

Corporate Presentation

February 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 cells ¹	T1D				WW
SC451	Stem-cell derived pancreatic islet cells	T1D				WW
SC379	Glial progenitor cells	HD, PMD, SPMS				WW

¹Investigator sponsored trial.

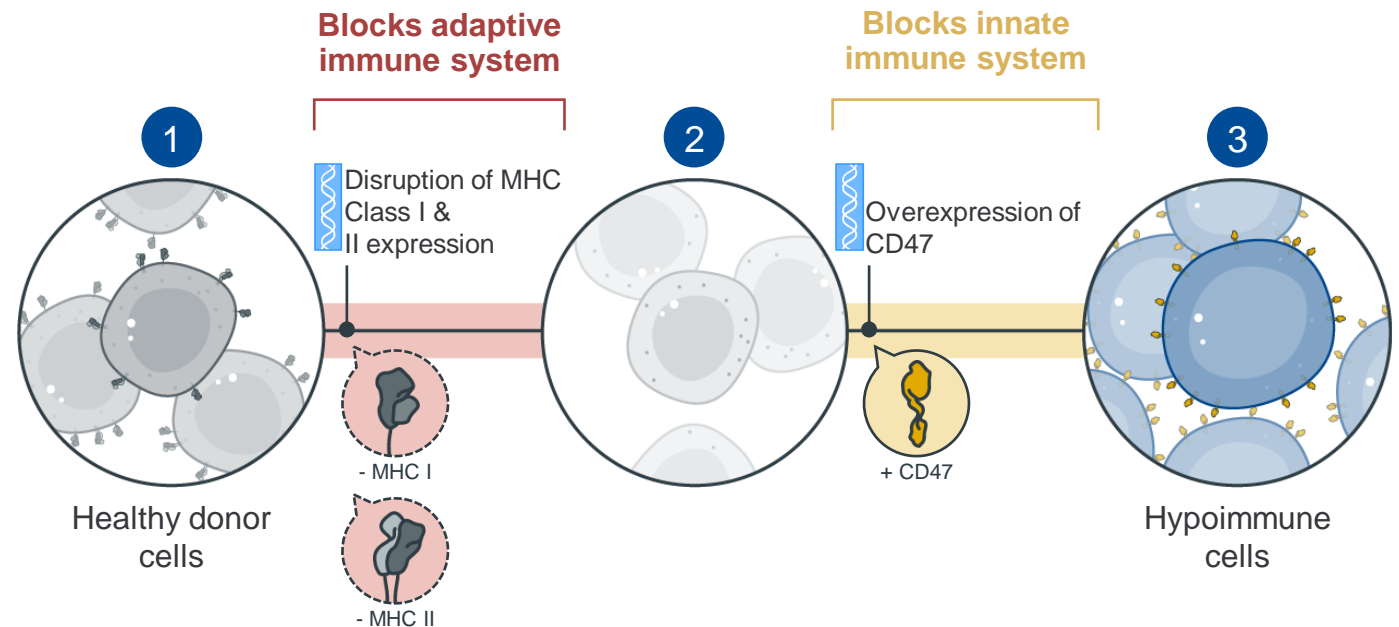
Abbreviations: AAV, ANCA-associated vasculitis; CLL, chronic lymphocytic leukemia; ERL, extrarenal systemic lupus erythematosus; HD, Huntington's disease; LN, lupus nephritis; MM, multiple myeloma; NHL, non-Hodgkin lymphoma; PMD, Pelizaeus-Merzbacher Disease; SPMS, secondary progressive multiple sclerosis;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



Current clinical platform with multiple ongoing approaches in research phase.

Sana's team has pioneered hypimmune technology



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

Tobias Deuse^{1,2}, Xiaomeng Hu^{1,2,3,7}, Alessia Gravina¹, Dong Wang^{1,2}, Grigol Tediashvili^{1,2,3}, Chandrav De⁴, William O. Thayer⁴, Angela Wahl¹, J. Victor Garcia⁴, Hermann Reichenspurner^{2,3}, Mark M. Davis⁵, Lewis L. Lanier^{6,8} and Sonja Schrepfer^{1,1*}



ARTICLE

The SIRPα-CD47 immune checkpoint in NK cells

Tobias Deuse^{1*}, Xiaomeng Hu^{1,2*}, Sean Agbor-Enoh^{1,4}, Moon K. Jang¹, Malik Alawi¹, Ceren Saygi¹, Alessia Gravina¹, Grigol Tediashvili¹, Vinh Q. Nguyen¹, Yuan Liu¹, Hannah Valantine^{1,5}, Lewis L. Lanier^{1,2,6*}, and Sonja Schrepfer^{1,2,7*}

Here we report on the existence and functionality of the immune checkpoint signal regulatory protein α (SIRPα) in NK cells and describe how it can be modulated for cell therapy. NK cell SIRPα 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 NKG2D. Elevated expression of CD47 protected K562 tumor cells and mouse and human MHC class I-deficient target cells against SIRPα⁺ primary NK cells, but not against SIRPα⁺ NK1.1 or NK92 cells. SIRPα deficiency or antibody blockade increased the killing capacity of NK cells. Overexpression of rhesus monkey CD47 in human MHC-deficient cells prevented cytotoxicity by rhesus NK cells in a xenogeneic setting. The SIRPα-CD47 axis was found to be highly species specific. Together, the results demonstrate that disruption of the SIRPα-CD47 immune checkpoint may augment NK cell antitumor responses and that elevated expression of CD47 may prevent NK cell-mediated killing of allogeneic and xenogeneic tissues.

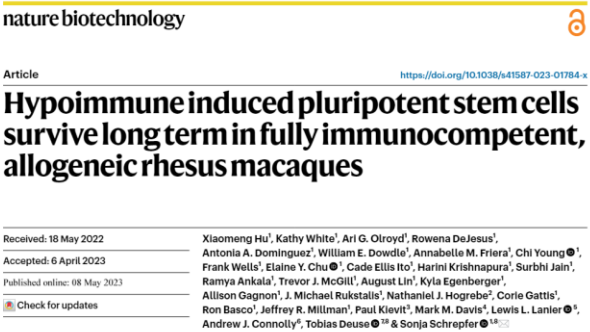
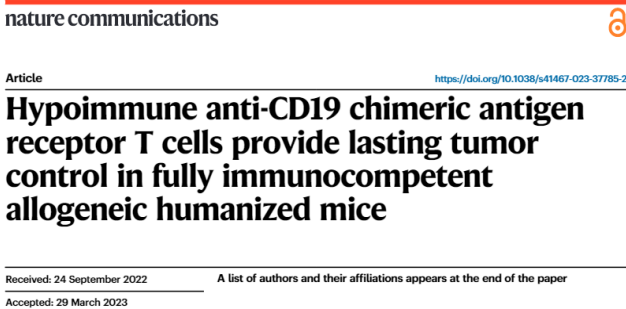


Hypoimmune induced pluripotent stem cell-derived cell therapeutics treat cardiovascular and pulmonary diseases in immunocompetent allogeneic mice

Tobias Deuse^{1,2}, Grigol Tediashvili^{1,2,3}, Xiaomeng Hu^{1,2,3,7}, Alessia Gravina¹, Annika Tamenang^{1,2}, Dong Wang¹, Andrew Connolly^{1,2}, Christian Mueller^{1,2}, Benat Mallavia¹, Mark R. Looney^{1,3}, Malik Alawi¹, Lewis L. Lanier^{1,2,6}, and Sonja Schrepfer^{1,2,7}

¹Division of Cardiothoracic Surgery, Department of Surgery, Transplant and Stem Cell Immunobiology Laboratory, University of California, San Francisco, CA 94143; ²Department of Cardiovascular Surgery, University Heart Center Hamburg, 20246 Hamburg, Germany; ³German Center for Cardiovascular Research (DZHK) partner site Hamburg/Kiel/Luebeck, 20246 Hamburg, Germany; ⁴Sana Biotechnology Inc., South San Francisco, CA 94080; ⁵Department of Pathology, University of California, San Francisco, CA 94143; ⁶Horae Gene Therapy Center, University of Massachusetts, Worcester, MA 01605; ⁷Department of Pediatrics, University of Massachusetts, Worcester, MA 01605; ⁸Department of Medicine, University of California, San Francisco, CA 94143; ⁹Department of Laboratory Medicine, University of California, San Francisco, CA 94143; ¹⁰Bioinformatics Core, University Medical Center Hamburg-Eppendorf, 20246 Hamburg, Germany; and ¹¹Department of Microbiology and Immunology and the Parker Institute for Cancer Immunotherapy, University of California, San Francisco, CA 94143

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



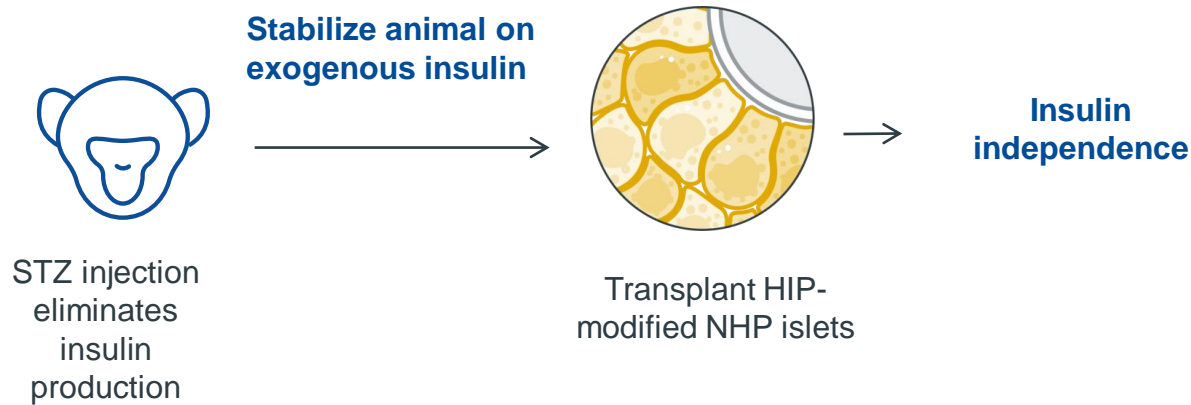
Brief Report Hypoimmune islets achieve insulin independence after allogeneic transplantation in a fully immunocompetent non-human primate

Xiaomeng Hu¹, Kathy White¹, Chi Young¹, Ari G. Olroyd¹, 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

