Corporate Presentation August 2024



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Sana Biotechnology

Changing the Possible for Patients

Sana's hypoimmune technology goal is to overcome allogeneic rejection

HIP technology provides foundation for potential multiple drugs across many therapeutic areas

Begin 2024 with four clinical programs treating seven diseases

- SC291 oncology NHL and CLL
- SC291 B-cell mediated autoimmune lupus nephritis, extrarenal lupus, and ANCA-associated vasculitis
- SC262 oncology r/r NHL, initially in CD19 CAR T failures
- UP421 HIP primary islet cells in patients with type 1 diabetes

Pipeline positioned to deliver additional clinical data over time

- Regenerative medicine: SC379 (CNS disorders) and SC451 (type 1 diabetes)
- Hypoimmune allogeneic CAR T cells: SC255 (BCMA) and beyond

Balance sheet allows potential for multiple data readouts



Sana pipeline positioned to deliver meaningful clinical data

PRODUCT CANDIDATE	MECHANISM	INDICATIONS	PRECLINICAL IND-ENABLING	PHASE 1	PHASE 2/3	SANA'S RIGHTS	
Oncology							
SC291	CD19-directed allo CAR T	NHL	ARDENT			WW	
SC291	CD19-directed allo CAR T	CLL	ARDENT			WW	
SC262	CD22-directed allo CAR T	NHL (CD19 failures)	VIVID			WW	
SC255	BCMA-directed allo CAR T	MM				WW	
B-cell Mediated Autoimmune Diseases							
SC291	CD19-directed allo CAR T	LN	GLEAM			WW	
SC291	CD19-directed allo CAR T	ERL	GLEAM			WW	
SC291	CD19-directed allo CAR T	AAV	GLEAM			WW	
SC291	CD19-directed allo CAR T	Other indications				WW	
Regenerative Medicine							
UP421	HIP primary islet cells1	T1D				WW	
SC451	Stem-cell derived pancreatic islet cells	T1D				WW	
SC379	Glial progenitor cells	HD, PMD, SPMS				WW	

¹Investigator sponsored trial.

Abbreviations: AAV, ANCA-associated vasculitis; CLL, chronic lymphocytic leukemia; ERL, extrarenal systemic lupus erythematosus; HD, Huntington's disease; LN, lupus nephritis; MM, multiple myeloma; NHL, non-Hodgkin lymphoma; PMD, Pelizaeus-Merzbacher Disease; SPMS, secondary progressive multiple sclerosis; T1D, type 1 diabetes; WW, worldwide.

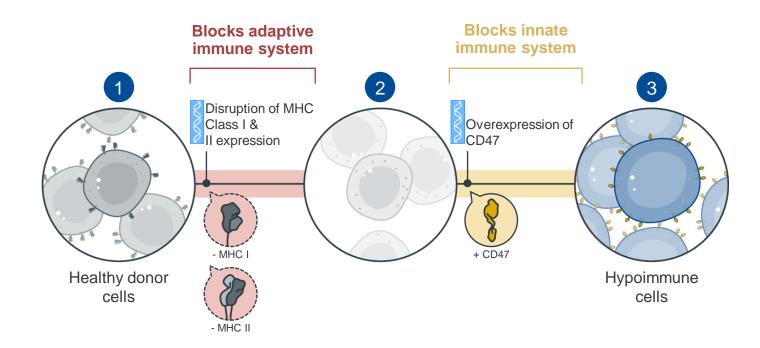


Overcoming allogeneic immune rejection has been key limitation in transplant and cellular medicine

Allogeneic cell rejection

- ~75 years of transplants immune rejection remains the largest problem
- Lifelong immunosuppression is current standard
- Genome modification efforts to date have generally been incomplete
- Autologous therapies have limited scalability and are only available for a small number of cell types

Sana's hypoimmune approach







Sana's team has pioneered hypoimmune technology



Hypoimmunogenic derivatives of induced pluripotent stem cells evade immune rejection in fully immunocompetent allogeneic recipients

Tobias Deuse^{1,7}, Xiaomeng Hu^{1,2,3,7}, Alessia Gravina¹, Dong Wang^{1,2}, Grigol Tediashvilli^{1,2,3}, Chandrav De⁴, William O. Thayer⁴, Angela Wahl⁴, J. Victor Garcia⁴, Hermann Reichenspurner^{2,3}, Mark M. Davis⁵, Lewis L. Lanier ^{0,6} and Sonja Schrepfer ^{0,1*}

Check for updates



The SIRPa-CD47 immune checkpoint in NK cells

Tobias Deuse¹, M. Xiaomeng Hu^{1,2}, Sean Agbor-Enoh^{3,4}, Moon K. Jang⁴, Malik Alawi⁴, Ceren Saygi⁴, Alessia Gravina¹, Grigol Tediashviñ⁴, Vinh Q. Nguyen⁴, Yuan Liu², Hannah Valantine^{8,9}, Lewis L. Lanier¹⁰⁺⁴, and Sonja Schrepfer^{1,2+4}

Here we report on the existence and functionality of the immune checkpoint signal regulatory protein a (SIRPa) in NX cells and describe how it can be modulated for cell therapy. NX cell SIRPa is up-regulated upon IL-2 stimulation, interacts with target cell CD47 in a threshold-dependent manner, and counters other stimulatory signals, including IL-2, CD16, or NXCGD. Elevated expression of CD47 protected K562 tumor cells and mouse and human MHC class I-deficient target cells against SIRPa⁻¹ primary NX cells, but not against SIRPa⁻¹ NKL or NX92 cells. SIRPa deficiency or antibody blockade increased the killing capacity of NX cells. Overexpression of rhesus monkey CD47 in human MHC-deficient cells prevented cytotoxicity by rhesus NX cells in a xenogeneic setting. The SIRPa-CD47 axis was found to be highly species specific. Together, the results demonstrate that disruption of the SIRPa-CD47 immune checkpoint may augment NX cell antitumor responses and that elevated expression of CD47 may prevent NX cell-mediated killing of allogeneic and xenogeneic tissues.





