Sana Biotechnology Presents Data at ISSCR 2022 Annual Meeting Showing Survival of Transplanted Hypoimmune iPSC-Derived Differentiated Cell Types Without Immunosuppression in Non-Human Primates

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First demonstration of the survival of allogeneic islet cells, cardiomyocytes, and retinal pigment epithelium cells transplanted into an immunocompetent non-human primate model without any immune suppression

The islet autoimmune data suggest that cells with hypoimmune (HIP) edits evade allogeneic immune response and autoimmune response in a type 1 diabetes mouse model

Transplanting allogeneic cells into a non-human primate without immune suppression represents a key step toward development of engineered cells for the treatment of disease

SEATTLE, June 17, 2022 (GLOBE NEWSWIRE) -- Sana Biotechnology, Inc. (NASDAQ: SANA), a company focused on creating and delivering engineered cells as medicines, presented data showing survival of transplanted allogeneic, hypoimmune cells of several different types in a variety of locations in non-human primates (NHPs). The transplanted cells were induced pluripotent stem cell (iPSC)-derived cardiomyocytes, retinal pigment epithelium (RPE) cells, and islet cells, which were engineered to include Sana's hypoimmune gene modifications that enable immune evasion. Data were presented by Sonja Schrepfer, M.D., Ph.D., Head of Hypoimmune Platform at Sana, during sessions at the International Society for Stem Cell Research (ISSCR) 2022 Annual Meeting taking place from Wednesday, June 15 through Sunday, June 19 in San Francisco.

"These data, demonstrating that three types of transplanted cells are able to survive and function in NHPs without immunosuppression, highlight the transformative potential of Sana's hypoimmune platform across a number of different cell types that can address a variety of diseases," said Steve Harr, Sana's President and Chief Executive Officer. "As an example, the use of allogeneic islet transplant has had limited success in treating type 1 diabetes due to morbidities from the necessary immunosuppression. In contrast, our data indicate that we successfully engineered HIP human pancreatic islet cells to evade immune recognition, and these cells persisted and normalized glucose levels in *in vivo* models. We are applying the hypoimmune platform to a number of programs in our pipeline, including SC291, our CD19 targeted allogeneic CAR T therapy for blood cancers, with a goal of an IND this year, and SC451, our islet cell program with a goal of an IND for the treatment of type 1 diabetes in 2023."

Transplanting cells or tissues from a donor to a different recipient currently requires intense immunosuppression to prevent rejection of the transplant. Sana's HIP platform goal is to eliminate the need for immunosuppression by cloaking cells from immune recognition. The platform includes disruption of the major histocompatibility (MHC) class I and MHC class II expression to hide cells from the adaptive immune system, which includes antibody and T cell responses. These changes alone make cells susceptible to innate immune cell killing, in particular by natural killer (NK) cells. However, Sana's HIP platform additionally provides for evasion from innate cell killing, including via the overexpression of CD47, a molecule that protects HIP-modified cells from innate cell killing involving either NK cells or macrophages. HIP-modified pluripotent stem cells can serve as the starting material for the differentiation of specialized cell types to serve as cell-based therapeutics. Sana's goal is to use these HIP-modified cells to replace damaged or missing cells in the body in a number of different diseases, including, among others, cancer, type 1 diabetes, and cardiac disease.

Survival of HIP-modified islet cells for type 1 diabetes

Primary NHP pancreatic islet cells
In this study, allogeneic primary pancreatic islet cells were HIP edited and transplanted intramuscularly into a healthy NHP without immunosuppression (n=1) as proof-of-concept. Islet cell survival was followed by *in vivo* bioluminescence imaging. The imaging showed that transplanted cells survived for the duration of the study (three months at data lock) with no evidence of a systemic immune response, including no T cell activation, antibody production, or NK cell activity as seen previously with other HIP edited cell types in NHPs (iPSC, cardiomyocytes, and RPE). Allogeneic unmodified primary pancreatic islet cells disappeared rapidly within 2 weeks.

Autoimmune mice
Type 1 diabetes is a disease in which the patient's immune system attacks and kills their pancreatic beta cells. Therefore, allogeneic transplanted cells in type 1 diabetes need to overcome both allogeneic and autoimmune rejection. Autoimmune diabetes arises spontaneously in non-obese diabetic (NOD) mice, and the pathophysiology of this disease shares many similarities with human type 1 diabetes. Since its development in 1980, this model has represented the gold standard of spontaneous disease models, allowing for investigation of autoimmune diabetes disease progression and susceptibility traits, as well as to test a wide array of potential treatments and therapies.

In this study, syngeneic or allogeneic mouse islet cells were transplanted intramuscularly without immunosuppression into diabetic autoimmune mice (n=15), split into three cohorts. The first cohort received unmodified syngeneic islet cells, the second cohort received unmodified allogeneic islet cells, and the third cohort received allogeneic HIP islet cells. The unmodified cells disappeared rapidly in the allogeneic setting (within 10 days) as well as in the syngeneic setting (within two weeks) due to autoimmune recognition. Neither cohort had a decrease in glucose levels. The HIP islet cells survived in all five diabetic mice for the duration of the study (one month at data lock), and glucose levels dropped, demonstrating therapeutic function of the HIP islet cells.

