



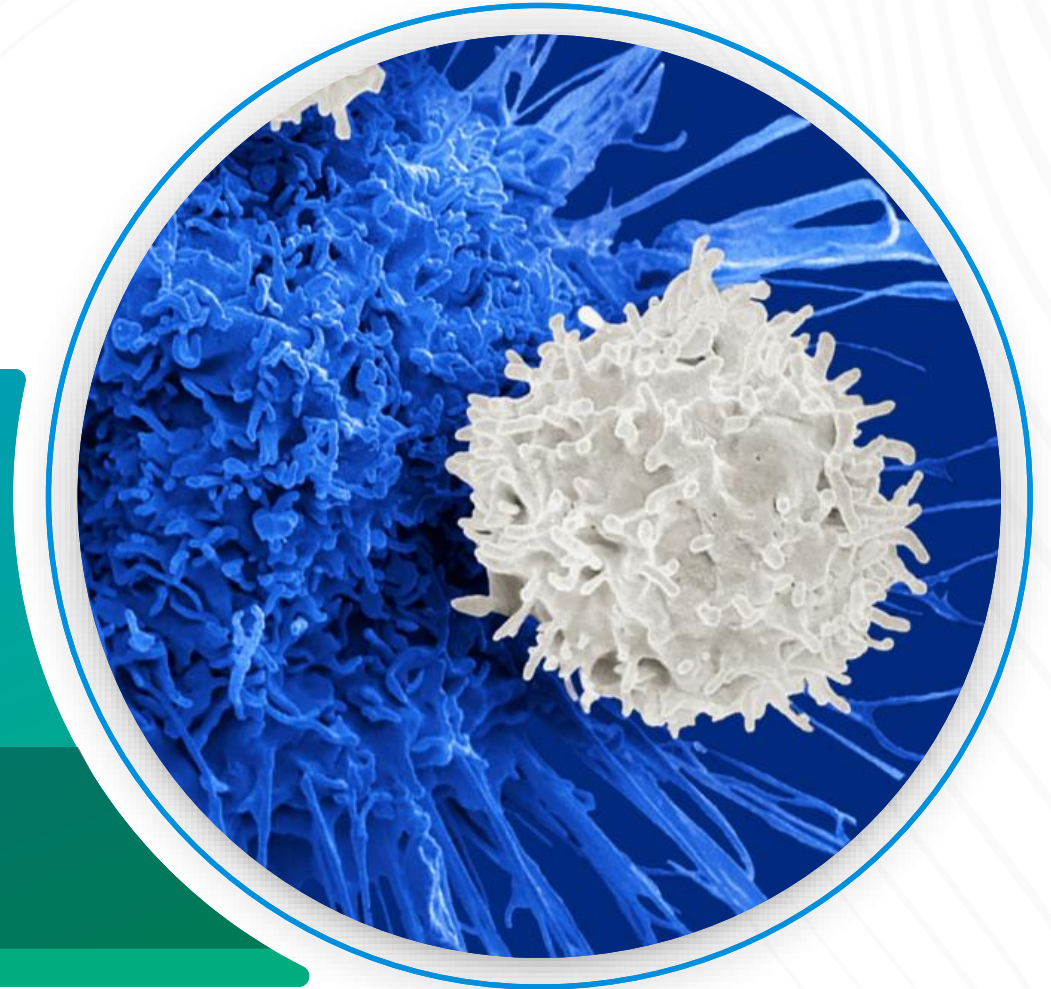
CENTURY
THERAPEUTICS

CNTY-813:

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

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Disclosures



Presenter
**G. Grant
Welstead, PhD**



Relevant Financial Relationship

- Employee, Century Therapeutics



Presentation Information

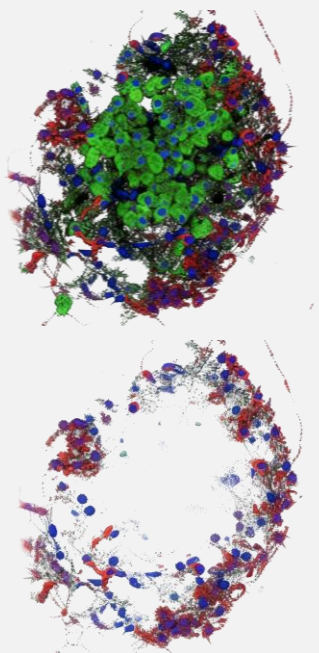
- This presentation describes preclinical research related to CNTY-813, an investigational iPSC-derived islet cell therapy for T1D
- The content is intended for scientific and educational discussion
- No clinical recommendations will be made

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 preclinical data, 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 Investigational New Drug (IND) or Clinical Trial Application (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, islet cells are destroyed

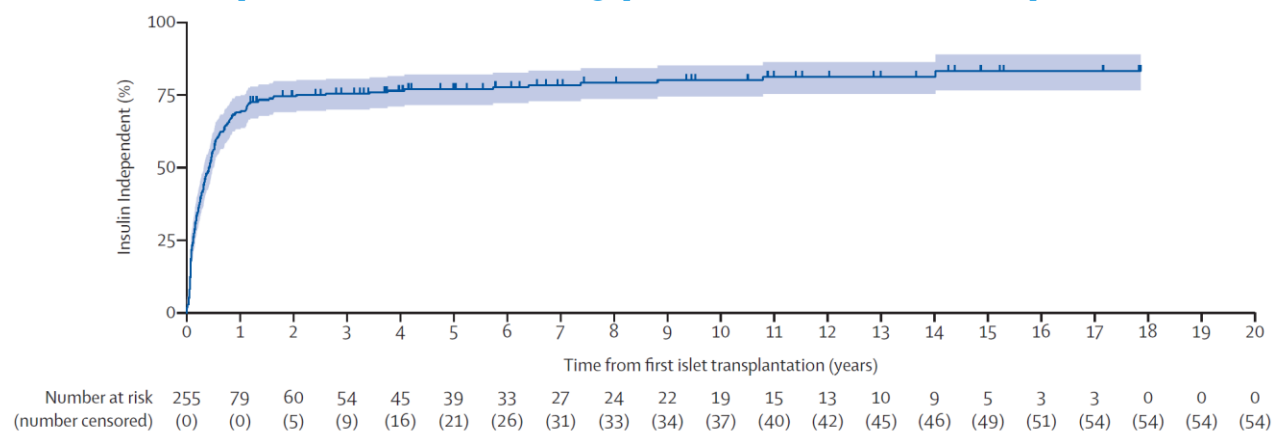


Healthy islet cells produce insulin (green)