Hypoimmune induced pluripotent stem cell-derived cell therapeutics treat cardiovascular and pulmonary diseases in immunocompetent allogeneic mice

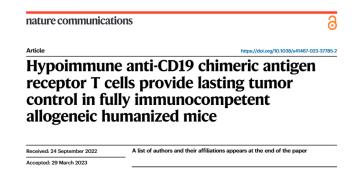
Tobias Deuse^{a,1}, Grigol Tediashvili^{a,b,1}, Xiaomeng Hu^{a,b,c,d,1}, Alessia Gravina^a, Annika Tamenang^{a,b}, Dong Wang^a, Andrew Connolly¹, Christian Mueller^{f,g}, Beñat Mallavia^h, Mark R. Looney^{h,J}, Malik Alawi^J, Lewis L. Lanier^{k,2,3}, and Sonja Schrepfer^{d,2,3}

*Division of Cardishrorais Caugery, Department of Surgey, Transplant and Stem Cell Immunobiology Laboratory, University of California, San Francisco, CA 94142. *Department of Cardisoraudus Surgey, University Heart Control Hamburgy, 2004; Hemburgy, Gormany Centrol Certain Control Cardisoraudus Research (D2HQ) partner site Hemburg/Kel-fluxbeck, 20246 Hamburg, Germany, "Sana Biotechnology Inc., South San Francisco, CA 94109; "Department of Pathology, University of California, San Francisco, CA 94104;" Therapy Centrol, University of Massachusetts, Worcster, MA 01605; "Department of Medicine, University of Laifornia, San Francisco, CA 94142; "Department of Medicine, University of Laifornia, San Francisco, CA 94142; "Department of Medicine, University of Laifornia, San Francisco, CA 94142; "Department of Medicine, University of Laifornia, San Francisco, CA 94142; "Department of Medicine, University of Laifornia, San Francisco, CA 94142; "Department of Medicine, University of Laifornia, San Francisco, CA 94142; "Department of Microbiology and Immunology and the Parker Institute for Cancer Immunotherapy, University of California, San Francisco, CA 94142; "Department of Microbiology and Immunology and the Parker Institute for Cancer Immunotherapy, University of California, San Francisco, CA 94142; "Department of Microbiology and Immunology and the Parker Institute for Cancer Immunotherapy, University of California, San Francisco, CA 94142; "Department of Microbiology and Immunology and the Parker Institute for Cancer Immunotherapy, University of California, San Francisco, CA 94142; "Department of Microbiology and Immunology and Immunolog

Contributed by Lewis L. Lanier, May 25, 2021 (sent for review October 22, 2020); reviewed by John Cooke and Yuji Shiba

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Article	https://doi.org/	0.1038/s41587-023-01784-x				
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Received: 18 May 2022	Xiaomeng Hu ¹ , Kathy White ¹ , Ari G. Olroyd ¹ , Rowena De. Antonia A. Dominguez ¹ , William E. Dowdle ¹ , Annabelle					
Accepted: 6 April 2023	Frank Wells ¹ , Elaine Y. Chu • ¹ , Cade Ellis Ito ¹ , Harini Kris	ells¹, Elaine Y. Chu 10¹, Cade Ellis Ito¹, Harini Krishnapura¹, Surbhi Jain¹,				
Published online: 08 May 2023	Ramya Ankala¹, Trevor J. McGill¹, August Lin¹, Kyla Egen Allison Gagnon¹, J. Michael Rukstalis¹, Nathaniel J. Hogi					

Ron Basco¹, Jeffrey R. Millman¹, Paul Kievit³, Mark M. Davis⁴, Lewis L. Lanier • Andrew J. Connolly •, Tobias Deuse • ¹⁸ & Sonia Schrepfer • ¹⁸



Cell Stem Cell



Brief Report

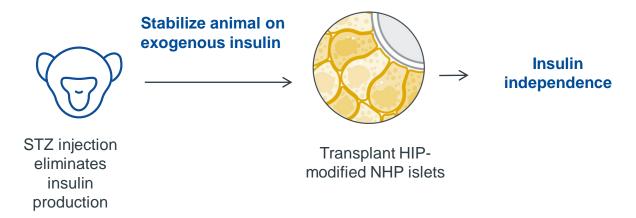
Hypoimmune islets achieve insulin independence after allogeneic transplantation in a fully immunocompetent non-human primate

Xiaomeng Hu,¹ Kathy White,¹ Chi Young,¹ Ari G. Olroyd,¹ Paul Kievit,^{1,2} Andrew J. Connolly,^{1,3} Tobias Deuse,^{1,4,5} and Sonja Schrepfer^{1,5,6,*}



HIP-modified allogeneic islet cells to control glucose in a type 1 diabetic NHP model

Type 1 diabetes is a disease of missing pancreatic beta cells



Study Design (N=1)

- NHP treated with STZ
- Glucose stabilized with exogenous insulin
- Allogeneic NHP primary islet cells isolated and HIP-modified
- Cells injected intramuscularly without immunosuppression

Key goals of study

- Demonstrate survival and function of HIPmodified allogeneic islet cells in diabetic NHP without immunosuppression
- Demonstrate long-term glucose normalization in diabetic NHP without exogenous insulin or immunosuppression
- Demonstrate the principle of graft ablation/safety switch with anti-CD47 antibody

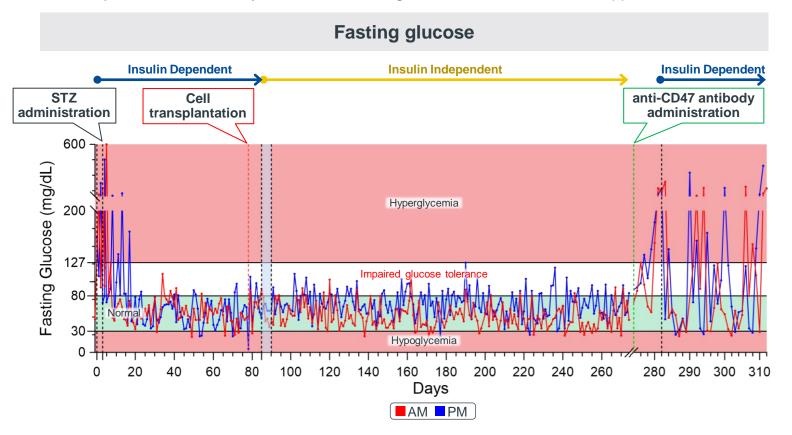
Abbreviations: NHP, non-human primate; STZ, Streptozotocin.

