the ongoing single-dose intravenous Phase 1b study in chronic inducible urticaria. New data presented at GUF include 12 week treatment results for the 1.5 mg/kg cohort in cold urticaria and long term follow up data from the 3.0 mg/kg cohorts in cold urticaria and symptomatic dermographism. A randomized, double-blind, placebo-controlled, multi-dose Phase 2 subcutaneous study of barzolvolimab is currently enrolling patients with both cold urticaria and symptomatic dermographism. Subcutaneous doses of 150 mg Q4 weeks and 300 mg Q8 weeks are being evaluated, which result in similar exposure to the intravenous 1.5 mg/kg and 3.0 mg/kg doses, respectively, evaluated in the Phase 1b study.

Data Summary

Cold Urticaria 1.5 mg/kg intravenous cohort oral presentation: *"Cold urticaria patients achieve complete response with 1.5 mg/kg barzolvolimab"*

10 patients received a single intravenous infusion of barzolvolimab at 1.5 mg/kg. Patients had high disease activity as assessed by provocation threshold testing with a mean baseline critical temperature threshold of 18.4°C or 65°F with a range from 6 to 27°C or 43 to 81°F. All patients had disease refractory to antihistamines and five patients had disease refractory to omalizumab. Safety results are reported for all 10 patients; activity results are reported for the 9 patients who received a full dose of barzolvolimab, including four patients with omalizumab refractory disease. The Company presented these new 1.5 mg/kg dose cohort data alongside the previously presented 3.0 mg/kg dose cohort to allow for comparison between the dose levels.

- All 9 of 9 (100%) patients evaluable for activity treated at 1.5 mg/kg experienced a complete response as assessed by provocation threshold testing, including 4 patients with disease refractory to omalizumab.
    - To date, 19 of 19 (100%) patients with cold urticaria treated with either a single dose of barzolvolimab at 1.5 or 3.0 mg/kg in this Phase 1b study have experienced a completed response by provocation testing, including 5 patients with omalizumab refractory disease.
- Rapid onset of responses after dosing and sustained durability were observed in the 1.5 mg/kg cohort. As expected, the duration of response was dose dependent.

    - 6 of 9 treated at 1.5 mg/kg achieved a complete response within a week of dosing.
    - The median duration of response for patients treated at 1.5 mg/kg was 51+ days (7+ weeks) compared to 77+ days (11+ weeks) for the patients with cold urticaria treated at 3.0 mg/kg.
- Improvements in disease activity as reported by Urticaria Control Test (UCT) were consistent with the completed responses as measured by provocation testing.
    - All patients in the 1.5 mg/kg cohort entered the study with poorly controlled disease (mean UCT score at baseline of 5.9 and a range of 1-11).
    - Following barzolvolimab administration, all patients treated at 1.5 mg/kg achieved well controlled disease (>12 UCT) with 7 of 9 achieving complete control (>16 UCT). These results were consistent with improvements seen in UCT in patients treated at 3.0 mg/kg.
- A single 1.5 mg/kg dose of barzolvolimab resulted in rapid, marked and durable suppression of serum tryptase.
    - The kinetics of tryptase depletion mirrored changes in provocation threshold and UCT.
- Barzolvolimab was generally well tolerated and the safety profile at 1.5mg/kg was similar to the profile observed with 3.0 mg/kg. No new treatment emergent AEs of concern were noted. While mild, transient and asymptomatic decreases in hemoglobin and WBC parameters were noted, consistent with prior studies, the hematology parameters generally remained within the normal range.

Long-term follow up 3.0 mg/kg intravenous cold urticaria and symptomatic dermographism poster presentation:
"Barzolvolimab-induced response and mast cell suppression are durable and linked"

21 patients received a single infusion of barzolvolimab at 3.0 mg/kg, including 11 (10 evaluable for activity) patients with cold urticaria and 10 with symptomatic dermographism. Patients had high disease activity as assessed by provocation threshold testing at baseline and poorly controlled disease by UCT. All patients had disease refractory to antihistamines and three patients had disease refractory to omalizumab. As previously reported, a single 3.0 mg/kg IV dose was generally well tolerated and demonstrated a 95% complete response (negative provocation testing) and 100% well controlled urticaria by Urticaria Control Test (UCT), including in all patients with disease refractory to omalizumab. Profound reduction in serum tryptase and skin mast cells during the 12 week follow up period were observed.

14 patients consented to the optional long term follow up evaluation (6 cold, 8 symptomatic dermographism); 10 of the 14 still had complete control of their disease as assessed by provocation testing at week 12. Data were collected at one or more timepoints beyond week 12 through week 36.

- Most patients had return of symptoms and/or loss of urticaria control between 12 and 36 weeks. Remarkably, two patients remained provocation negative at 36 weeks, and four had well controlled disease (UCT ≥12) 36 weeks post dosing.
- Serum tryptase exhibits a similar rate of recovery as clinical symptoms, while skin mast cells return at a slower rate.
    - Tissue KIT signaling, as approximated by SCF levels, was rapidly inhibited after dose administration and fully reactivated approximately 18 weeks after dosing.
    - Tryptase levels return to pretreatment levels during follow up, while mast cells continue to recover.
- Drug related adverse events noted during the study all resolved.

Additional Presentations: Encore presentations reviewing previously presented data from the Phase 1b study in chronic spontaneous urticaria and on wound healing are also being presented at GUF. The presentations will be made available on the Celldex website and do not include new data.

Webcast and Conference Call
The Company will host a conference call/webcast to discuss the results today at 8:00 a.m. ET. 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 (800) 715-9871 (within the United States) or (646) 307-1963 (outside the United States). The conference ID is 4307990.

About Chronic Inducible Urticaria
Chronic inducible urticarias are forms of urticaria that have an attributable trigger associated with them, typically resulting in wheals (hives) or angioedema. Approximately 0.5% of the total population suffers from chronic inducible urticarias. Celldex is exploring the three most common forms, cold-induced, dermographism (scratch-induced) and cholinergic (exercise/sweat-induced). People afflicted with cold urticaria experience symptoms like itching, burning wheals and angioedema when their skin is exposed to temperatures below skin temperature. Symptomatic dermographism is characterized by the development of a wheal and flare reaction in response to stroking, scratching or rubbing of the skin and usually occurs within minutes of the inciting stimulus. Cholinergic urticaria is triggered by the body's sweating response to active or passive body warming, and is characterized by small (1–4 mm) wheals surrounded by bright red flares. Common triggers include exercise, hot baths/showers, fever, occlusive dressings, eating spicy foods and emotional stress. 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.

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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