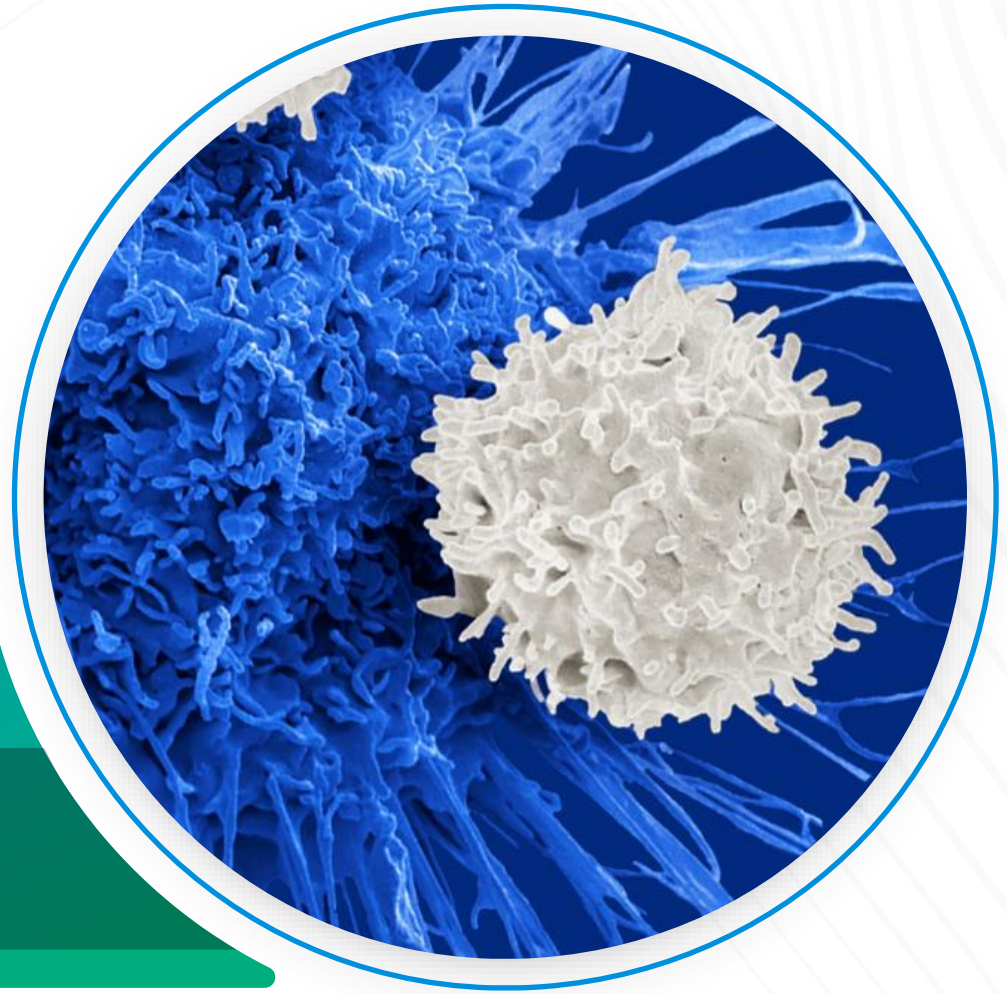
CENTURY THERAPEUTICS



CNTY-813: Scalable Production of Allo-Evasion 5.0-Engineered iPSC Islets for Off-the-Shelf Cell Therapies

Leonardo Velazco-Cruz, PhD

Disclosures

- **Presenter**
  - Leonardo Velazco-Cruz, PhD
- **Relevant Financial Relationship**
  - Employee, Century Therapeutics
  - Stock/Shareholder: Century Therapeutics
- **Presentation Information:**
  - This presentation describes preclinical research related to CNTY-813, an investigational iPSC-derived islet cell therapy for T1D
  - The content is intended for scientific and educational discussion
  - No clinical recommendations will be made

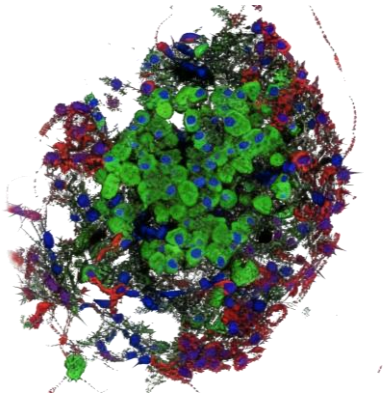
Forward-looking statements

This presentation contains forward-looking statements within the meaning of, and made pursuant to the safe harbor provisions of, The Private Securities Litigation Reform Act of 1995. All statements contained in this presentation, other than statements of historical facts or statements that relate to present facts or current conditions, including but not limited to, statements regarding our clinical development plans and timelines and the initial safety and efficacy profiles of CNTY-813 and statements regarding our preclinical development programs, including initial preclinical data and development plans and timelines are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “should,” “expect,” “plan,” “aim,” “seek,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “forecast,” “potential” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this presentation are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition, and results of operations. These forward-looking statements speak only as of the date of this presentation and are subject to a number of risks, uncertainties and assumptions, some of which cannot be predicted or quantified and some of which are beyond our control, including, among others: our ability to successfully advance our current and future product candidates through development activities, preclinical studies, and clinical trials; our ability to progress CNTY-813 through clinical development; our ability to meet development milestones on anticipated timelines; uncertainties inherent in the results of preliminary data, pre-clinical studies and earlier-stage clinical trials, which may not be predictive of final results or the results of later-stage clinical trials; our ability to obtain clearance of our future IND or CTA submissions and commence and complete clinical trials on expected timelines, or at all; our reliance on the maintenance of certain key collaborative relationships for the manufacturing and development of our product candidates; the timing, scope and likelihood of regulatory filings and approvals, including final regulatory approval of our product candidates; the impact of geopolitical issues, trade disputes and tariffs, banking instability and inflation on our business and operations, supply chain and labor force; the performance of third parties in connection with the development of our product candidates, including third parties conducting our clinical trials as well as third-party suppliers and manufacturers; our ability to successfully commercialize our product candidates and develop sales and marketing capabilities, if our product candidates are approved; our ability to recruit and maintain key members of management and our ability to maintain and successfully enforce adequate intellectual property protection. These and other risks and uncertainties are described more fully in the “Risk Factors” section of our most recent filings with the Securities and Exchange Commission and available at www.sec.gov. You should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that we may face. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

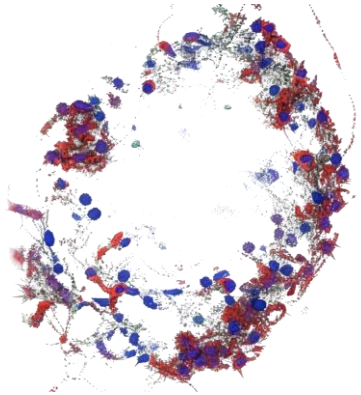
Islet cell transplantation provides potential for curative therapy in T1D