In T1D, islet cells are destroyed

Islet transplantation provides a potentially curative therapy for T1D

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

Insulin independence achieved for one year in **~70%** of patients receiving allogeneic cadaveric islet transplantation¹

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., 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

Generation of islets with a 29-day defined process

High purity and reproducible across batches

iPSC

**Definitive
Endoderm**

Stage 1

**Primitive
Gut Tube**

Stage 2

**Pancreatic
Progenitor I**

Stage 3

**Pancreatic
Progenitor II**

Stage 4

Endocrine

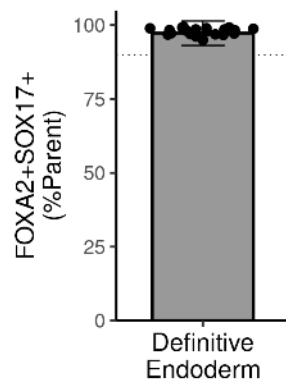
Stage 5

β Cell

Stage 6

Stage 1

Definitive Endoderm

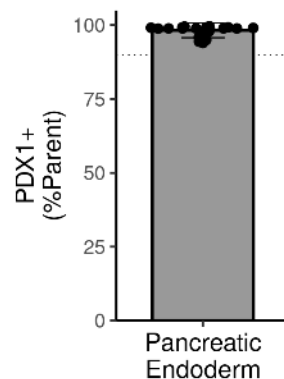


Mean (n)

97.3 (20)

Stage 4

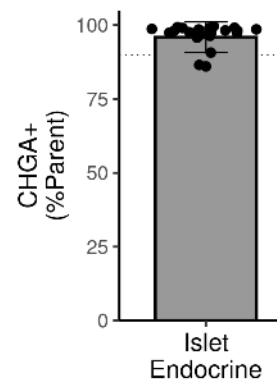
Pancreatic Progenitor II



98.2 (24)

Stage 6

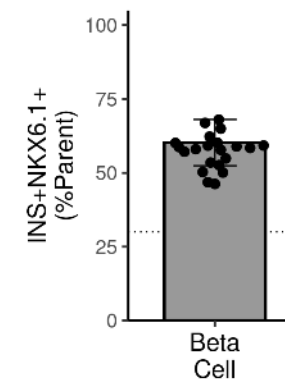
Islet Endocrine



95.9 (32)

Stage 6

Beta Cell



60.2 (32)

Consistent Differentiation

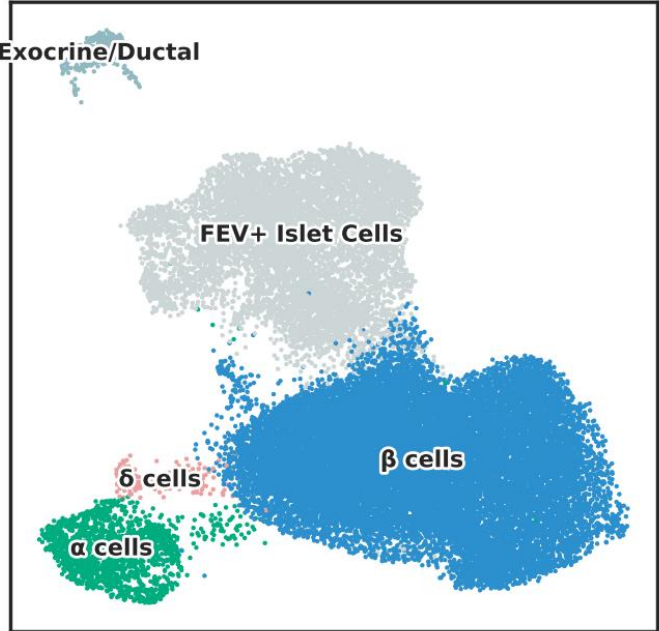
Surpassed necessary
purity at every stage

>95% Endocrine

50–60% Beta Cells
(Insulin Producing)

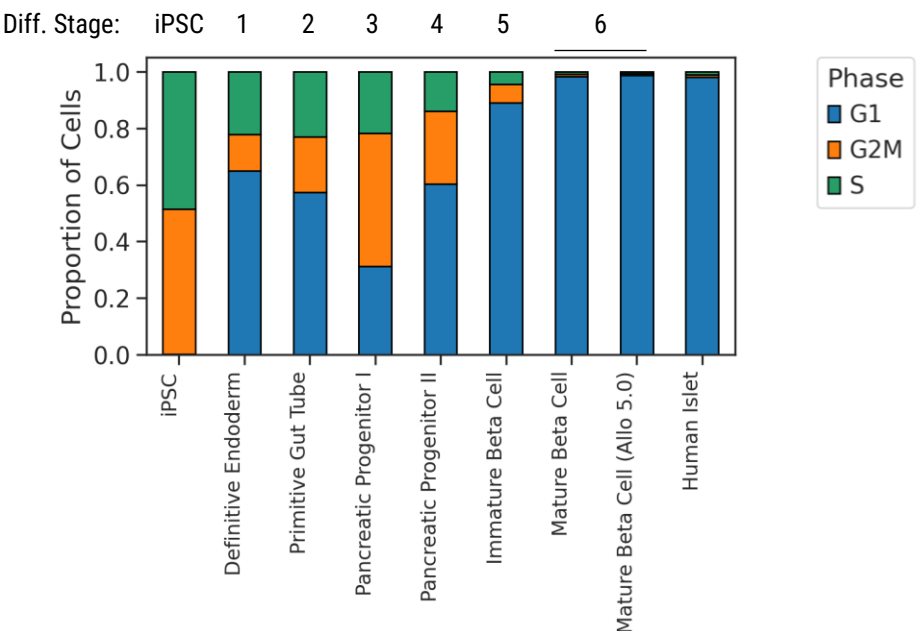
CNTY-813 islets contain defined, terminally differentiated endocrine cell populations

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

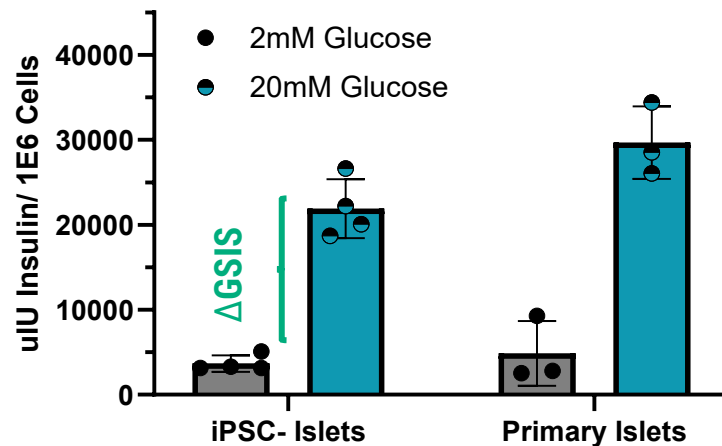


- CNTY-813 manufacturing achieves a defined islet endocrine composition, with beta cells as the predominant population
- Data is consistent with cell cycle exit on par with primary islets by end of manufacture (>98% G1 phase identity)

