Century Therapeutics Presents New Preclinical Data Highlighting iPSC-derived Cell Therapy Platform Technology at the 2024 American Association for Cancer Research (AACR) Annual Meeting

April 8, 2024

PHILADELPHIA, April 08, 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 that preclinical data from the Company's iPSC-derived cell therapy platform was presented at the AACR Annual Meeting 2024. The posters highlight the Company's end-to-end capabilities in iPSC reprogramming and differentiation, gene editing, synthetic biology, protein engineering and computational biology.

"Together, the promising preclinical data showcase Century's continued dedication to driving the field of allogeneic cell therapy through the incorporation of a suite of innovations into next generation product candidates," said Hy Levitsky, M.D., President of Research and Development at Century Therapeutics. "We presented new data advancing our Allo-Evasion™ platform through the transgenic expression of HLA-G, which along with HLA-E can augment the protection against host natural killer cell-mediated rejection of iPSC derived cells also engineered to resist T cell recognition through the elimination of HLA-I and HLA-II expression. This enhanced protection against rejection is designed to enable Century's multi-dosing strategy that increases the period of drug exposure, potentially leading to deeper and more durable responses for patients in need. We also presented new data describing our novel, dual-targeting CAR for B cell mediated malignancies which demonstrated promising *in vitro* and *in vivo* cytotoxicity and resisting antigen loss, and which we believe expands the potential of allogeneic CAR-T cell therapy beyond currently available options in oncology that only target CD19. Along with other important preclinical data presented at AACR, the findings to date highlight our unique gene editing, protein engineering, and manufacturing capabilities that are the foundations of our industry-leading allogeneic cell therapy pipeline and platform."

Details of the posters presented on Sunday, April 7th and Monday, April 8th are as follows:

The Discovery of a Novel CD19xCD22 Dual-Targeting CAR For the Development of an iPSC-Derived Cell Therapy
Poster Board Number**:** 4
Session Title**:** Adoptive Cell Therapies 2: CAR-T Cells
Session Date & Time**:** Sunday, April 7, 2024**,** at 1:30 PM - 5:00 PM PT

Through its industry leading engineering capabilities, Century has developed a CD19xCD22 bispecific, CD22 biparatopic chimeric antigen receptor (CAR), which was transduced into primary T cells and demonstrated cytotoxicity activity against CD19 and CD22-positive tumor cells, as well as CD19 knockout and CD22 knockout cell lines *in vitro* and in *in vivo* mouse xenograft models. This novel CAR was engineered and tested in iPSC-derived gamma-delta T cells, showing *in vitro* tumor cell cytotoxicity. These findings support the continued examination of a CD19xCD22 bispecific CAR for off-the-shelf allogeneic cell therapy to expand patient access beyond CD19 CAR-T cell therapies.

Engineered Expression Of HLA-E And HLA-G Protects iPSC-Derived Cells from Killing by Primary NK Cells
Poster Board Number: 3
Session Title: CAR-K, NK Engagers, and NK Modulators
Session Date & Time: Monday, April 8, 2024, at 9:00 AM - 12:30 PM PT

In this study, the Company showed that the combination of HLA-E and HLA-G expression was the most effective in protecting allogeneic drug products from elimination of genetically dissimilar cells. Investigators assessed allo-evasion from natural killer (NK) cells by iPSC-derived cells engineered to express HLA-E and -G. NK cells across donors expressed heterogeneous combinations of HLA-E and -G ligands. K562 and iPSC-derived cells lacking HLA-I were susceptible to killing by PBMCs. Overexpression of HLA-E and -G offered protection to K562 and iPSC-derived cells against all tested donors. HLA-E offered more protection than HLA-G, and the combination of both HLA-E and -G was most potent. When a genetically dissimilar HLA Class I protein family is deleted to prevent T cell mediated graft rejection, expression of the more-conserved HLA-E and -G can effectively protect allogeneic drug products from elimination. We believe this data further reinforces the Company's proprietary Allo-Evasion™ technology and its potential to evade identification by the host immune system, which would allow for repeat dosing without rejection, enabling increased persistence of the cells during the treatment period and potentially leading to deeper and more durable responses.

