# Celldex Therapeutics Presents Positive Data from CDX-0159 Phase 1b Study in Chronic Inducible Urticaria at EAACI 2021

July 9, 2021

*- 95% complete response rate after single dose of CDX-0159 -*
*- Rapid, profound and durable responses offer patients opportunity for quick, lasting, meaningful relief -*
*- Median duration of response 77+ days in Cold Urticaria and 57+ days in Symptomatic Dermographism -*
*- Serum tryptase and skin mast cell depletion mirror clinical activity -*
*- Favorable safety profile -*
*- Company to host webcast conference call on Monday, July 12 at 8:15 a.m. ET -*

HAMPTON, N.J., July 09, 2021 (GLOBE NEWSWIRE) -- Celldex Therapeutics, Inc. (NASDAQ:CLDX) today announced updated data from the Company's ongoing, open label Phase 1b clinical trial of CDX-0159 in patients with antihistamine refractory cold urticaria and symptomatic dermographism, the two most common forms of chronic inducible urticaria. These diseases, which are often severe and debilitating, can significantly impact patients' lives. CDX-0159 is a humanized monoclonal antibody that specifically binds the receptor tyrosine kinase KIT with high specificity and potently inhibits its activity.

All 19/19 (100%) patients who received a single full dose of CDX-0159 experienced a clinical response to provocation testing. 18/19 (95%) experienced a complete response and 1/19 (5%) experienced a marked partial response. Responses were rapid, profound, and durable and correlated with a depletion of skin mast cells. CDX-0159 was generally well tolerated. These data were presented by Dr. Marcus Maurer, Professor of Dermatology and Allergy at Charité – Universitätsmedizin, in Berlin during a late-breaking poster discussion session (#1046) as part of the European Academy of Allergy and Clinical Immunology (EAACI) Annual Congress 2021.

"The achievement of a 95% complete response rate, rapid onset and sustained durability after a single dose is unprecedented in this patient population and clearly demonstrates that CDX-0159 has the potential to become an important new treatment option for patients suffering with chronic inducible urticaria," commented Anthony S. Marucci, President and Chief Executive Officer of Celldex Therapeutics. "We believe these impressive early data show that CDX-0159 safely depletes mast cells which indicates its potential to impact other diseases with mast cell involvement. We continue to make excellent progress across the CDX-0159 development program in urticaria and expect to expand into prurigo nodularis later this year, and additional indications with mast cell involvement in the future."

"These early-stage results are stunning and represent a major breakthrough for patients with inducible urticarias where current treatment options have been unable to provide relief from often severe symptoms," said Marcus Maurer, M.D., Professor of Dermatology and Allergy at Charité - Universitätsmedizin in Berlin, who is conducting the study. "While individuals with inducible urticaria go to great lengths to avoid disease triggers in their daily lives, many find it impossible to do so and are impacted by severe itching and burning hives that impair all parts of their lives—their work, their concentration, their sleep and their social behavior. CDX-0159 clearly provided a real benefit to these patients and has meaningfully improved their lives. This novel mast cell depleting mechanism is especially exciting because it can provide insights into the involvement of mast cells across many diseases where their role is not yet well understood by the scientific community."

**Summary of data from ongoing Phase 1b Trial of CDX-0159:**

As of the data cut-off on June 11, 2021, 20 patients had received a single intravenous infusion of CDX-0159 at 3 mg/kg, including 11 patients with cold urticaria and 9 patients with symptomatic dermographism. Patients had high disease activity as assessed by provocation threshold testing. In patients with cold urticaria and symptomatic dermographism baseline critical temperature thresholds were 18.9°C/66°F (range: 5-27°C/41-80.6°F) and FricTest® thresholds were 3.8 (range: 3-4) of 4. Safety results are reported for all 20 patients; activity results are reported for the 19 patients who received a full dose of CDX-0159. 14 of 19 patients completed the 12-week study observation period and five were ongoing (range of 2-8 weeks) as of June 11, 2021.

