

Corporate Presentation

January 2023



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Sana Biotechnology

Engineered Cells as Medicines

Sana's ambition is to repair or replace any cell in the body. Technologies address fundamental barriers:

- **Hypoimmune (HIP) technology:** Overcoming immune rejection of allogeneic cells
- **Fusogen technology:** *In vivo* delivery of genomic modification reagents in a cell-specific manner

Overcoming immune rejection of allogeneic cells has potential to change cell therapy:

- Allogeneic CAR T cells that perform clinically like autologous CAR T cells can transform treatment of hematological malignancies
- Key to unlocking the potential of stem cell-derived therapies such as pancreatic islet cells for the treatment of type 1 diabetes

Two opportunities in 2023 for clear clinical proof of concept:

- SC291: Cell persistence and clinical efficacy
- HIP primary islets in patients with type 1 diabetes
- Results will provide insights in CAR T cell and stem-cell based platforms – ability to overcome allogeneic and autoimmune cell rejection

Pipeline poised to deliver multiple clinical data readouts over next several years:

- **Hypoimmune allogeneic CAR T cells:** SC291 (CD19), SC262 (CD22), SC255 (BCMA), and beyond
- **Regenerative medicine:** SC451 (type 1 diabetes) and SC379 (CNS disorders)
- ***In vivo* fusogen platform:** SG295

Balance sheet allows potential for multiple data readouts

Sana's platforms, technology, and programs

Pipeline poised to deliver multiple clinical data readouts over next several years

Product Candidates	Mechanism	Potential Indications	Expected Clinical Milestones	
			2023	2024
SC291 (HIP)	CD19-targeted allo CAR T	NHL/ALL/CLL	●	●
HIP primary islet cells ¹		Type 1 Diabetes	● ●	●
SG295 (Fusogen)	<i>In vivo</i> CAR T (CD8/CD19)	NHL/ALL/CLL	●	●
SC262 (HIP)	CD22-targeted allo CAR T	NHL/ALL/CLL	●	●
SC451 (HIP)	Stem-cell derived pancreatic islet cells	Type 1 Diabetes		● ●
SC255 (HIP)	BCMA-targeted allo CAR T	Multiple Myeloma		●
SC379	Glial progenitor cells	PMD, HD, SPMS		●
SG239 (Fusogen)	<i>In vivo</i> CAR T (CD8/BCMA)	Multiple Myeloma		
SG242 (Fusogen)	<i>In vivo</i> CAR T (CD4/CD19)	NHL/ALL/CLL		
SG221 (Fusogen)	<i>In vivo</i> CAR T (CD4/BCMA)	Multiple Myeloma		
SG233 (Fusogen)	<i>In vivo</i> CAR T (CD8/CD22)	NHL/ALL/CLL		
SC418 (Fusogen)	<i>In vivo</i> hematopoietic stem cells	SCD, Beta-Thalassemia		

● IND filing
● Clinical data

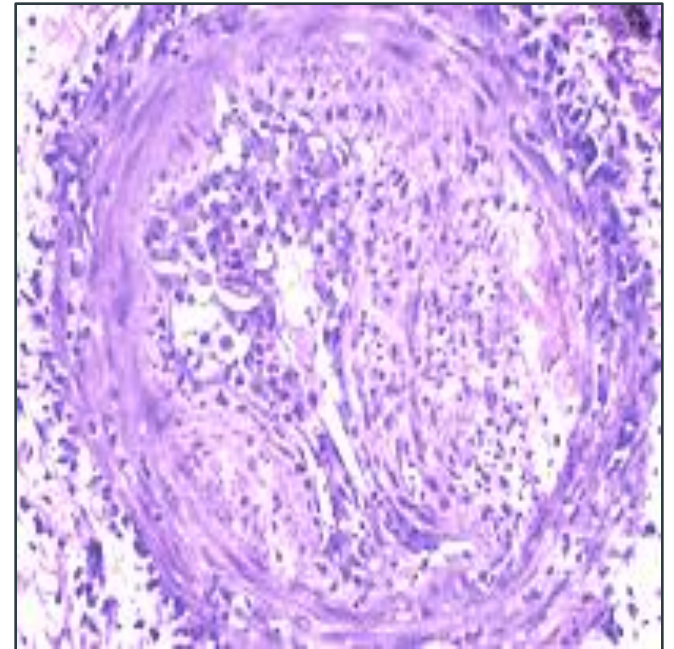
¹IST, investigator sponsored trial.

Abbreviations: ALL, acute lymphoblastic leukemia; CLL, chronic lymphocytic leukemia; HD, Huntington's disease; IND, investigational new drug; NHL, non-Hodgkin's lymphoma; PMD, Pelizaeus-Merzbacher Disease; SCD, sickle cell disease; SPMS, Secondary Progressive Multiple Sclerosis.

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

- ~75 years of organ and bone marrow transplants – immune rejection remains the largest problem
- Cell-based medicines face similar immune rejection challenges
- Significant 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
- Red blood cell transfusions are the only example of successful, broadly available transplanted allogeneic cells
- Overcoming immune rejection of foreign cells has potential to unlock entire field of cellular medicine

Biopsy of acute rejection of a pancreas transplant



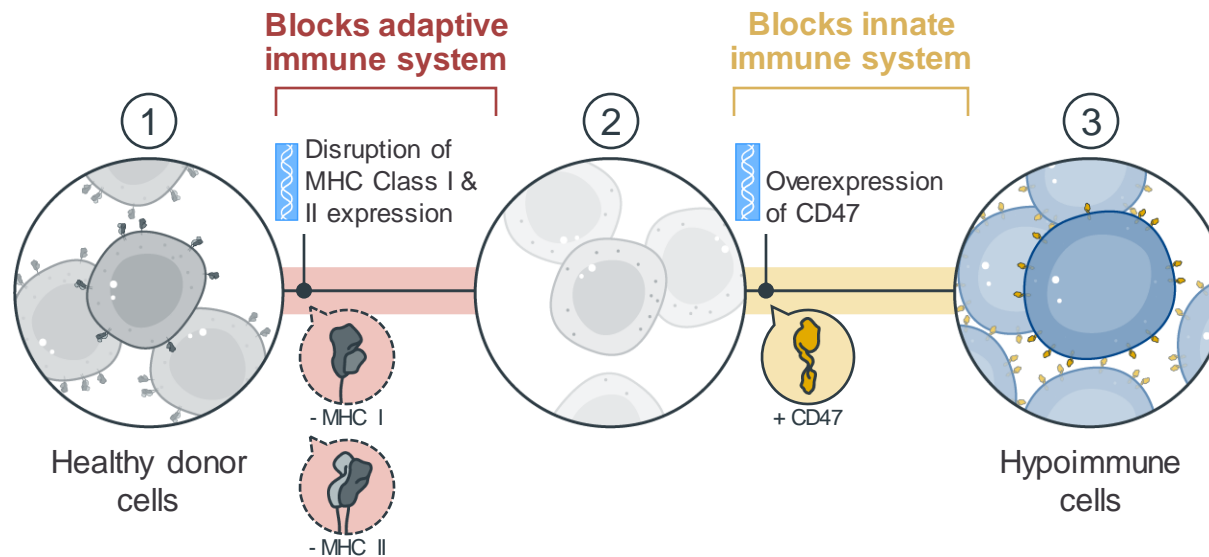
Drachenberg et al. *Am. J. Transplant.* 2008

Sana's hypoimmune solution: Leverage insights from nature

Leverage insights from nature to create hypoimmune cells

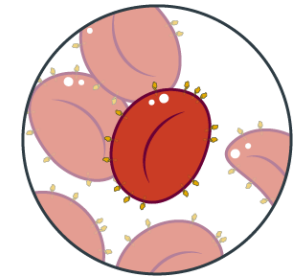


Sana's hypoimmune approach



Red blood cells

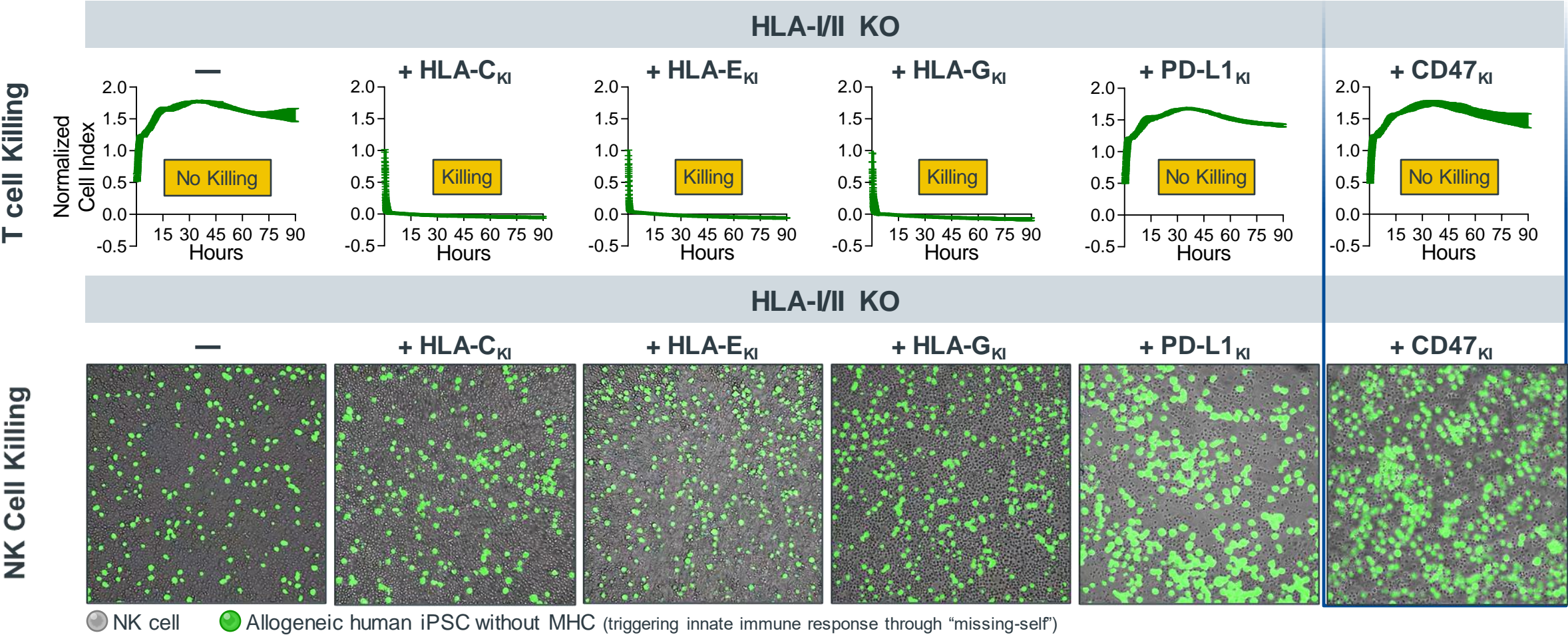
- Overexpress CD47
- Do not express MHC Class I and II



Red blood cells

Abbreviations: MHC, major histocompatibility complex; RBC, red blood cell.
Current clinical platform with multiple ongoing approaches in research phase.