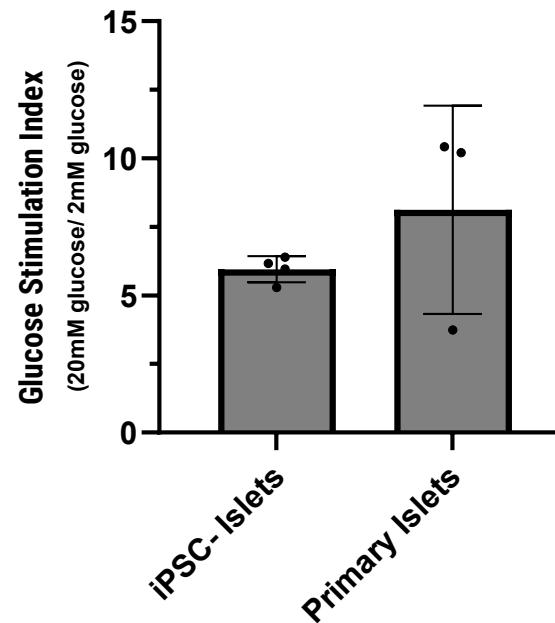
CNTY-813 islet cells demonstrate robust glucose-responsive function

Nonclinical Potency

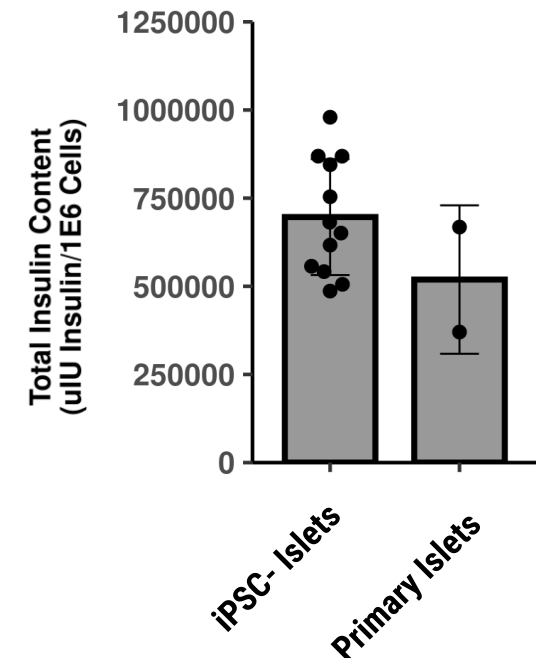
Glucose Stimulated Insulin Secretion



Stimulation Index



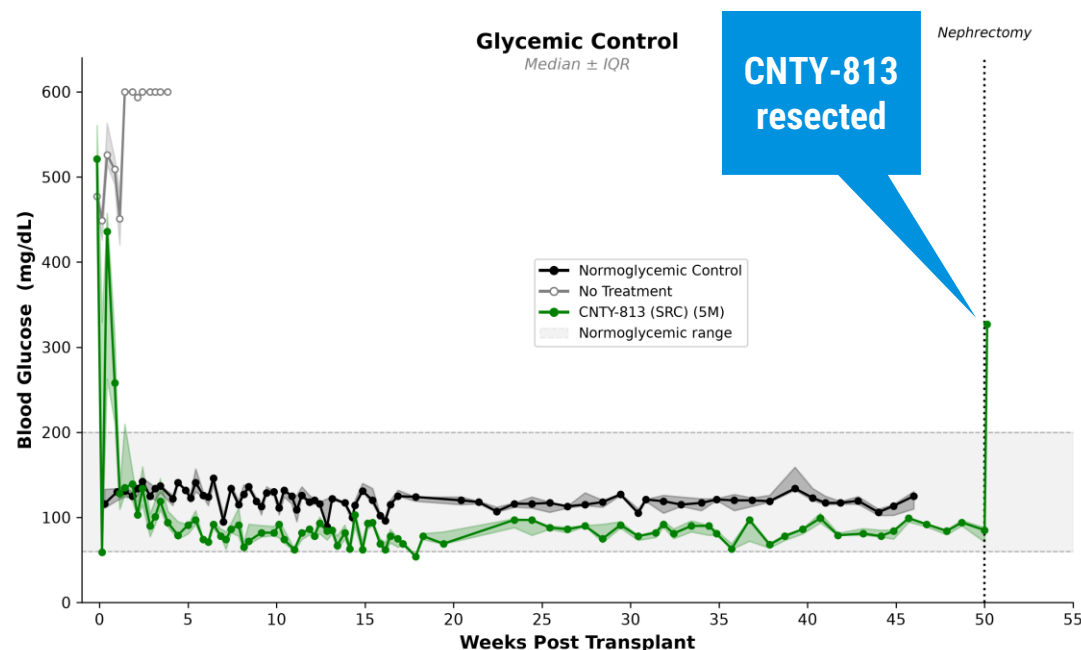
Total Insulin Content



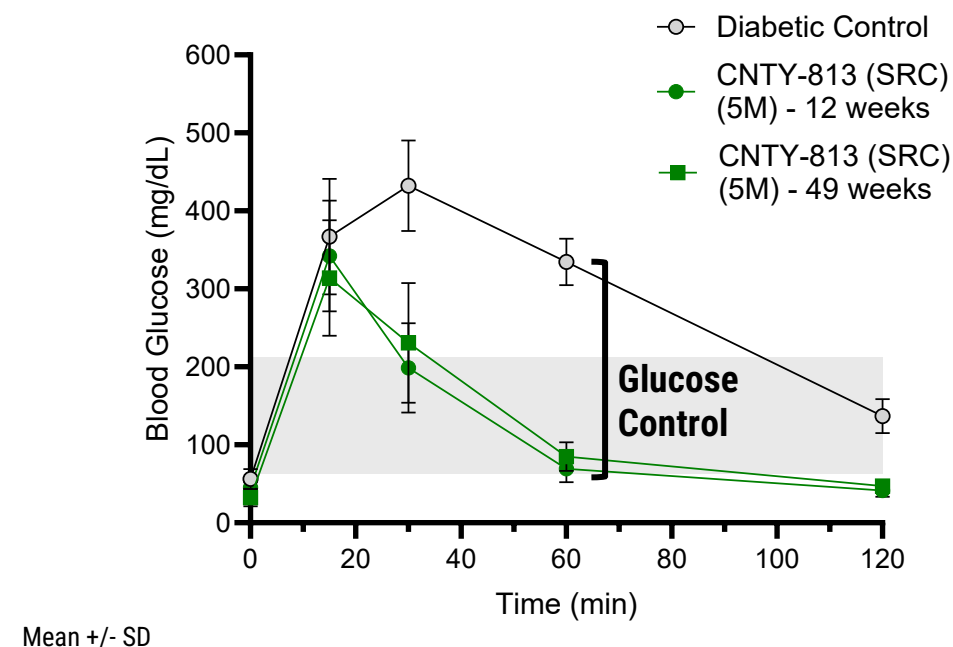
CNTY-813 islets rapidly restored normoglycemia in STZ-induced diabetic mice