- All 19/19 (100%) patients experienced a clinical response as assessed by provocation threshold testing; 18/19 (95%) experienced a complete response and 1/19 (5%) experienced a partial response.
    - 10/10 (100%) patients with cold urticaria experienced a complete response.
    - 8/9 (89%) patients with symptomatic dermographism experienced a complete response and 1/9 (11%) experienced a partial response.
    - Compete responses were observed in all 3 patients (1 cold urticaria; 2 symptomatic dermographism) with prior Xolair® (omalizumab) experience, including two who were Xolair refractory.
- Rapid onset of responses after dosing and sustained durability were observed.
    - Most patients with cold urticaria and symptomatic dermographism experienced a complete response by week 1 and by week 4, respectively.
    - The median duration of response for patients was 77+ days for cold urticaria and 57+ days for symptomatic dermographism.
- Improvements in disease activity as reported by physician's and patient's global assessment of disease severity were consistent with the complete responses as measured by provocation testing.

- A single 3 mg/kg dose of CDX-0159 resulted in rapid, marked and durable suppression of serum tryptase and depletion of skin mast cells (87% depletion) as measured through biopsy.
    - The kinetics of serum tryptase and skin mast cell depletion mirrored clinical activity.
    - This confirmed that serum tryptase level is a robust pharmacodynamic biomarker for assessing mast cell burden and clinical activity in inducible urticaria and potentially in other diseases with mast cell driven involvement.
- CDX-0159 was generally well tolerated. The most common adverse events were hair color changes, mild infusion reactions, and transient changes in taste perception.
    - Hair color changes (generally small areas of hair color lightening) and taste disorders (generally partial changes of ability to taste salt) are consistent with inhibiting KIT signaling in other cell types and are expected to be fully reversible.
    - As previously reported, a single severe infusion reaction of brief loss of consciousness was observed in a patient with a history of fainting. The patient rapidly recovered. Importantly, no evidence of mast cell activation as measured by serum tryptase monitoring was observed.
    - There was no evidence of clinically significant decreases in hematology parameters—an important finding for a KIT inhibitor.
- One patient with symptomatic dermographism enrolled in the study also had a diagnosis of prurigo nodularis. After a single dose of CDX-0159, this patient experienced both a complete response of symptomatic dermographism and notable improvement of the prurigo nodularis. Celldex plans to initiate a study in prurigo nodularis in the fourth quarter of 2021.

The Phase 1b study is an open label clinical trial designed to evaluate the safety of a single dose of CDX-0159 in patients with cold urticaria or symptomatic dermographism who are refractory to antihistamines. The study was recently amended to also add a cohort of patients with cholinergic urticaria. 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. CDX-0159 is administered intravenously (3.0 mg/kg) as add on treatment to H1-antihistamines and patients are followed for 12 weeks after dosing. For additional information on this trial (NCT04548869), please visit www.clinicaltrials.gov.

The poster presented at EAACI can be viewed on the "Publications" page of the Celldex website.

As previously announced here, in addition to the on demand pre-recorded poster discussion at EAACI which was made available today, a Q&A with the session chair will also take place on Monday, July 12, 2021 at 12:30-13:30 p.m. CET (6:30-7:30 a.m. ET).

The subcutaneous formulation of CDX-0159 is planned to enter the clinic in the third quarter of 2021. The Company plans to initiate a study in prurigo nodularis in the fourth quarter of 2021. Celldex remains on track to initiate the Phase 2 studies in both spontaneous and inducible urticaria in the first half of 2022. Initial results from the cholinergic cohort are planned for presentation at a scientific congress in the first quarter of 2022. Treatment results from the Phase 1b study in chronic spontaneous urticaria are planned for presentation at a scientific congress in early summer of 2022. The Company plans to expand development into a fourth indication by year end 2022.

**Webcast and Conference Call**
The Company will host a conference call/webcast along with Dr. Marcus Maurer to discuss the results at 8:15 a.m. ET on Monday, July 12. 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 4493642. 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 4493642.

**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 CDX-0159**
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 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.

**Company Contact**
Sarah Cavanaugh
Senior Vice President, Corporate Affairs & Administration
(508) 864-8337
scavanaugh@celldex.com

Patrick Till
Senior Director, Investor Relations & Corporate Communications
(484) 788-8560
ptill@celldex.com

Source: Celldex Therapeutics, Inc.