Century Therapeutics Presents Preclinical Data Highlighting Advances in iPSC Platform Technology and Programs at 2024 ASGCT Annual Meeting

May 10, 2024

- *In vitro data showcases CNTY-101's ability to induce CD19-specific cytolysis of B-cells and potential to treat B-cell driven autoimmune diseases including systemic lupus erythematosus (SLE)*
- *Preclinical data demonstrates potential utility of using a synthetic ligand targeting CD300a as a universal strategy for preventing NK mediated rejection in allogeneic cell therapies*

PHILADELPHIA, May 10, 2024 (GLOBE NEWSWIRE) -- Century Therapeutics (NASDAQ: IPSC), an innovative biotechnology company developing induced pluripotent stem cell (iPSC)-derived cell therapies in immuno-oncology and autoimmune and inflammatory disease, today announced two poster presentations at the ASGCT 27th Annual Meeting. The data presented highlights the potential of the Company's lead candidate, CNTY-101, to treat B-cell driven autoimmune diseases including SLE. Additionally, the Company presented data which further demonstrates the capabilities of its Allo-Evasion™ technology through new preclinical data of a CD300a agonist which can potentially inhibit natural killer (NK) cell alloreactivity.

"As demonstrated today, we remain dedicated to continuously investing in the evolution of our Allo-Evasion™ platform to further enable our iPSC candidates to have a more controlled, durable and tolerable profile than other cell therapies currently in development to treat autoimmune disease," said Hy Levitsky, M.D., President of Research and Development at Century Therapeutics. "The data demonstrate CNTY-101, an allogeneic iPSC-derived NK cell therapy engineered using Allo-Evasion™ edits, eliminates CD19+ B-cells *in vitro* while enhancing persistence and durability with less inflammatory cytokine secretion after target killing. We are also excited to highlight preclinical data of a novel synthetic ligand to CD300a, a potent inhibitory receptor found in nearly all NK cells tested across a wide sampling of the population to render engineered cells resistant to NK cell mediated rejection, potentially offering greater protection for a variety of allogeneic cell therapies currently in development. Together, these capabilities have the potential to allow us not only to protect allogeneic cell therapies better than leading alternatives, but also improve outcomes and deliver a broadly beneficial treatment option across a range of indications."

Details of the posters are as follows:

Characterization of CNTY-101, an Allogeneic Anti-CD19 iPSC-Derived NK Product, for the Treatment of B Cell-Driven Autoimmune Diseases
Poster Board Number: 1815
Session Title: Immune Targeting and Approaches with Genetically-Modified Cells and Cell Therapies
Session Date & Time: Friday, May 10th, 2024, at 12:00 PM -7:00 PM ET

B-cell targeted allogeneic iPSC-derived immune effector cells have the potential to deliver long-term remission in autoimmune diseases mediated by pathogenic B-cells, including SLE. Century's lead candidate, CNTY-101, is currently being evaluated in patients with B-cell Non-Hodgkin Lymphoma, and studies in SLE patients will soon begin. Early clinical experience with this iPSC-derived NK cell demonstrates the potential for tight control over drug exposure, potentially enabling B-cell depletion without causing prolonged B-cell aplasia. CNTY-101 was engineered with multiple precision gene edits, incorporating a CD19-specific CAR, homeostatic cytokine support for enhanced persistence, Allo-Evasion™ edits to prevent rejection by the patients' immune system, and a safety switch. In non-clinical studies the Company demonstrated that CNTY-101 was more potent *in vitro* than peripheral blood mononuclear cell (PBMC) derived CAR-T cells in inducing CD19-specific cytolysis of B-cells isolated from multiple healthy and SLE patient donors with less detectable inflammatory cytokine secretion after B-cell depletion.

Beyond HLA-E: Universal Protection of Allogeneic T Cells from Natural Killer Cells Via CD300a Agonism
Poster Board Number: 1816
Session Title: Immune Targeting and Approaches with Genetically-Modified Cells and Cell Therapies
Session Date & Time: Friday, May 10th, 2024, at 12:00 PM -7:00 PM ET