In T1D, beta cells are destroyed

Healthy beta cells produce insulin (green)



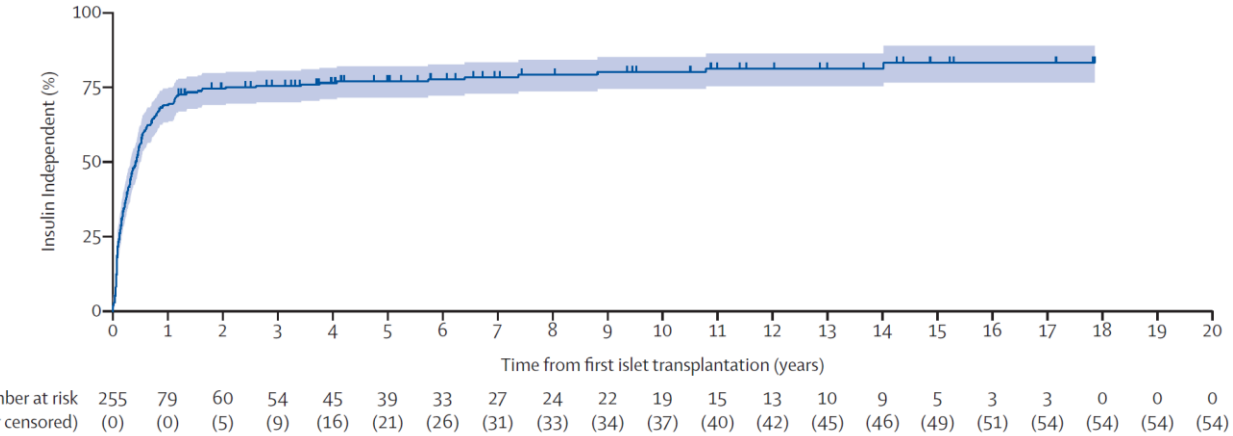
In T1D, beta cells are destroyed



Islet transplantation provides a potentially curative therapy for T1D

Insulin independence achieved for one year in ~70% of patients receiving allogenic cadaveric islet transplantation[1]

Insulin independence following pancreatic islet transplantation



Source: Marfil-Garza et al. 2022; Pancreatic islet transplantation in type 1 diabetes: 20-year experience from a single-centre cohort in Canada

Supply and chronic immunosuppression limit the broader use of T1D cell therapies

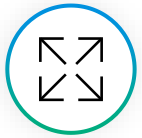
CNTY-813: Century's islets with Allo-Evasion 5.0 are designed to address key challenges in T1D cell therapy

1. Approximately 1500 patients reported in https://www.citregistry.org/system/files/CITR%2012th%20Allograft%20Report_2025_Final.pdf

CNTY-813 design integrates key capabilities for off-the-shelf T1D cell therapy

DIFFERENTIATION PLATFORM

- Scalable iPSC-derived islet manufacturing
- Reproducible islet differentiation
- Clinical manufacturing process from GMP MCB



FUNCTIONAL ISLETS

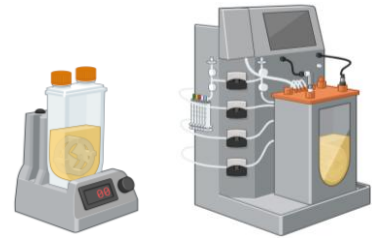
- Glucose-responsive insulin secretion
- In vivo glucose control in diabetic mice
- No safety events observed to date in preclinical models
  - i.e., cyst or tumor formation

ALLO-EVASION™ 5.0

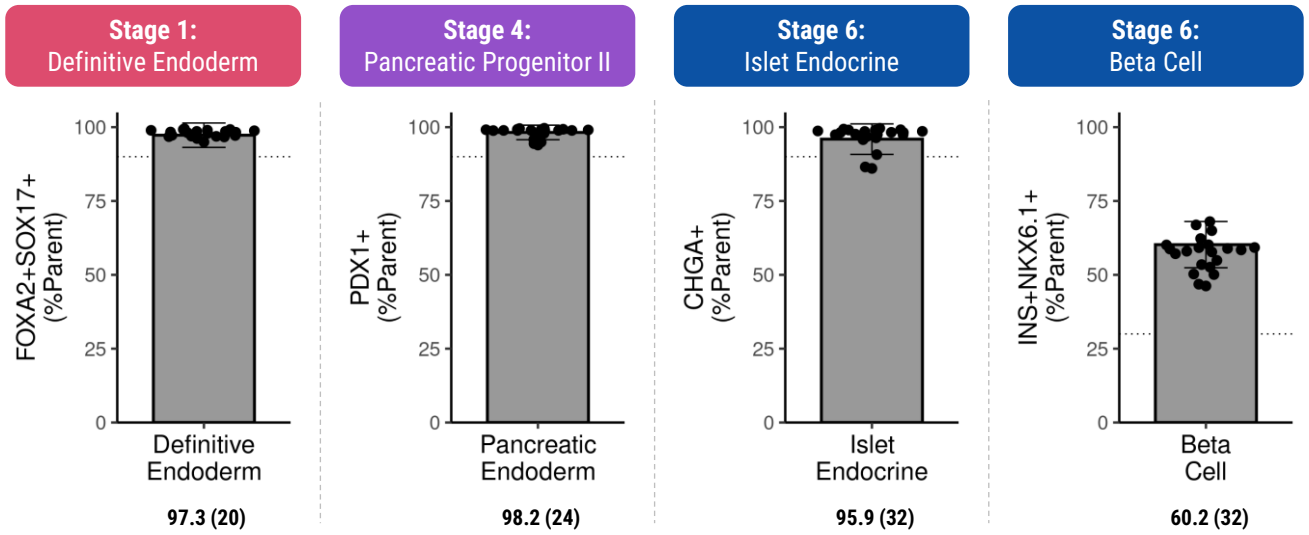
- T cell protection
- NK cell protection
- Reduced humoral immune clearance

Scalable manufacturing, islet function, and immune-evasive engineering address key barriers for T1D cell replacement