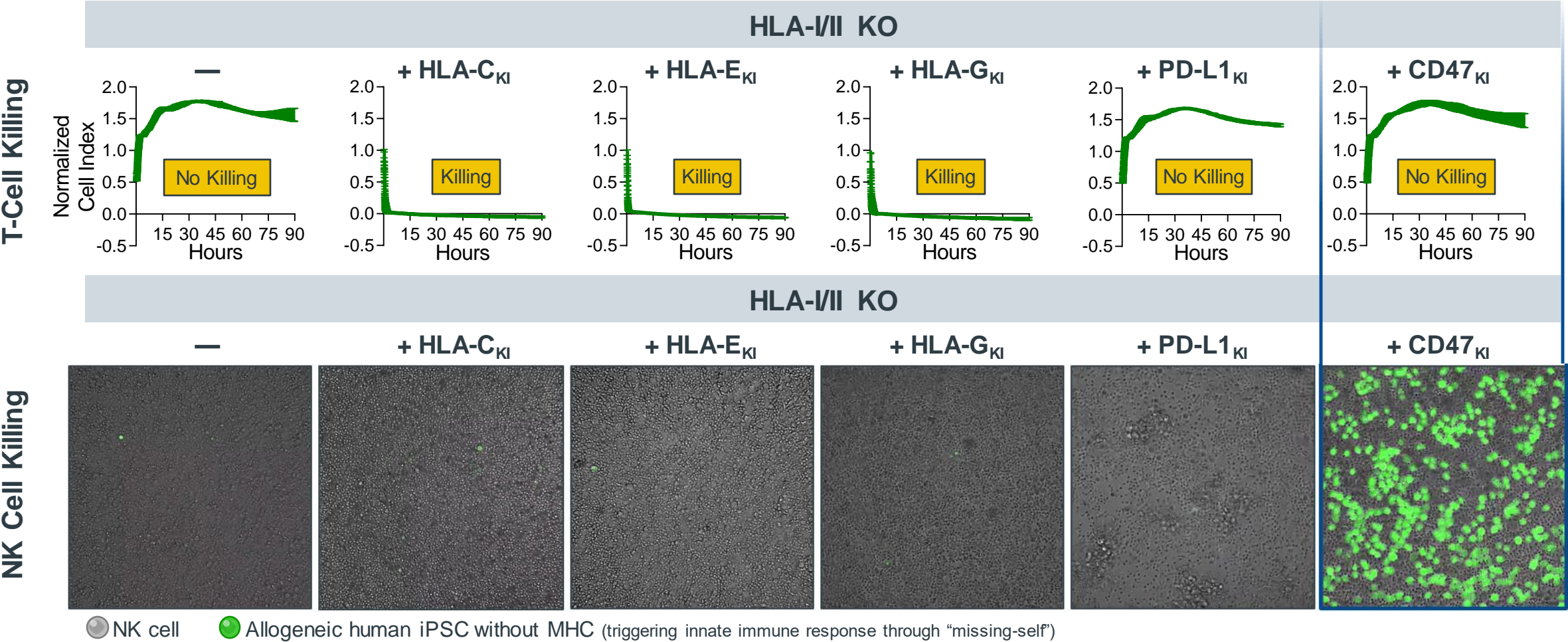
Sana's HIP modifications offer superior protection from innate cell killing



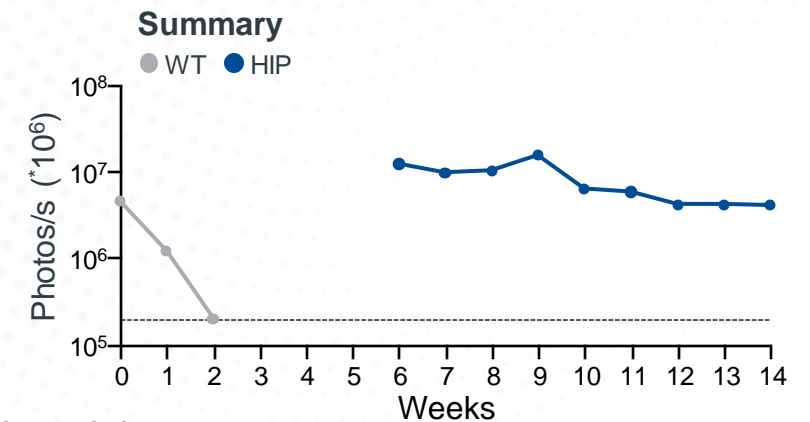
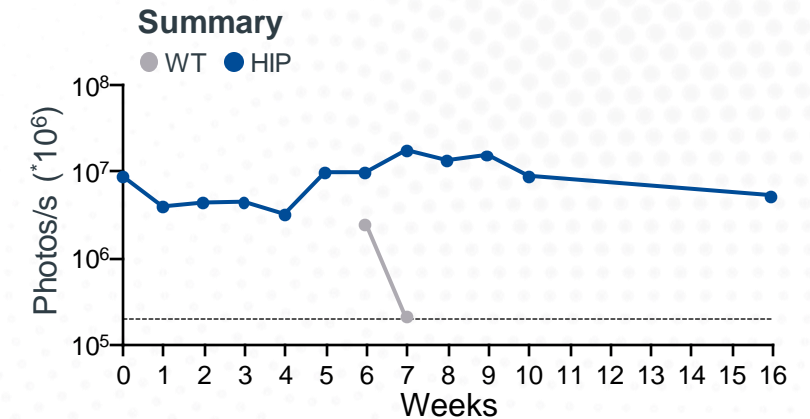
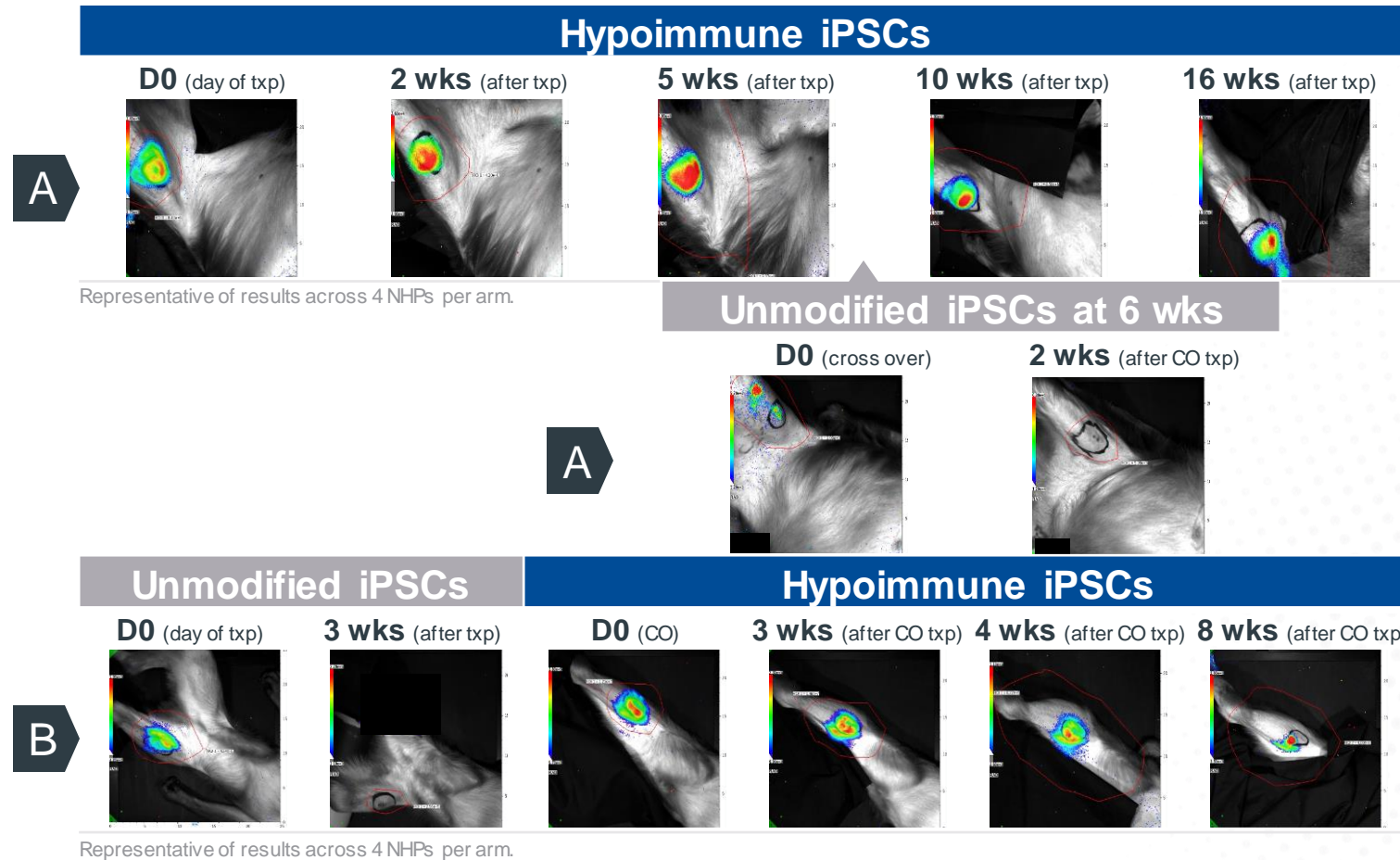
Abbreviations: HLA, human leukocyte antigen; iPSC, induced pluripotent stem cells; KI, knock-in; KO, knock-out; NK, natural killer; PD-L1, Programmed death-ligand 1.



Sana's HIP modifications offer superior protection from innate cell killing



Hypoimmune cells survive *in vivo* when transplanted in NHP while unmodified iPSCs get rejected



- NHP unmodified iPSCs (wt) & NHP hypoimmune iPSCs (HIP) were transplanted into 8 allogeneic recipients

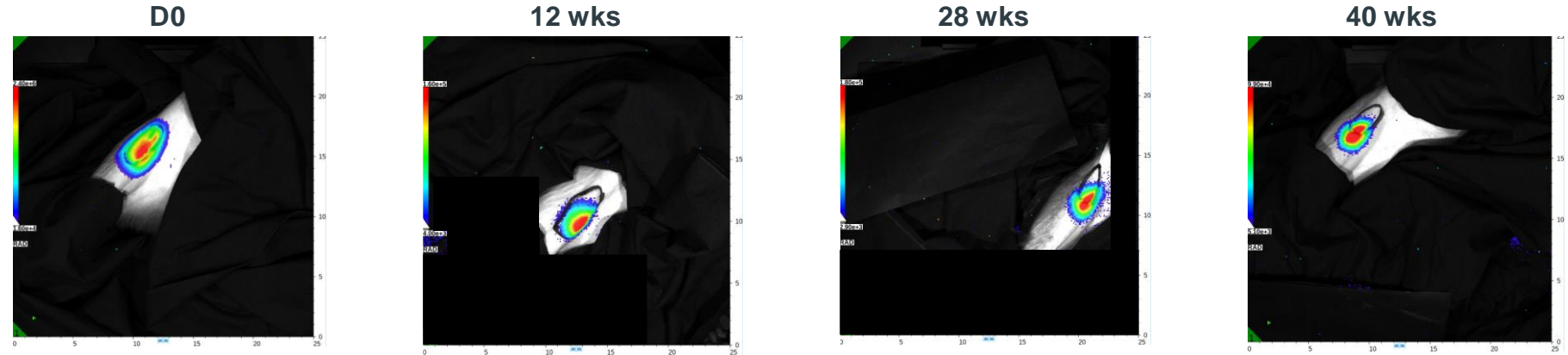
CO, cross over; Txp, transplant

Survival of allogeneic hypoimmune pancreatic islet cells for 10+ months without immunosuppression

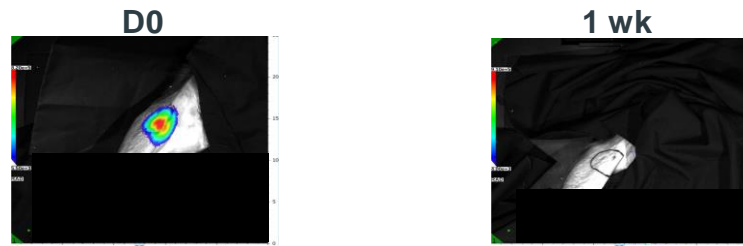
Study design:

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

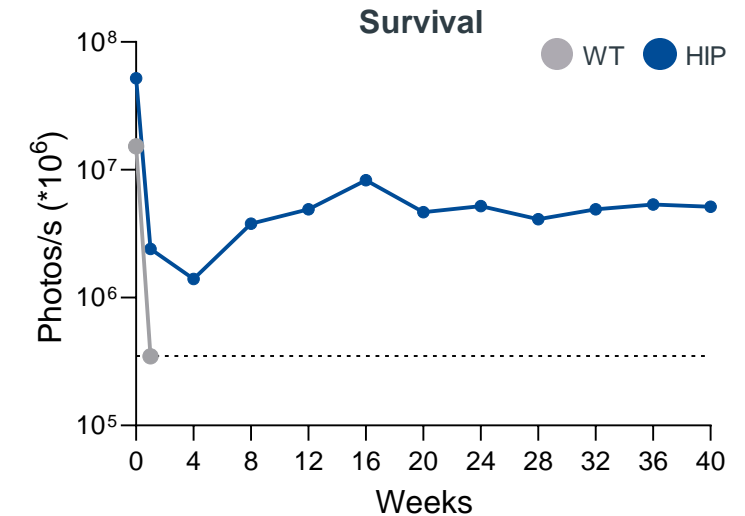
HIP results (follow up shown: 10 months). Study ongoing.