Nonclinical Potency

Non-Fasted Blood Glucose



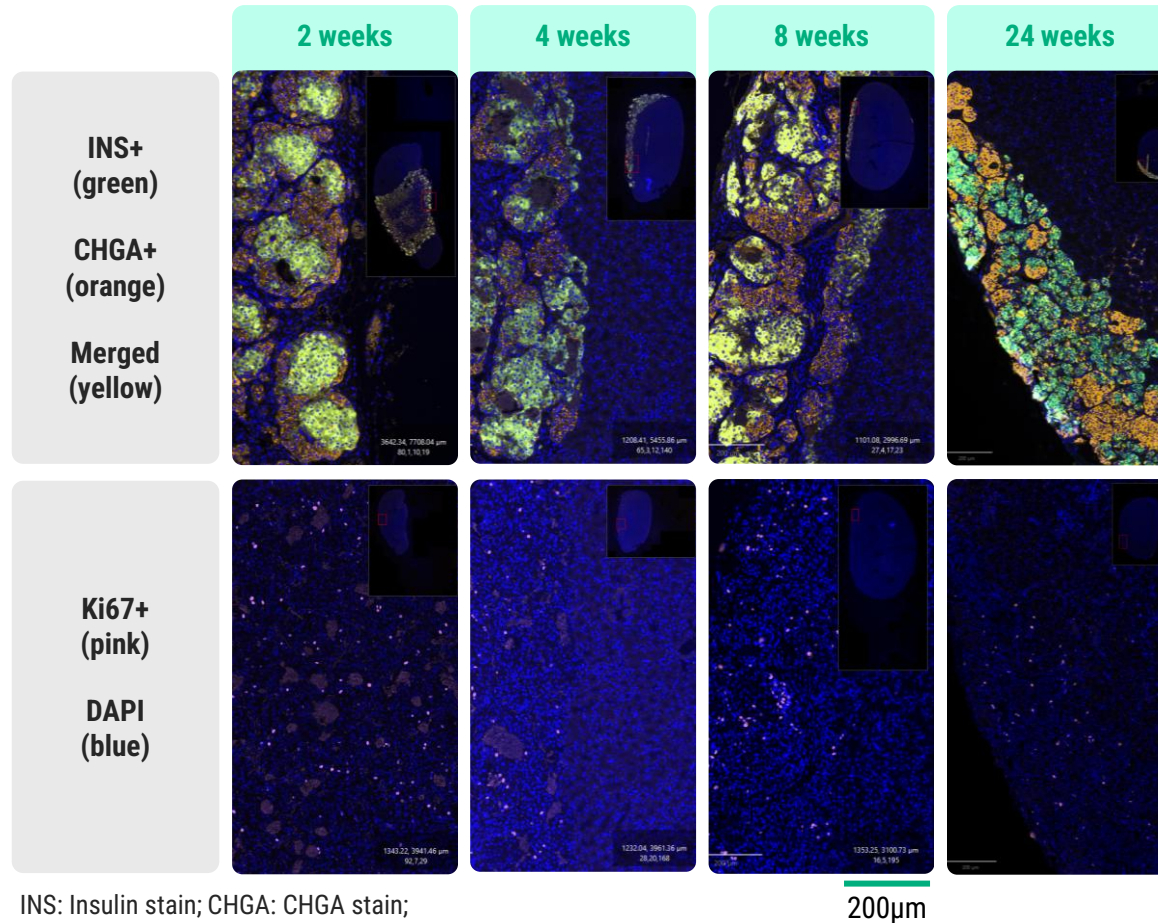
Glucose Tolerance Test



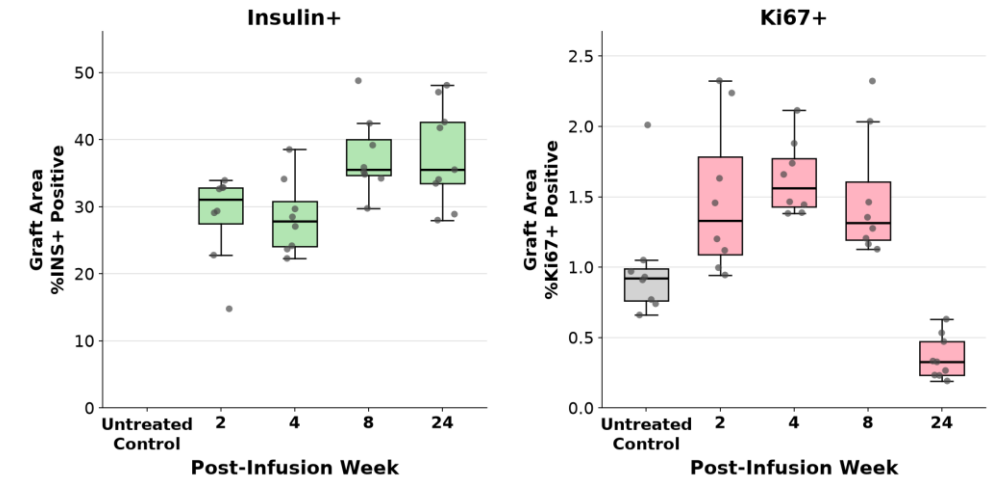
**CNTY-813 provided durable glycemic control for >11 months,
with reversal after graft removal demonstrating clear pharmacological activity**