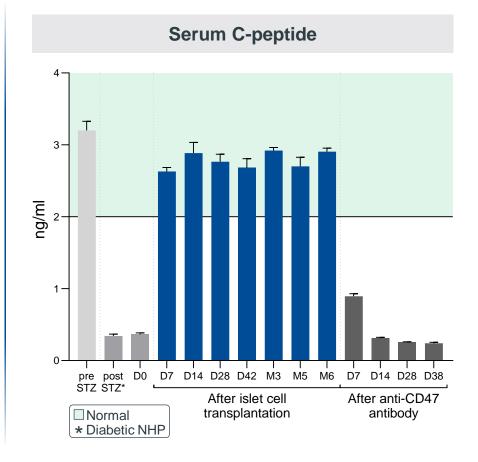


Survival and function of allogeneic hypoimmune pancreatic islet cells in diabetic NHP 6 months without immunosuppression

Study Design (N=1)

- NHP primary islet cells isolated and HIP-modified
- Cells injected intramuscularly into a diabetic, allogeneic NHP without immunosuppression







Potential near-term opportunities to apply HIP modifications to validated mechanisms with unmet need

Blood cancers:

>100,000 patients/year^{1,2,3}



B-cell mediated autoimmune diseases: >5 million patients⁴



Type 1 diabetes: >8 million patients worldwide⁵



¹Avezbakiyev et al. *Blood*. 2022

⁴Sana internal analysis; SciVida Autoimmune Factbook 2023, U.S. ⁵t1dindex.org

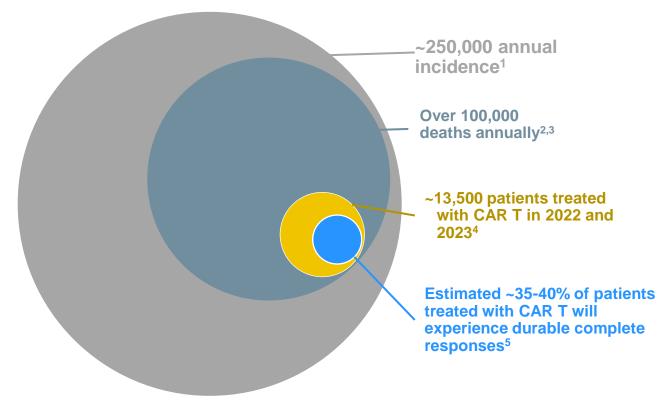


²Durie et al. *The Oncologist*. 2020

³US and EU5

Hematologic cancers continue to have a high unmet need

High mortality in lymphoma, leukemia, and myeloma in the US and EU5



¹Leukemia & Lymphoma Society and Clarivate DRG Market Forecast 2022; internal analysis of secondary EPI data.

Abbreviations: EU5, France, Germany, Italy, Spain, UK



Challenges

- Autologous CAR T cell scalability
- Many patients fail CAR T treatment
- Allogeneic CAR T cell immune rejection limits persistence and efficacy

Opportunity

- Known targets
- Known efficacy and safety bar

Sana's HIP CAR T platform can address challenges and exploit opportunities

²Avezbakiyev et al. *Blood*. 2022

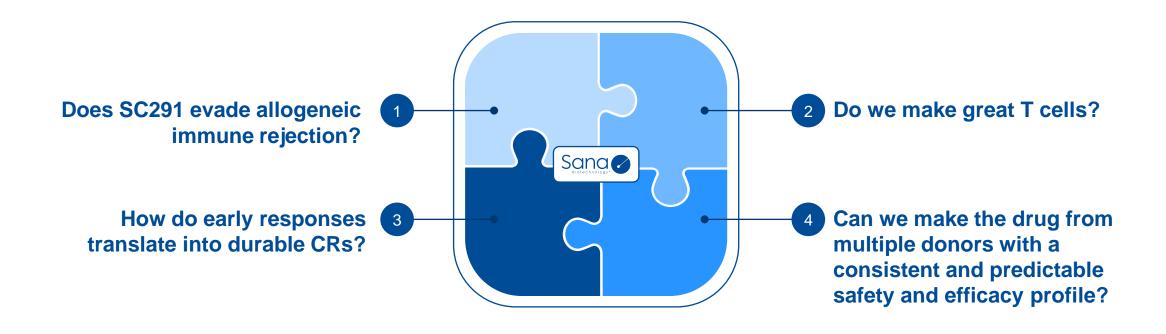
³Durie et al. *The Oncologist*. 2020

⁴Available 10-K filings 2022-2023 and Evaluate Pharma 2022; internal analysis of secondary EPI data.

⁵Scivida 2022 NHL Factbook

Defining success for SC291 in oncology

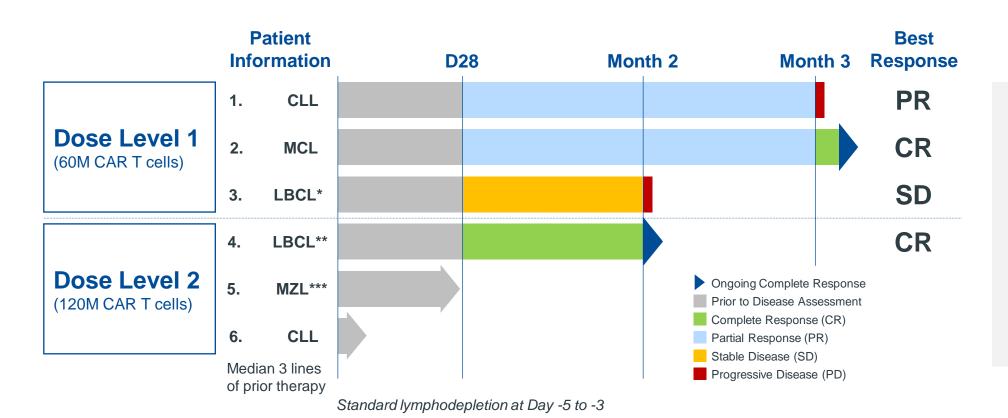
Understanding levels of evidence as data mature





ARDENT: 3 of 4 evaluable patients had at least a partial response, with 2 ongoing complete responses

6 patients treated to date; dose escalation ongoing



Safety

- No dose limiting toxicities
- No GvHD
- No SC291-related SAEs
- No CRS or ICANS
- No Grade 3 or higher infections

Clinical data as of: January 5, 2024

^{*}Transformed DLBCL from FL. **Transformed DLBCL from MZL. ***Assessment ongoing as of January 5, 2024.