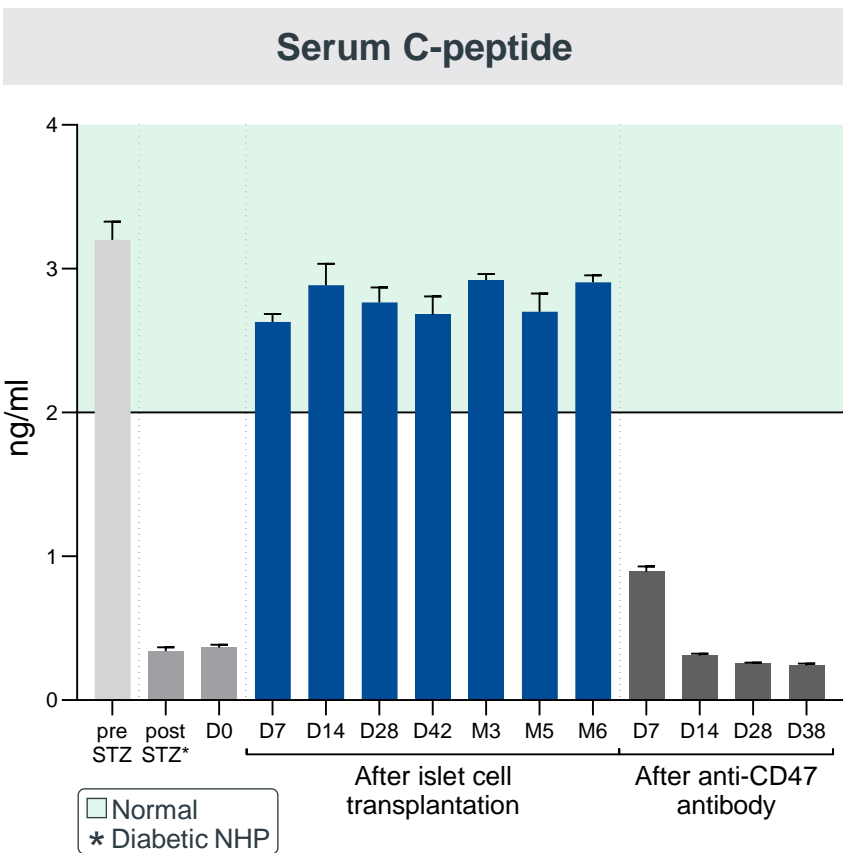
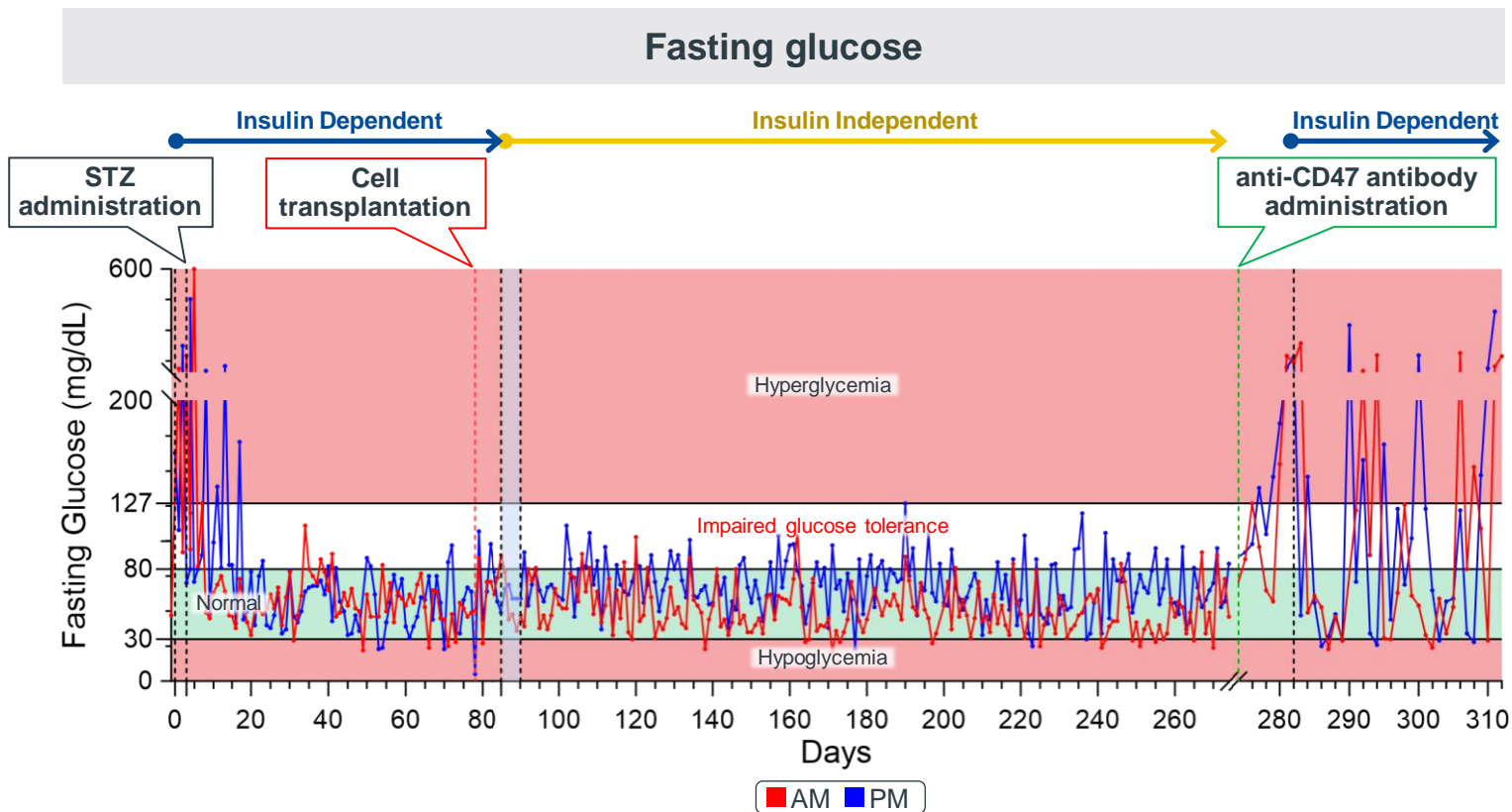
- Demonstrate survival and function of HIP-modified allogeneic islet cells in diabetic NHP without immunosuppression
- Demonstrate long-term glucose normalization in diabetic NHP without exogenous insulin or immunosuppression
- Demonstrate the principle of graft ablation/safety switch with anti-CD47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

²Durie et al. *The Oncologist*. 2020

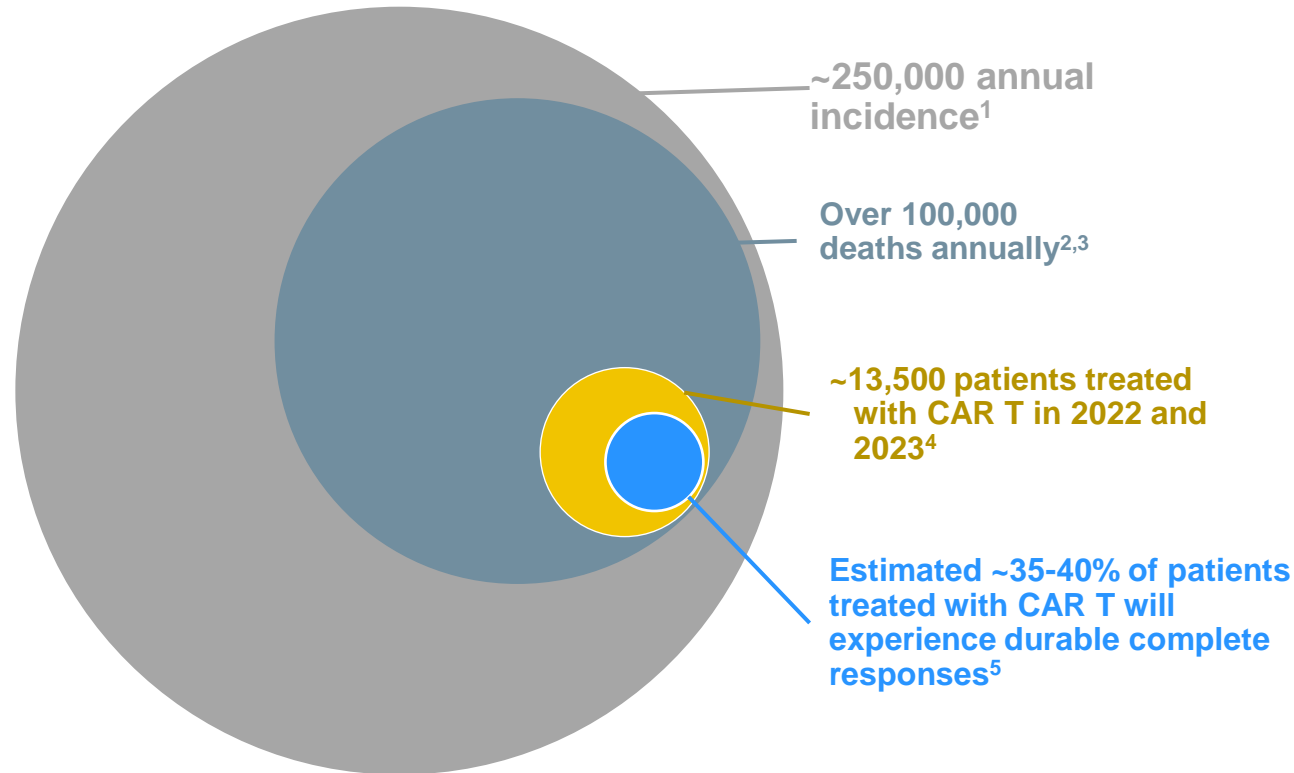
³US and EU5

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

⁵t1dindex.org

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.