Defined, Multi-stage Bioreactor Enabled Differentiation Process



Adapted to a Scalable Bioreactor Suspension System



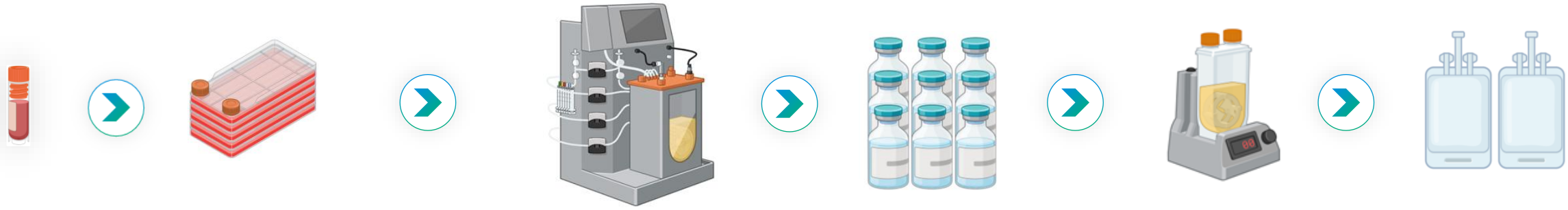
Consistent Differentiation

- Surpassed the necessary purity at every stage
- >95% Endocrine
- 50-60% Beta Cells (Insulin Producing)

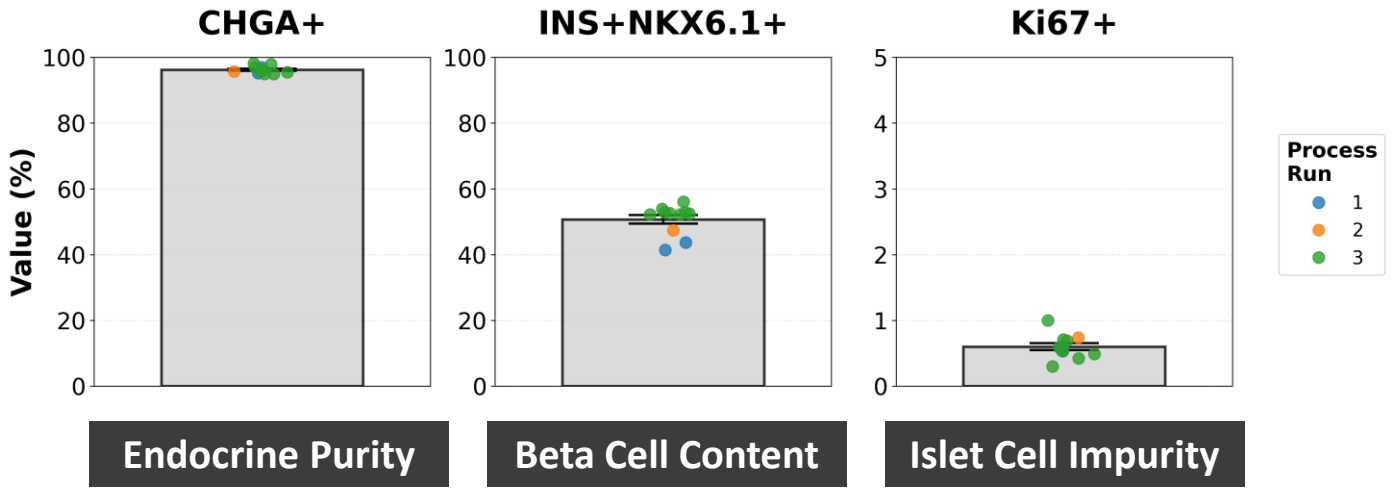
- Dotted lines: success criteria
- N are independent batches.
- Source: Company data on file

Phase 1 clinical manufacturing process established and executed from MCB across 3 independent batches

MCB Thaw → iPSC Expansion → Bioreactor Differentiation → Cryopreserved Intermediate → Post-Thaw Maturation → Final Fresh Product



Consistent final product flow cytometry profiles across 3 at-scale batches



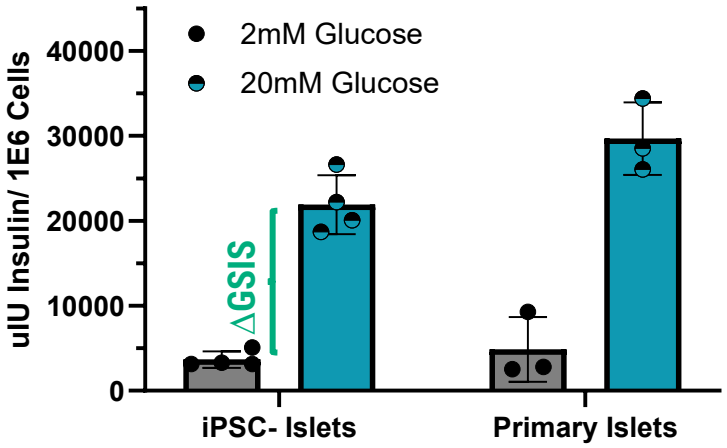
- 3 Batches
- 11 Samples

Source: Company data on file

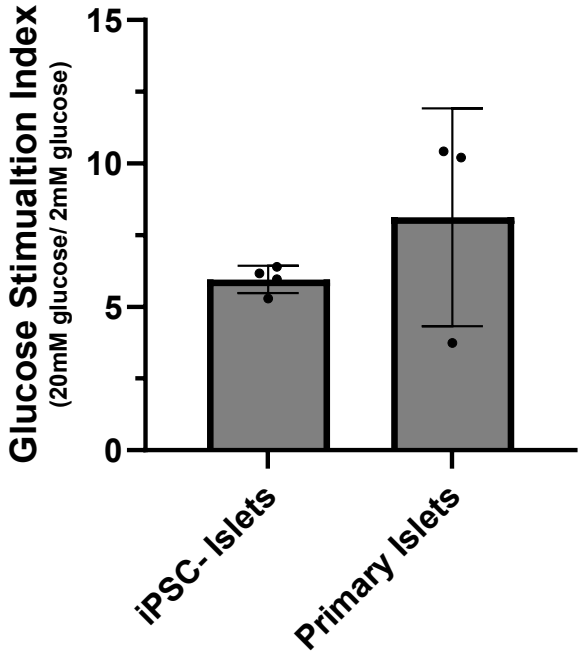
CNTY-813 islet cells demonstrate robust glucose-responsive function