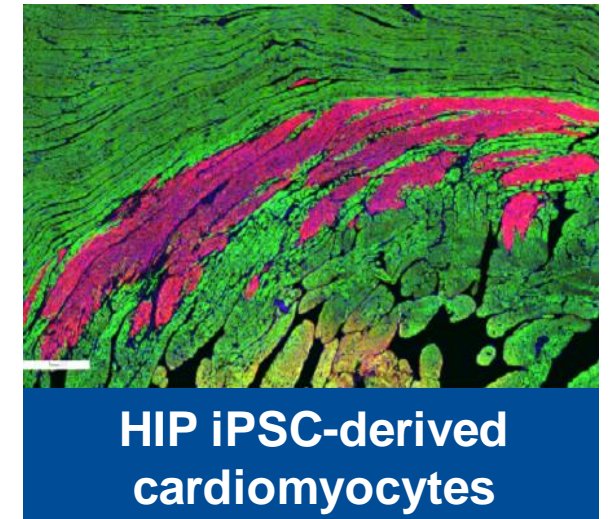
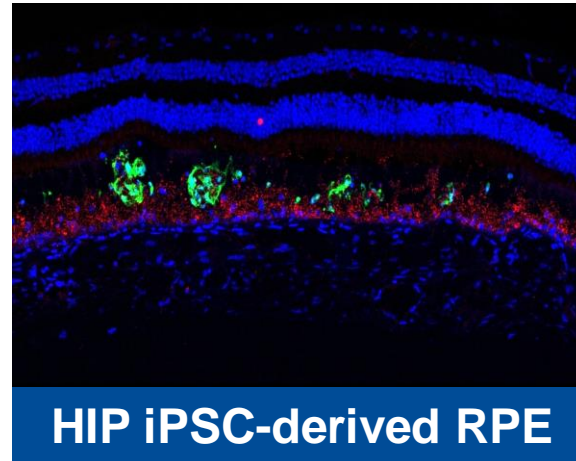
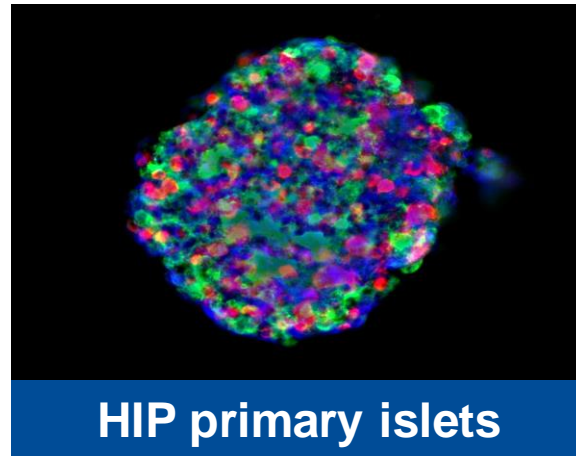
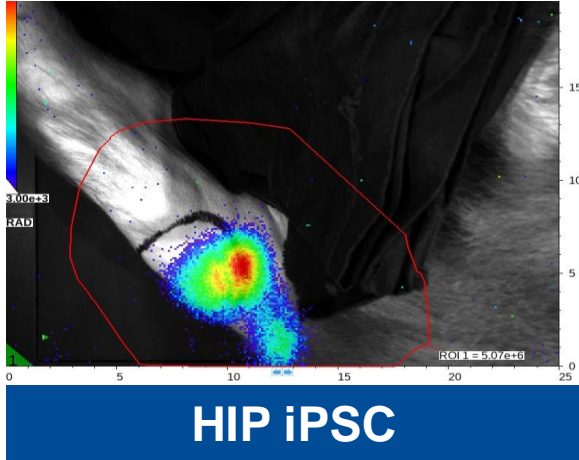
WT results (no survival after 1 wk)



n=1 HIP primary islet cells; n=1 WT primary islet cells.



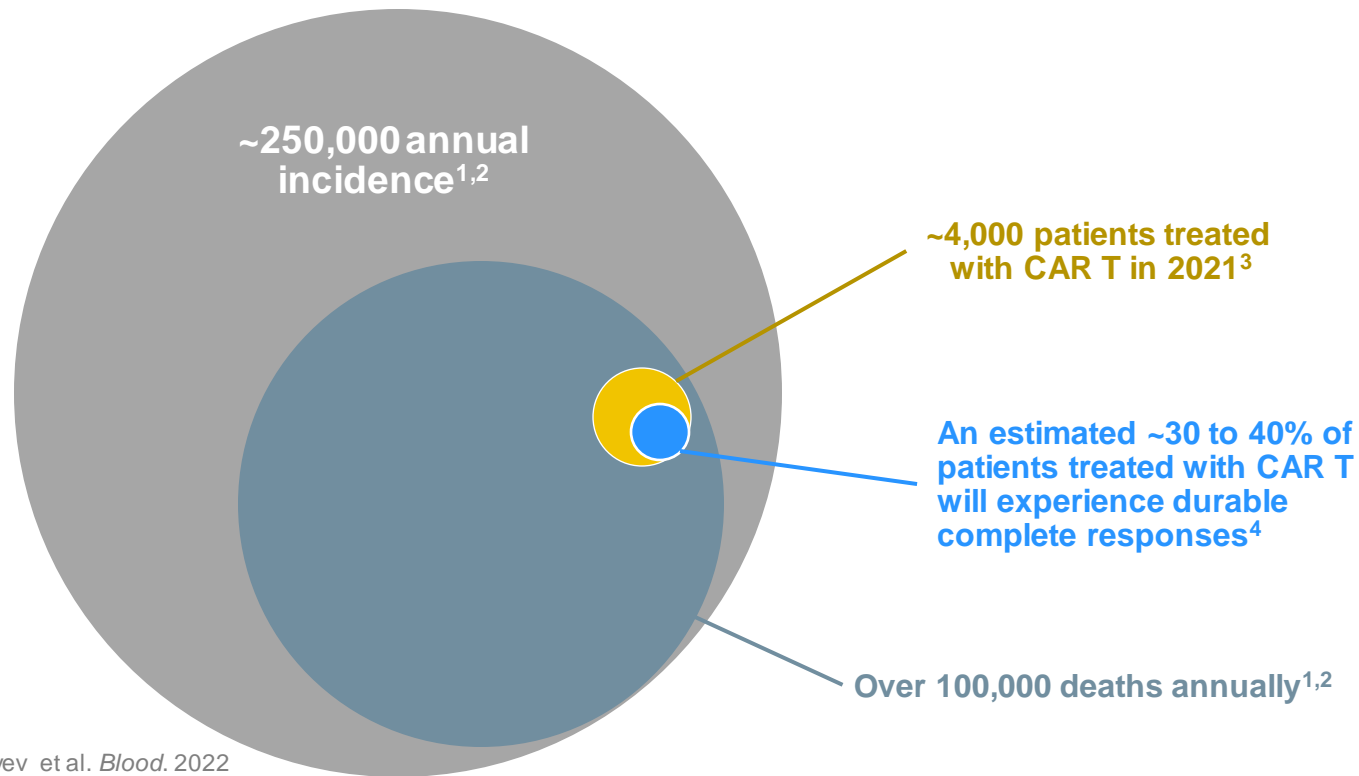
Survival and immune evasion after transplant for different cell types in multiple NHP studies



Abbreviations: RPE, retinal pigment epithelium.

Hematologic cancers continue to have a high unmet need

High mortality in lymphoma and myeloma in the US and EU5



¹Avezbakiyev et al. *Blood*. 2022

²Durie et al. *The Oncologist*. 2020

³Clarivate DRG NHL Market Forecast Nov 2021

⁴Scivida 2022 NHL Factbook

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

Challenges

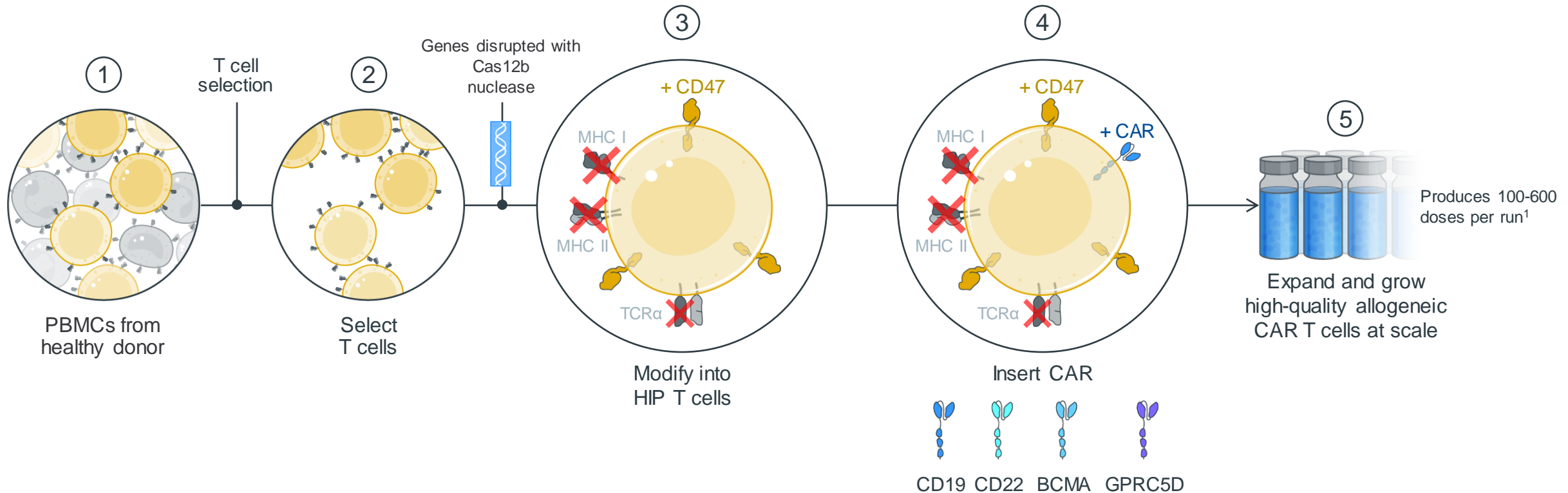
- Autologous CAR T cell scalability
- Many patients fail CAR T treatment
- Allogeneic CAR T cells immune rejection limits persistence and efficacy

Opportunity

- Known targets
- Known efficacy and safety bar

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

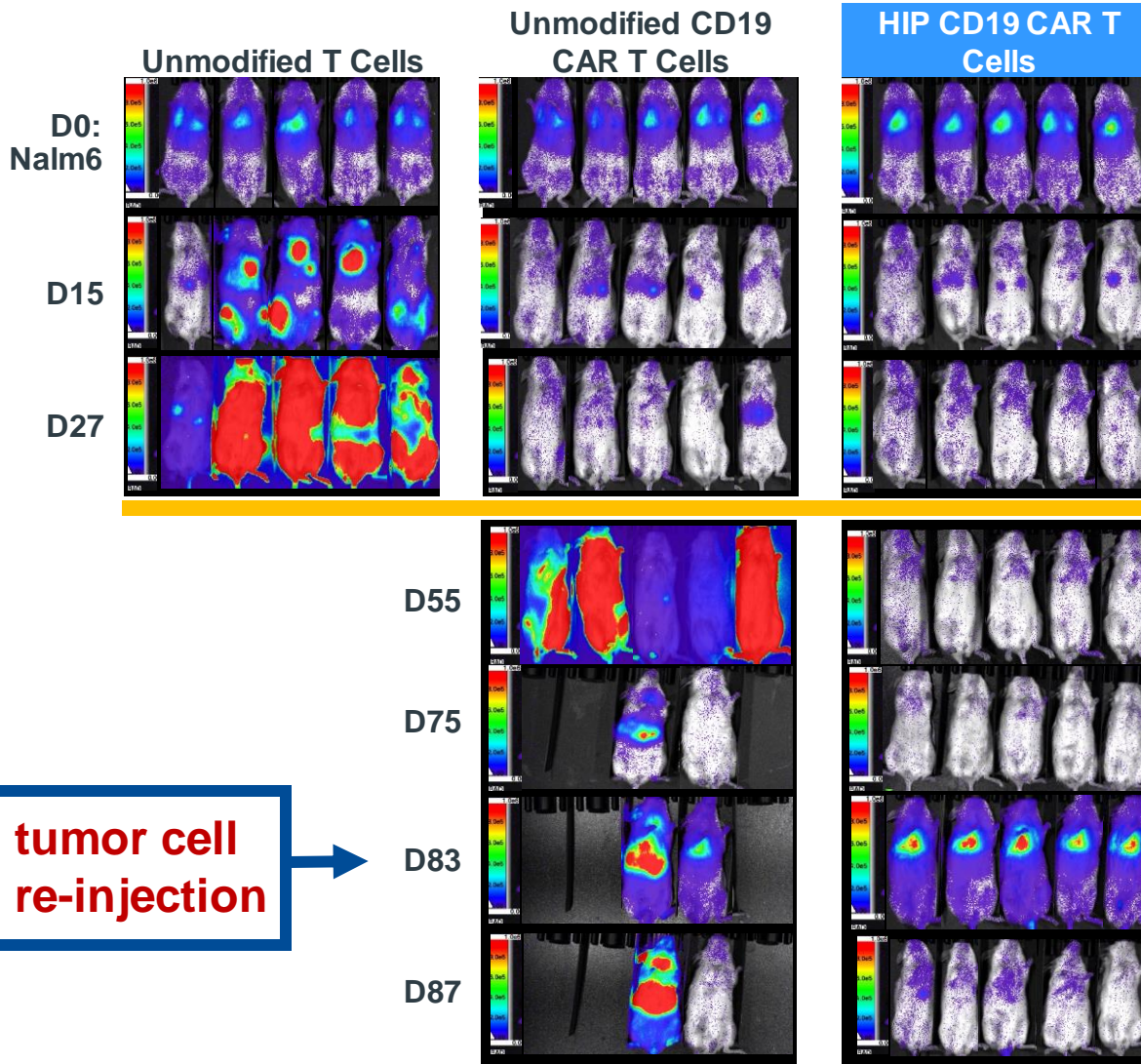
Sana's HIP platform can create a regenerative pipeline for allogeneic CAR T therapies



¹Based on current scale, assuming 50% hold back for analytical and other testing, and variability in dose in Phase 1 study.