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

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

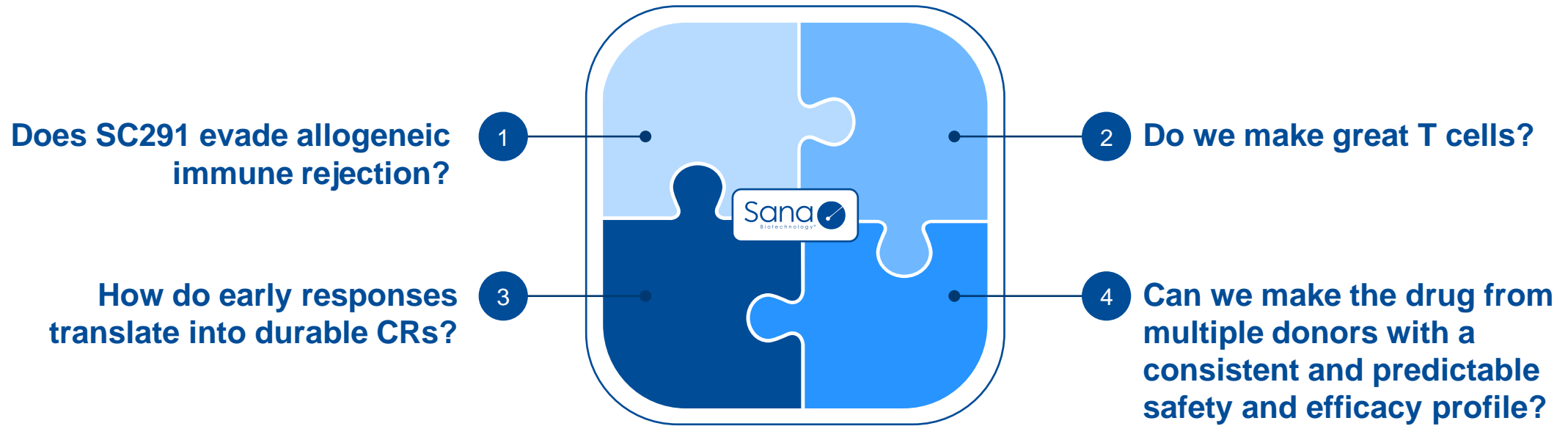
Opportunity

- Known targets
- Known efficacy and safety bar

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

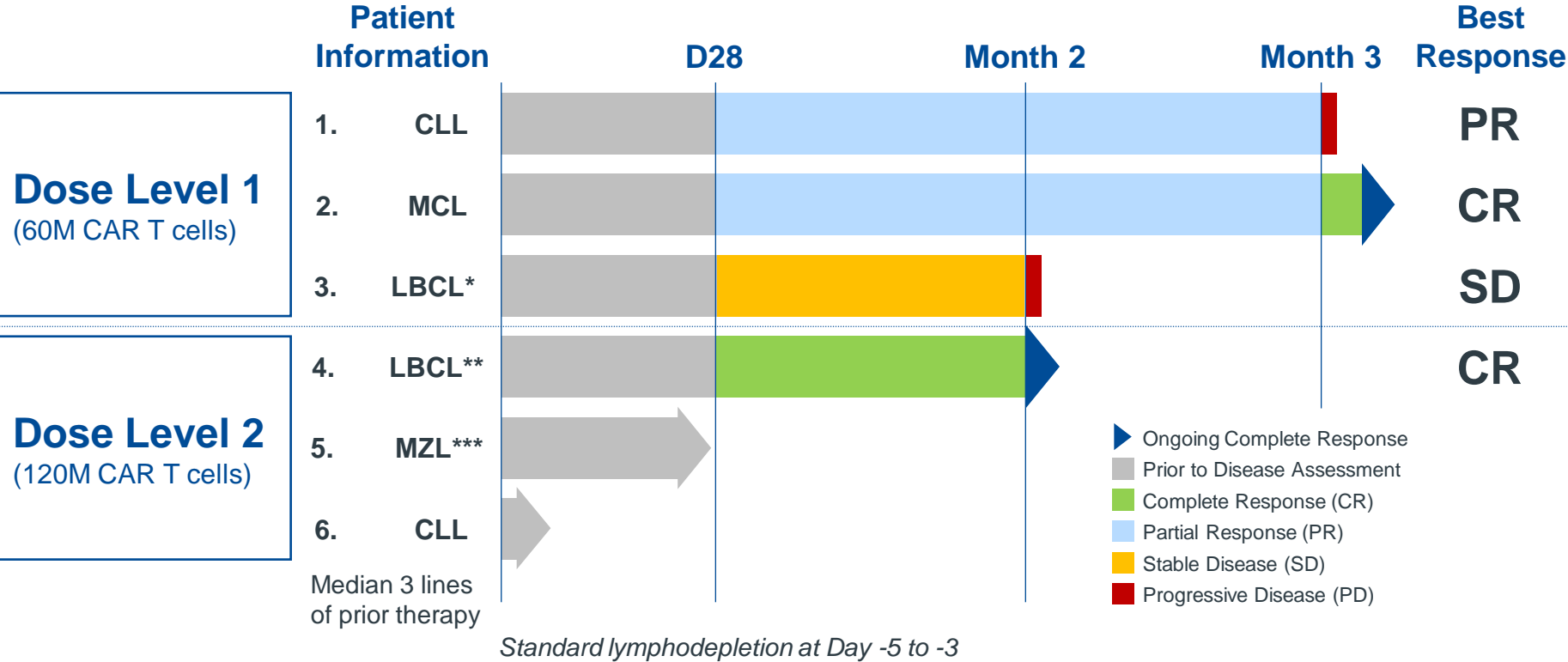
Defining success for SC291 in oncology

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

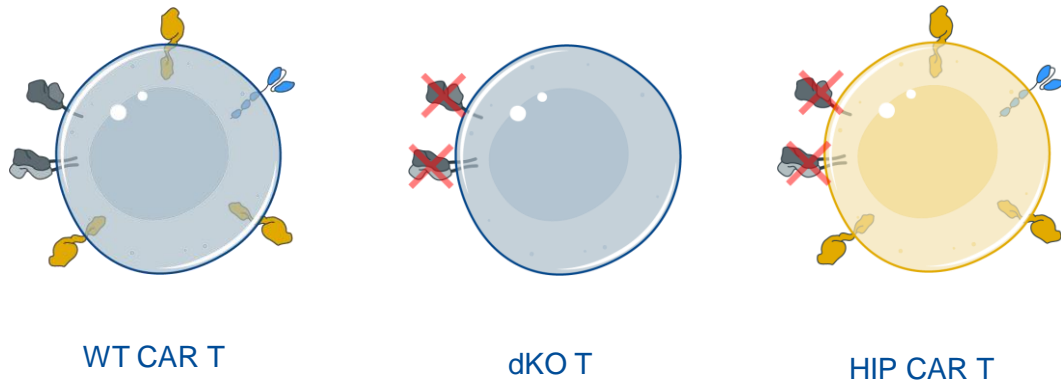
- No dose limiting toxicities
- No GvHD
- No SC291-related SAEs
- No CRS or ICANS
- No Grade 3 or higher infections

Clinical data as of: January 5, 2024
“evaluable” defined as patients treated with SC291 and had at least one disease assessment
*Transformed DLBCL from FL. **Transformed DLBCL from MZL. ***Assessment ongoing as of January 5, 2024.

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



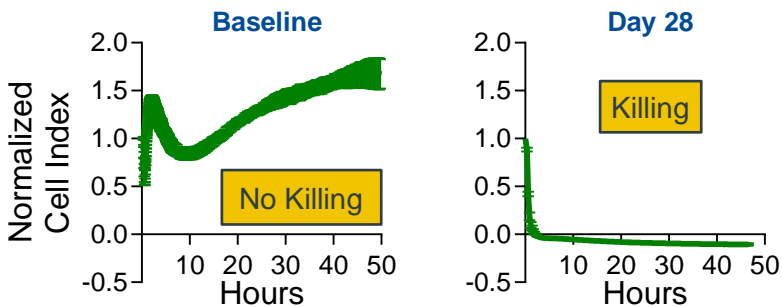
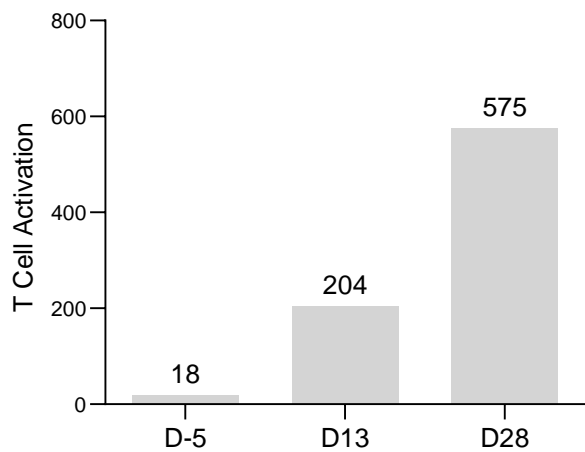
T Cell Population	Genetic Modifications
WT CAR T	CD47-CD19 CAR
dKO T	HLA I/II deficient
HIP CAR T	CD47-CD19 CAR; HLA I/II deficient

2 Test the patient's immune system against SC291

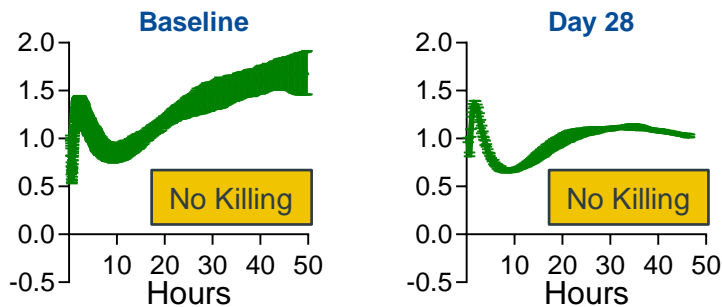
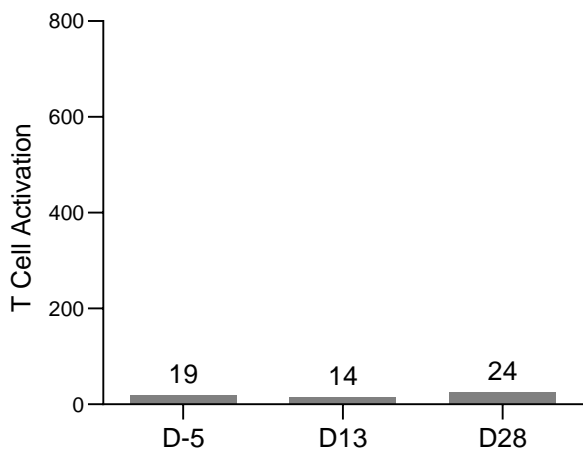
Cell	Day 28			
	T cell	Ab	NK cell	Blood
WT CAR T				
dKO T				
HIP CAR T				

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

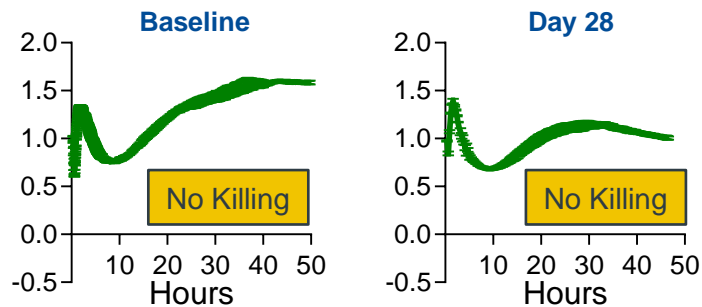
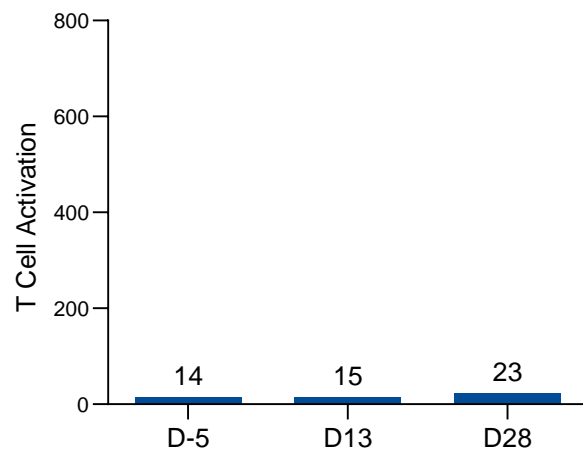
Patient T cells kill
WT CAR T cells



Patient T cells do not kill
dKO T cells



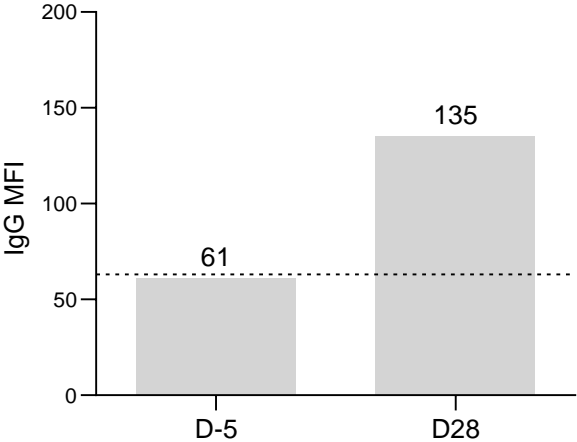
Patient T cells do not
kill HIP CAR T cells



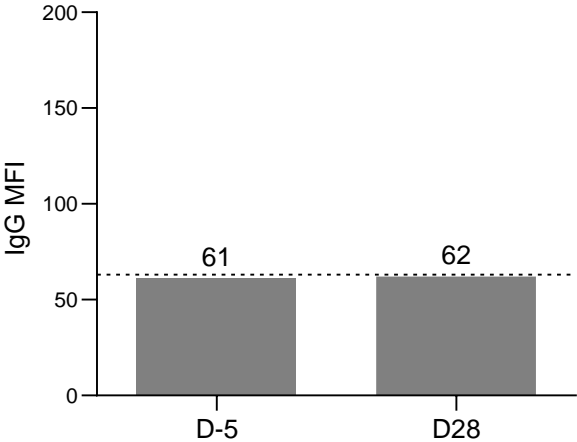
From Patient #1 in the ongoing ARDENT trial.