Potency

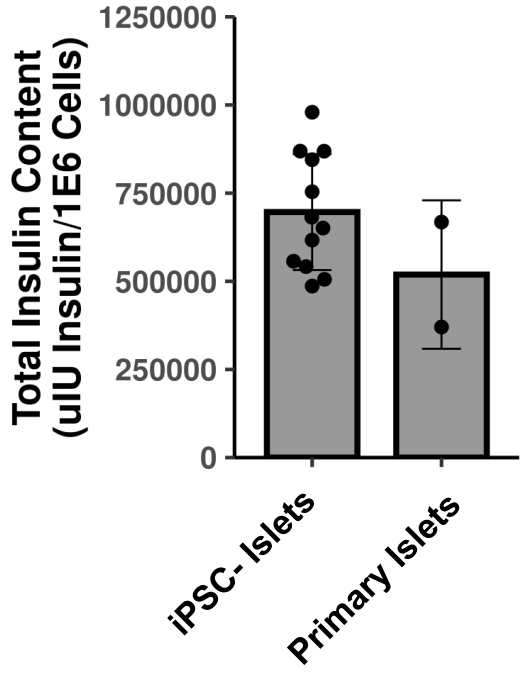
Glucose Stimulated Insulin Secretion



Stimulation Index



Total Insulin Content



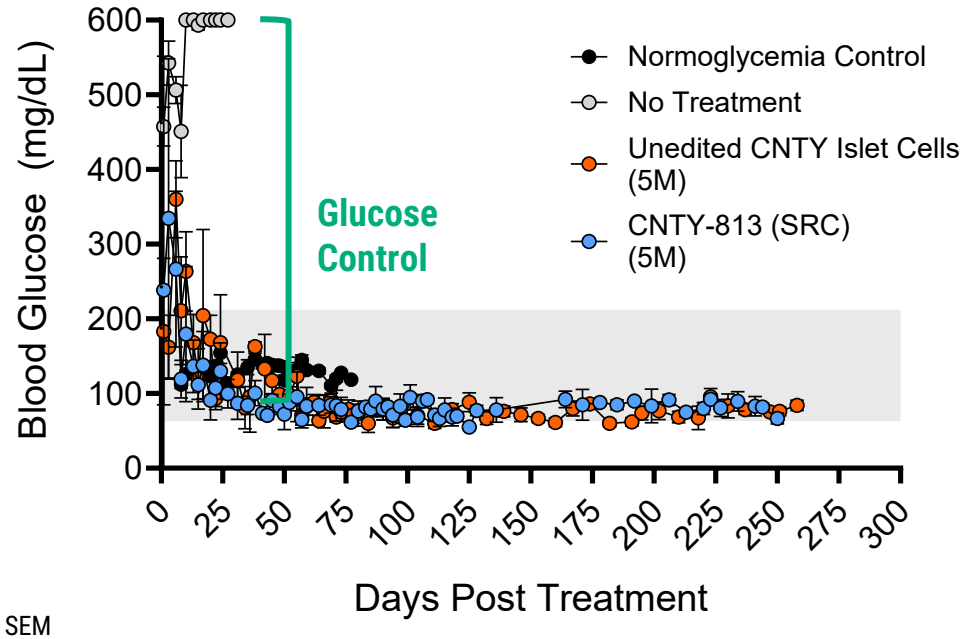
Mean +/- SD is shown in graphs

Source: Company data on file

CNTY-813 islets rapidly restored normoglycemia in STZ-induced diabetic mice

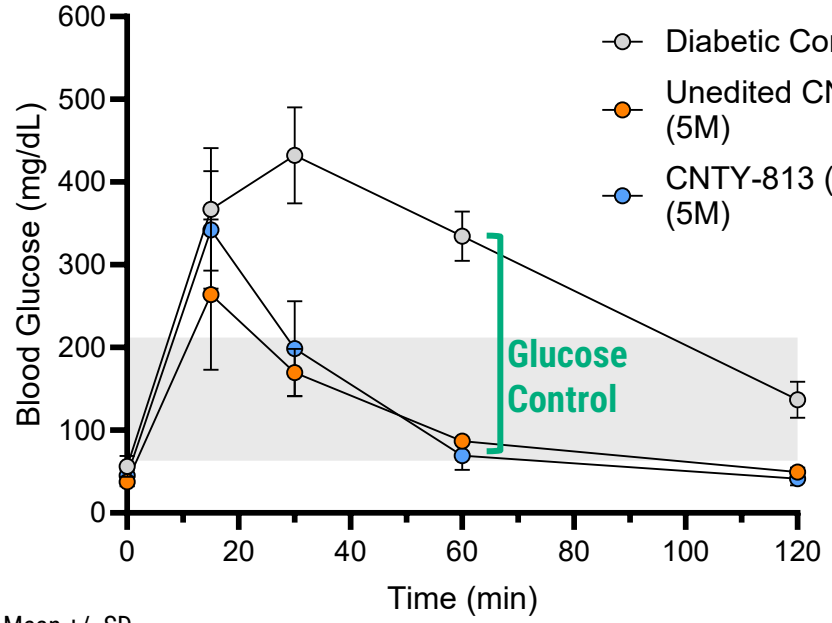
Potency

Non-Fasted Blood Glucose



Mean +/- SEM

Glucose Tolerance Test



Mean +/- SD

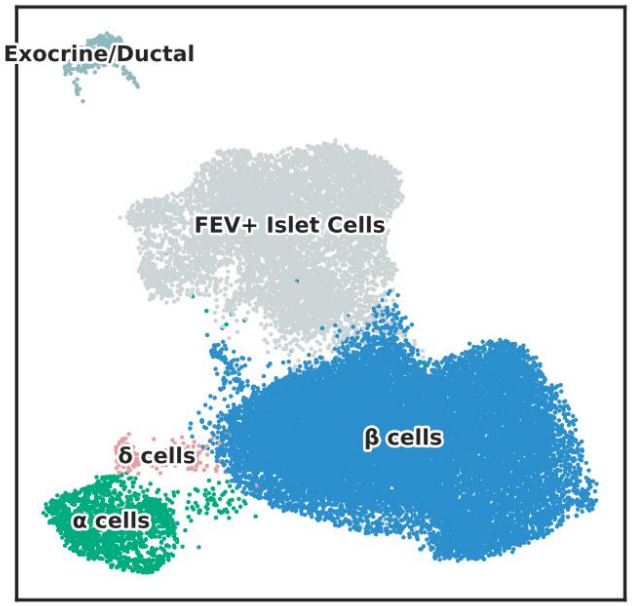
Allo-Evasion 5.0-edited CNTY-813 restored glucose control comparable to unedited islets and persists for >8 months

STZ = Streptozotocin | SRC = Sub renal capsule implantation, Gray shaded area = normal blood glucose range