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

Endocrine graft identity over time



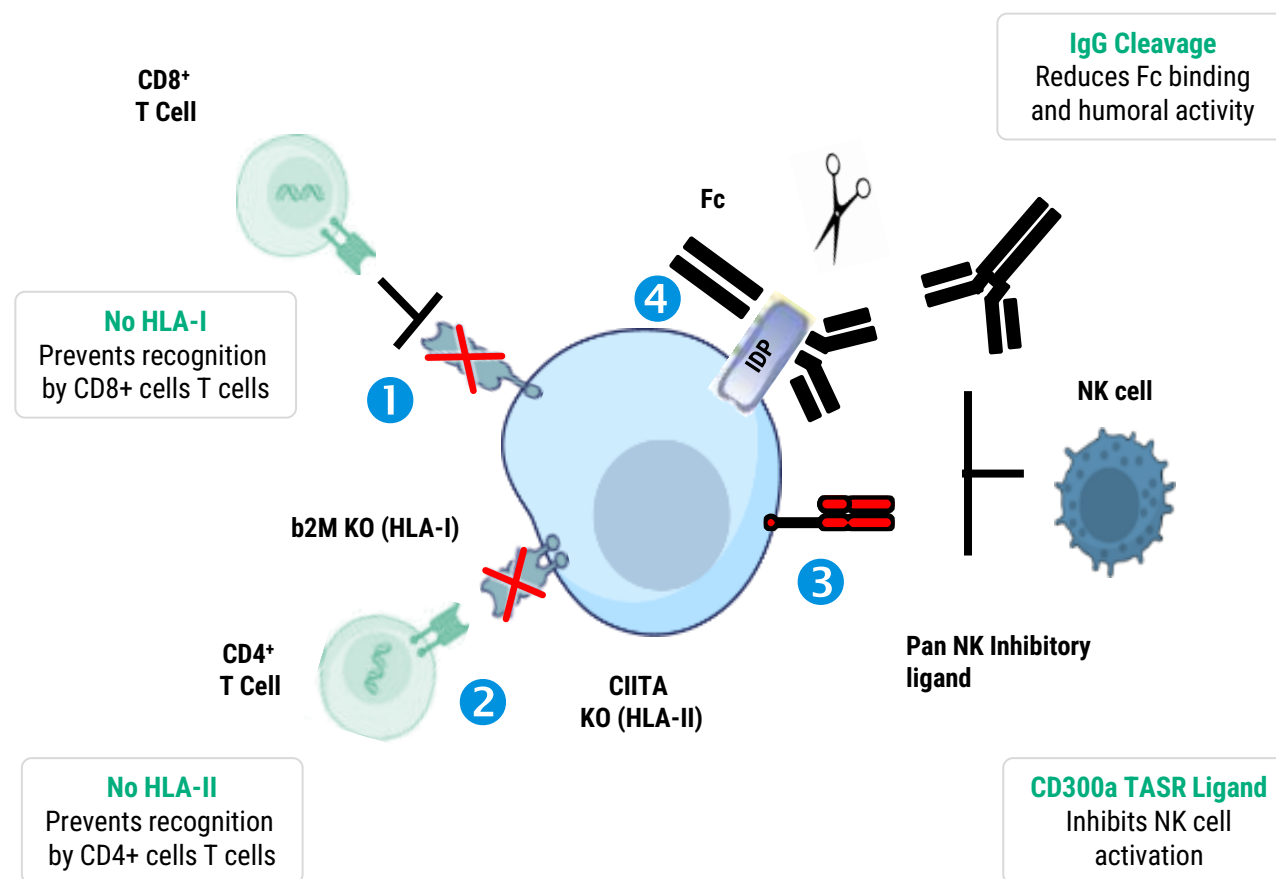
INS: Insulin stain; CHGA: CHGA stain;
Ki67: Stain for human and mouse Ki67; DAPI: nuclear stain



- ✓ Endocrine graft morphology maintained
- ✓ Stable Insulin and low Ki67 staining post engraftment
- ✓ No tumorigenesis observed in >140 mice with >3-month follow up (>1B cells infused)
- ✓ All CNTY-813 infused mice achieve normoglycemia

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

ALLO-EVASION™ 5.0



Protection from

T cells

1 Deletion of HLA-I

2 Deletion of HLA-II

NK cells

3 Insertion of CD300a TASR pan-NK inhibitory ligand^{1, 2}

Humoral Immunity

4 Insertion of cell-surface enzyme to degrade IgG antibodies³

1. https://www.centurytx.com/wp-content/uploads/ASH_Welstead_Universal-Protection-of-Allogeneic-T-Cells-Final.pdf

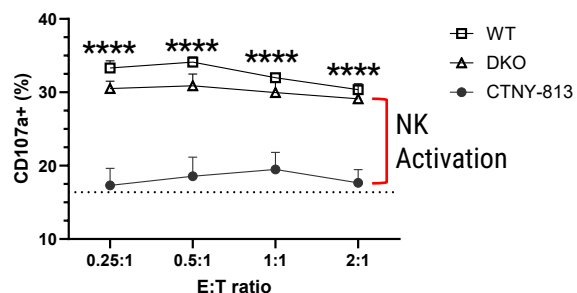
2. <https://ashpublications.org/bloodadvances/article/doi/10.1182/bloodadvances.2024013436/518079/Universal-Protection-of-Allogeneic-T-Cell>

3. Peraro et al, Mol. Therapy 2021, 29(12), 3398-3409; <https://pmc.ncbi.nlm.nih.gov/articles/PMC8636170>

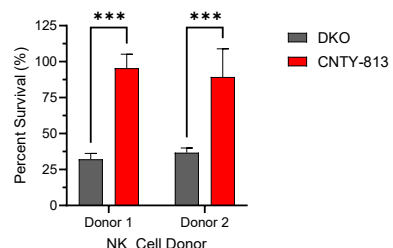
CNTY-813 demonstrated protection from multiple immune effector mechanisms

01 NK-CELL Protection

Reduced NK Cell Activation



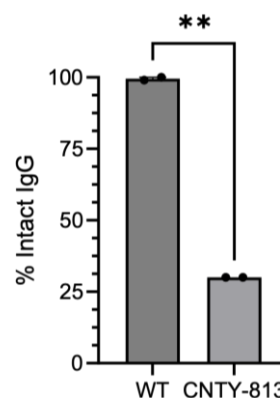
Reduced NK Cell Cytotoxicity



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

02 IgG Cleavage

Rapid IgG Cleavage

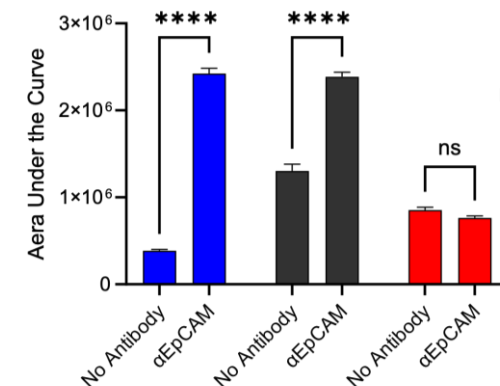


Significant reduction in intact IgG after 1 hour in cleavage assay

CNTY-813 degraded IgG antibodies in vitro

03 Protected from phagocytosis

Reduced Antibody-Dependent Phagocytosis (ADCP)