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

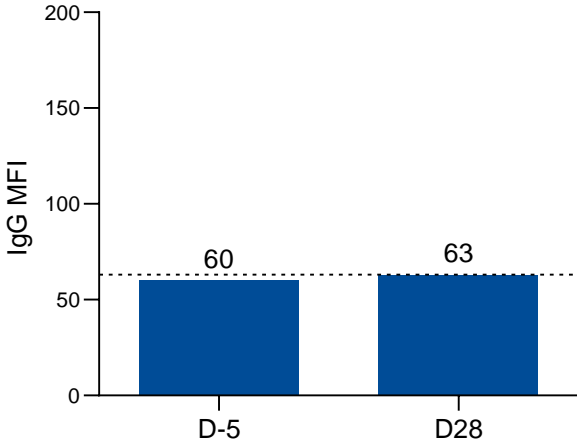
WT CAR T cells induce an antibody response



dKO T cells do not induce an antibody response



HIP CAR T cells do not induce an antibody response



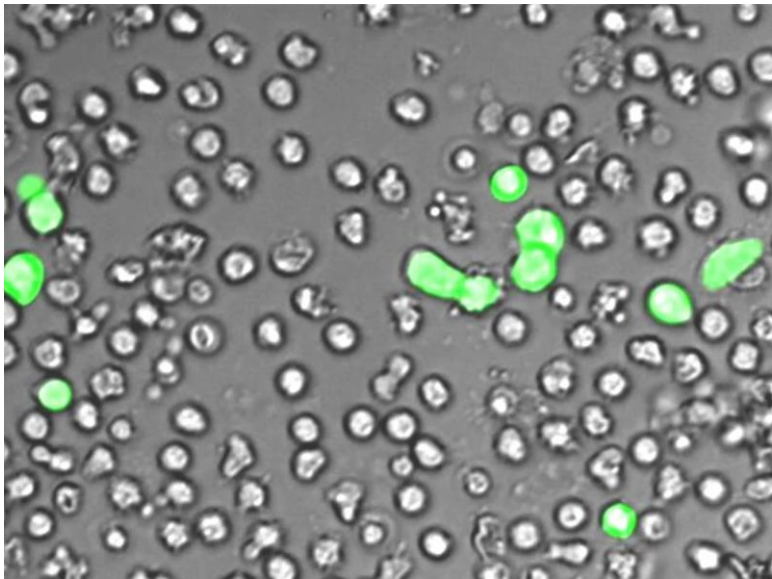
From Patient #1 in the ongoing ARDENT trial.

Only HIP CAR T cells avoid NK cell killing

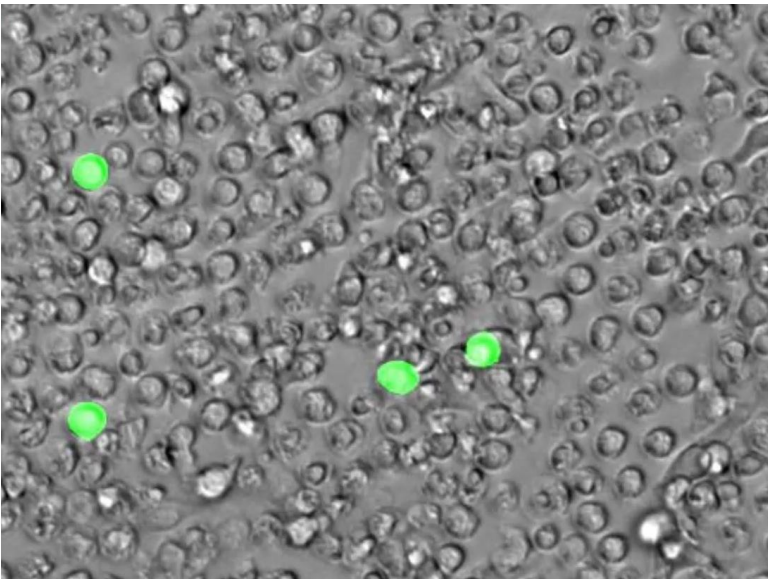
NK cells taken from patient's blood

Patient's NK cells from day 13 after SC291 dosing

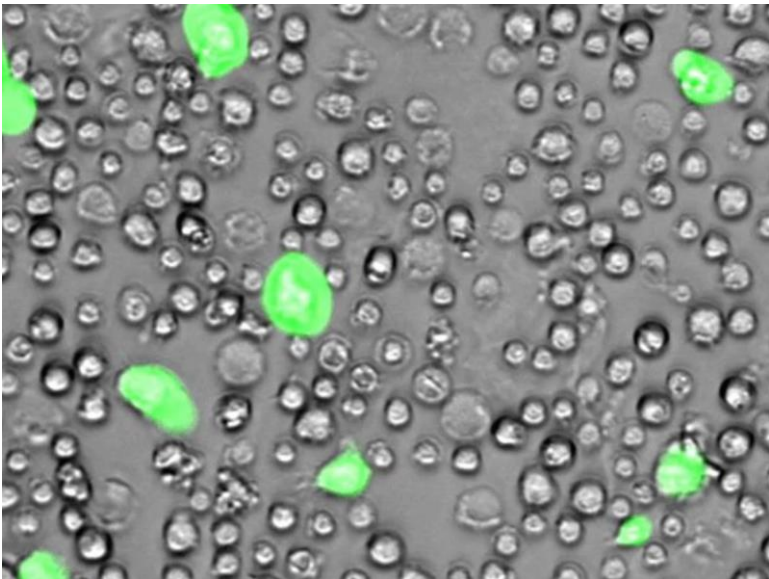
NK cells kill dKO T cells




NK cells kill dKO T cells with HLA-E overexpression




NK cells do NOT kill HIP CAR T cells



Actual assay time = 4 hours.



T cell with editing profile in column title



NK cells

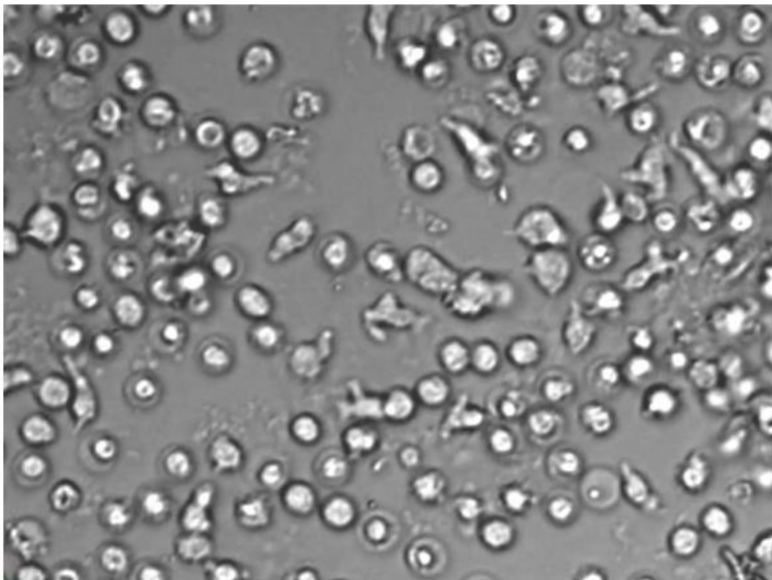
From Patient #1 in the ongoing ARDENT trial.

Only HIP CAR T cells avoid NK cell killing

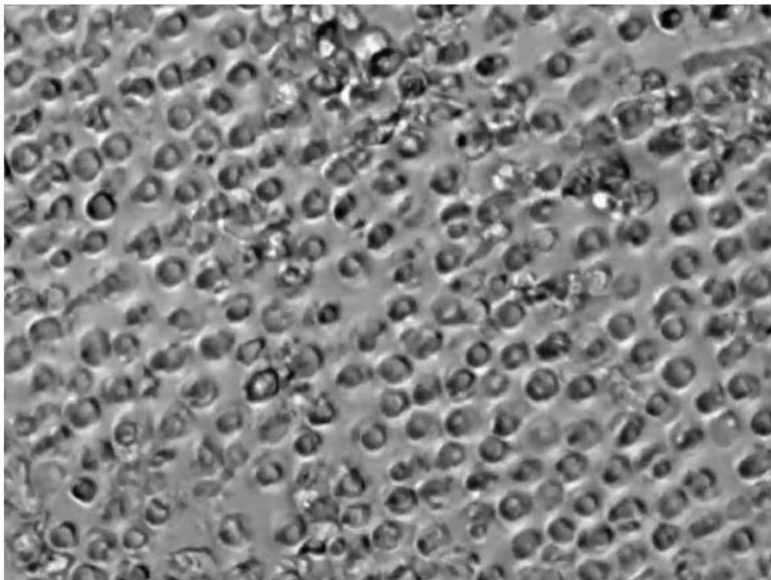
NK cells taken from patient's blood

Patient's NK cells from day 13 after SC291 dosing

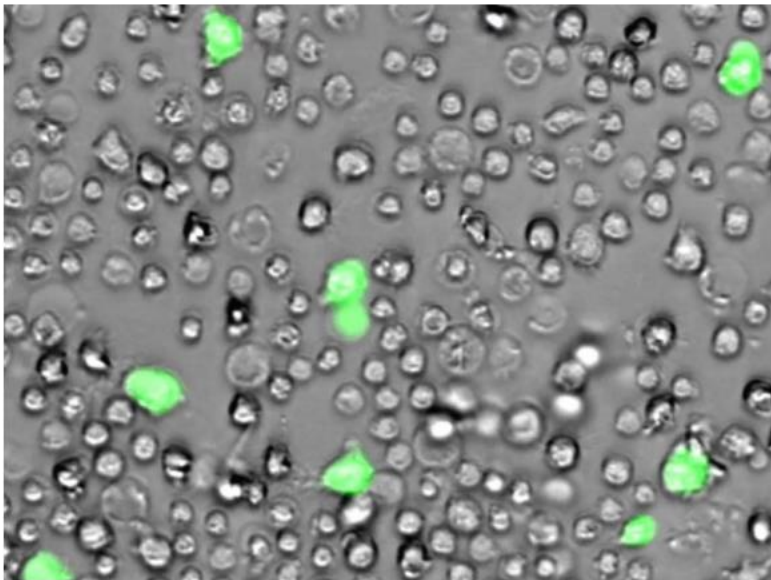
NK cells kill dKO T cells



NK cells kill dKO T cells with HLA-E overexpression



NK cells do NOT kill HIP CAR T cells



Actual assay time = 4 hours.