Source: Company data on file

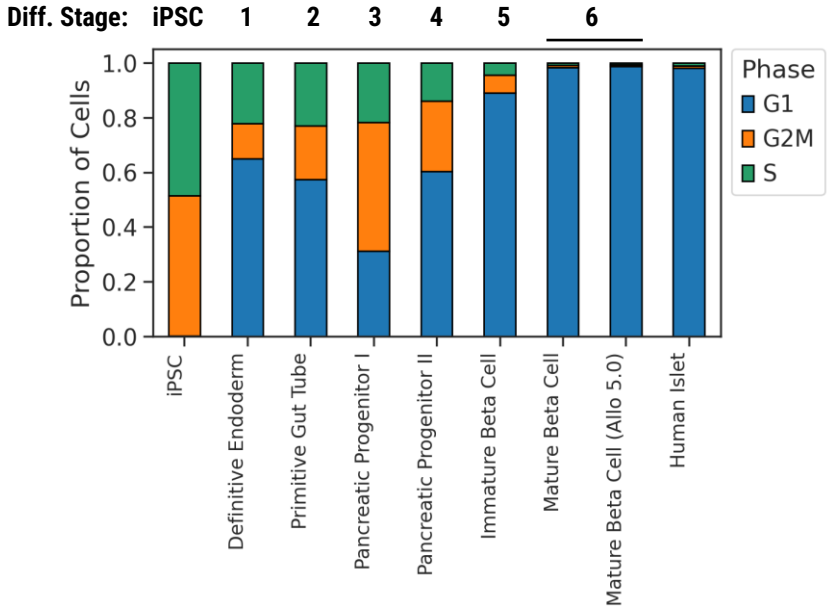
CNTY-813 islets contain defined endocrine cell populations

scRNAseq Cell Type Annotations



Population (30,151 total)	Frequency
β cells:	**66.3%**
FEV+ Islet Cells	26.4%
α cells	5.5%
δ cells	0.8%
Exocrine/Ductal	1.0%

scRNAseq Cell Cycle Annotations



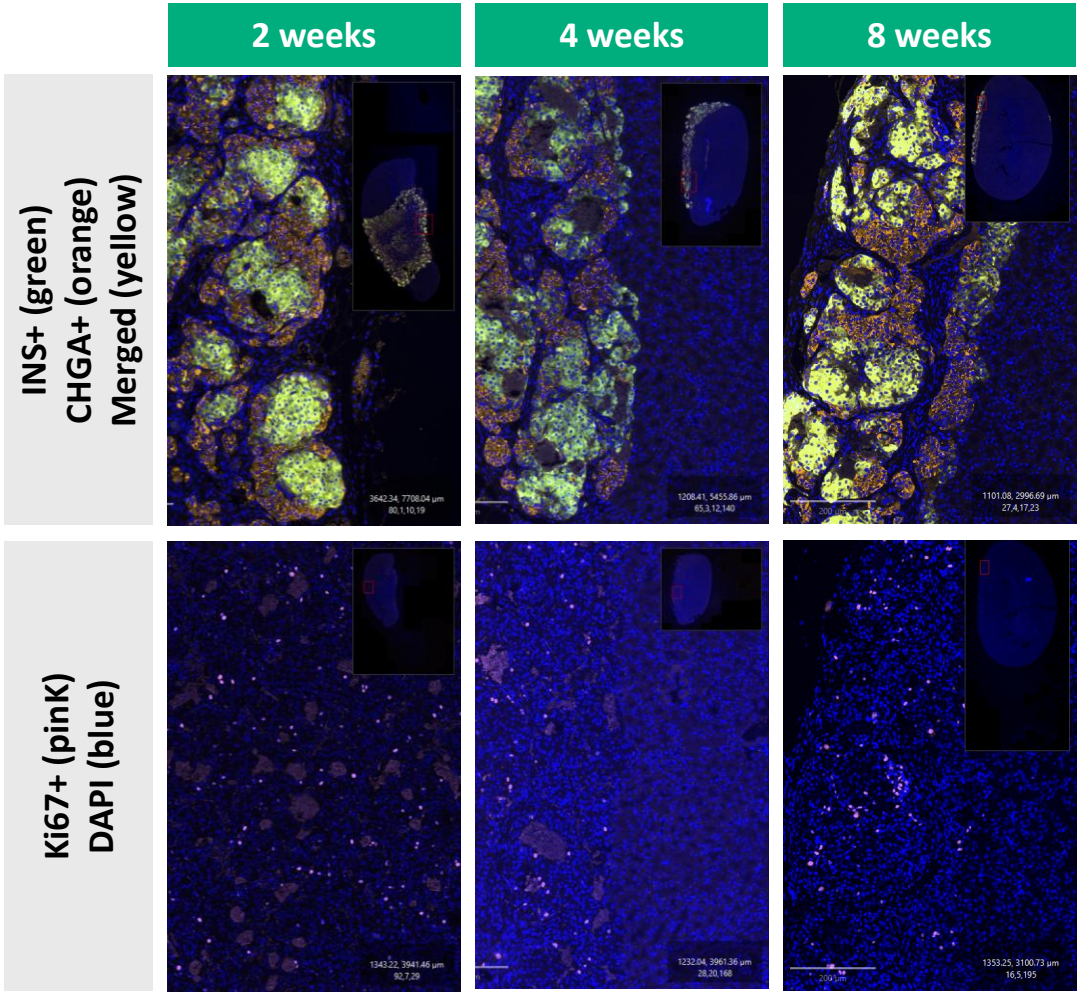
- CNTY-813 achieves a defined islet endocrine composition, with beta cells as the predominant population
- Data is consistent with cell cycle exit on par with primary islets by end of manufacture (>98% G1 phase identity)

CNTY-813 data represents four combined end-of-process samples

Population Enriched Markers: β-cell: INS, NKX6.1; α-cell: GCG,ARX; δ-cell: SST; Exocrine/Ductal: KRT19; FEV+ Islet Cell: FEV+SLC18A1+

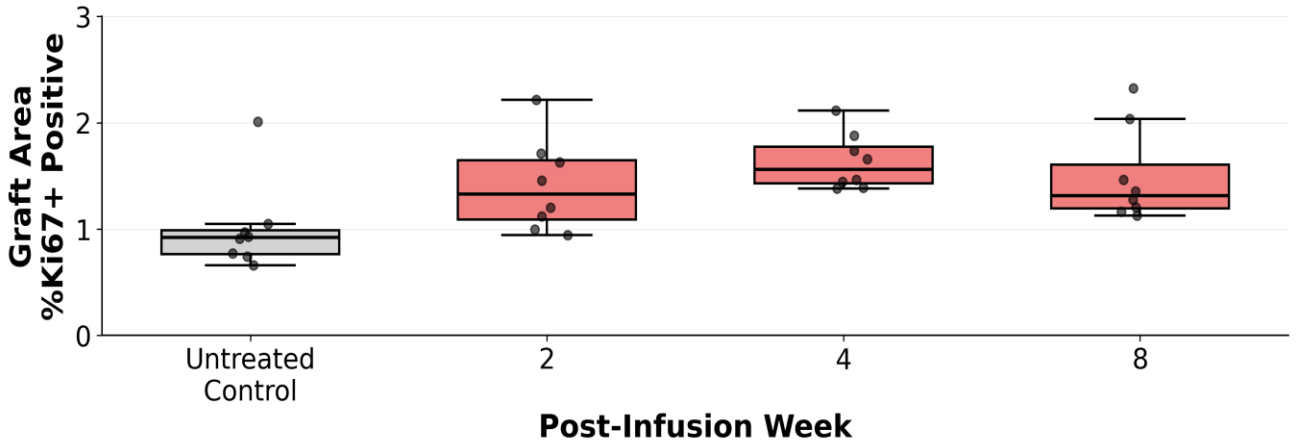
CNTY-813 grafts maintain endocrine identity with no evidence of tumorigenesis