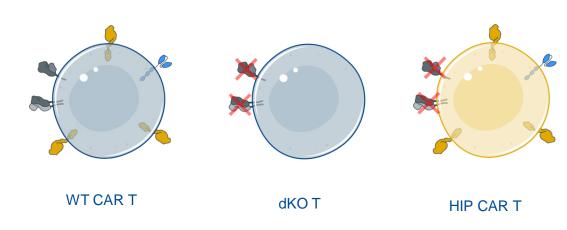


[&]quot;evaluable" defined as patients treated with SC291 and had at least one disease assessment

Immune response data provide important early insights

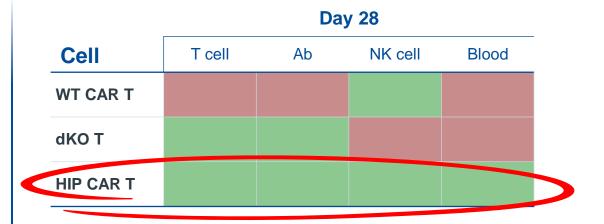
Translating preclinical data to people

1 SC291 is a mixture of HIP and non-HIP CAR T cells



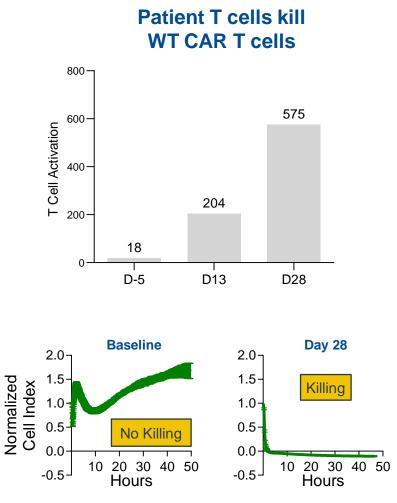
T Cell Population	Genetic Modifications
WT CAR T	CD47-CD19 CAR
dKO T	HLA I/II deficient
HIP CAR T	CD47-CD19 CAR; HLA I/II deficient

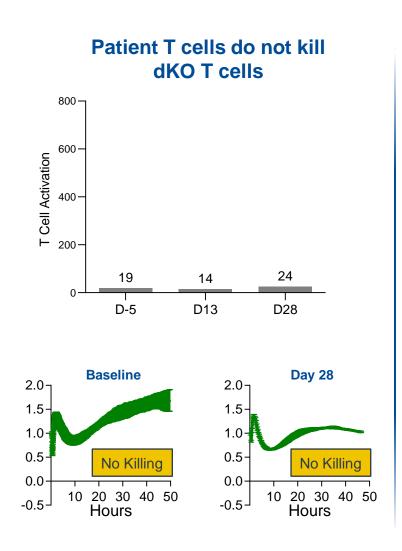
2 Test the patient's immune system against SC291

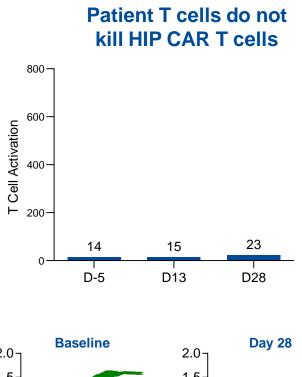


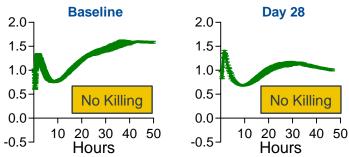


Patient T cells kill WT CAR T cells but do not kill dKO T cells or HIP CAR T cells







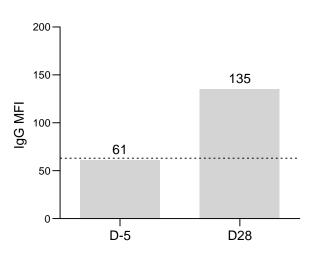


From Patient #1 in the ongoing ARDENT trial.

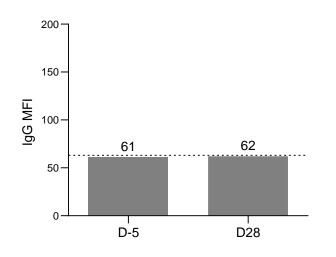


Patient generates antibodies against WT CAR T cells but not dKO T cells or HIP CAR T cells

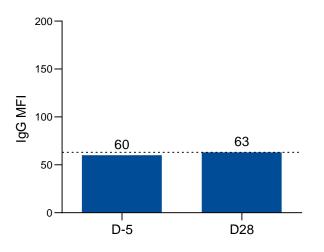
WT CAR T cells induce an antibody response



dKO T cells do not induce an antibody response



HIP CAR T cells do not induce an antibody response



From Patient #1 in the ongoing ARDENT trial.

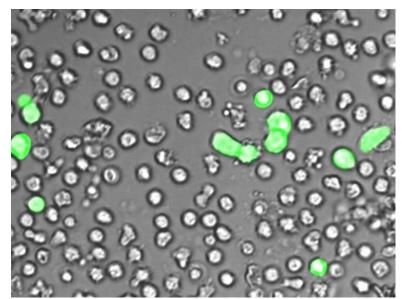


Only HIP CAR T cells avoid NK cell killing

NK cells taken from patient's blood

Patient's NK cells from day 13 after SC291 dosing

NK cells kill dKO T cells

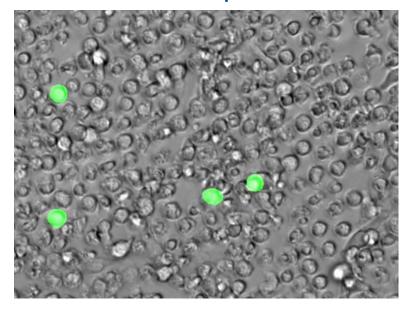


Actual assay time = 4 hours.