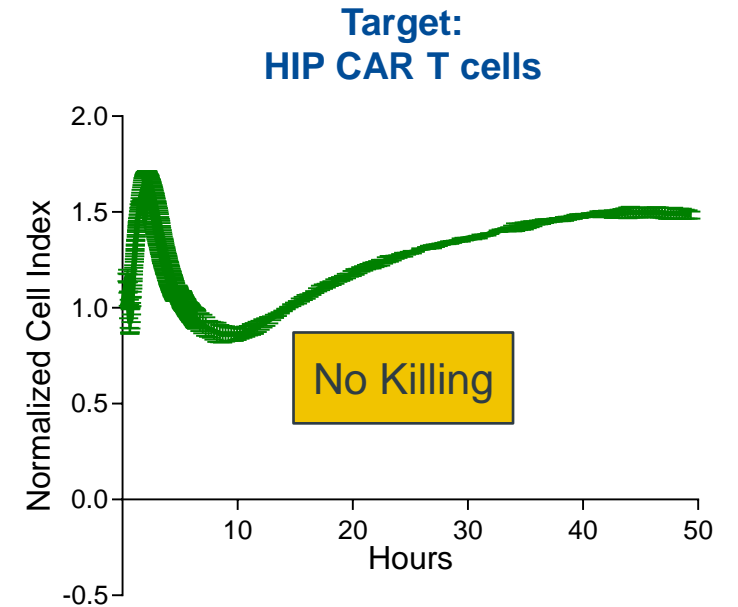
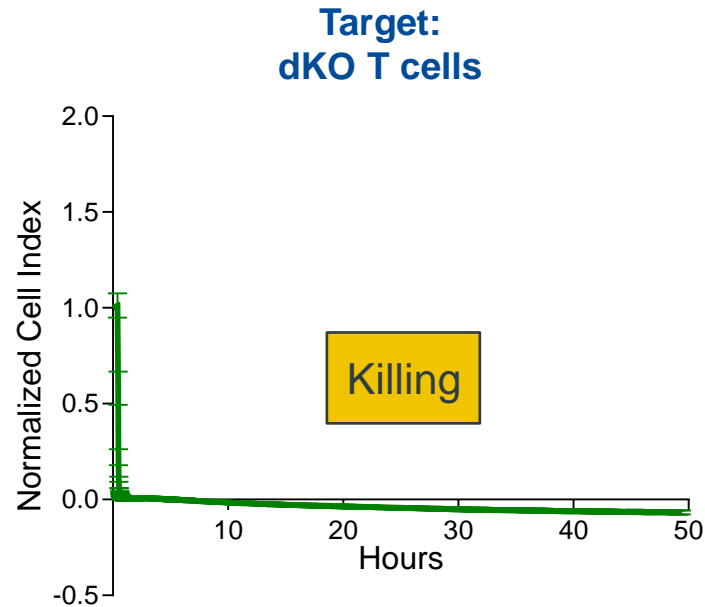
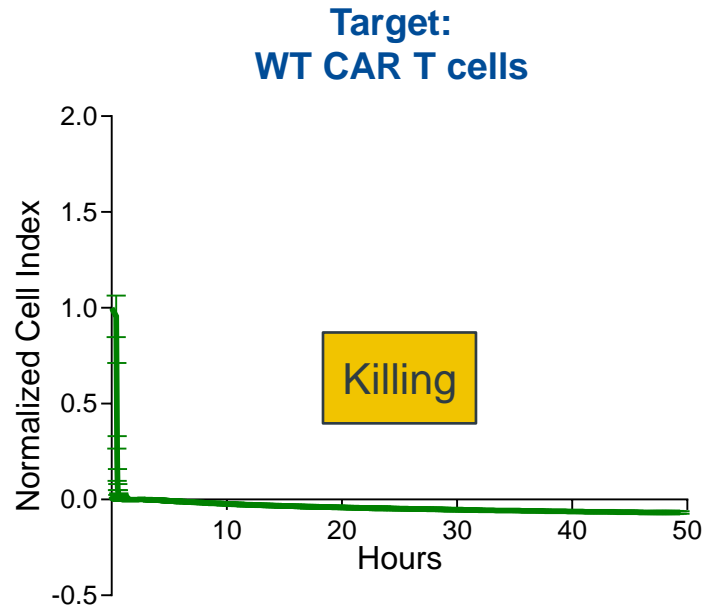
T cell with editing profile in column title

NK cells

From Patient #1 in the ongoing ARDENT trial.

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

D28 blood sample

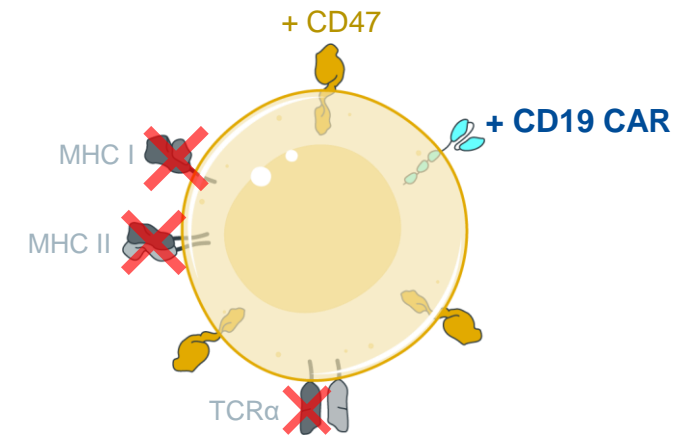


From patient #1 in the ongoing ARDENT trial.

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

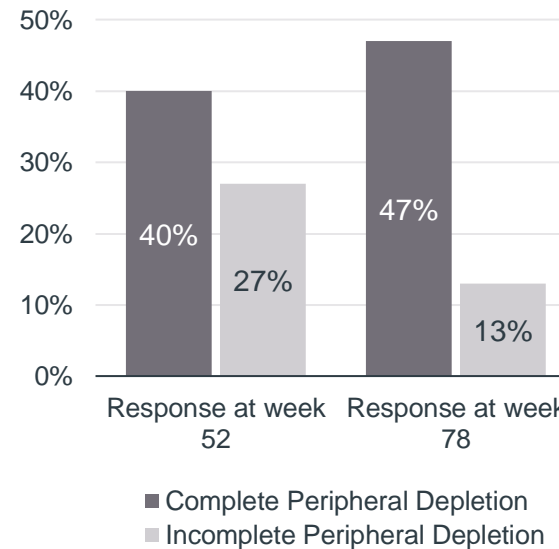
Autoimmune diseases have emerged as promising opportunity

1 B-cell targeting therapies have been efficacious across many autoimmune diseases¹

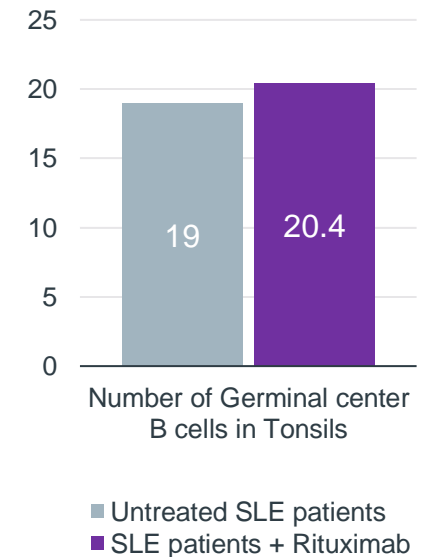
- SLE
- Vasculitis (granulomatosis with polyangiitis & microscopic polyangiitis)
- Neuromyelitis optical spectrum
- Pemphigus
- Relapsing and progressive MS
- Rheumatoid arthritis
- Lupus nephritis
- Sjogren syndrome
- NMDAR encephalitis
- Thrombocytopenic purpura
- Amyloidosis
- Scleroderma
- Autoimmune 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



3 Germinal center B cells are unaffected by rituximab treatment³



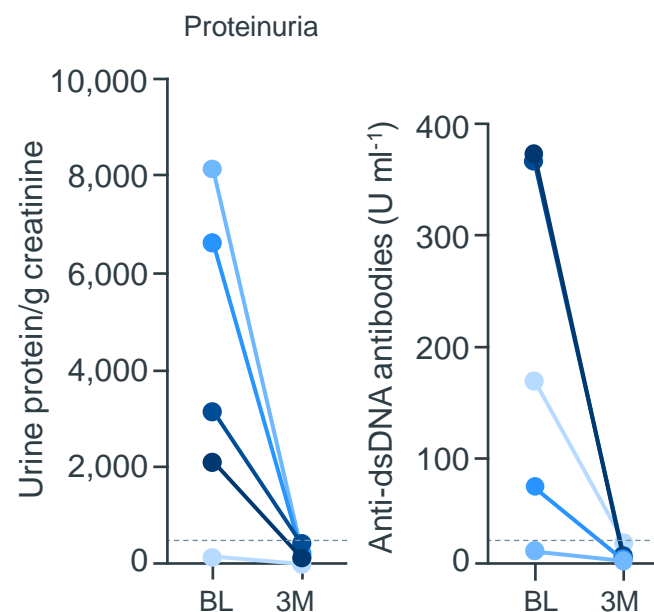
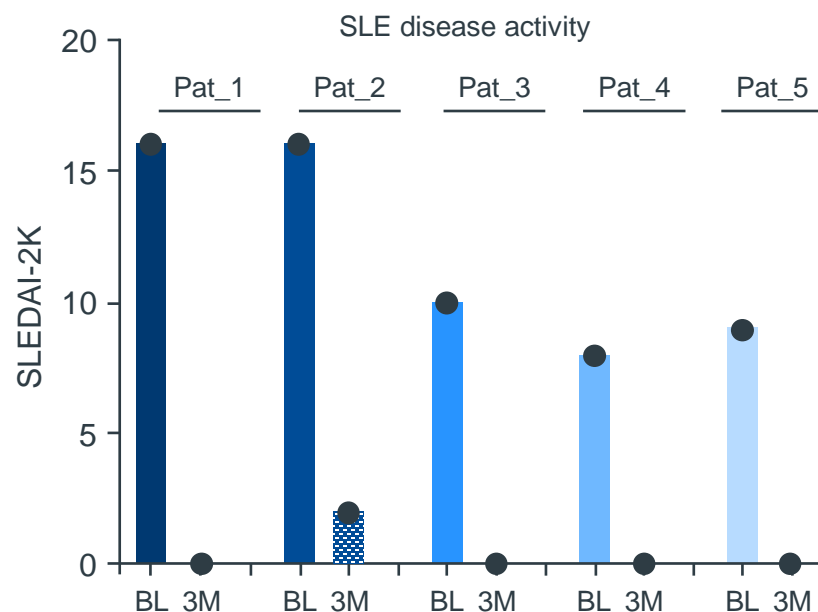
¹Adapted from Zhang et al. *Frontiers in Immunology*. 2023; Oh et al. *Immune Network*. 2023; Lee et al. *Nature Reviews Drug Discovery*. 2021.

²Mendez et al. *Clinical Journal of the American Society of Nephrology*. 2018.

³Anolik et al. *Arthritis and Rheumatism*. 2007.