Survival of HIP-modified cardiomyocytes (iPSC-derived)
In this study, allogeneic iPSC-derived cardiomyocytes were transplanted without immunosuppression into the hearts of healthy NHPs split into two cohorts. The first cohort received unmodified allogeneic iPSC-derived cardiomyocytes (WT; n=2), while the second cohort received allogeneic HIP iPSC-derived cardiomyocytes (HIP; n=4). The unmodified cells were almost eliminated in all NHPs, with significant T cell activation in addition to antibody production and binding. The HIP cardiomyocytes survived in all four monkeys for the duration of the study (up to two months at data lock), and there was no evidence of a systemic immune response, including no T cell activation, antibody production, or NK cell activity. After two months, injection sites were recovered, and local immune cells were analyzed for their donor-specific cell recognition and killing. While local immune cells kill unmodified cardiomyocytes, HIP cardiomyocytes were not recognized by these immune cells.

Survival of HIP-modified retinal pigmental epithelial (RPE) cells (iPSC-derived)
In this study, allogeneic iPSC-derived RPEs were transplanted into the eye of healthy NHPs without immunosuppression split into two cohorts. The first cohort received unmodified allogeneic iPSC-derived RPE (WT; n=3), while the second cohort received allogeneic HIP iPSC-derived RPE (HIP; n=3). The unmodified cells were almost completely eliminated in all NHPs within three weeks, with significant T cell activation, antibody production and local microglial activation, demonstrating in this context that the eye is not an “immunoprivileged” site.

The HIP RPE survived in all three monkeys for the duration of the study (three weeks at data lock), and there was no evidence of a systemic immune response, including no T cell activation, antibody production, microglial or NK cell activity. Two weeks after the initial dose, the NHPs were re-injected with the same cell type into the second eye, so that the NHPs received a total of two doses. Unmodified WT RPEs again evoked a rapid systemic immune response in all NHPs, with activation of T cells and antibody production, and cells almost completely eliminate within one week. HIP RPE cells continued to survive even after re-injection without stimulation of adaptive or innate immune responses. These data suggest the potential to re-administer HIP RPE cells.

Sana intends to submit the data behind its presentations for publication in a peer-reviewed journal.

About Hypoimmune Platform
Sana’s hypoimmune platform is designed to create cells *ex vivo* that can “hide” from the patient’s immune system to enable the transplant of allogeneic cells without the need for immunosuppression. We are applying the hypoimmune technology to both pluripotent stem cells, which can then be differentiated into multiple cell types, and to donor-derived allogeneic T cells, with the goal of making potent and persistent CAR T cells at scale. Preclinical data demonstrates across a variety of cell types that these transplanted allogeneic cells are able to evade both the innate and adaptive arms of the immune system while retaining their activity. Our most advanced programs utilizing this platform include an allogeneic CAR T program targeting CD19+ cancers and stem-cell derived beta islet cells for patients with type 1 diabetes.

About Sana Biotechnology
Sana Biotechnology, Inc. is focused on creating and delivering engineered cells as medicines for patients. We share a vision of repairing and controlling genes, replacing missing or damaged cells, and making our therapies broadly available to patients. We are a passionate group of people working together to create an enduring company that changes how the world treats disease. Sana has operations in Seattle, Cambridge, South San Francisco, and Rochester. For more information about Sana Biotechnology, please visit https://sana.com/.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements about Sana Biotechnology, Inc. (the “Company,” “we,” “us,” or “our”) within the meaning of the federal securities laws, including those related to the company’s vision, progress, and business plans; expectations for its development programs, product candidates and technology platforms, including its pre-clinical, clinical and regulatory development plans and timing expectations; the potential ability to make allogeneic, hypoimmune cells, including iPSC-derived cardiomyocytes, RPE cells, and islet cells, that survive and evade the immune system without immunosuppression and the potential persistence and efficacy of such hypoimmune cells; and the Company’s expectations with respect to the submission and publication of data. All statements other than statements of historical facts contained in this press release, including, among others, statements regarding the Company’s strategy, expectations, cash runway and future financial condition, future operations, and prospects, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “design,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “positioned,” “potential,” “predict,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. The Company has based these forward-looking statements largely on its current expectations, estimates, forecasts and projections about future events and financial trends that it believes may affect its financial condition, results of operations, business strategy and financial needs. In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. These statements are subject to risks and uncertainties that could cause the actual results to vary materially, including, among others, the risks inherent in drug development such as those associated with the initiation, cost, timing, progress and results of the Company’s current and future research and development programs, preclinical and clinical trials, as well as the economic, market and social disruptions due to the ongoing COVID-19 public health crisis. For a detailed discussion of the risk factors that could affect the Company’s actual results, please refer to the risk factors identified in the Company’s SEC reports, including but not limited to its Quarterly Report on Form 10-Q dated May 10, 2022. Except as required by law, the Company undertakes no obligation to update publicly any forward-looking statements for any reason.

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