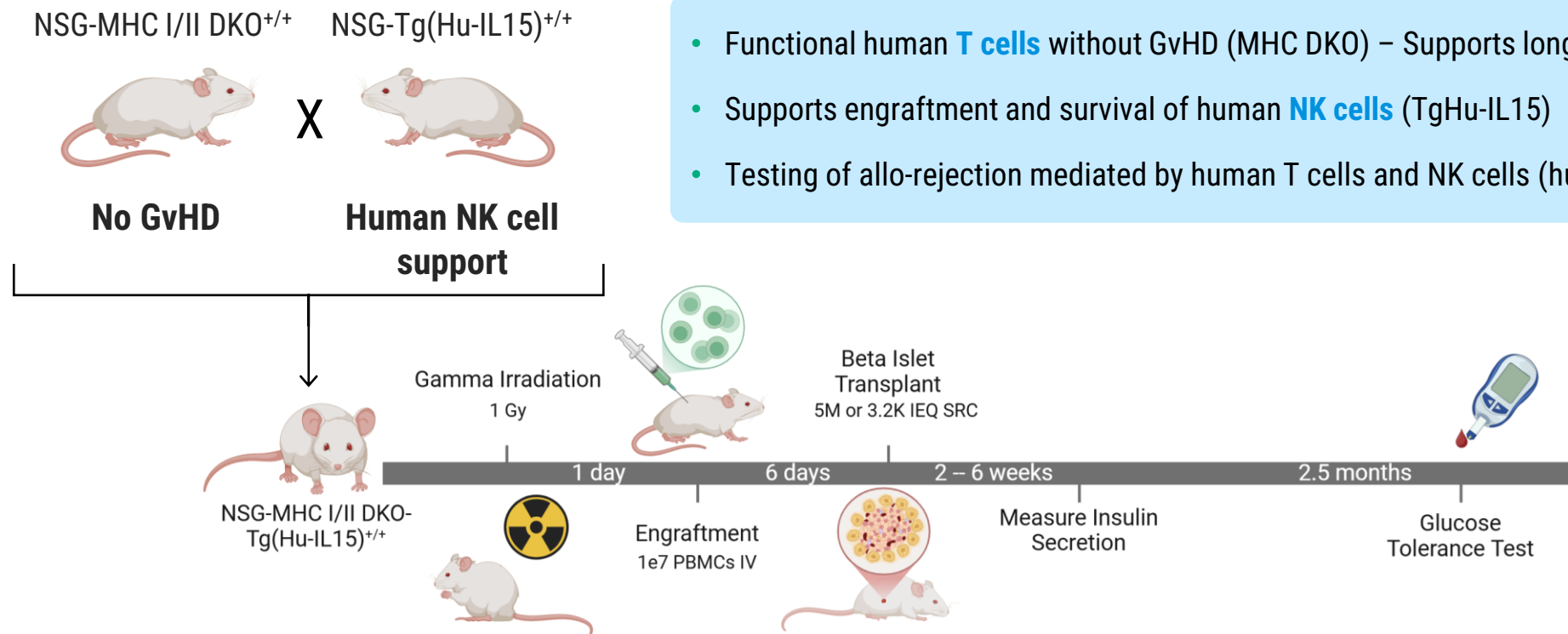


Protection from ADCP achieved against an antibody targeting EpCAM

CNTY-813 protection from Ab-mediated phagocytosis

Employing a humanized mouse model to study allogeneic graft rejection

Humanized Mouse Engrafted with Healthy Donor PBMCs

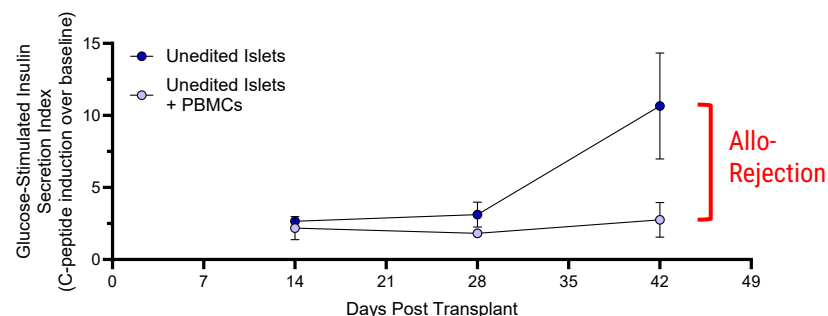


Human immune-cell engraftment supports functional testing of allo-rejection in vivo