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

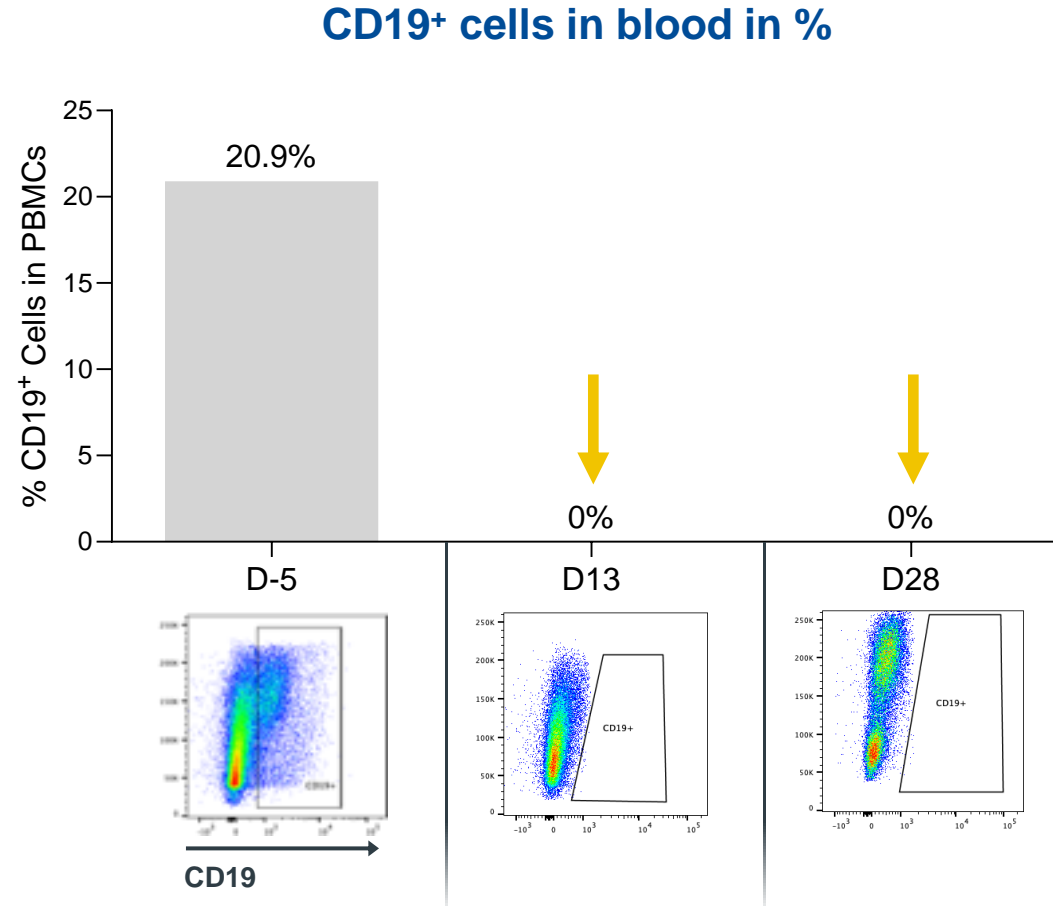


- Well tolerated – mild CRS (Grade 1) and no ICANS seen
- 5/5 patients are in a durable complete remission and off all drugs
- All known disease biomarkers rapidly normalized and have remained so thus far
- 24+ months of drug-free remission seen in patients constituting a potential functional cure
- 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.

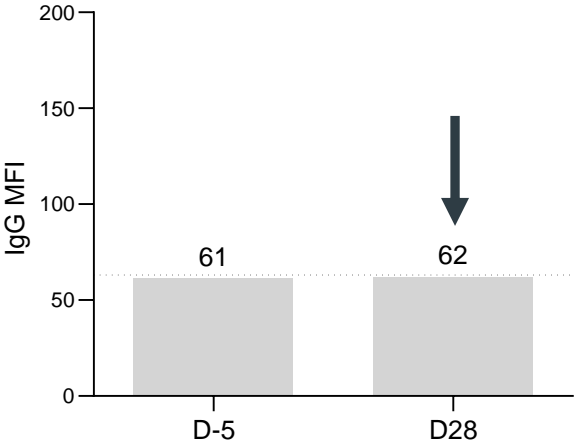
ARDENT trial: SC291 treatment leads to deep B cell depletion in oncology patient



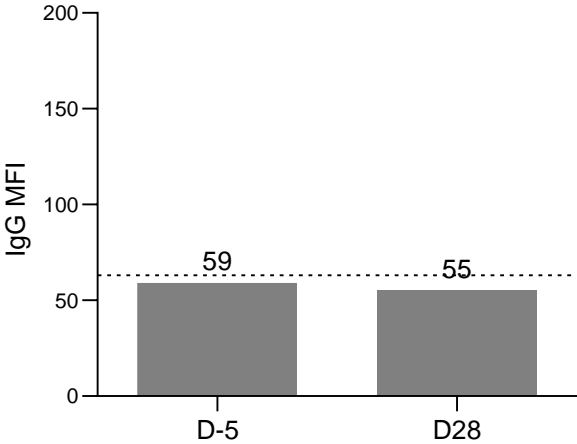
From Patient #4 in the ongoing ARDENT trial.

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

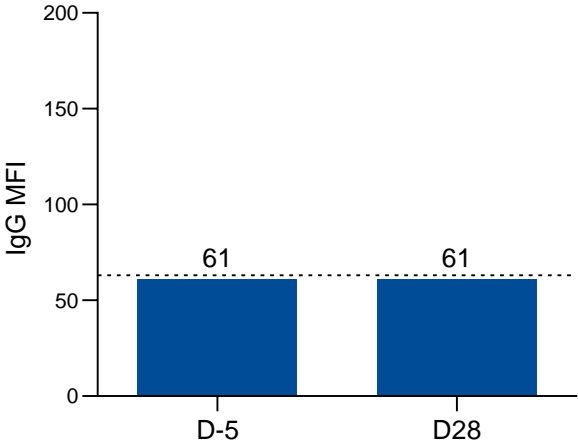
No anti-HLA antibody production against WT CAR T cells suggests complete B cell depletion



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

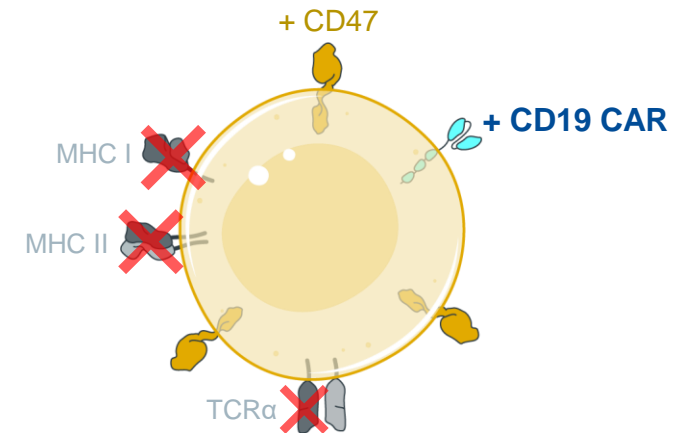
³US, EU5, and Japan

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

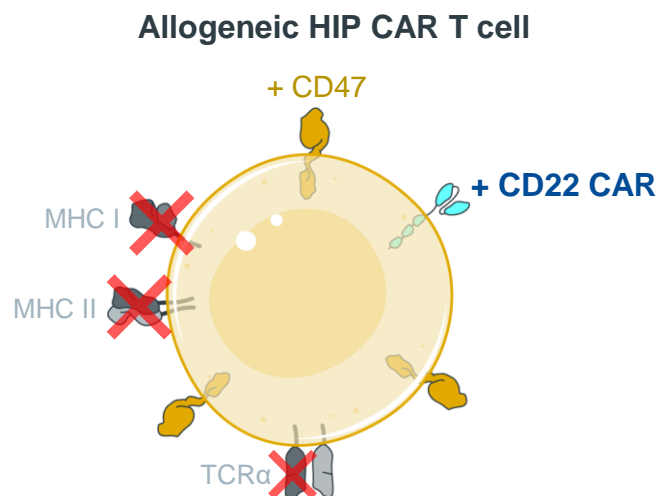


- Potential of ~7,500 CAR T failures annually in 2027²
- Median survival of ~5 months post-CD19 CAR T therapy failure³

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

 = 1,000 people

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

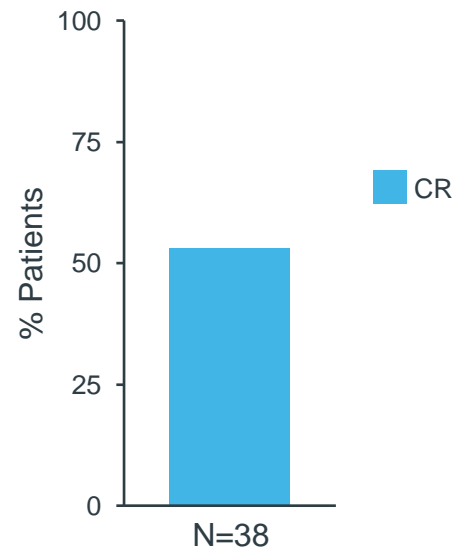


¹US, EU5, and Japan. ²Clarivate DRG NHL Market Forecast Nov 2021; 2027 Forecast is 2L+ LBCL patients; internal analysis of secondary EPI data.

³Di Blasi et al. *Blood*. 2022; DESCAR-T registry. ⁴DiBlasi et al. *Blood*. 2022

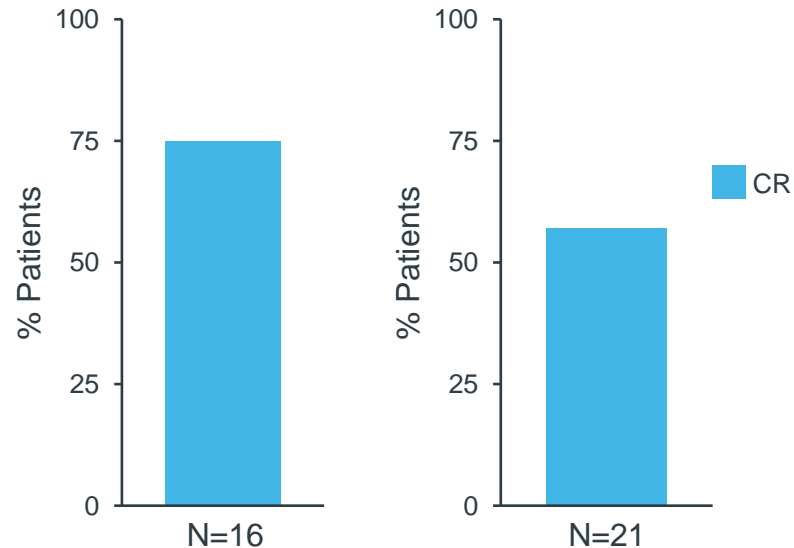
SC262: Licensed CD22 CAR produced strong clinical data in CD19 failures when part of autologous CAR T

>50% CR rate in CD19 CAR failure DLBCL patients



2023 ASH Yi-Jiun Su

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



2022 ASH Miklos/Stanford

2018 *Nature Med* Fry, et al.