Abbreviations: Cas 12b, CRISPR associated protein 12b; GPRC5D, G protein-coupled receptor, class C, group 5, member D; PBMC, peripheral blood mononuclear cell.

HIP CD19 CAR T cells demonstrate persistence and continued efficacy in humanized mice model

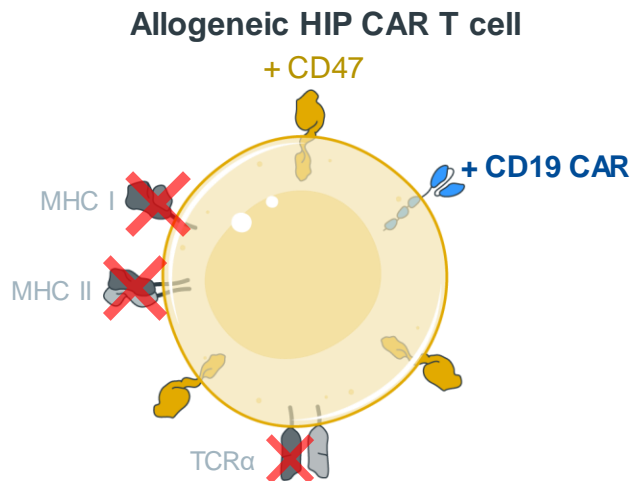


- SC291 tumor control comparable at early timepoints to standard CD19 CAR T cells
- SC291 tumor control superior at later timepoints to standard CD19 CAR T cells
- SC291 controls tumors when animals are rechallenged with tumor

Improved persistence can lead to best-in-class allogeneic CAR T platform

SC291: Sana's CD19 HIP allogeneic CAR T

- IND cleared
- First clinical data in 2023

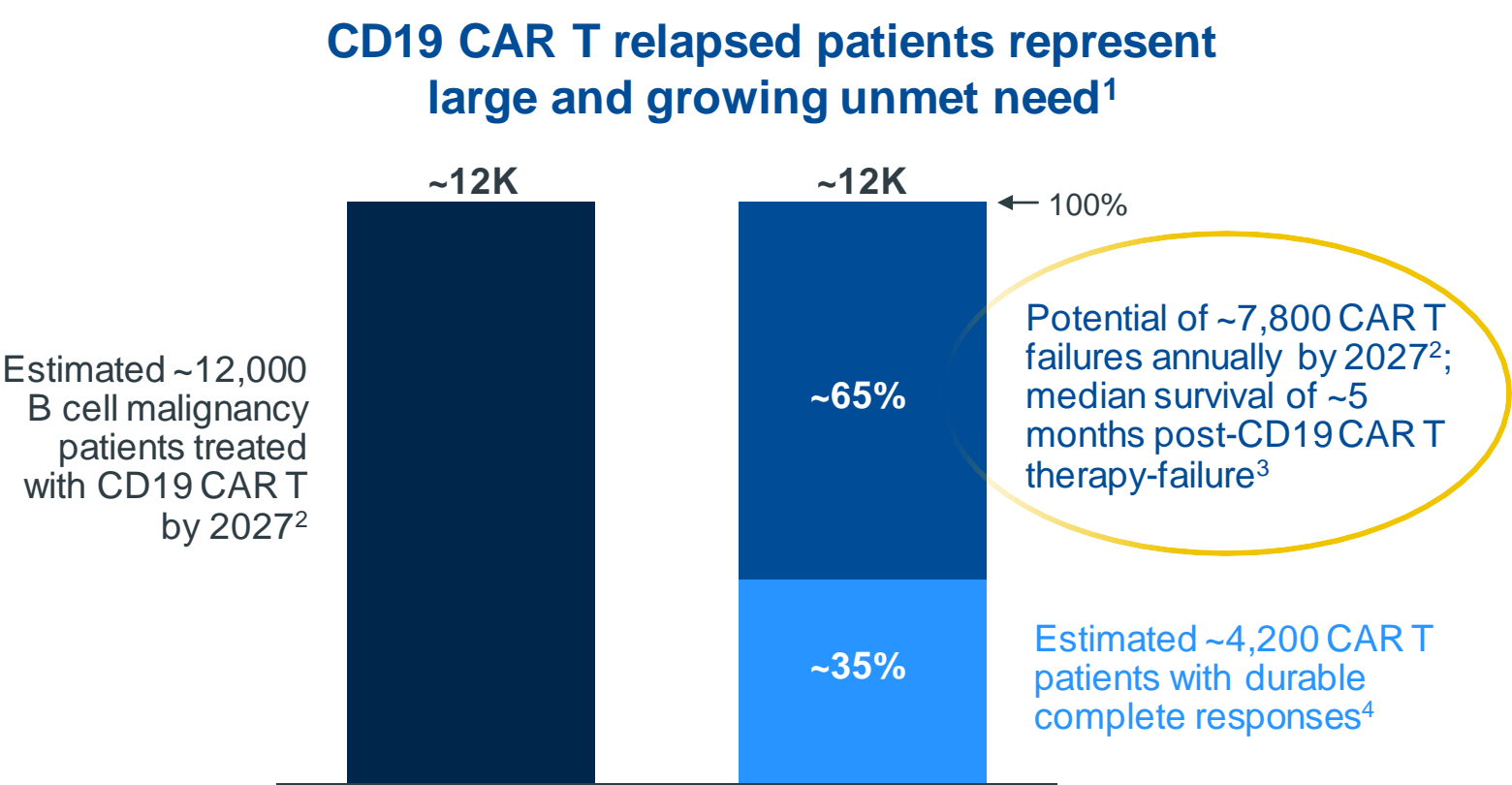


Data show CAR T cell persistence correlates with long term complete response (CRs) rates¹

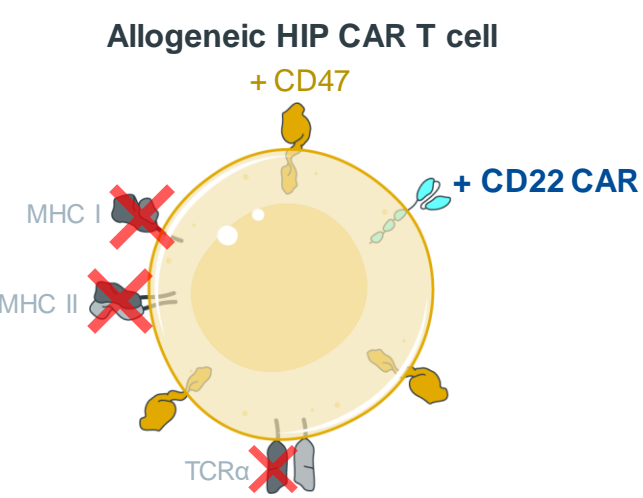
CAR T Persistence		Potential Efficacy Outcome
≤ 1 month	➤➤➤	Comparable to existing Allo CAR T
2 to 3 months	➤➤➤	Best-in-class Allo CAR T
3 to 6 months	➤➤➤	Comparable to Auto CAR T
≥ 6 months	➤➤➤	Better than Auto CAR T

¹Porter et al. *Science Translational Medicine*. 2015

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



SC262 utilizes a clinically-validated CD22 CAR



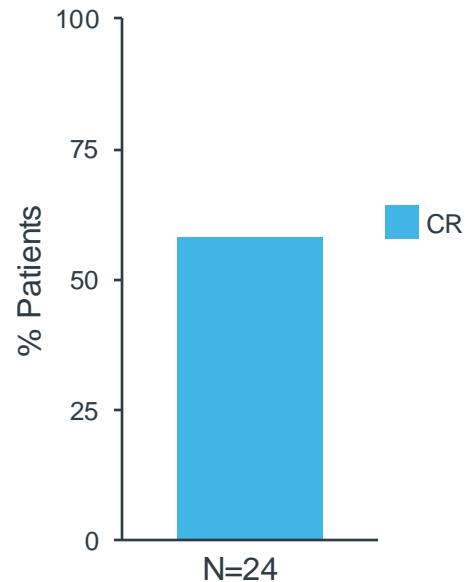
¹US, EU5, and Japan.

²Clarivate DRG NHL Market Forecast Nov 2021; 2027 Forecast is 2L+ LBCL patients.

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

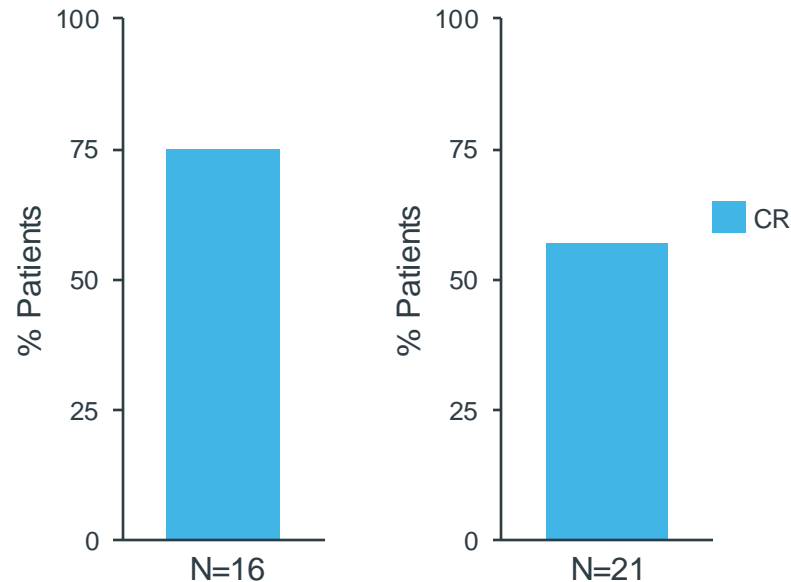
SC262: Licensed CD22 CAR produced strong clinical data in CD19 failures when part of autologous CAR T

>50% 6-month CR rate in CD19 CAR failure DLBCL patients



2021 ASH Miklos/Stanford

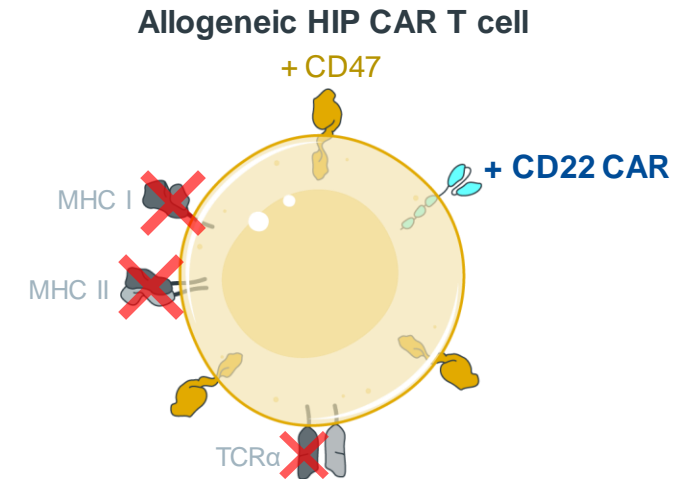
High rate of CRs in CD19 failure ALL patients
~80% patients with prior CD19 therapy