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

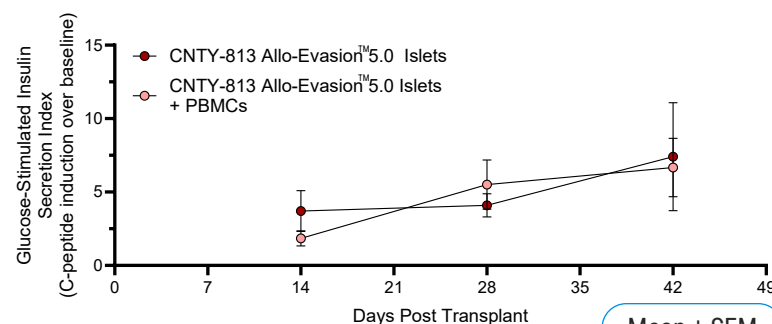
Glucose Stimulation Index

Unedited Islets



↓
Reduced function with PBMC engraftment

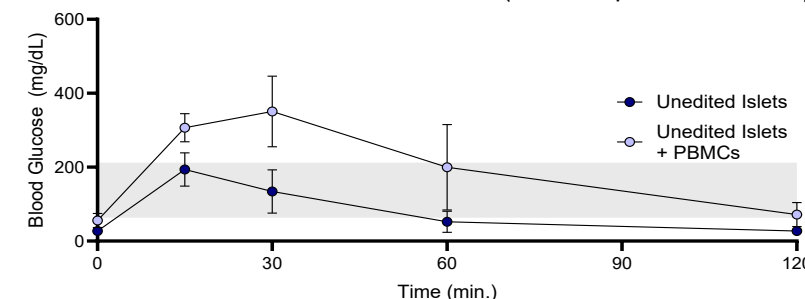
Allo-Evasion™ 5.0 Islets



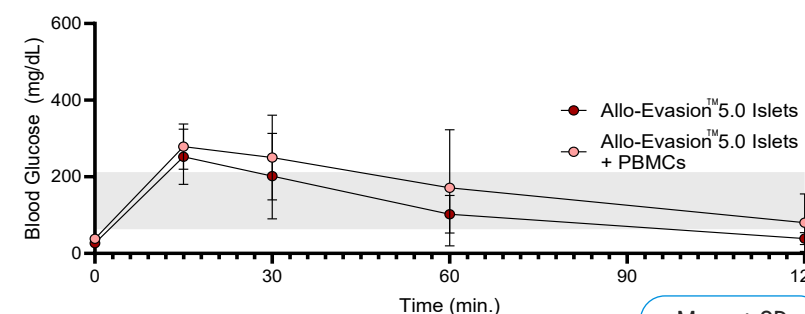
≡
Maintained function with PBMC engraftment

Glucose Tolerance Test (GTT)

(11 weeks post-islet infusion)



Unedited Islets

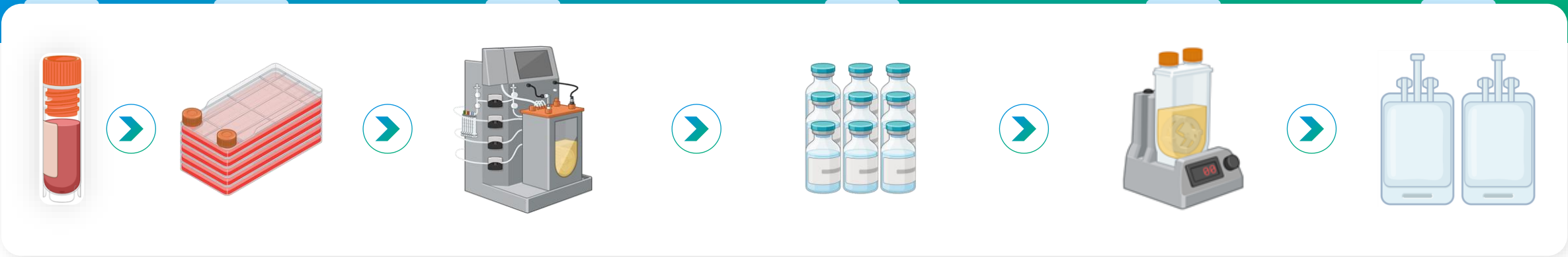


Allo-Evasion™ 5.0 Islets

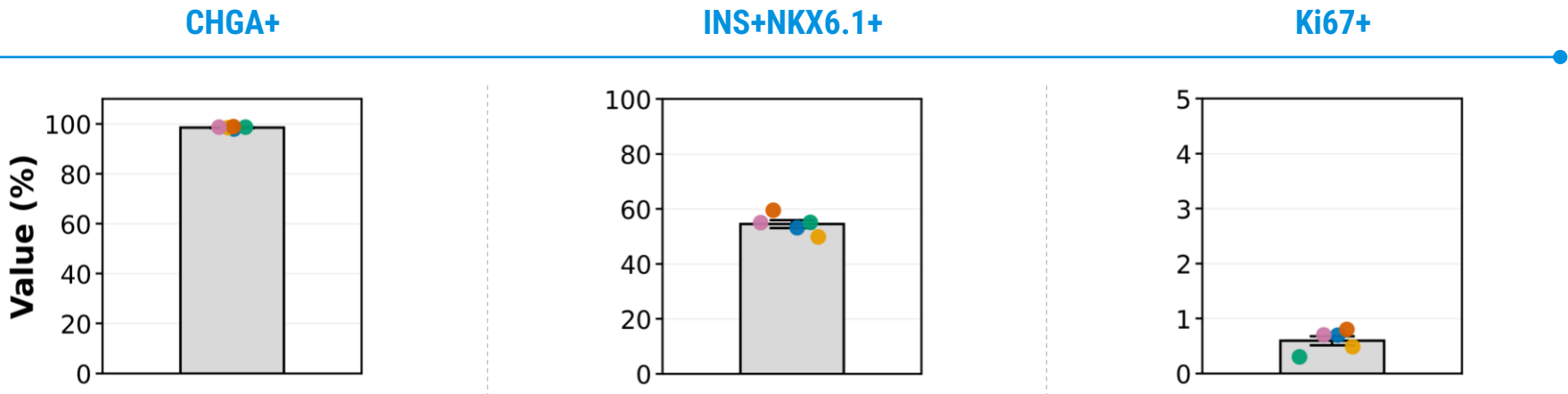
Allo-Evasion™ 5.0 maintained CNTY-813 Glucose Stimulated Insulin Secretion and GTT performance in vivo1

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

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



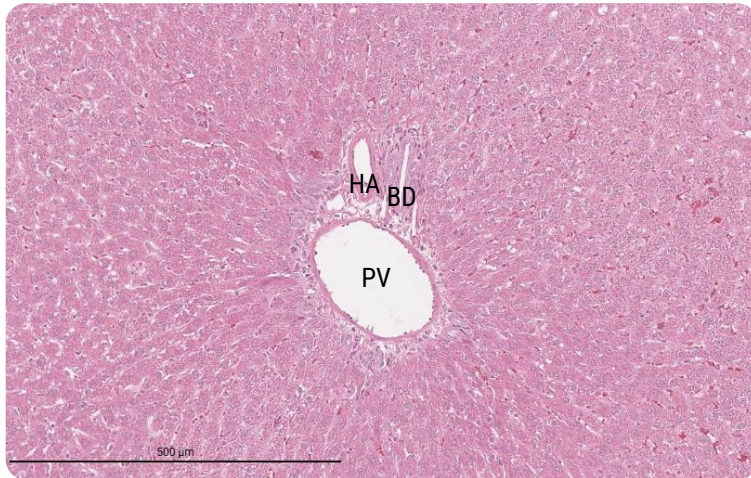
Consistent final product flow cytometry profiles across 5 clinical-scale batches