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 insulin-producing 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

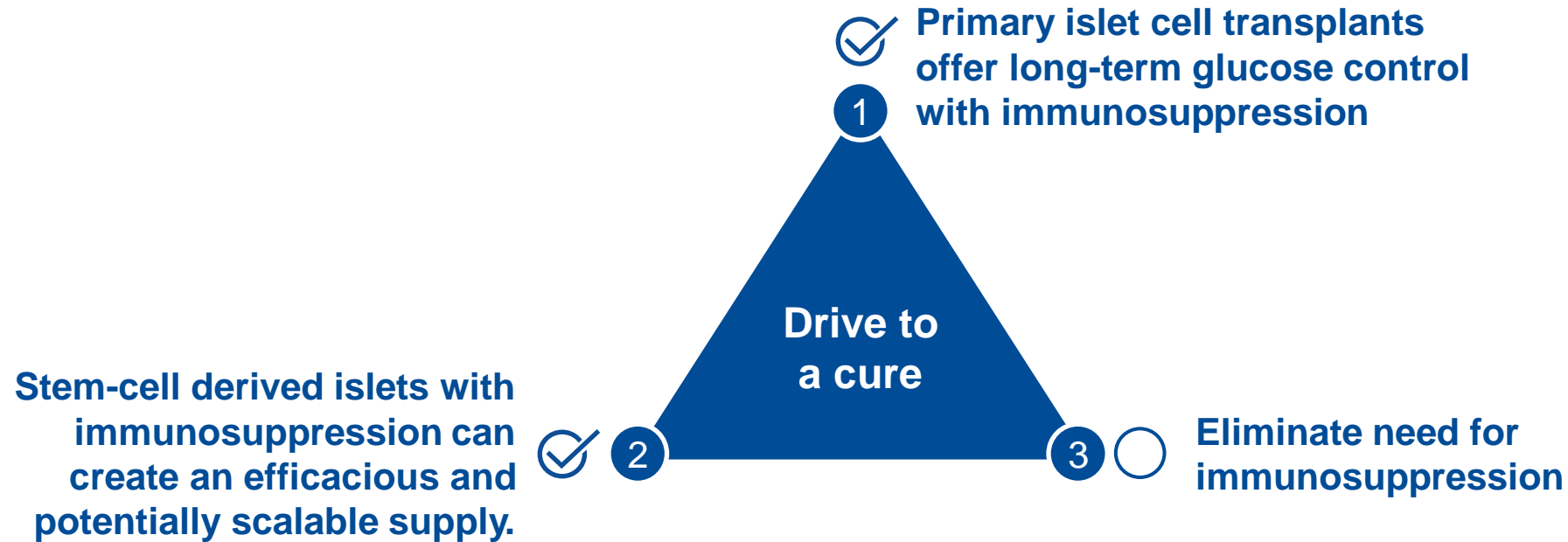


¹Rawshani et al. *Lancet*. 2018

²t1dindex.org

Emerging data suggest a cure is possible

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

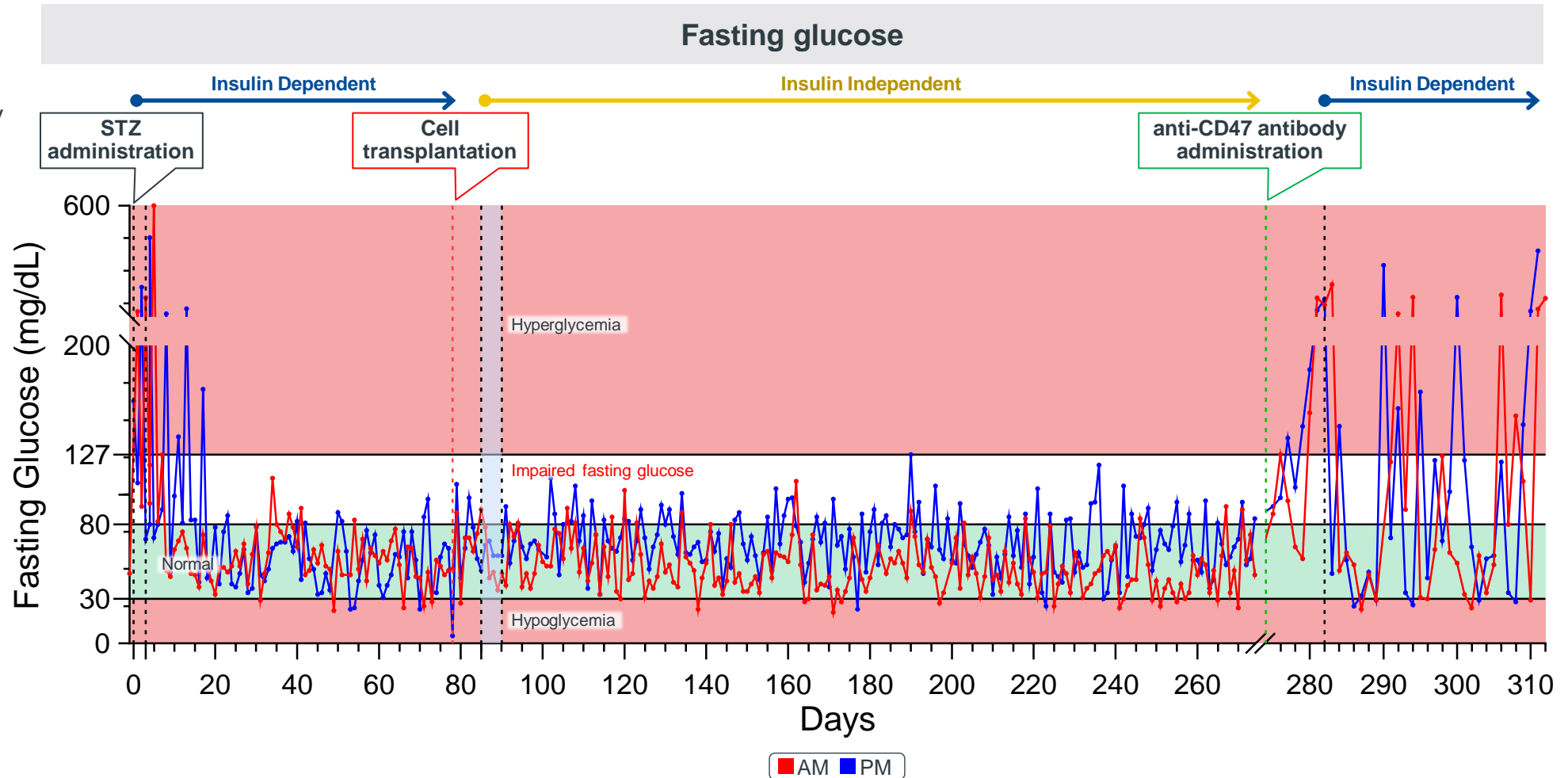


Goal – single treatment with long-term normal blood glucose without immunosuppression or insulin

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

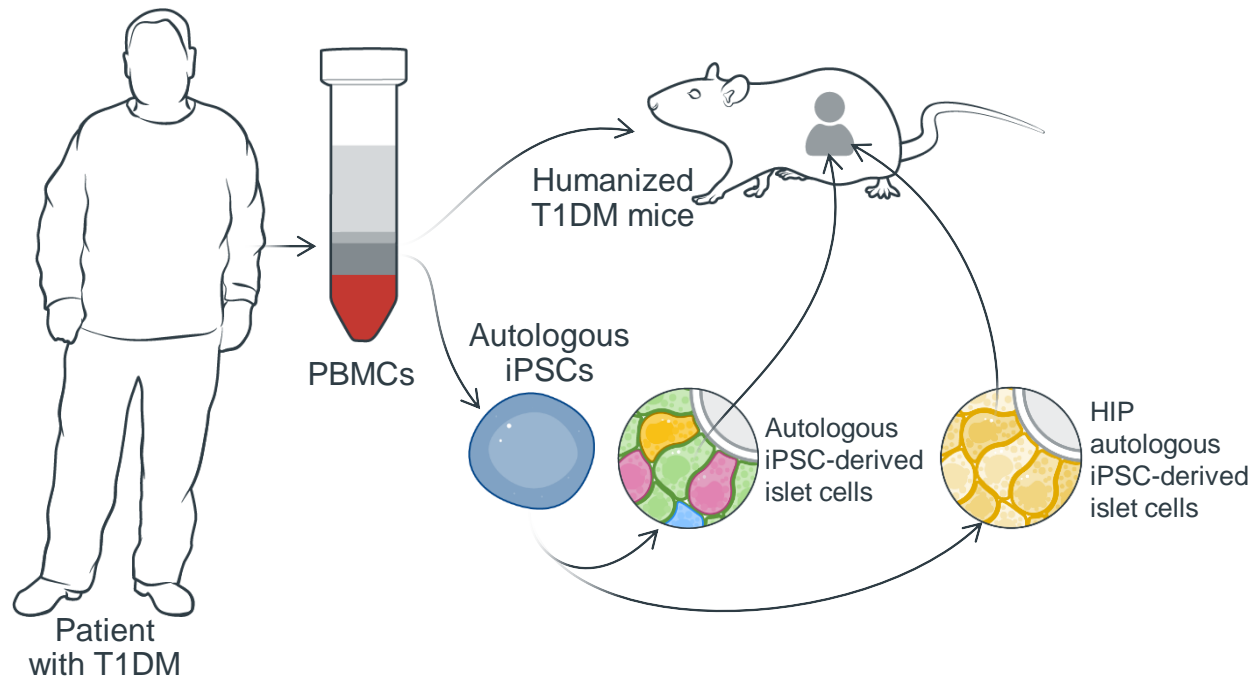
Study Design (N=1)

- 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

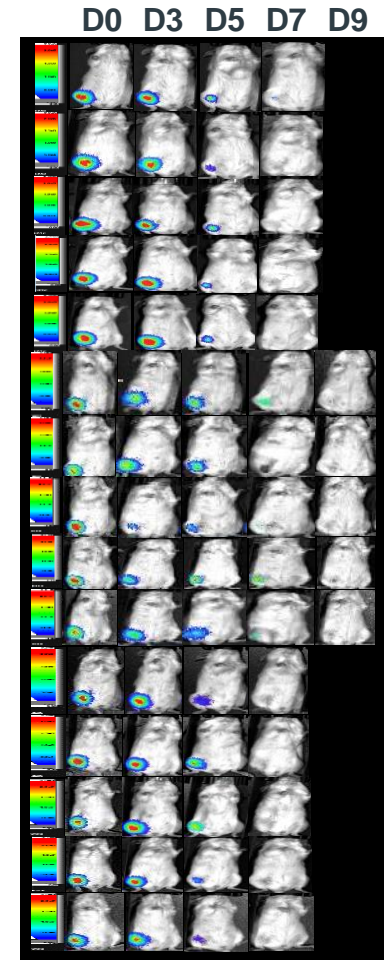
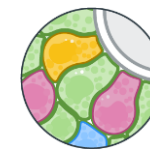
PBMCs from patient with T1DM used to generate stem cell-derived islet cells and to humanize immune system in mice