2022 ASH Miklos/Stanford

2018 Nature Med Fry, et al.

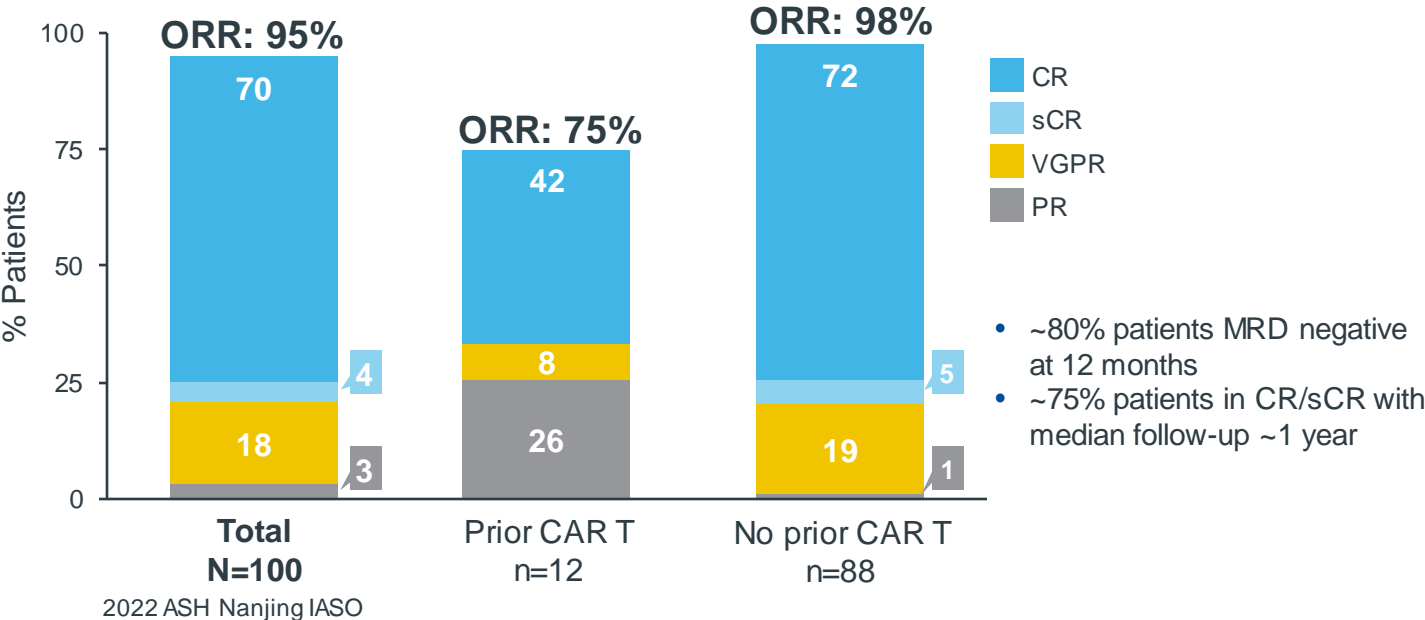
Expand our allo T platform to CD22 with Sana's SC262 candidate



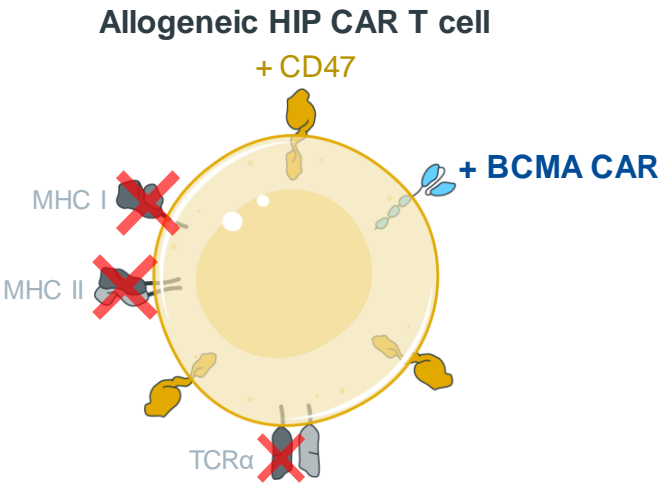
SC262 Goals: File IND this year; clinical data in 2024

SC255: Licensed BCMA CAR produced strong clinical data in myeloma when part of autologous CAR T

High response rate in multiple myeloma with 95% of patients MRD negative



Expand our allo T platform to BCMA with Sana's SC255 candidate



SC255 Goal: File IND as early as 2024

Abbreviations: CR, complete response; ORR, objective response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

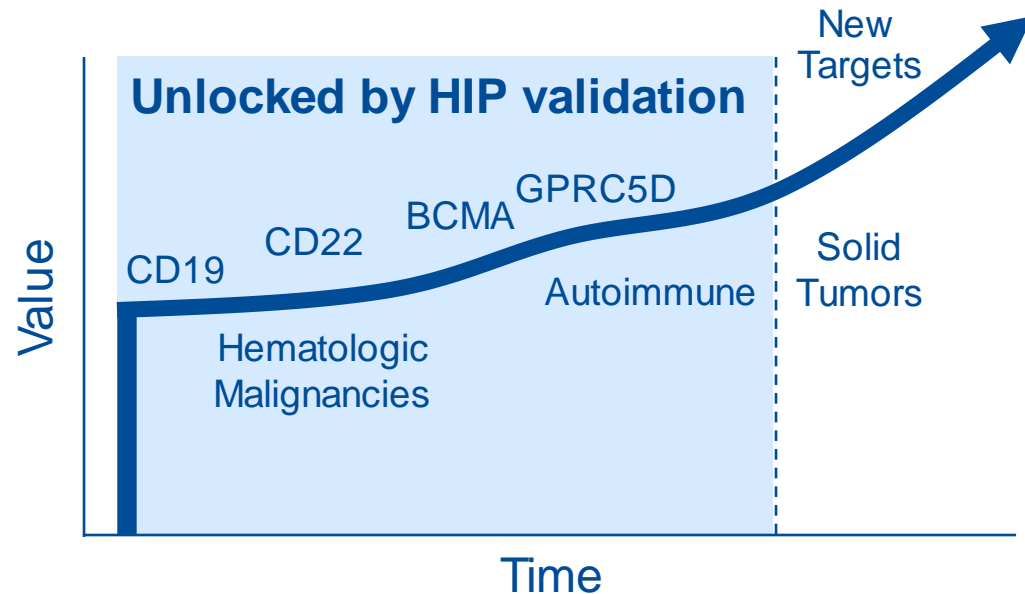
Goal is to build a best-in-class CAR T portfolio to treat patients with a range of cancers and beyond

Known

- ☒ Validated targets
- ☒ Validated CAR constructs
- ☒ >100,000 potential cancer patients worldwide^{1,2}
- ☒ HIP platform understood in preclinical models

Future State

- ☐ Potential for SLE and other autoimmune disorders
- ☐ Solid Tumors
- ☐ HIP platform understood in humans



Unlocking the potential of our allogeneic CAR T franchise across multiple patient populations

¹Avezbakiyev et al. *Blood*. 2022

²Durie et al. *The Oncologist*. 2020

Abbreviations: SLE, systemic lupus erythematosus.

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

- Disease caused by autoimmune destruction of insulin-producing beta cells in the pancreas; results in inability to control blood glucose
- Type 1 diabetes is a large unmet need with 1.6M patients in the U.S. and 2.4M in Europe²
- Long-term complications: end-organ damage, including heart attack, stroke, blindness, and kidney failure
- SC451 goal is euglycemia without exogenous insulin or immunosuppression



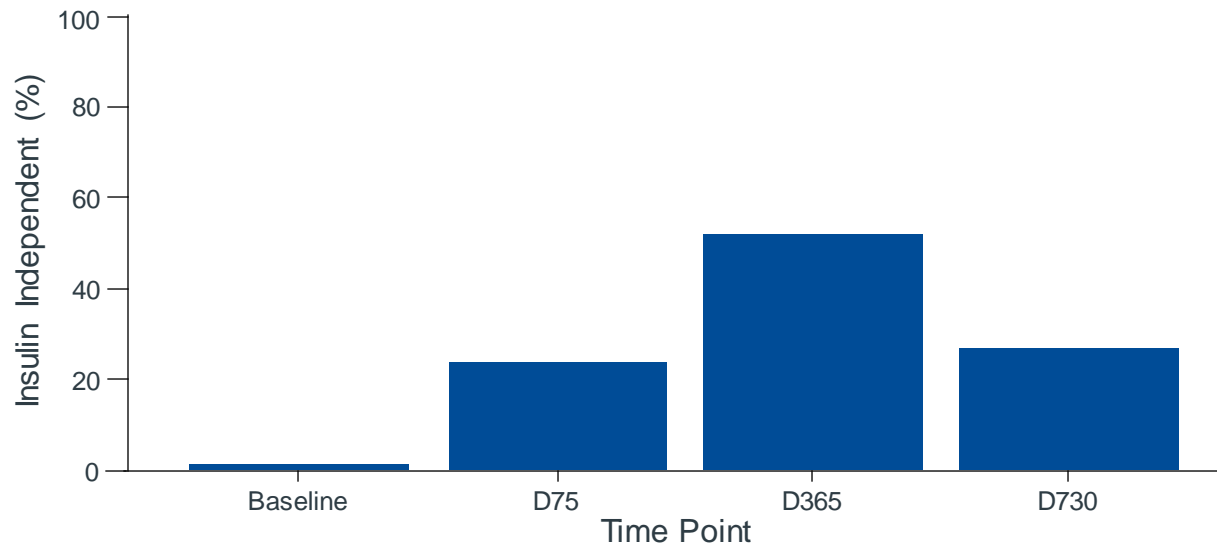
¹Rawshani et al. *Lancet*. 2018

²Centers for Disease Control and Prevention, *Diabetes Report*, 2017-2018.

Islet cell transplantation has been shown to work in type 1 diabetes

Islet cell transplants result in insulin independence in type 1 diabetics

- Phase 3 trial of primary islets showed 52% & 42% of patients become insulin independent at 1 & 2 years, respectively
- Utilization limited by need for lifelong immunosuppression

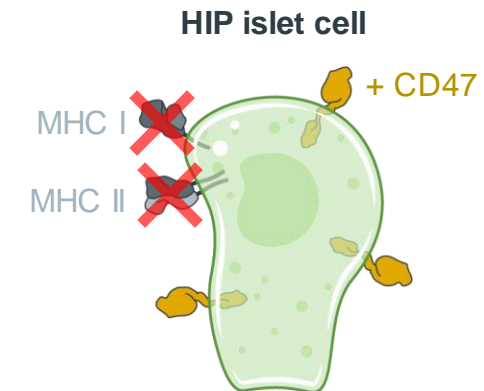


Hering et al, *Diabetes Care*. 2016.

N= 48 adults; demonstrated efficacy of islet transplant with 87.5%/71% achieving primary endpoint (HbA1c <7% and no serious hypoglycemia) at 1 and 2 years.

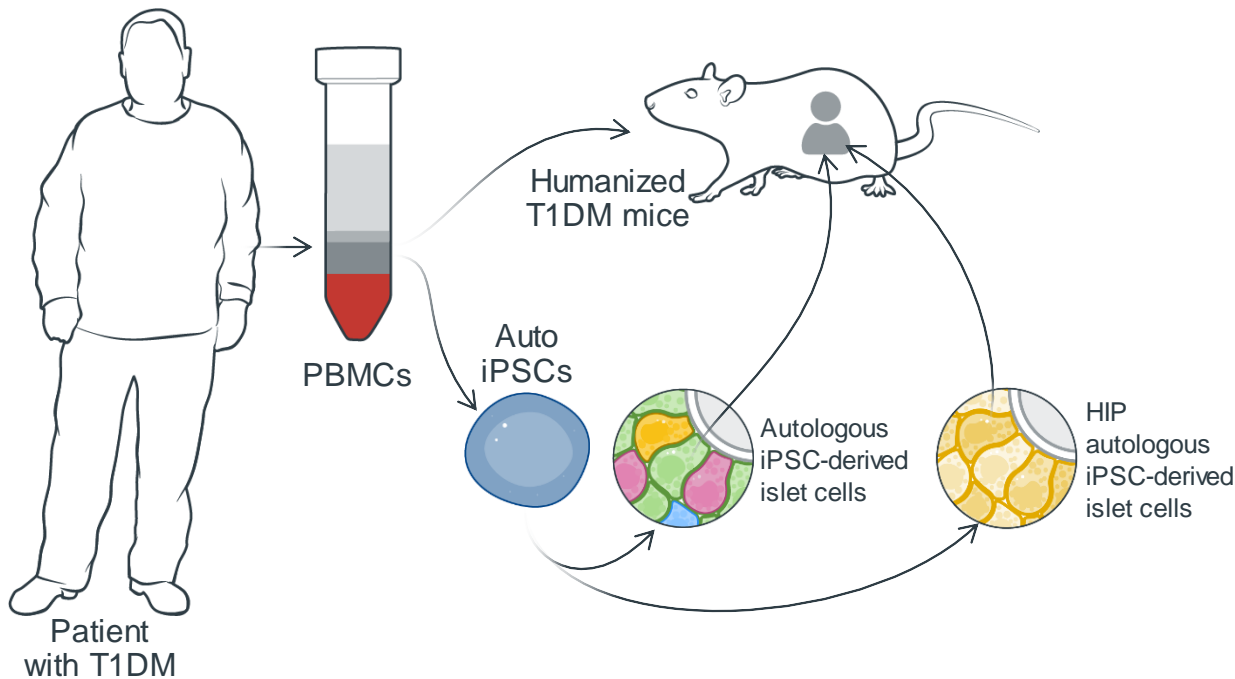
Sana's solution: Hypoimmune islet cells for type 1 diabetes (SC451)

- PSCs can provide scale and product consistency
- HIP has potential to eliminate immunosuppression, protecting against both allogeneic and autoimmune rejection