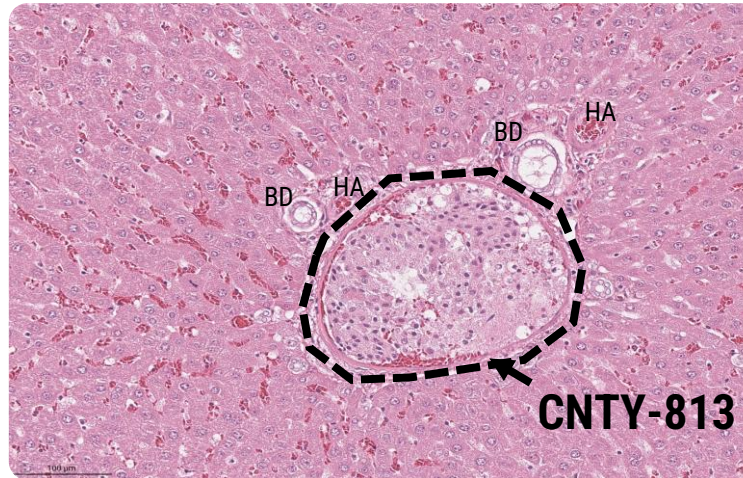
Clinical Scale Run 1 2 3 4 5

Successful CNTY-813 engraftment in rat livers via portal vein injection

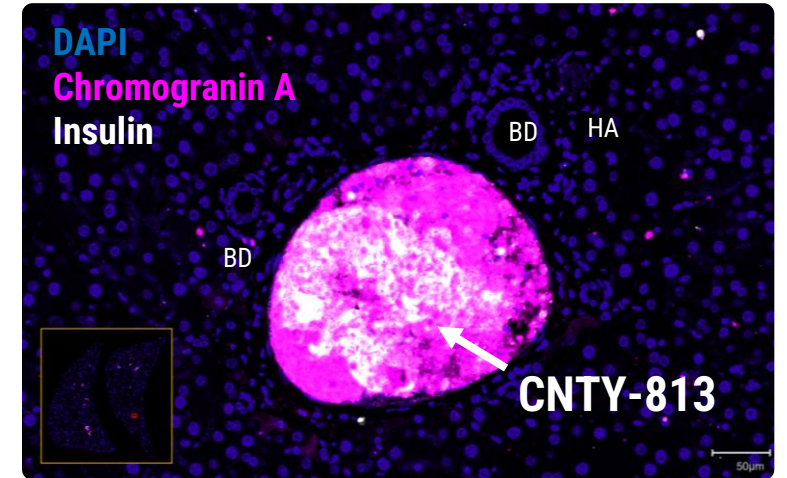
Vehicle Control



CNTY-813 – H&E



CNTY-813 – IF

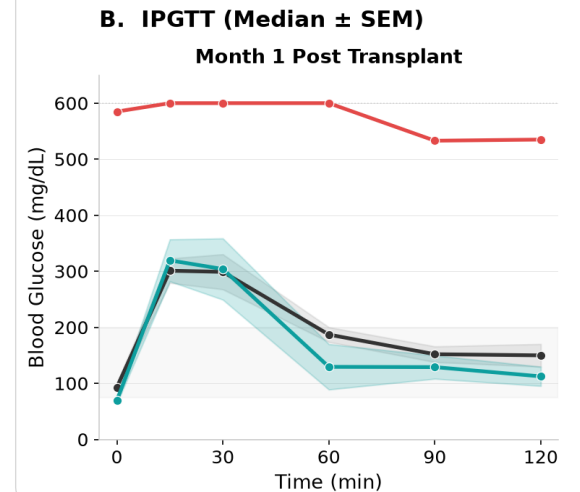
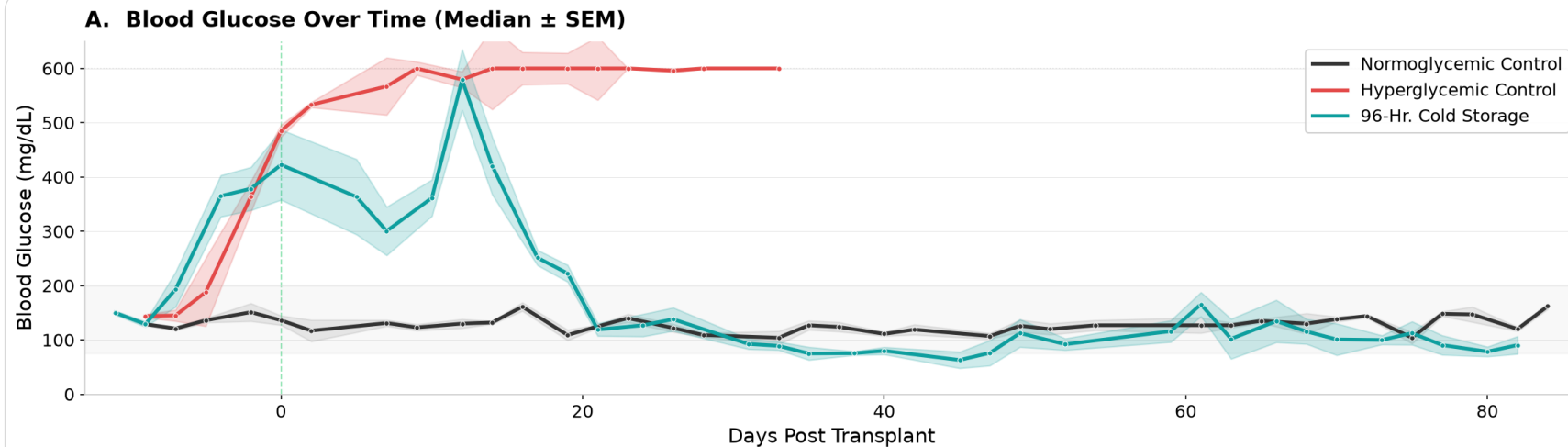


CNTY-813 aggregates are identified in the liver at 1-month post-transplant



Islets stain positive for chromogranin A and Insulin

Clinical-scale islets restored durable normoglycemia after 96-hours in cold storage



Clinical-scale product with 96-hour cold storage stability

Islets manufactured at clinical scale retained full functionality after 96-hours in cold storage solution

Rapid restoration of glycemic control

Transplanted mice normalized blood glucose within 30 days post-transplant and maintain stable normoglycemia through 3 months of follow-up

Glucose tolerance equivalent to healthy controls

IPGTT glucose clearance in treated mice was indistinguishable from normoglycemic controls by 1-month post-transplant

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

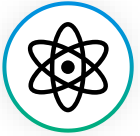


ALLO-EVASION™ 5.0

- 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

Acknowledgements



Entire Century Team



Mike Brehm & Lab – UMASS Chan School of Medicine and Diabetes Center of Excellence