Unmodified stem cell-derived islet cells from patient with T1DM do not survive

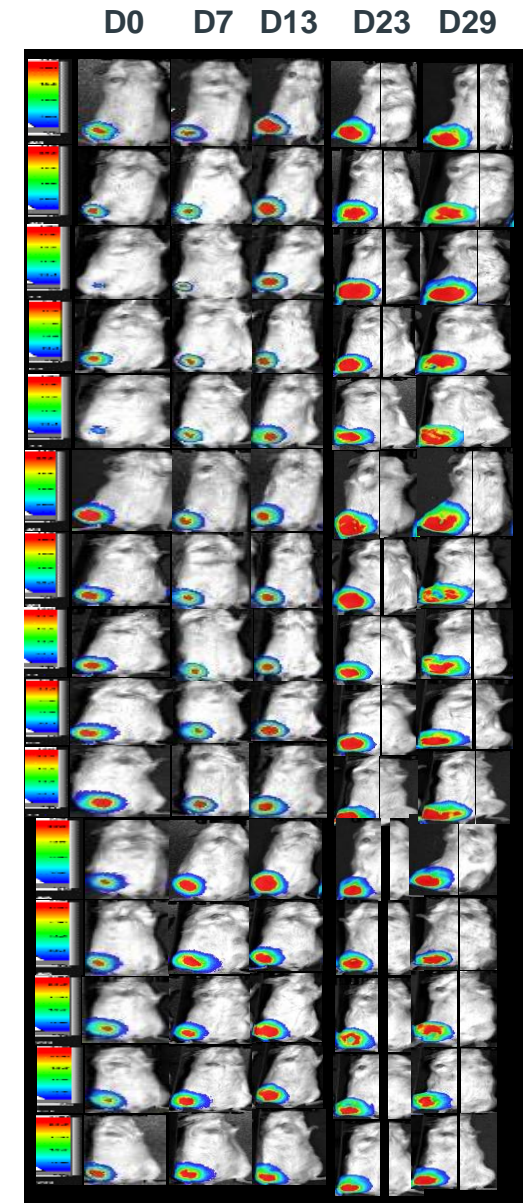
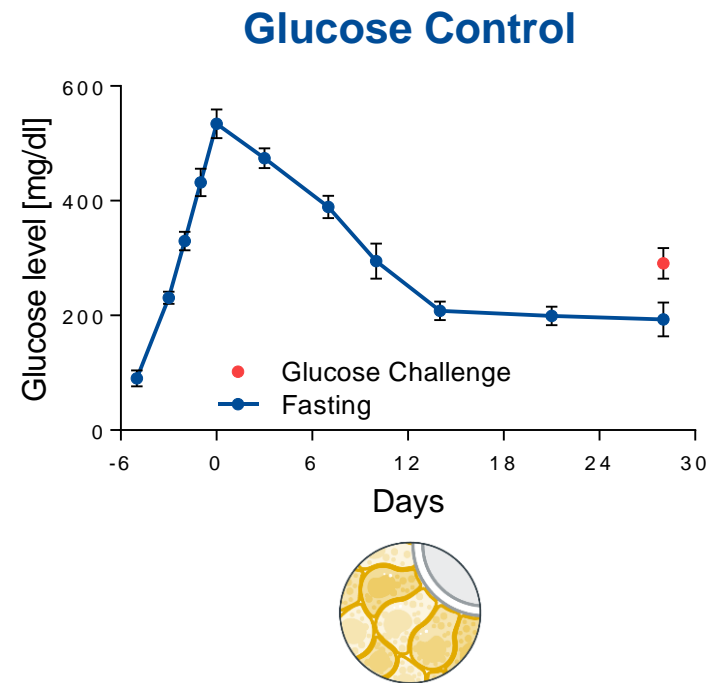
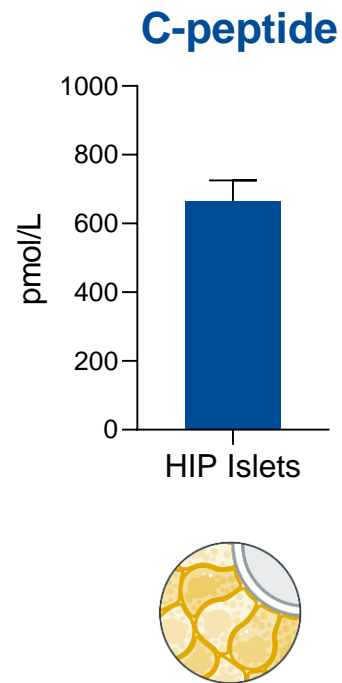
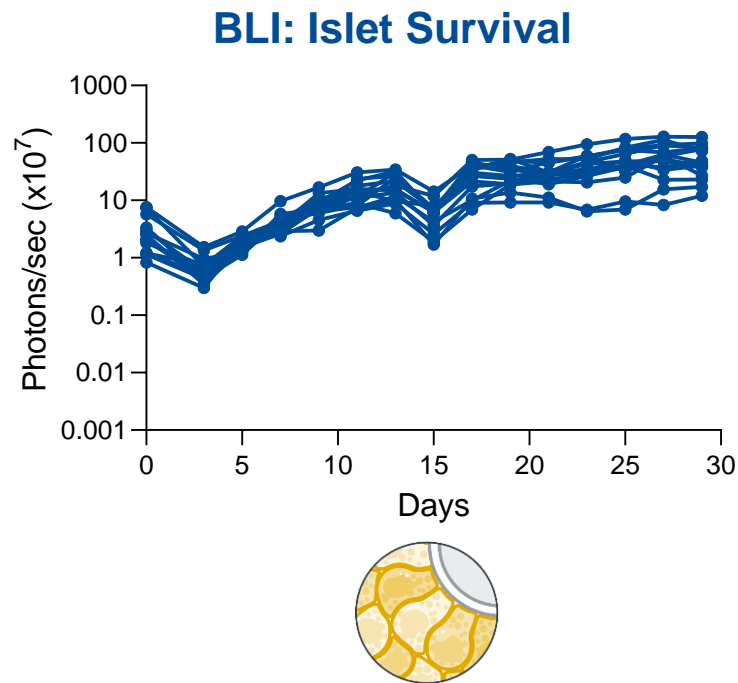


Patient T cells eliminate islet cells due to autoimmunity



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

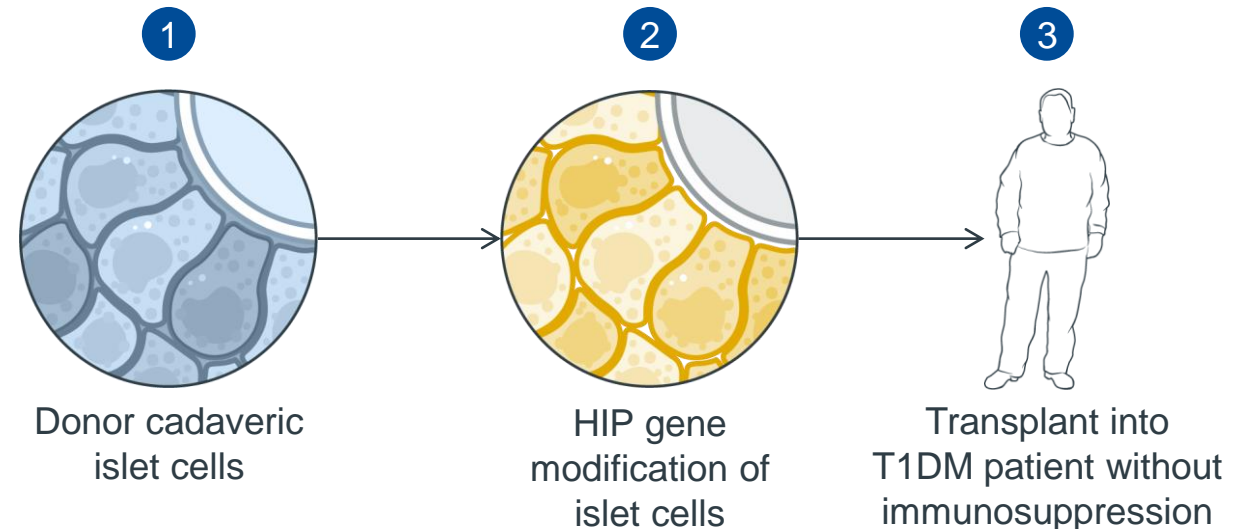


Abbreviations: BLI, bioluminescence imaging
Hu et al. *Sci Transl Med*. 2023.

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

IST Design

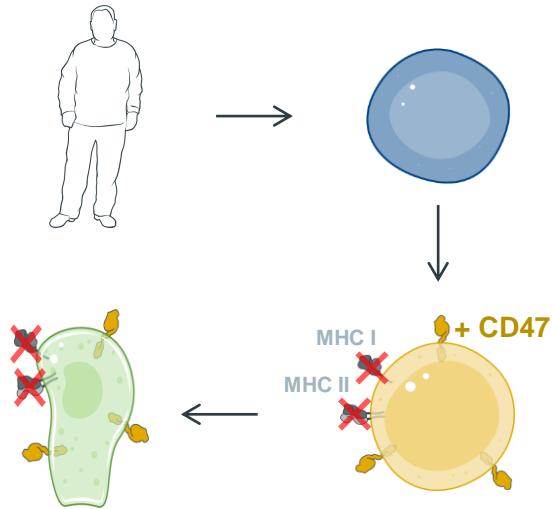


Key Measured Outcomes

Cell survival & immune evasion
C-peptide
Glycemic control

Sana's approach to treat type 1 diabetes

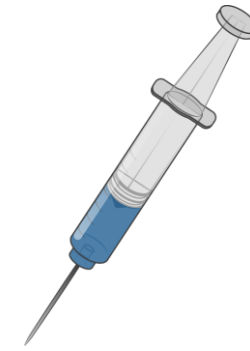
1 Make hypoimmune islet cells from stem cells



2 Manufacture at scale

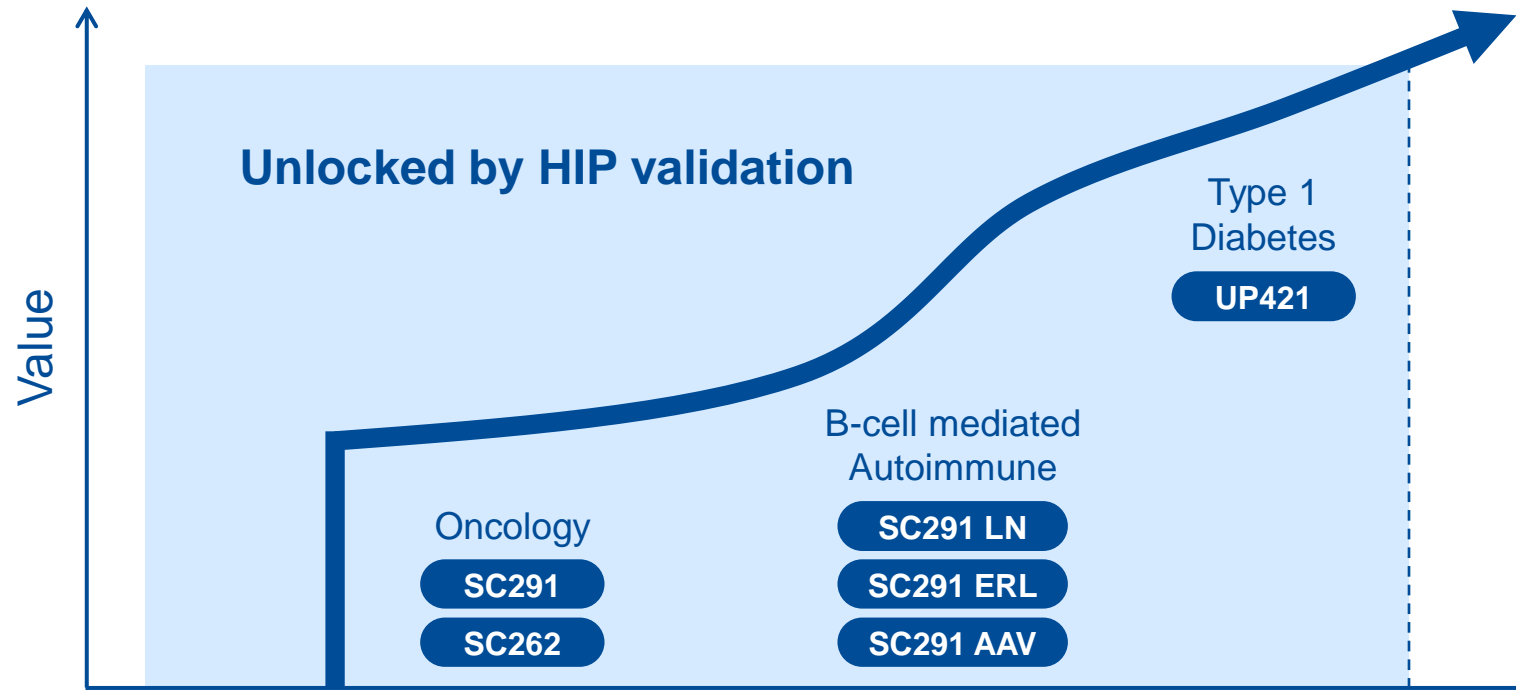


3 Deliver as a single therapy



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

Sana Biotechnology
www.sana.com