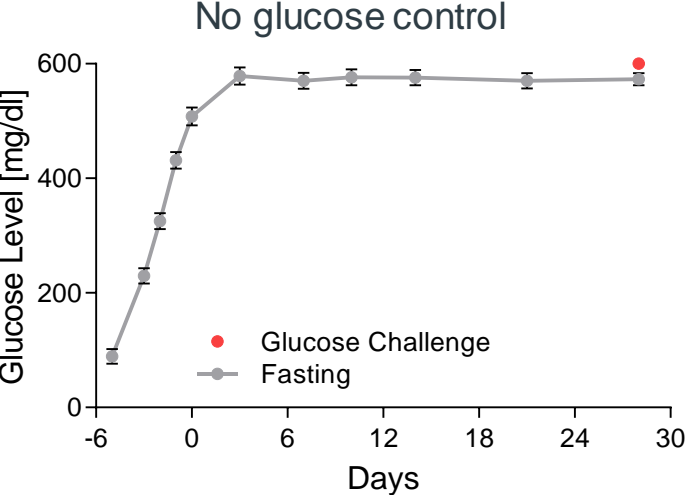


Sana's immunology, gene modification, & stem cell capabilities create proprietary type 1 diabetes model

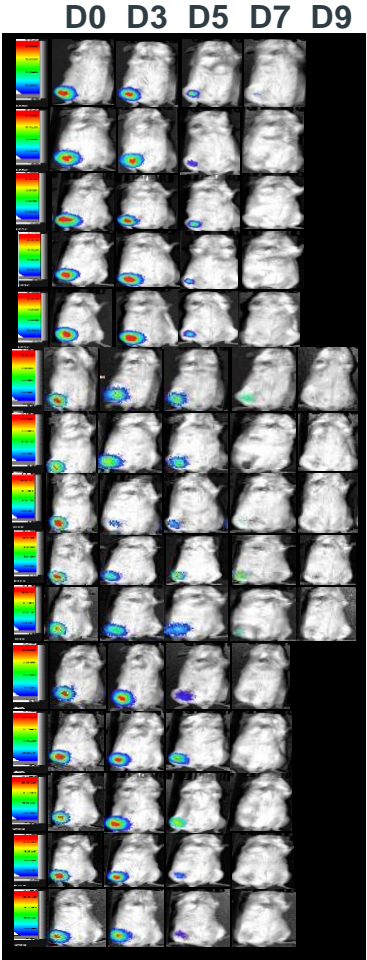
Type 1 diabetic PBMCs used to generate stem cell-derived islet cells and to humanize immune system in mice



Unmodified patient stem cell-derived islet cells do not survive

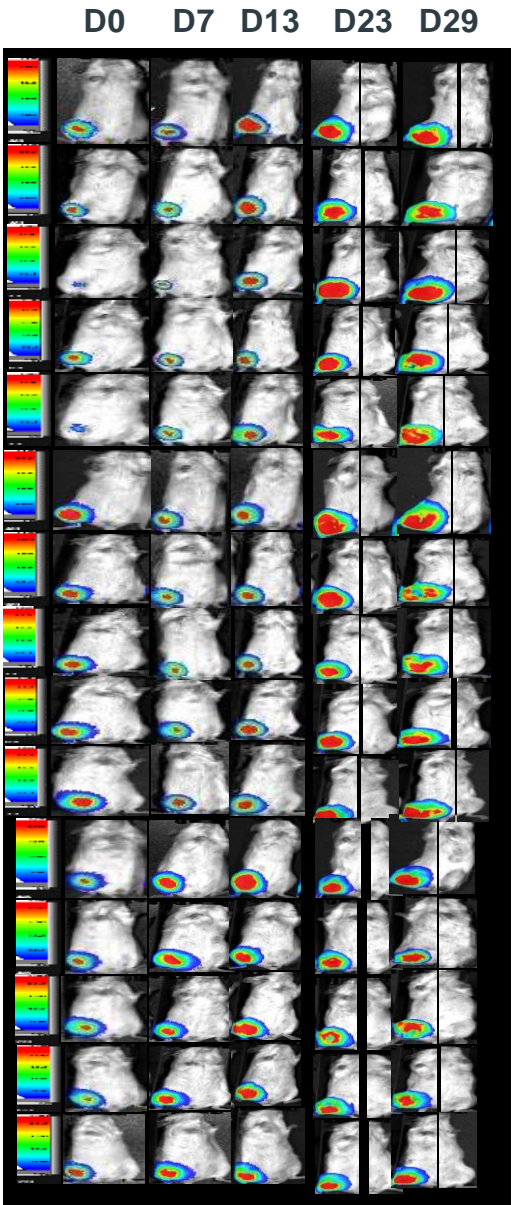
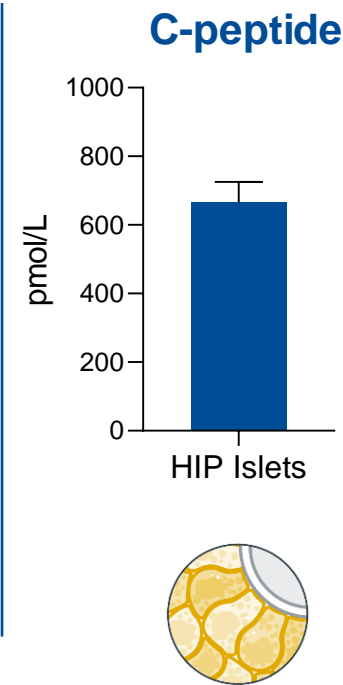
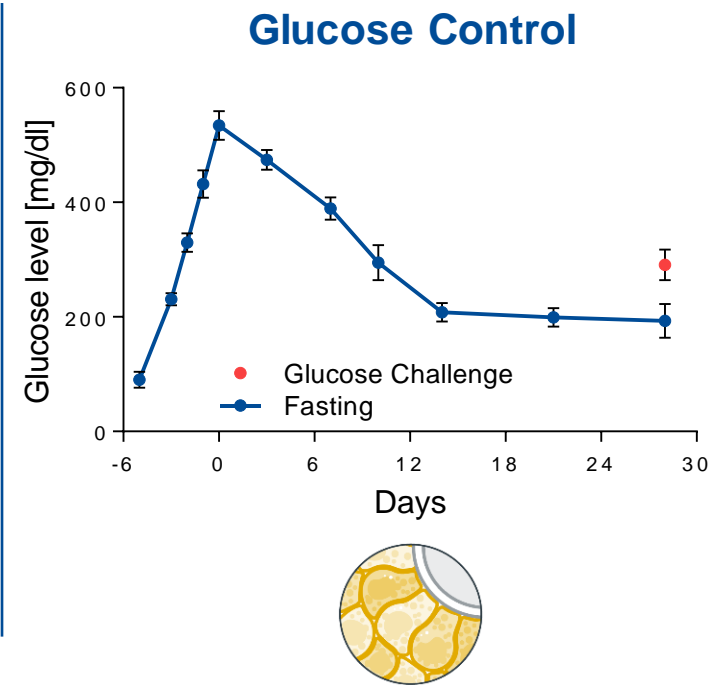
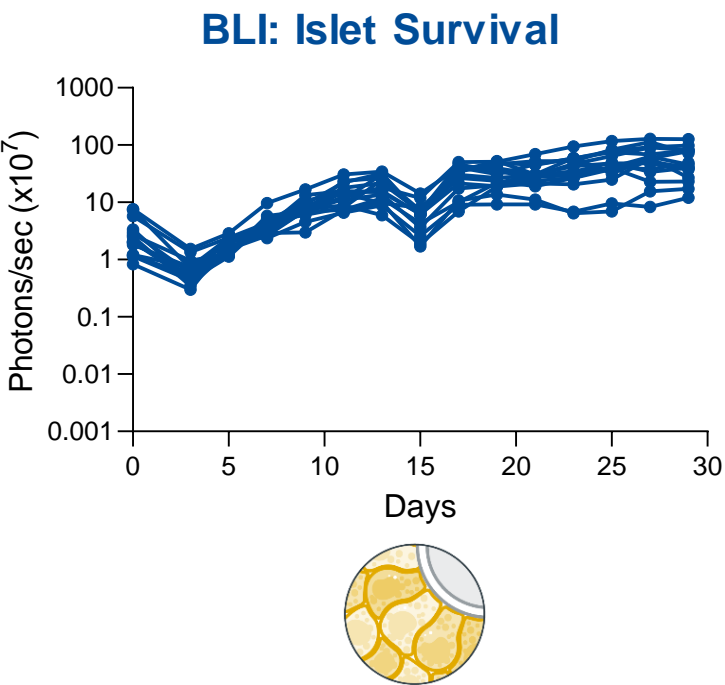


Patient T cells eliminate islet cells due to autoimmunity



Abbreviations: T1DM, type 1 diabetes mellitus.

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

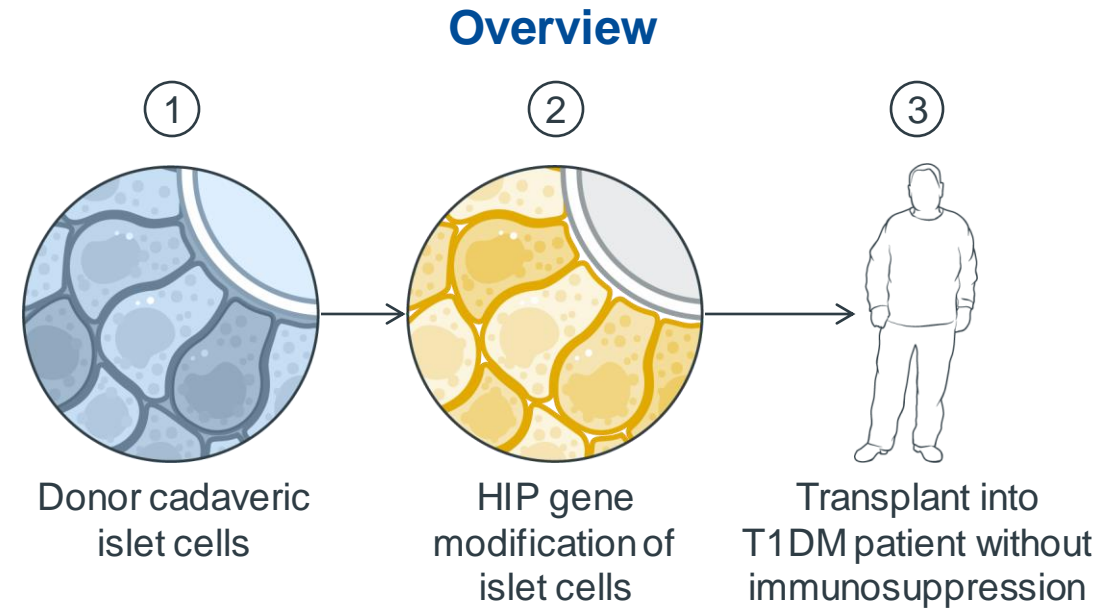


SC451 Goal: File IND and share clinical data in 2024

Abbreviations: BLI, bioluminescence imaging.