Endocrine graft identity over time



INS: Insulin stain; CHGA: CHGA stain; Ki67: Stain for Ki67; DAPI: nuclear stain

Quantification of Ki67+ over time



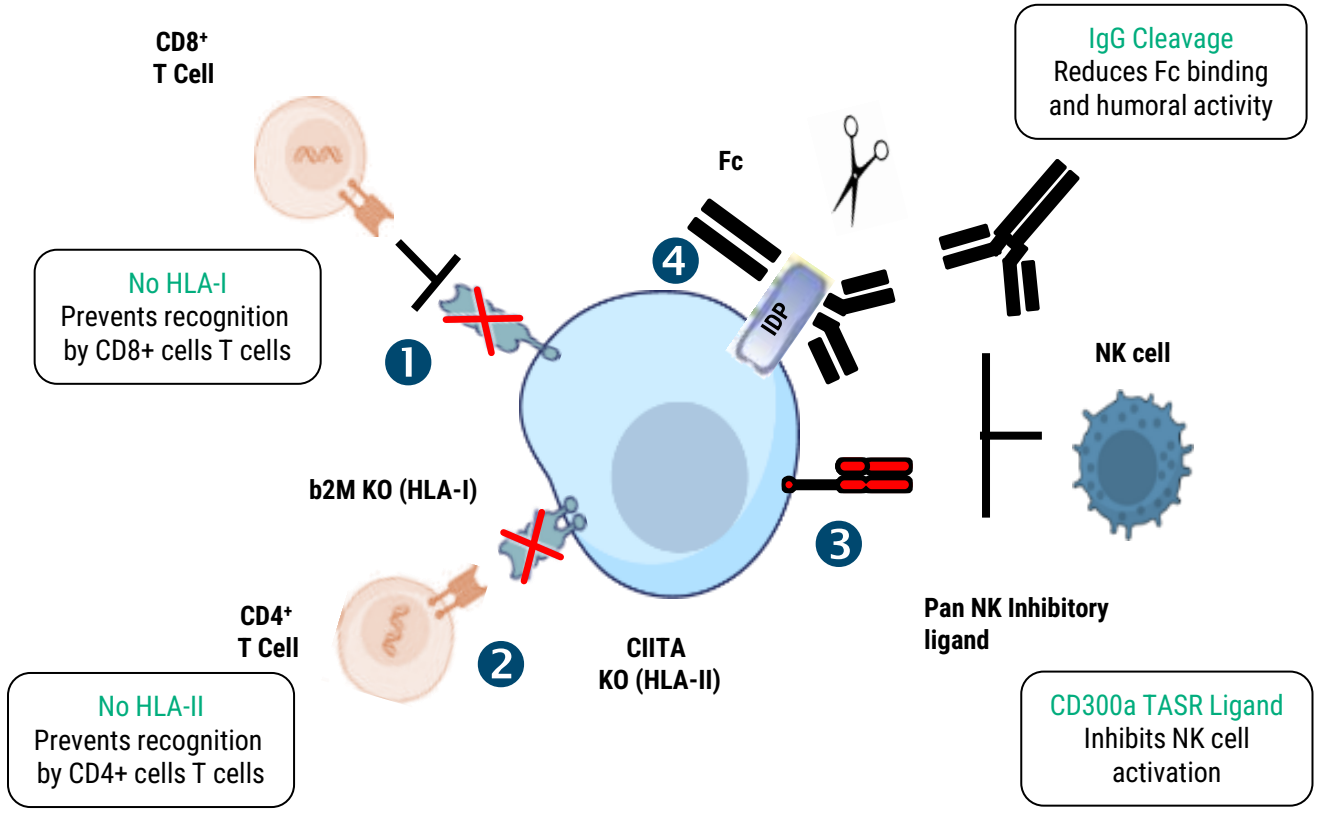
Ki67 staining includes host-derived cells; not human specific.

- ✓ **Endocrine graft morphology maintained** through 8 weeks
- ✓ **No Ki67 increase or cyst formation** was observed through 8 weeks
- ✓ **No tumorigenesis observed in >140 mice** with >3-month follow up (>1B cells infused)

Source: Company data on file

CNTY-813 is engineered to evade T cell, NK cell, and humoral responses

ALLO-EVASION™ 5.0



Protection from:

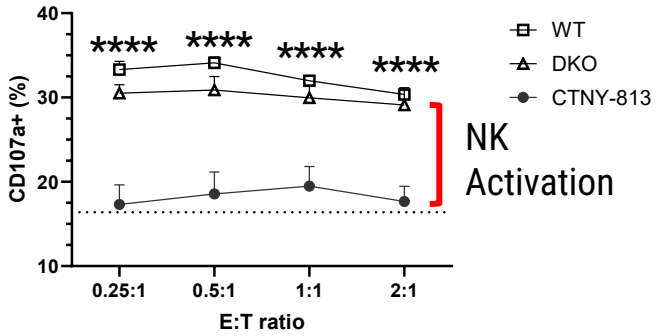
T cells	❶ Deletion of HLA-I ❷ Deletion of HLA-II
NK cells	❸ Insertion of CD300a TASR pan-NK inhibitory ligand[1, 2]
Humoral Immunity	❹ Insertion of cell-surface enzyme to degrade IgG antibodies[3]

1. https://www.centurytx.com/wp-content/uploads/ASH_Welstead_Universal-Protection-of-Allogenic-T-Cells-Final.pdf
2. https://ashpublications.org/bloodadvances/article/doi/10.1182/bloodadvances.2024013436/518079/Universal-Protection-of-Allogeneic-T-Cell
3. Peraro et al, *Mol. Therapy* 2021, 29(12), 3398-3409; https://pmc.ncbi.nlm.nih.gov/articles/PMC8636170

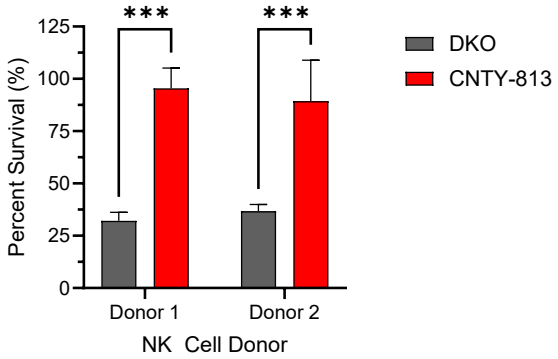
CNTY-813 demonstrated protection from multiple immune effector mechanisms