The therapeutic potential of allogeneic, off-the-shelf T cell therapies is hindered by immune-mediated rejection by the host. While ablation of human leukocyte antigen (HLA) removes most T cell and humoral alloreactivity, this renders the cells vulnerable to attack by natural killer (NK) cells. Expression of natural inhibitory ligands such as HLA-E can diminish NK mediated killing, however, the extent of this resistance varies from host to host and a solution that allows for universal protection again NK cell response has not been found. To overcome this challenge, Century is engineering a class of synthetic ligands called trans antigen signaling receptors (TASRs), which agonize CD300a, an inhibitory receptor present on the vast majority of NK cells across a broad sampling of the population. Researchers assessed expression of a CD300a TASR on T cells edited to lack HLA-I in a large human cohort study. CD300a TASR outperformed leading alternatives, including CD47 and HLA-E, both in terms of protection against NK mediated killing as well as enhanced CAR-T cell efficacy under allogeneic pressure. Notably, peripheral blood from CMV-seropositive donors (>50% of the population) expressed NK cell subsets with relative resistance to HLA-E mediated inhibition, while cells expressing CD300a TASR were protected, broadening the population with the potential to be effectively treated by next-generation allogeneic cell therapies. As such, surface expression of an engineered CD300a agonist acted as a universal ligand against NK cell alloreactivity. CD300a TASR has the potential to be a solution to a key constraint against the broad use of allogeneic cell therapies for hematologic malignancies, cancer, autoimmunity and beyond. These results further strengthen Century's Allo-Evasion™ platform, focused on designing cells capable of evading identification and destruction by the host immune system while simultaneously allowing for repeat dosing of CAR-modified cell therapies to generate durable responses across autoimmune and inflammatory diseases as well as hematologic and solid tumors.

A preprint of the data from the poster was shared in *bioRix* and can be viewed here.

About Allo-Evasion™

Century's proprietary Allo-Evasion™ technology is used to engineer cell therapy product candidates with the potential to evade identification by the host immune system so they can be dosed multiple times without rejection, enabling increased persistence of the cells during the treatment period and potentially leading to deeper and more durable responses. More specifically, Allo-Evasion™ 1.0 technology incorporates three gene edits designed to avoid recognition by patient/host CD8+ T cells, CD4+ T cells and NK cells. Knockout of beta-2-microglobulin or β2m, designed to prevent CD8+ T cell recognition, knock-out of the class II major histocompatibility complex transactivator, or CIITA, designed to prevent CD4+ T cell recognition, and knock-in of the HLA-E gene, designed to enable higher expression of the HLA-E protein to prevent killing of CNTY-101 cells by host NK cells. Allo-Evasion™ technology may allow the implementation of more flexible and effective repeat dosing protocols for off-the-shelf product candidates.

About Century Therapeutics

Century Therapeutics (NASDAQ: IPSC) is harnessing the power of adult stem cells to develop curative cell therapy products for cancer and autoimmune and inflammatory diseases that we believe will allow us to overcome the limitations of first-generation cell therapies. Our genetically engineered, iPSC-derived cell product candidates are designed to specifically target hematologic and solid tumor cancers, with a broadening application to autoimmune and inflammatory diseases. We are leveraging our expertise in cellular reprogramming, genetic engineering, and manufacturing to develop therapies with the potential to overcome many of the challenges inherent to cell therapy and provide a significant advantage over existing cell therapy technologies. We believe our commitment to developing off-the-shelf cell therapies will expand patient access and provide an unparalleled opportunity to advance the course of cancer and autoimmune and inflammatory disease care. For more information on Century Therapeutics please visit www.centurytx.com.

Century Therapeutics Forward-Looking Statement

This press release contains forward-looking statements within the meaning of, and made pursuant to the safe harbor provisions of, The Private Securities Litigation Reform Act of 1995. All statements contained in this press release, other than statements of historical facts or statements that relate to present facts or current conditions, including but not limited to, statements regarding our clinical development plans and timelines, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "might," "will," "should," "expect," "plan," "aim," "seek," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "forecast," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this press release are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition, and results of operations. These forward-looking statements speak only as of the date of this press release and are subject to a number of risks, uncertainties and assumptions, some of which cannot be predicted or quantified and some of which are beyond our control, including, among others: our ability to successfully advance our current and future product candidates through development activities, preclinical studies, and clinical trials; our dependence on the success of our lead product candidate, CNTY-101; the ability of CNTY-101 to be administered as part of a multi-dose strategy and to enable responses without lymphodepletion; uncertainties inherent in the results of preliminary data, pre-clinical studies and earlier-stage clinical trials, which may not be predictive of final results or the results of later-stage clinical trials; the timing of and our ability to initiate and successfully enroll the Phase 1 SLE trial; our ability to obtain FDA clearance of our future IND submissions and commence and complete clinical trials on expected timelines, or at all; our reliance on the maintenance of certain key collaborative relationships for the manufacturing and development of our product candidates; the timing, scope and likelihood of regulatory filings and approvals, including final regulatory approval of our product candidates; the impact of geopolitical issues, banking instability and inflation on our business and operations, supply chain and labor force; the performance of third parties in connection with the development of our product candidates, including third parties conducting our clinical trials as well as third-party suppliers and manufacturers; our ability to successfully commercialize our product candidates and develop sales and marketing capabilities, if our product candidates are approved; our ability to recruit and maintain key members of management and our ability to maintain and successfully enforce adequate intellectual property protection. These and other risks and uncertainties are described more fully in the "Risk Factors" section of our most recent filings with the Securities and Exchange Commission and available at www.sec.gov. You should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that we may face. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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