Path to potential clinical validation of hypoimmune islet cells in T1DM patients in 2023

- Investigator sponsored trial
- Primary human HIP islet cells transplantation in type 1 diabetes patients
- Goal: Cell survival with no immunosuppression
- Goal: Data in 2023
- Insight for SC451

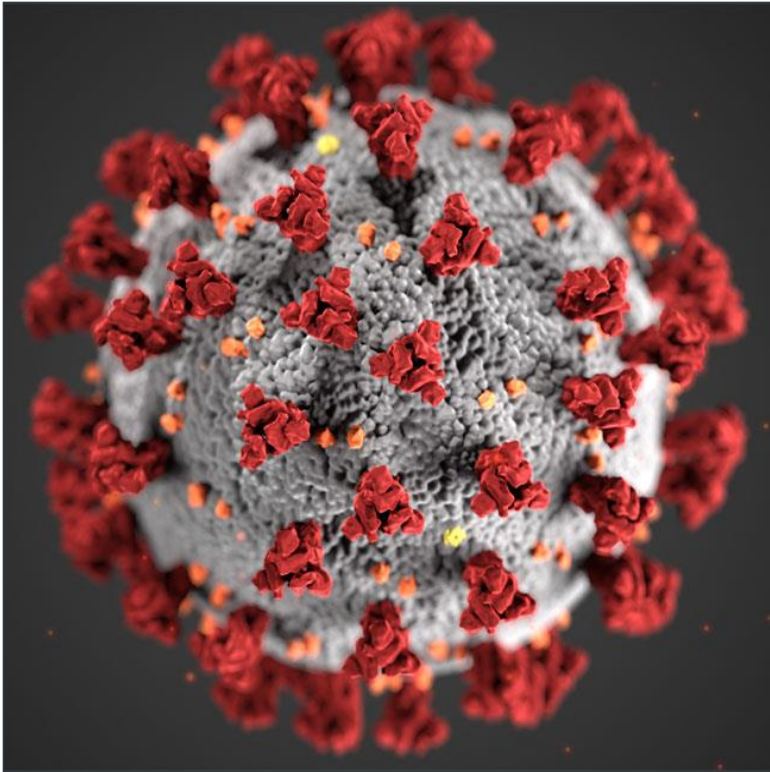


Key Measured Outcomes

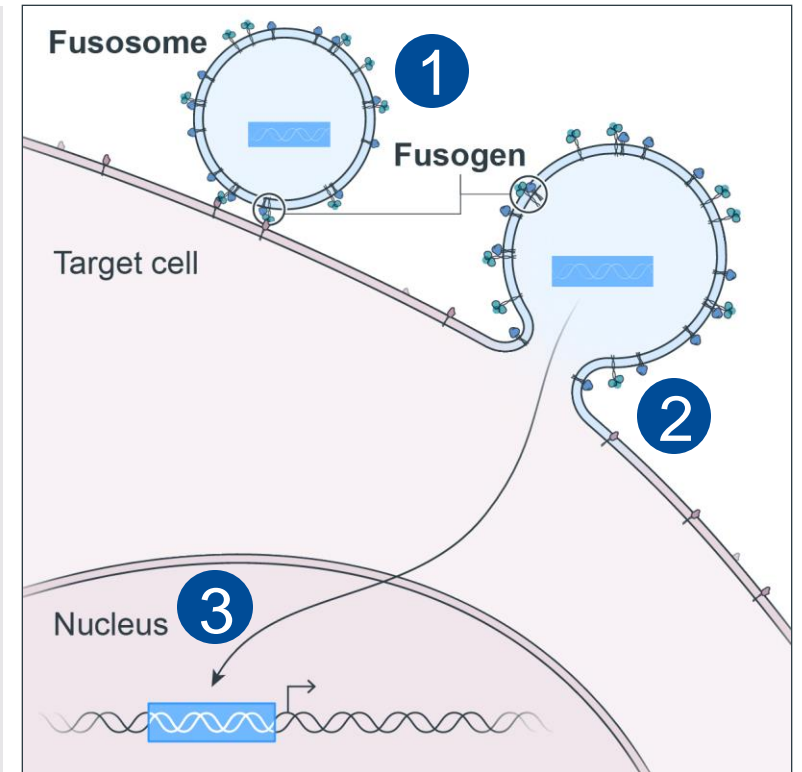
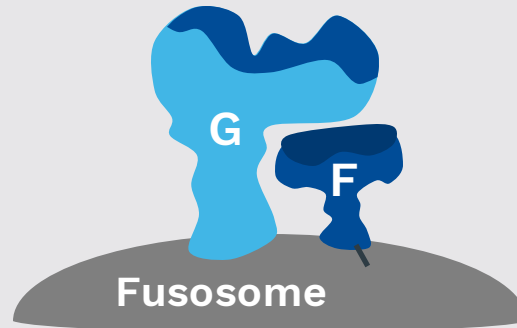
Cell survival & immune evasion
C-peptide
Glycemic control

Fusosome technology: Development of cell-specific *in vivo* delivery platform

Sana approach: Leverage insights from nature to deliver various payloads to specific cells



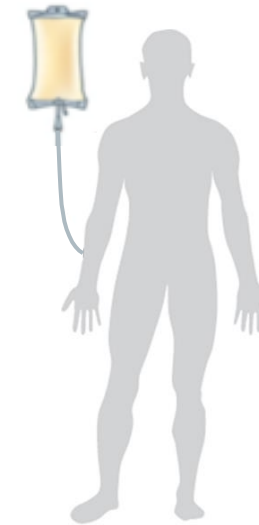
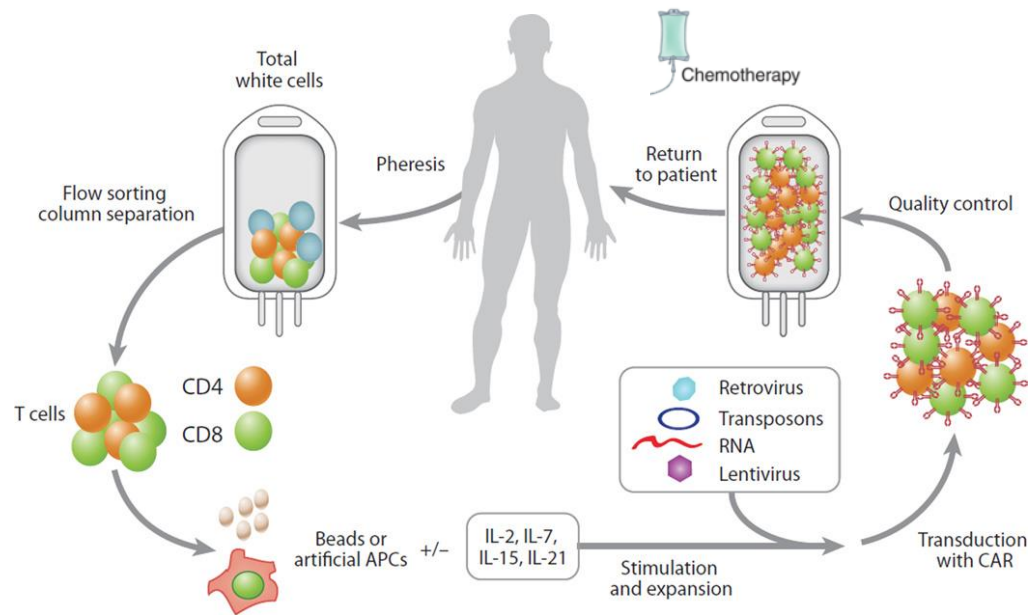
Source: CDC website



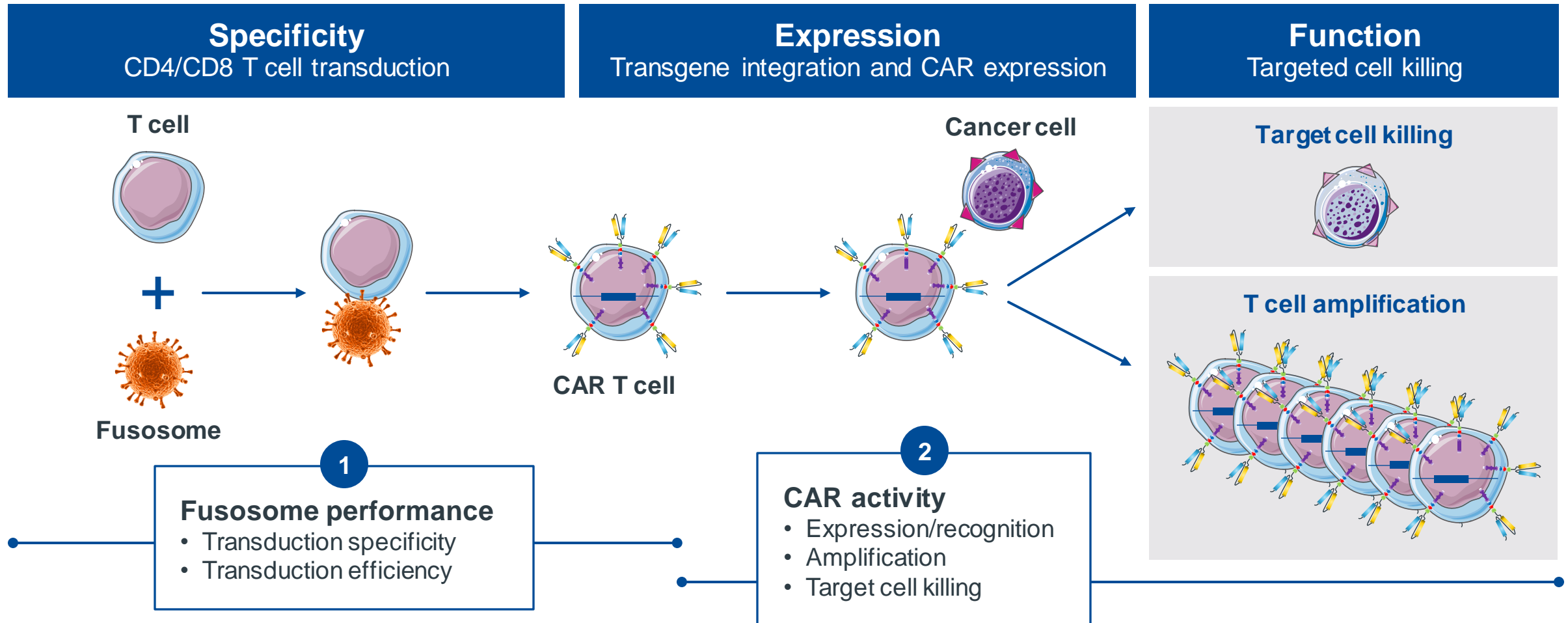
Fusogen technology has potential to eliminate conditioning chemotherapy and *ex vivo* manufacturing