1. NK-CELL PROTECTION

Reduced NK Cell Activation

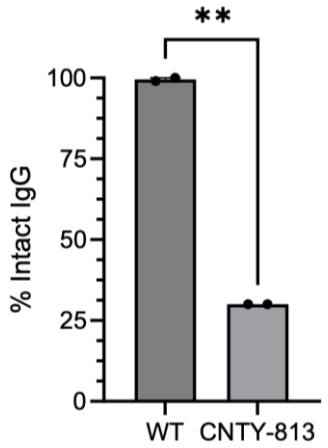


Reduced NK Cell Cytotoxicity



2. IgG CLEAVAGE

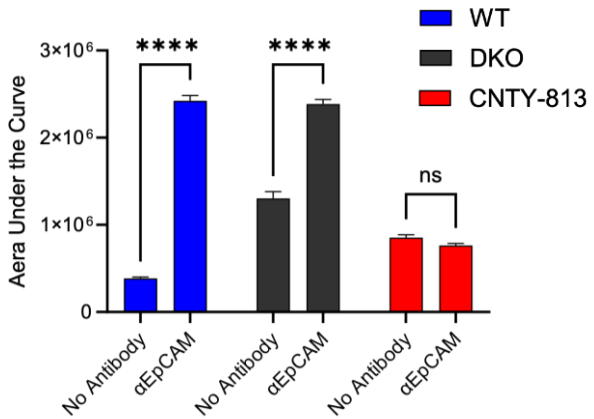
Rapid IgG Cleavage



Significant reduction in intact IgG after 1 hour in cleavage assay

3. PROTECTED FROM PHAGOCYTOSIS

Reduced Antibody-Dependent Phagocytosis (ADCP)



Protection from ADCP achieved against an antibody targeting EpCAM

CNTY-813 did not activate or get cleared by NK cells

CNTY-813 degraded IgG antibodies in vitro

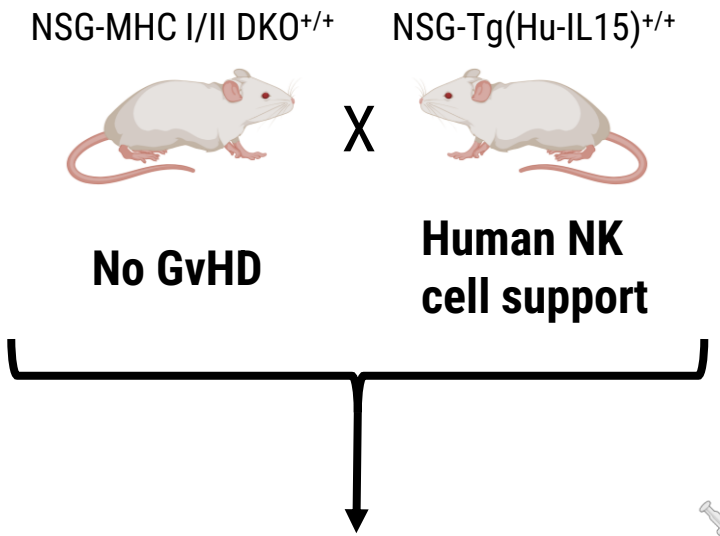
CNTY-813 protection from Ab-mediated phagocytosis

**, p<0.05; **, p<0.01; ***, p<0.001; ****, p<0.0001*

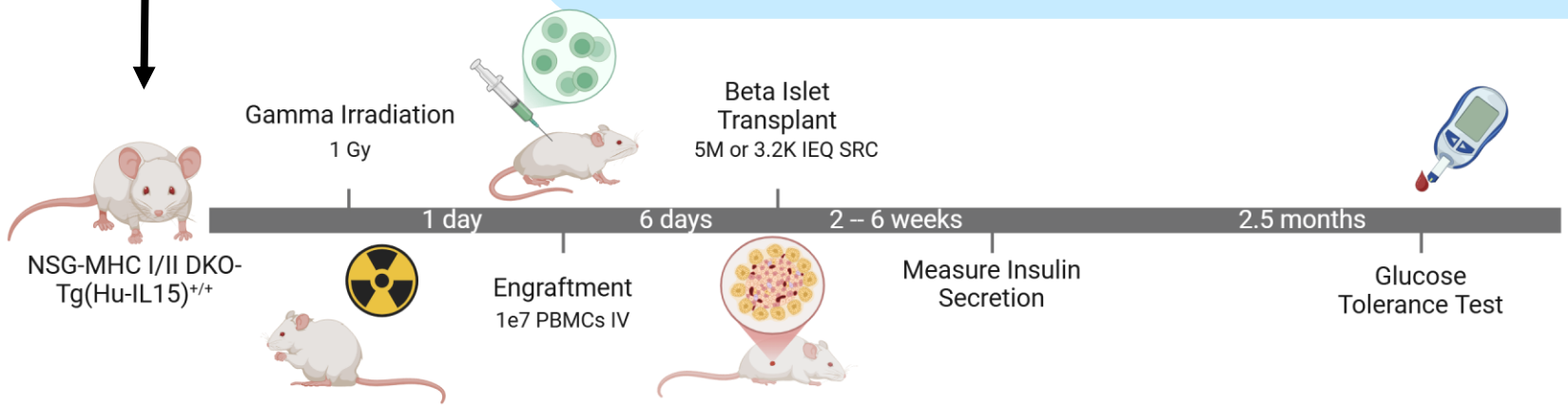
Source: Company data on file

Employing a humanized mouse model to study allogeneic graft rejection

Humanized Mouse Engrafted with Healthy Donor PBMCs



- Functional human **T cells** without GvHD (MHC DKO) – supports longer study durations
- Supports engraftment and survival of human **NK cells** (TgHu-IL15)
- Testing of allo-rejection mediated by human T cells and NK cells (huPBMCs)

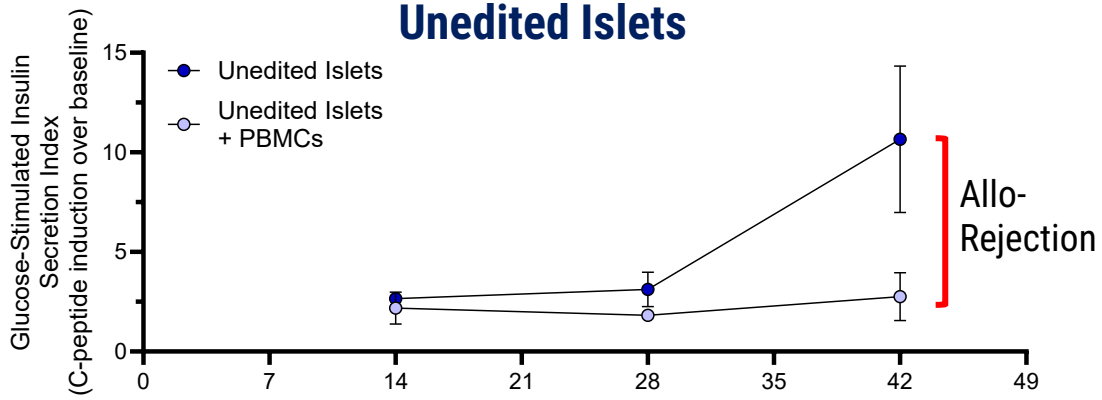


Human immune-cell engraftment supports functional testing of allo-rejection in vivo