Screening iPSC Lines for Optimal Characteristics of Differentiation into Immune Effector Cells for Clinical Programs
Poster Board Number: 19
Session Title: Adoptive Cellular Therapy 1
Session Date & Time: Monday, April 8, 2024, at 1:30 PM - 5:00 PM PT

Century outlined the genomic characterization of both its clinical-grade PBMC-derived and its gamma-delta T cell-derived iPSC lines (PiPSCs and TiPSCs, respectively). The Company successfully reprogrammed these cell lines from multiple donors and analyzed them through its genomic characterization pipeline and tiered them based on potential genetic liabilities to determine those best suited for clinical development. Multiple lines were then identified and iPSC and TiPSC were successfully differentiated to immune effector cells. d35 iT cells exhibited diverse phenotypes, yields, and function. These lines can then be specialized into effector cells exhibiting heightened functionality, applicable to conditions including autoimmune disorders and oncology indications, among others. Once differentiated, Century further screened the lines for their *in vitro* cytotoxicity and post target-engagement persistence, thereby discovering those that were most suitable for further clinical development.

Discovery of a Novel NECTIN4 iPSC-derived Cell Therapy for the Treatment of Solid Tumors
Poster Board Number: 27
Session Title: Antibody Drug Conjugates and Bispecific Antibodies
Session Date & Time: Monday, April 8, 2024, at 9:00 AM - 12:30 PM PT

Century is developing an iPSC-derived cell therapy targeting NECTIN4, an established biomarker linked to carcinogenesis, worse prognosis, and disease severity, for the treatment of NECTIN4 expressing solid tumors. In these preclinical studies, Century identified novel single-domain antibodies (VHH) that bind to multiple epitopes on the NECTIN4 extracellular domain. The VHH antibodies were engineered into CAR formats and characterized for expression, cell activation through antigen engagement, and cytotoxicity activity in primary T cells. Selected binders demonstrated efficacy in multiple CAR formats in primary T cells in a mouse xenograft model using OVCar-3 tumor cells. The lead CARs engineered into primary T cells demonstrated tumor inhibition similar to a reference CAR using the ASG-5ME antibody (Enfortumab) as the NECTIN4 binder. The CARs were engineered into Century's iPSC-derived iNK and iT cells and demonstrated cytotoxicity activity against a panel of cell lines with a range of cell surface expression of NECTIN4. We believe these findings support the advancement of Century's lead NECTIN4 binder for the development of an iPSC-derived cell therapy to treat NECTIN4 positive solid tumors.

Century will also be sharing two additional posters at AACR on Tuesday, April 9th and Wednesday, April 10th. Details are as follows:

Discovery Of Inhibitory CAR Target DSG1 for Damping NECTIN4 On-Target Off-Tumor Toxicity in iPSC-Derived CAR-T Cell Therapy
Poster Board Number: Section 2, 18
Session Title: Adoptive Cell Therapies 3: CAR-T Cells
Session Date & Time: Tuesday, April 9, 2024, at 9:00 AM -12:30 PM PT

Century is developing NECTIN4 targeted iPSC-derived CAR-T cell therapy. In a NECTIN4 targeted antibody drug conjugate, enfortumab vedotin, severe skin adverse events are seen in some patients, thought to be driven by on-target off-tumor toxicity against NECTIN4 displaying skin keratinocytes. In this study, Century compared the expression levels of NECTIN4 to targets associated with tissue and cell-type specific on-target off-tumor toxicity in primary CAR-T cell clinical trials. These findings support the incorporation of a DSG1-directed inhibitory CAR into NECTIN4 specific CAR-T cell therapeutic candidates to combat skin related adverse reactions.

CXCR4 Transgene Improves In Vivo Migration and Efficacy of Engineered iPSC-Derived Natural Killer Cells
Poster Board Number: 7
Session Title: Chemokines and Cytokines in Cancer
Session Date & Time: Wednesday, April 10, 2024, at 9:00 AM - 12:30 PM PT

In this poster, Century describes its novel engineering of iPSCs resulting in efficient migration and efficacy of iPSC-derived natural killer (iNK) cells. To ensure effective treatment of bone marrow cancers and certain hematologic malignancies, efficient migration to relevant disease sites is crucial. By engineering iPSCs with CXCR4, Century demonstrated improved migration and efficacy of iNK cells without affecting cell differentiation, phenotype or iNK yield. iNK^{CXCR4} cells significantly enhanced anti-tumor efficacy, effectively eliminating bone disease *in vivo*. These findings suggest that the addition of the CXCR4 transgene in iPSC-derived effector cells may allow for a higher therapeutic response, especially in tumors located in axial-skeletal regions.

Century's 2024 AACR posters will be available for download shortly after their scheduled presentation on the Scientific Resources page of the Company's site.

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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