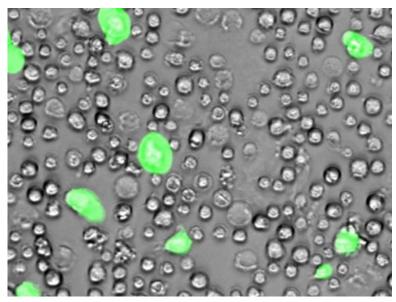


From Patient #1 in the ongoing ARDENT trial.

NK cells kill dKO T cells with **HLA-E** overexpression



NK cells do NOT kill HIP CAR T cells







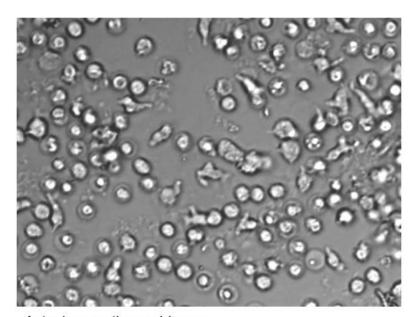


Only HIP CAR T cells avoid NK cell killing

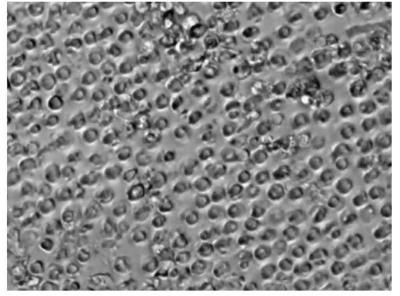
NK cells taken from patient's blood

Patient's NK cells from day 13 after SC291 dosing

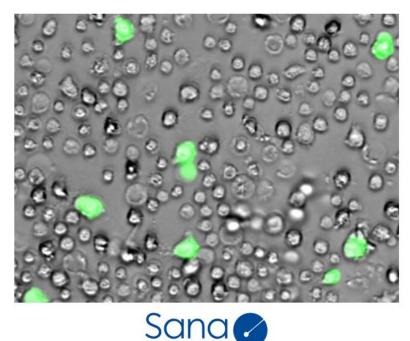
NK cells kill dKO T cells

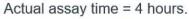


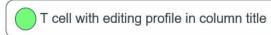
NK cells kill dKO T cells with **HLA-E** overexpression



NK cells do NOT kill HIP CAR T cells









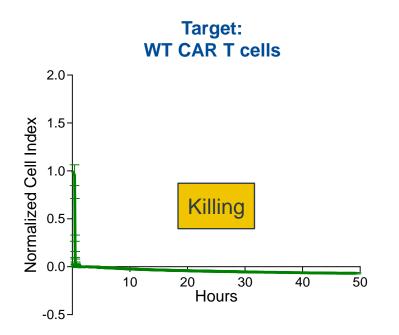


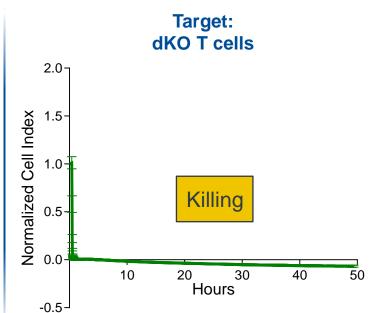


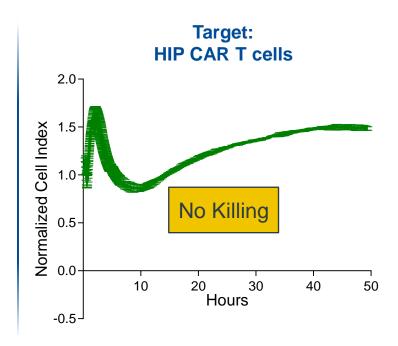


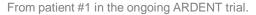
No detectable immune response in the patient toward HIP CAR T cells

D28 blood sample







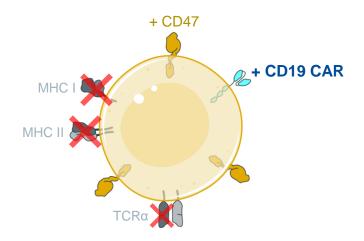




SC291: ARDENT trial continues enrollment with more data expected in 2024

- Early data suggest ability to dose safely, the desired immune evasion profile, and clinical efficacy
- Expect more data to come
 - Immune evasion
 - Safety profile
 - Response rate
 - Cell persistence
 - Durability of responses

Allogeneic HIP CAR T cell



An effective allogeneic CAR T cell therapy offers potential to transform outcomes for patients



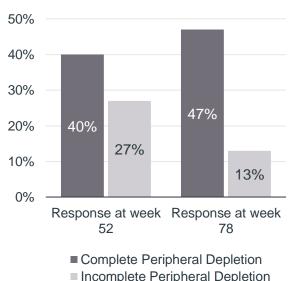
Autoimmune diseases have emerged as promising opportunity

- 1 B-cell targeting therapies have been efficacious across many autoimmune diseases¹
 - SLE
 - Vasculitis (granulomatosis with polyangiitis & microscopic polyangiitis)
 - Neuromyelitis optical spectrum
 - Pemphigus
 - Relapsing and progressive MS
 - Rheumatoid arthritis
 - Lupus nephritis
 - Sjogren syndrome

- NMDAR encephalitis
- Thrombocytopenic purpura
- Amyloidosis
- Scleroderma
- Autoimmune hemolytic anemia
- Chronic immune demyelinating polyradiculoneuropathy
- Immune-mediated necrotizing myopathy
- Membranous nephropathy

2 Depth of B cell depletion with treatment predicts efficacy in early trials²

Complete B-cell depletion resulted in greater complete responses in Lupus Nephritis patients²

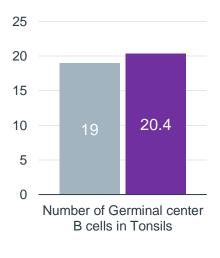


¹Adapted from Zhang et al. Frontiers in Immunology. 2023; Oh et al. Immune Network. 2023; Lee et al. Nature Reviews Drug Discovery. 2021. ²Mendez et al. Clinical Journal of the American Society of Nephrology, 2018.