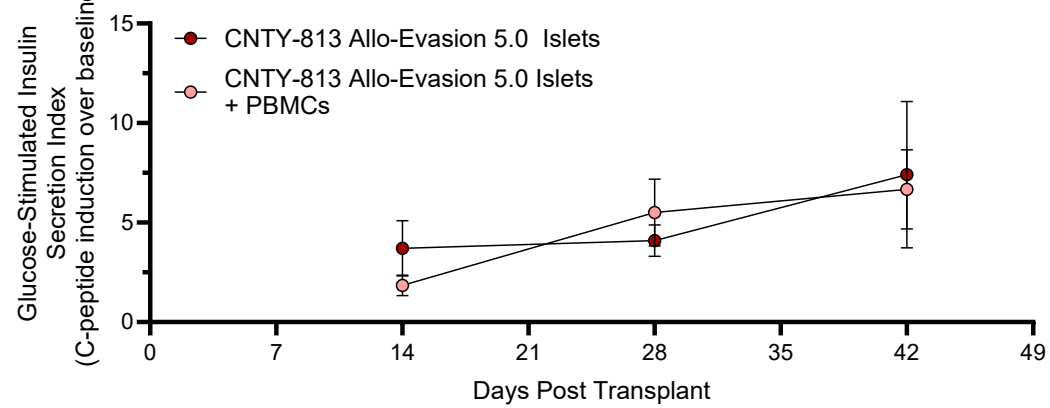
Allo-Evasion 5.0 protected CNTY-813 from rejection in humanized mice

Glucose Stimulation Index

Unedited Islets



Allo-Evasion 5.0 Islets



Reduced function with PBMC engraftment

Maintained function with PBMC engraftment

Readout

Human C-peptide stimulation index (over-baseline)

Interpretation

Higher response indicates preserved graft insulin secretion

Mean ± SEM

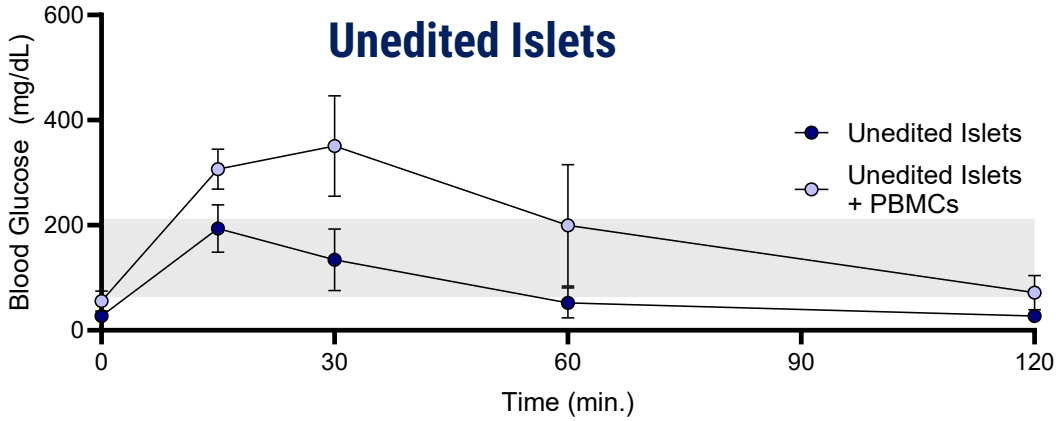
Allo-evasion 5.0™ maintains CNTY-813 Glucose Stimulated Insulin Secretion

C-Peptide is a surrogate for insulin

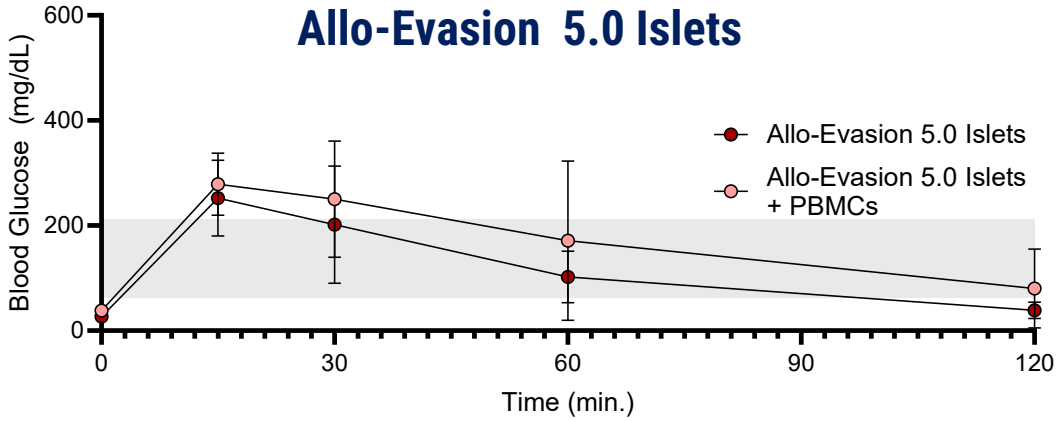
Source: Company data on file

Allo-Evasion 5.0 protected CNTY-813 from rejection in a humanized mouse

Glucose Tolerance Test (GTT) (11 weeks post-islet infusion)



Reduced function with PBMC engraftment



Maintained function with PBMC engraftment

Readout

Human blood glucose as depicted by area under the curve (AUC) during glucose tolerance test

Interpretation

Lower AUC indicates faster glucose clearance and better glucose control

Mean ± SD

Allo-evasion 5.0™ maintained CNTY-813 GTT performance

Source: Company data on file

CNTY-813 demonstrated reproducible differentiation, durable glucose control, and immune-evasive function in preclinical models

DIFFERENTIATION PLATFORM

- Reproducible, bioreactor-enabled differentiation from GMP MCB
- Phase 1 clinical manufacturing process established
- CNTY-813 specs:
  - >95% islet endocrine
  - >50% beta cell identity

FUNCTIONAL ISLETS

- GSIS potency similar to primary islets
- Rapid and durable glucose control observed in diabetic mice
- Maintained graft identity with a favorable safety profile

ALLO-EVASION™ 5.0

- Engineered to reduce T-cell, NK-cell, and humoral immune recognition
- Protection from NK and humoral clearance demonstrated
- Preserved graft function under alloimmune pressure in vivo

These data support the development of CNTY-813 as a potentially broadly accessible off-the-shelf cell therapy for Type 1 Diabetes