Current *ex vivo* approaches have limitations

Fusogen platform offers potential to overcome these limitations

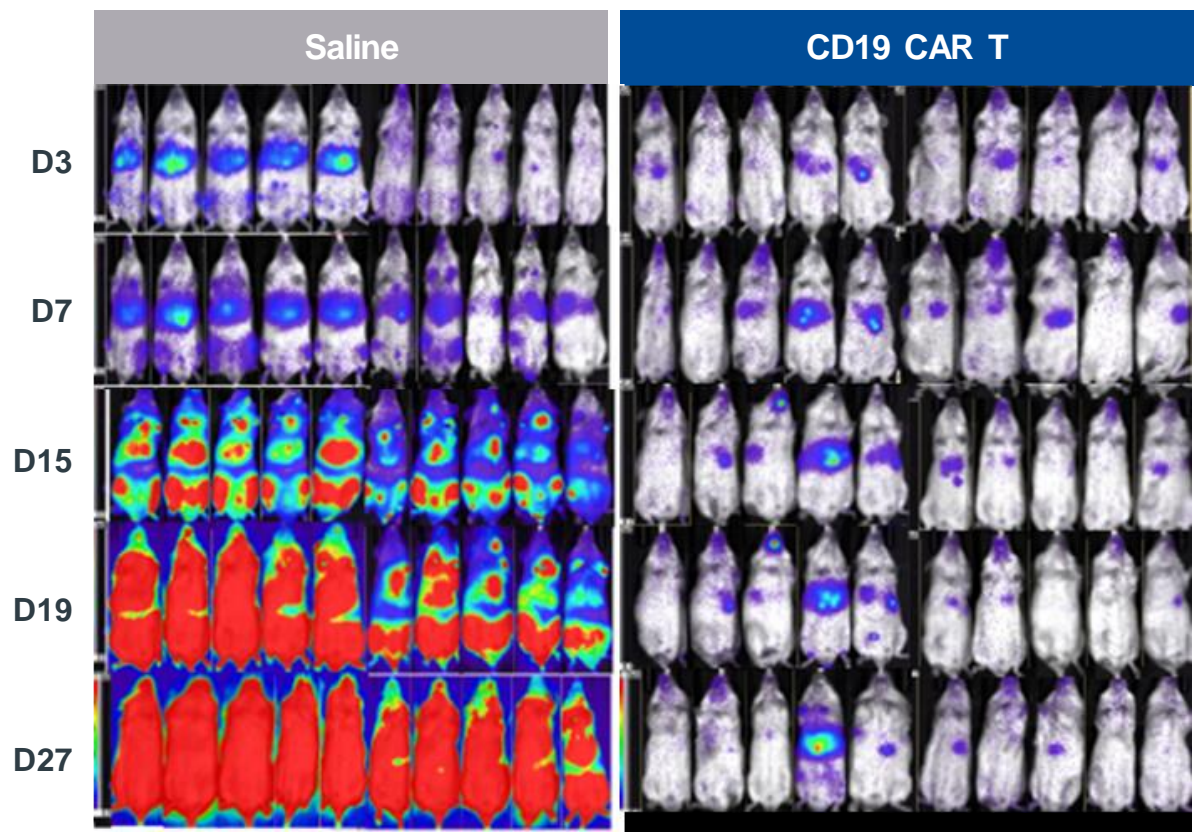


T cell fusosome delivers CAR construct directly to T cells *in vivo*

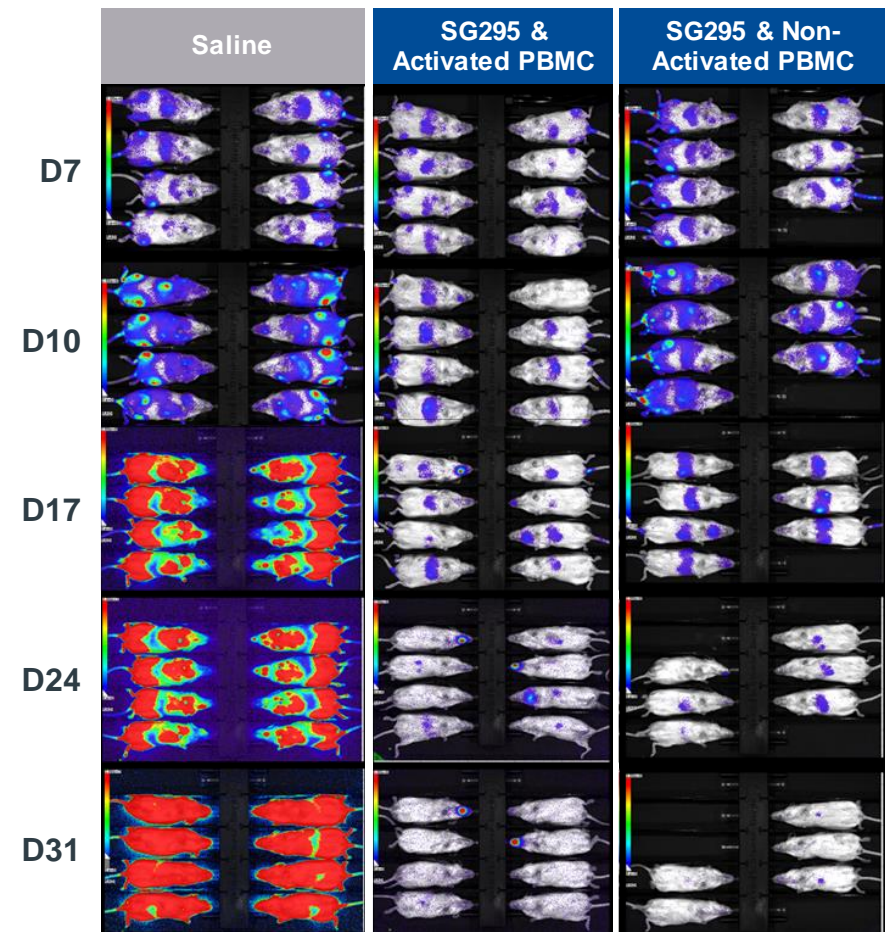


IV administration of CD19 CAR delivered by fusosome can clear B cell tumors in humanized mice comparably to *ex vivo* CD19 CAR T

CD19 CAR T: *ex vivo*

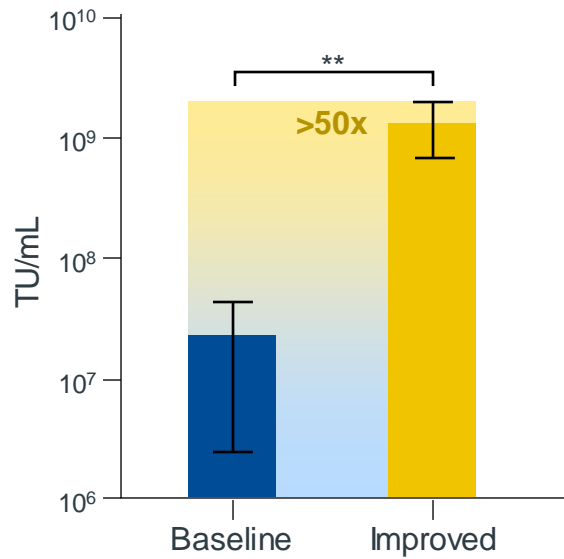


CD19 CAR delivered by fusosome: *in vivo*



Significant improvements in manufacturing process may lead to a better therapy

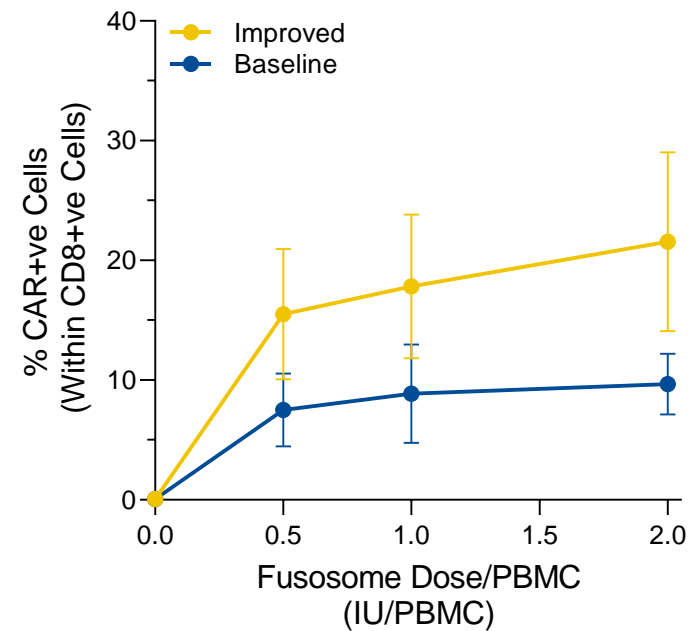
SG295 made with V2.0 process results in >50X potency improvement



Potential for:

- Better efficacy
- Greater safety
- Higher yields and lower cost of goods

SG295 made with V2.0 process transduces more T cells at the same dose



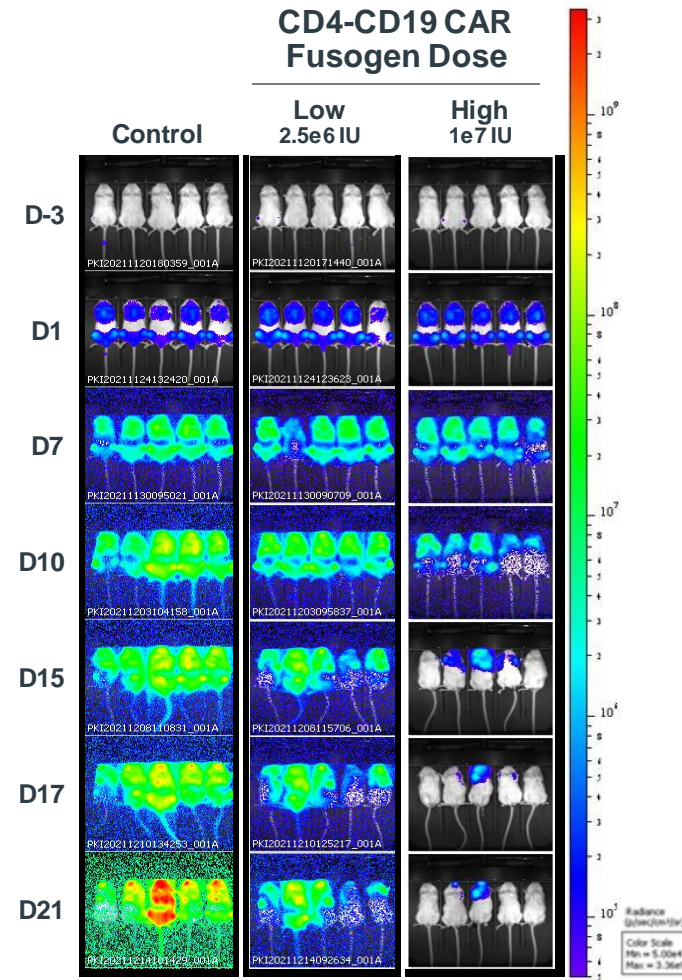
First clinical study incorporates SG295 made with V2.0 process

SC295 Goals: File IND in 2023; clinical data in 2024

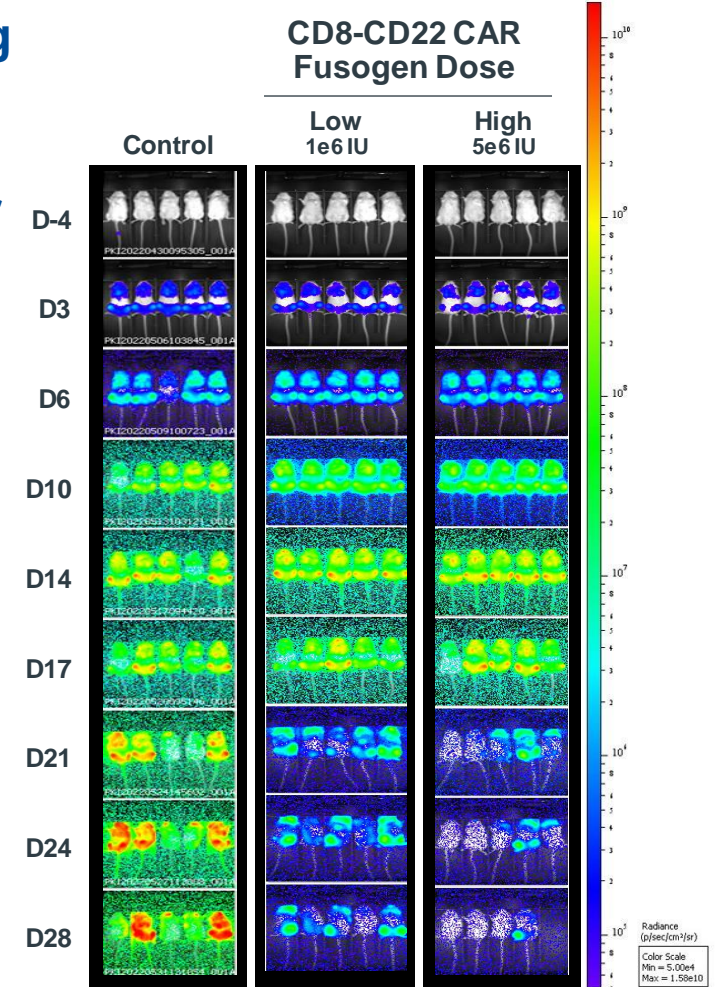
Abbreviations: TU, transduction units.

Tumor control achieved with fusosomes targeting other cell types and alternate tumor antigens

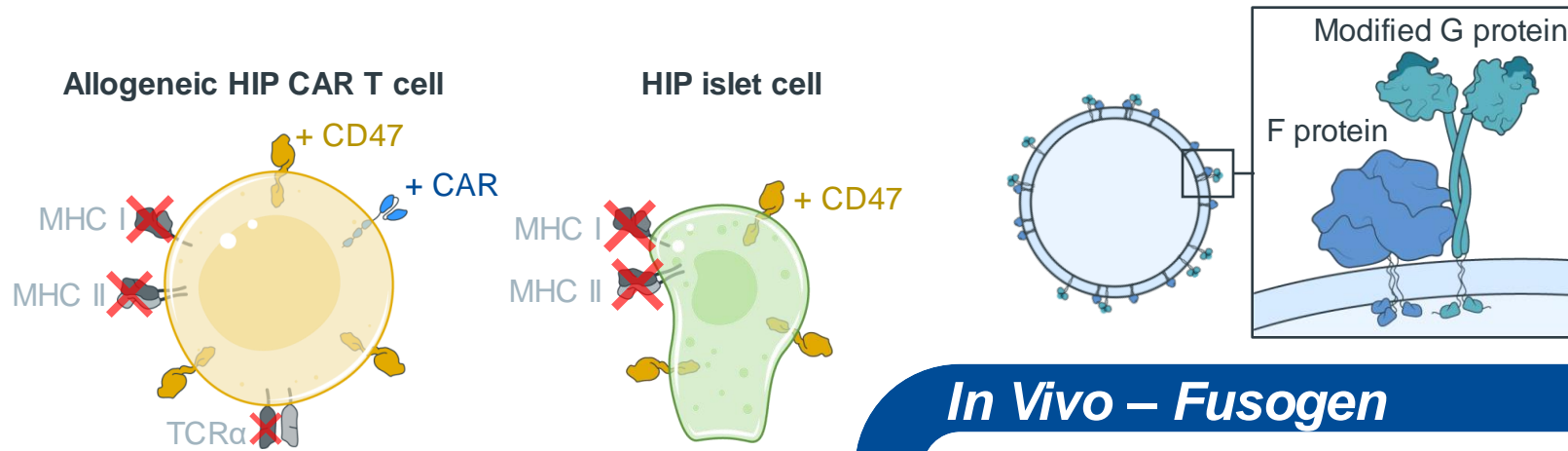
**CD4 T cell targeting
fusosomes
delivering CD19
CAR achieve tumor
control in mice**



**CD8 T cell targeting
fusosomes
delivering CD22
CAR achieve tumor
control in mice**



Sana aspiration: Engineered cells as medicines



Ex Vivo – Hypoimmune

Allogeneic CAR T Franchise

- Oncology: SC291, SC262, SC255
- Autoimmune

Stem Cell-Derived

- Type 1 Diabetes: SC451
- CNS: SC379¹

In Vivo – Fusogen

- *In vivo* CAR T: SG295
- Cell-specific *in vivo* HSC editing: SG418
- Cell-specific delivery of genomic modification material

Engineered cells into new therapeutic areas

2023

¹Does not incorporate hypoimmune genomic modifications

Thank You

Sana Biotechnology
www.sana.com