³Anolik et al. Arthritis and Rheumatism. 2007.



3 Germinal center B cells are unaffected by rituximab treatment³

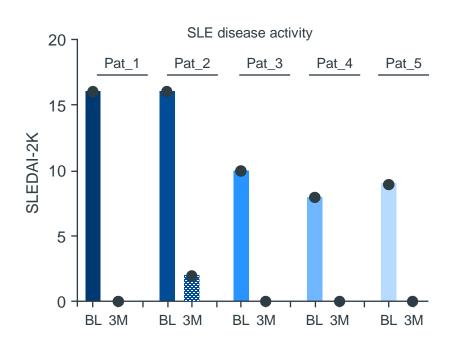


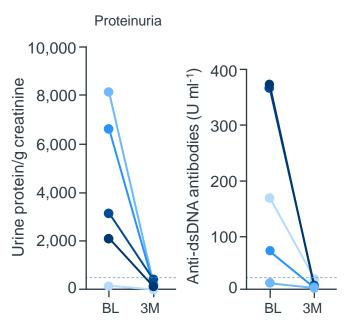
■ Untreated SLE patients

■ SLE patients + Rituximab

Autologous CD19 CAR T therapy results in durable drug-free remission in refractory SLE patients

Improvement in signs and symptoms of SLE after CD19 CAR T treatment





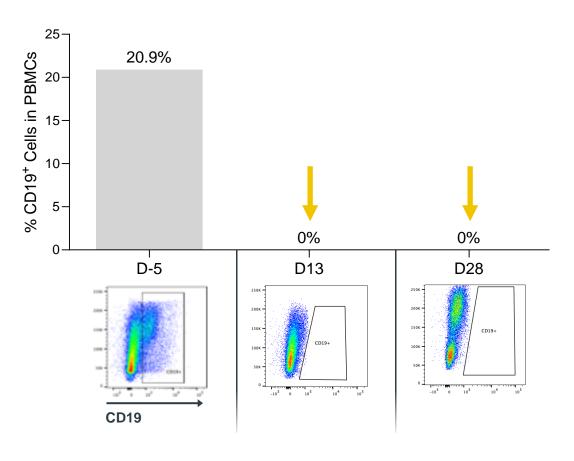
- Well tolerated mild CRS (Grade 1) and no ICANS seen
- 5/5 patients are in a durable complete remission and off all drugs
- All known disease biomarkers rapidly normalized and have remained so thus far
- 24+ months of drug-free remission seen in patients constituting a potential functional cure
- B-cell recovery and immune system reset in ~3 months with sustained SLE remission

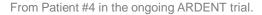
Mackensen et al. *Nature Medicine*. 2022 Abbreviations: BL, baseline; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; M, months; SLE, systemic lupus erythematosus.



ARDENT trial: SC291 treatment leads to deep B cell depletion in oncology patient

CD19+ cells in blood in %

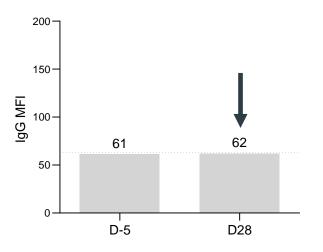




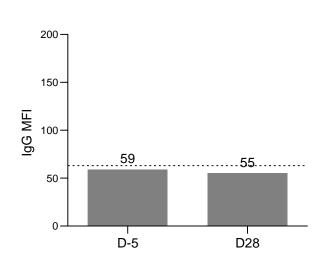


Complete B cell depletion may be even more important in autoimmune than oncology patients

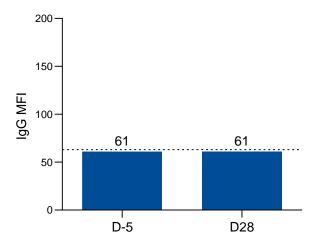
No anti-HLA antibody production against WT CAR T cells suggests complete B cell depletion



dKO T cells do not induce an antibody response



HIP CAR T cells do not induce an antibody response



From Patient #4 in the ongoing ARDENT trial.



SC291 offers potential for transformative treatment for B-cell mediated autoimmune diseases

Targeting multiple indications

Phase 1 trial – multiple autoimmune disorders

- 1 Lupus nephritis >230K^{1,2} patients³
- 2 Extrarenal SLE >160K¹ patients³
- 3 ANCA-associated vasculitis >60K4 in US

SC291 benefits versus autologous therapies

- 1 No patient apheresis
- 2 Product availability
- 3 Scaled manufacturing
- 4 Consistent T cell quality

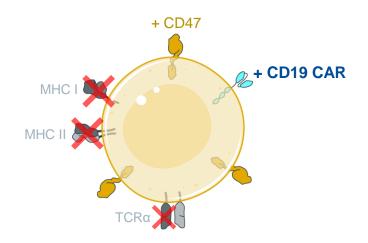
¹Lu et al. *Annals of Rheumatic Diseases*. 2023 ²Guzman et al. *Arthritis Rheum*. 2013 ³US, EU5, and Japan ⁴Jayne et al. ANCA-Associated Vasculitis: An Update



SC291: GLEAM Phase 1 trial goals are to understand safety, dose, and early efficacy

- Key features of Phase 1 trial (GLEAM)
 - Patients with refractory lupus nephritis, extrarenal SLE, and AAV
 - Starting dose of 90 million CAR T cells
 - Potential to expand beyond these indications over time
- Expect to generate and share data in 2024 from multiple indications
 - Safety and tolerability
 - Early response rates

Allogeneic HIP CAR T cell



An effective allogeneic CAR T offers potential to transform outcomes for patients



SC262: Targeting growing population of patients with inadequate response to CD19 therapy

CD19 CAR T relapsed patients represent large and growing unmet need¹

Estimated ~12,000 B cell malignancy patients treated with CD19 CAR T in 2027²

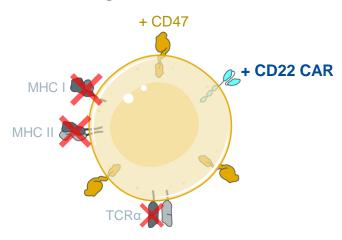


- Potential of ~7,500 CAR T failures annually in 2027²
- Median survival of ~5 months post-CD19 CAR T therapy failure³

