Sana Biotechnology Announces Preclinical Data Published in Nature Biotechnology Demonstrating its Hypoimmune-Engineered Cells Escape Immune Detection and Survive While Remaining Fully Functional

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Hypoimmune-modified allogeneic iPSCs evade immune response and rejection without immunosuppression in non-human primate model

Long-term survival and immune evasion of hypoimmune-modified allogeneic iPSCs at least equivalent to survival of autologous iPSCs

CD47 overexpression provided robust protection of hypoimmune-modified allogeneic cells from killing by the innate immune system versus other engineering approaches

SEATTLE, May 08, 2023 (GLOBE NEWSWIRE) -- Sana Biotechnology, Inc. (NASDAQ: SANA), a company focused on changing the possible for patients through engineered cells, today announced that *Nature Biotechnology* has published a paper titled “Hypoimmune induced pluripotent stem cells survive long term in fully immunocompetent, allogeneic rhesus macaques.” The preclinical studies published in this paper used Sana’s hypoimmune (HIP) technology to engineer HIP-modified allogeneic cells to escape immune detection in the absence of immune suppression. *In vivo* studies in fully immunocompetent non-human primates (NHPs) demonstrated that HIP-modified allogeneic cells survived without immunosuppression for the length of the studies (16 weeks and >40 weeks). An additional humanized mouse study showed that HIP-modified induced pluripotent stem cells (iPSCs) that are differentiated into pancreatic islet cells were immune evasive and ameliorated diabetes *in vivo*.

“We have demonstrated in numerous preclinical studies that our hypoimmune-engineered cells persist and function without eliciting an immune response,” said Doug Williams, PhD, Sana’s President of Research and Development. “These published data in rigorous translational models that closely imitate the human immune system support our previous findings, most importantly that HIP-modified allogeneic cells avoid immune recognition and rejection without immune suppression. We are incorporating the HIP technology into multiple therapeutic candidates in our pipeline and look forward to reporting our first human clinical data later this year.”

Allogeneic HIP Cells Avoid Immune Activation and Escape Systemic Immune Rejection in NHPs
NHP iPSCs were engineered using HIP technology to generate HIP-modified iPSCs. A cross-over study was performed where NHP HIP iPSCs (HIP^{allo}) were administered to NHPs previously sensitized to non-engineered NHP iPSCs (wt^{allo}) and wt^{allo} cells were administered to NHPs previously transplanted with HIP^{allo} cells. In NHPs first receiving HIP^{allo} cells, no cellular immune activation or killing of HIP^{allo} cells was observed after cell transplantation. Subsequent injection of wt^{allo} cells into these NHPs induced strong cellular immune responses similar to those observed in the group receiving wt^{allo} cells first. The HIP^{allo} cells survived with no evidence of immune recognition despite this immune response to wt^{allo} cells. In contrast, NHPs initially transplanted with wt^{allo} cells showed rapid immune sensitization, including strong T cell activation and killing of the wt^{allo} cells. Subsequent transplantation of HIP^{allo} cells showed survival and no cellular immune response to HIP^{allo} cells despite the previous immune activation to and killing of wt^{allo} cells.

In all instances, administration of HIP^{allo} cells did not generate de-novo antibodies and no antibody-related killing of HIP^{allo} cells was observed, regardless of the order of administration. In contrast, administration of wt^{allo} cells provoked a vigorous antibody and killing response against these cells.

In a separate study using human iPSCs, hypoimmune-modified human iPSCs (HIP^{xeno} iPSCs) and unmodified human iPSCs (wt^{xeno} iPSCs) were transplanted into NHPs. Similar results were observed and demonstrated the ability of HIP^{xeno} iPSCs to avoid immune activation and recognition, whereas wt^{xeno} iPSCs induced a strong immune response.

Human HIP iPSCs Differentiated into All Three Germ Layers, Collectively Avoiding Immune Recognition; HIP Primary Islet Cells Survive for Over 40 Weeks in NHP
In the allogeneic setting following transplantation into the NHP, iPSCs differentiated *in vivo* and gave rise to cells from all three germs layers (endoderm, medederm, and ectoderm). These HIP-modified cells avoided immune recognition, survived, and engrafted in immunocompetent NHPs, supporting the notion that cells remain hypoimmune through differentiation and that the various HIP derivatives are protected from immune recognition even after differentiation.

In another study, HIP-modified allogeneic primary islet cells achieved long-term survival after transplantation for over 40 weeks and evaded immune recognition without the use of immunosuppression in one NHP. An additional study in immunocompetent allogeneic humanized mice demonstrated that human HIP iPSC-derived islet cells are functional and ameliorated diabetes following transplantation.

Only Transgenic CD47 Overexpression Provided Widespread Protection Against the Innate Immune Response
The depletion of class I and II human leukocyte antigens (HLA) is an engineering strategy aimed at broadly avoiding recognition by the adaptive immune system. This depletion, however, triggers recognition by the innate system, including a killing response by NK cells and macrophages. Head-to-head comparisons of strategies to counteract this response were conducted and data showed that strategies using HLA-E, HLA-G, or PD-L1 did not prevent innate immune recognition. Only CD47 overexpression prevented both adaptive and innate immune recognition *in vitro* and *in vivo*.

About Sana’s 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 hypoimmune technology to both donor-derived allogeneic T cells, with the goal of making potent and persistent CAR T cells at scale, and pluripotent stem cells, which can then be differentiated into multiple cell types at scale. Preclinical data from a variety of cell types demonstrate that these transplanted allogeneic cells can evade both the innate and adaptive arms of the immune system while retaining their function. Our most advanced programs using hypoimmune technology include our allogeneic CAR T program targeting CD19+ cancers, our allogeneic CAR T program targeting CD22+ cancers, our allogeneic CAR T program targeting BCMA+ cancers, and our stem-cell derived pancreatic islet cell program 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.

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 expectations for availability and timing of clinical data; and the potential capabilities, benefits, and impact of the hypoimmune platform, including the potential ability 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. 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 economic, market, and social disruptions, including due to the 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 Securities and Exchange Commission (SEC) reports, including but not limited to its Quarterly Report on Form 10-Q dated May 8, 2023. Except as required by law, the Company undertakes no obligation to update publicly any forward-looking statements for any reason.

Investor Relations & Media:

Nicole Keith
investor.relations@sana.com
media@sana.com