Sana Biotechnology Announces Preclinical Data Published in Nature Communications Demonstrating the Ability of its Hypoimmune Allogeneic CD19-directed CAR T Cells to Evade Immune Rejection and Produce Durable Anti-Tumor Responses

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Hypoimmune-modified allogeneic CD19-directed CAR T cells can evade immune detection and kill tumor cells in a novel humanized allogeneic preclinical model in vivo, including following tumor cell reinjection

Findings suggest that hypoimmune-modified allogeneic CAR T cell therapeutics might overcome limitations associated with poor cell persistence of allogeneic CAR T cells

Initial clinical data from SC291, a hypoimmune-modified CD19-directed allogeneic CAR T therapy, in patients with B-cell malignancies expected later this year

IND submission expected this year for a second hypoimmune-modified CAR T, SC262, a hypoimmune-modified CD22-directed allogeneic CAR T therapy, in patients who failed CD19 CAR T cell therapy

Hypoimmune data consistent with Science Translational Medicine findings published earlier this week with hypoimmune pancreatic islet cells in preclinical type 1 diabetes models

SEATTLE, April 13, 2023 (GLOBE NEWSWIRE) -- Sana Biotechnology, Inc. (NASDAQ: SANA), a company focused on changing the possible for patients through engineered cells, today announced that *Nature Communications* has published a paper titled “Hypoimmune anti-CD19 chimeric antigen receptor T cells provide lasting tumor control in fully immunocompetent allogeneic humanized mice.” The preclinical studies published in this paper evaluated the performance of Sana’s hypoimmune (HIP) allogeneic chimeric antigen receptor (CAR) T cells versus unmodified allogeneic (allo) CAR T cells. The key findings demonstrate that HIP CAR T cells significantly outperformed unmodified allo CAR T cells in tumor studies using fully immunocompetent, humanized mice in both durability of tumor clearance as well as CAR T cell expansion and persistence. In additional *in vitro* assays and *in vivo* assays, the data demonstrate that HIP engineering does not impact CAR T cell specificity, impair cytotoxic function, accelerate T cell exhaustion, or weaken anti-tumor efficacy. The HIP CAR T cell persistence observed in allogeneic, fully immunocompetent, humanized mice resulted in durable tumor clearance as shown by the rapid clearance of a second tumor challenge at ninety days after HIP CAR T cell administration, highlighting the potential long-term persistence and efficacy in clearing any hidden or remaining tumor cells in a patient with cancer.

“We designed our hypoimmune allogeneic CAR T platform to overcome immune rejection challenges that have limited efficacy to date for allogeneic CAR T cell therapies and the access and product variability of autologous CAR T cells,” said Steve Harr, Sana’s President and CEO. “These preclinical data highlight that our hypoimmune CAR T cells can evade immune detection, persist, and clear tumor cells both acutely and over time. SC291, our hypoimmune CD19-targeted allogeneic CAR T therapy, has transformative potential for patients with B-cell malignancies if these results translate to our clinical studies, and we look forward to presenting initial clinical data later this year.”

HIP CAR T Cells Provide Lasting Tumor Killing Efficacy in Fully Immunocompetent Allogeneic Humanized Mice and Prevent Tumor Regrowth After Subsequent Reinjection of Tumor Cells
The ability to effectively kill tumors was assessed in immunocompetent humanized mice. Longitudinal bioluminescence imaging (BLI) showed that HIP CAR T cells provided lasting removal of tumor throughout the study period. In contrast, unmodified allogeneic CAR T cells only temporarily slowed the progression of tumor growth in this immunocompetent model and eventually failed to control cancer progression. In these same mice, CAR T cell efficacy was assessed after reinjection of tumor cells eighty-three days following the administration of the CAR T cells. HIP CAR T cell-treated mice rapidly cleared the tumor cells, demonstrating the persistence and effectiveness of the HIP CAR T cells even after three months. These findings demonstrate that HIP modified allogeneic CAR T cells persist and result in the effective suppression of CD19 expressing tumors. Consistent with the experience in patients to date, unmodified allogeneic CAR T cells show greatly reduced persistence and a high rate of tumor recurrence in this model.

HIP CAR T Cells are Equally Effective at Clearing Tumors in *In Vivo* Immunodeficient Models
The efficacy of HIP CAR T cells in clearing tumors was assessed in immunodeficient mice that received low, middle, and high doses of either HIP CAR T cells or unmodified allogeneic CAR T cells intravenously. HIP CAR T cells and unmodified allogeneic CAR T cells similarly reduced bone marrow cancer burden.

HIP Modifications Do Not Impair CAR T Function and HIP CAR T Cells Are Not Prone to Exhaustion
In vitro studies demonstrate that HIP engineering does not impact CAR T cell specificity, impair cytotoxic function, accelerate T cell exhaustion, or weaken anti-tumor efficacy across a number of parameters including TIM3, TIGIT, LAG3, CLTA-4, CD39, or PD-1.

Using an immunodeficient model to eliminate the contribution of allogeneic rejection, the longer-term function of HIP CAR T cells and unmodified allogeneic CAR T cells were evaluated in NSG mice receiving multiple injections of tumor cells at 15 and 27 days following CAR T cell administration. On day 63, mice treated with HIP CAR T cells showed significantly higher CAR+ cell numbers in the bone marrow and spleen and more effectively reduced CD19+ cancer cells in the bone marrow as compared to mice receiving unmodified allogeneic CAR T cells. No differences in CAR T cell exhaustion were observed between the groups.

HIP CAR T Cells can be Cleared Rapidly by Targeting CD47
Given the reliance of HIP CAR T cells on CD47 overexpression to protect these MHC class I- and II-disrupted cells against an innate immune

response, another study was conducted to evaluate the use of CD47-targeting fusion proteins to “hide” CD47 overexpression, enable innate immune cell killing, and serve as a safety switch to eliminate HIP CAR T cells. The administration of CD47-targeting fusion proteins resulted in a near-complete ablation of HIP CAR T cells. The effect was highly specific and did not target other tissue cell types that express HLA. Only HLA-deficient HIP CAR T cells were susceptible to innate immune clearance.

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 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, including the expected timing of IND submissions for the Company’s product candidates and indications for which the Company is developing its product candidates and for which such INDs will be submitted, expected impact of its product candidates and data from preclinical studies of cells made using hypoimmune technology, and expected availability and timing of data from the Company’s clinical trials; the potential ability of the Company’s allogeneic hypoimmune CAR T cells to address limitations of allogeneic CAR Ts and autologous CAR Ts, including by evading immune detection and demonstrating long-term persistence and efficacy; the potential ability of the hypoimmune platform 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, and the potential benefits associated therewith; and the potential ability to make potent and persistent CAR T cells at scale and of hypoimmune pluripotent stem cells to differentiate into multiple cell types at scale. 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 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 Securities and Exchange Commission (SEC) reports, including but not limited to its Annual Report on Form 10-K dated March 16, 2023. Except as required by law, the Company undertakes no obligation to update publicly any forward-looking statements for any reason.

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