Estimated ~35-40% of CAR T patients with durable complete responses⁴

Expand our allo T platform to CD22 with Sana's SC262 candidate

Allogeneic HIP CAR T cell



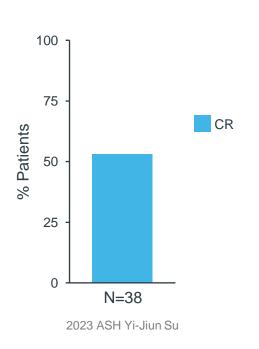


¹US, EU5, and Japan. ²Clarivate DRG NHL Market Forecast Nov 2021; 2027 Forecast is 2L+ LBCL patients; internal analysis of secondary EPI data. ³Di Blasi et al. *Blood*. 2022; DESCAR-T registry. ⁴DiBlasi et al. *Blood*. 2022

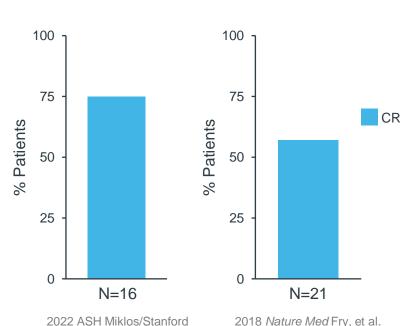


SC262: Licensed CD22 CAR produced strong clinical data in CD19 failures when part of autologous CAR T

>50% CR rate in CD19 CAR failure DLBCL patients



High rate of CRs in CD19 failure ALL patients ~80% patients with prior CD19 therapy



VIVID Phase 1 Trial

- CD19 CAR T exposed relapsed and/or refractory NHL
- Adult subjects
- Dose escalation study
- Cell dose: 90M, 150M, and 250M
- Standard lymphodepletion
- Primary Endpoints: Safety and tolerability
- Secondary Endpoints: Patient response



Type 1 diabetes represents a large unmet need with a loss of ~15 years of life¹

- Disease caused by autoimmune destruction of insulinproducing pancreatic beta cells, resulting in no insulin production
- Type 1 diabetes is a large unmet need with >8M WW²
- Short-term complications result from hypo- and hyperglycemia
- Long-term complications result from micro- and macrovascular disease and end-organ damage: including heart attack, stroke, blindness, and kidney failure
- SC451 goal is euglycemia without any immunosuppression or exogenous insulin

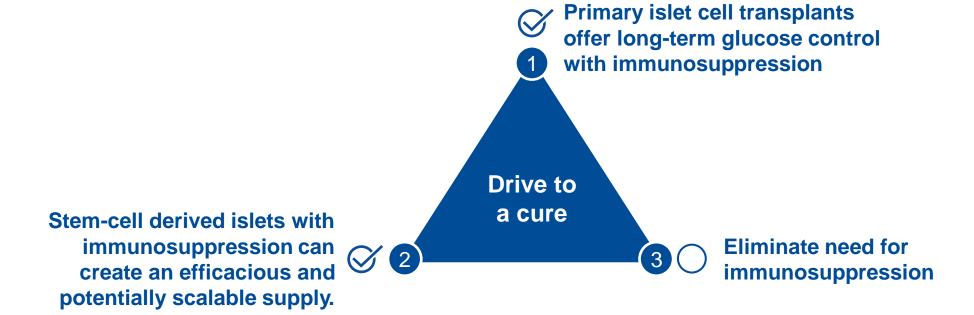






Emerging data suggest a cure is possible

Sana – combining stem cell, gene editing, and immunology expertise



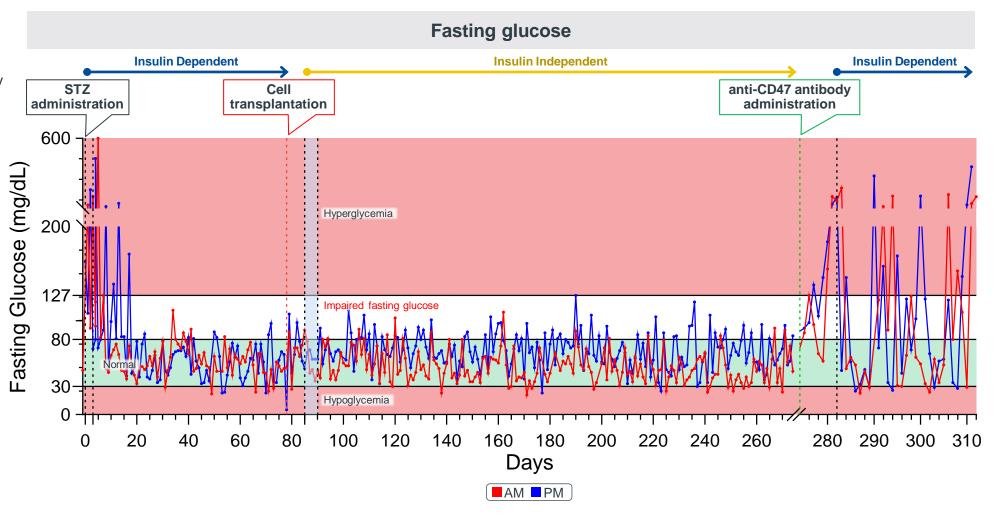
Goal – single treatment with long-term normal blood glucose without immunosuppression or insulin



Survival and function of allogeneic hypoimmune pancreatic islet cells in diabetic NHP 6 months without immunosuppression

Study Design (N=1)

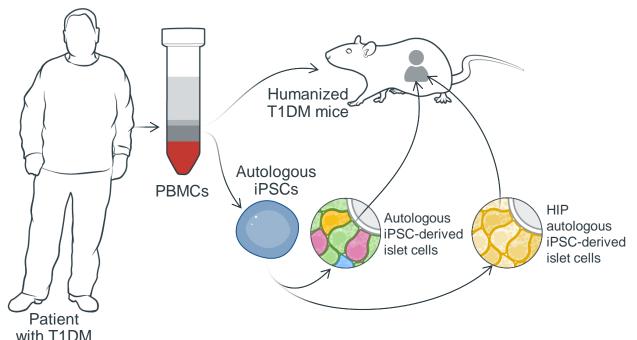
- NHP primary islet cells isolated and HIP-modified
- Cells injected intramuscularly into a diabetic, allogeneic NHP without immunosuppression

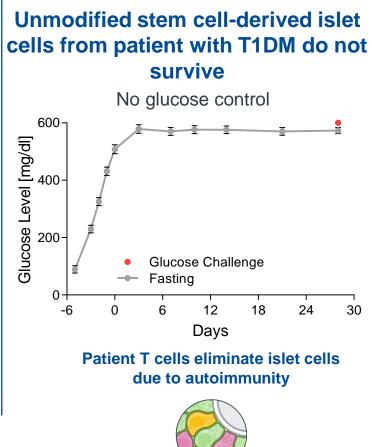


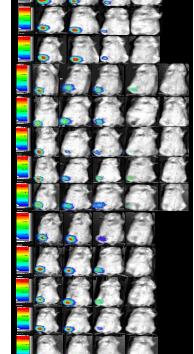


Type 1 diabetes model highlights potential to overcome autoimmune rejection of pancreatic beta cells

PBMCs from patient with T1DM used to generate stem cellderived islet cells and to humanize immune system in mice





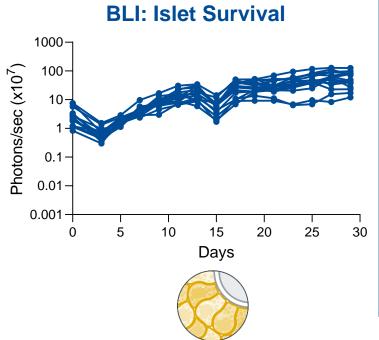


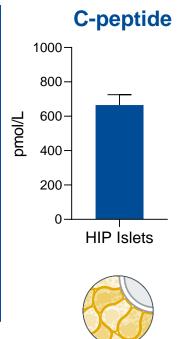
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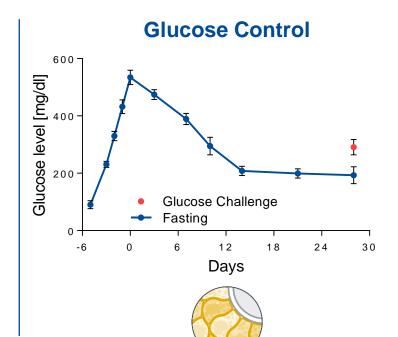
Abbreviations: T1DM, type 1 diabetes mellitus Hu et al. *Sci Transl Med.* 2023

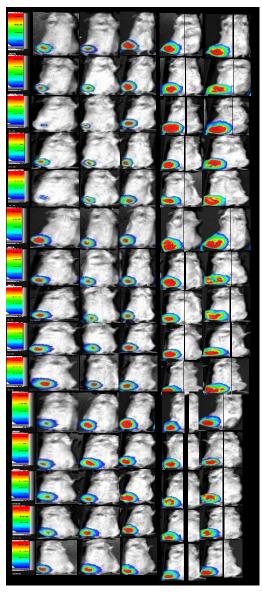


HIP iPSC-derived pancreatic islet cells from patient with T1DM evade autoimmune killing and control glucose







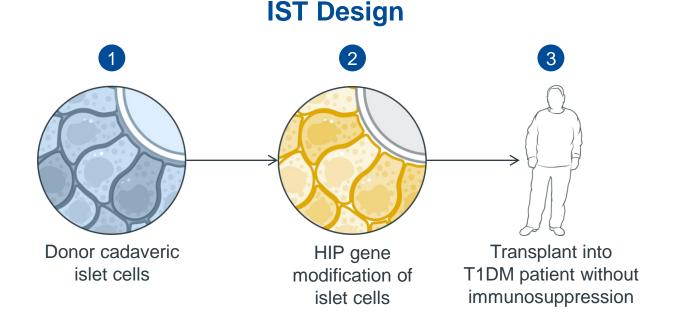


Abbreviations: BLI, bioluminescence imaging Hu et al. *Sci Transl Med.* 2023.



Potential clinical validation of hypoimmune islet cells in T1DM patients

- Trial authorized at Uppsala University Hospital
- Primary human HIP islet cells transplantation in type 1 diabetes patients
- Intramuscular administration in forearm
- No immunosuppression
- Insights for SC451



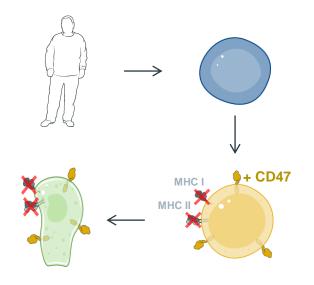
Key Measured Outcomes

Cell survival & immune evasion
C-peptide
Glycemic control



Sana's approach to treat type 1 diabetes

1 Make hypoimmune islet cells from stem cells



2 Manufacture at scale



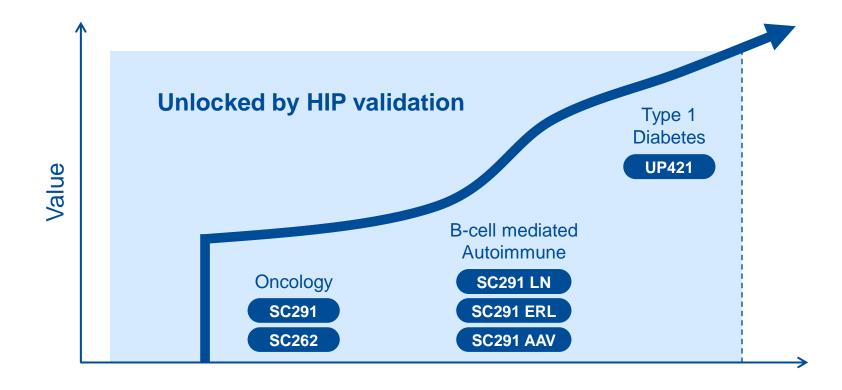
3 Deliver as a single therapy



SC451 program – HIP stem cell-derived islet cell therapy – delivered with no immunosuppression



We anticipate meaningful clinical data in multiple diseases in 2024



Unlocking the potential of our hypoimmune platform across multiple patient populations



Thank You

