



***Advancing cell therapeutics  
to provide ‘functional cures’***

TSX: SVA  
OTCQB:SEOVF  
FSE/XETRA:PSH

Sernova Annual General Meeting April 27, 2023

# Forward looking statements

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# 2023 AGM Presentation

## Agenda

- Brief Update on Sernova's type 1 diabetes (T1D) clinical program
  - Cohort 1 update
  - Cohort 2 enrolment update
- Sernova rationale using islets as a 'functional cure' for T1D as opposed to insulin injections
- Sernova's iPSC islet cluster technology being developed with Evotec: a commercially viable product
- Update from this week's IPITA conference with Sernova/Evotec's presentation
- Future milestones

# Sernova: Innovator and Leader

## Cell Therapeutics: Paradigm Shift for Superior Treatment of High-Maintenance, Lifelong Conditions

- Sernova's integrated **Cell Pouch System™** provides the potential for a '**functional cure**' for chronic medical conditions with **multi-billion dollar market potential**
- **Cell Pouch** implantable device forms organ like environment for immune protected therapeutic cells to **naturally produce missing proteins or hormones**, overcoming barriers associated with cell survival and function – **no fibrosis**
- **Type 1 Diabetes (T1D) lead program**, additional programs for **hypothyroidism and hemophilia A**
- Current **US Phase 1/2 clinical study** interim data **demonstrating insulin independence in multiple long-term T1D patients with hypoglycemia**; longest patient > 3.0 years
- **Partnership with Evotec (NASDAQ: EVO)** will provide **ethically derived best in class, commercially viable iPSC islet clusters** with potential to treat all insulin dependent patients
- **Strong cash position** through key milestones

# Phase 1/2 Study – Cohort 1 Informed / Guided to Cohort 2

## Advancing With A Higher Capacity Cell Pouch Product

- Cohort 1 (6 patients)
  - Patients demonstrated a **clear safety profile** for **Cell Pouch System**
  - Established threshold for islet dose and density optimization
  - Cohort 1 update coming at American Diabetes Association Meeting (podium presentation)
- Cohort 2 (up to 7 patients) – Provides optimized dosing regimen and shorter dosing timelines
  - Implementation of **10 channel Cell Pouch** with **>50% more islet capacity**
    - released to trial site for implantation commencing **November 2022**
    - first 4 patients enrolled **including Cell Pouch implantation**
    - **first 2 patients transplanted with the first dose of islets** – next transplants pending
    - intra-implantation cell dosing interval **reduced from 6 to 3 months**
    - engaged new patient recruitment agency for rapid enrollment of remaining study patients
  - Initial interim data with 10 channel Cell Pouch and islet transplants anticipated **H2 2023**
- Results from this study will inform the Phase 3 program and **support anticipated Biologic License Agreement (BLA) submission to FDA**



# The Advantages Of Pancreatic Islets Over Insulin Injection

## Alpha Cells

Alpha cells secrete the hormone **glucagon** in response to **low blood glucose**.

The effect of glucagon is to raise blood glucose.

## Insulin: A Single Component of Glucose Regulation

Insulin is only one way the body controls glucose. Using **solely insulin** to treat type 1 diabetes can **only lower blood glucose**, which can be dangerous and potentially life threatening.

## Beta Cells

Beta cells secrete the hormone **insulin** in response to **high blood glucose**.

The effect of insulin is to lower blood glucose.

## Delta Cells

Delta cells secrete the hormone **somatostatin** in response to **high levels of insulin or glucagon**.

The effect of somatostatin is to keep blood glucose from dropping too low or elevating too high by inhibiting the secretion of both hormones if they reach too high a level.

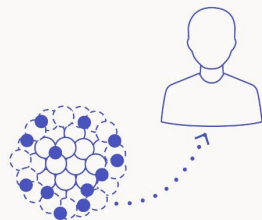
## Pancreatic Islets: The Complete Approach

Pancreatic islets are the primary mechanism behind the **global regulation** of blood glucose. Islets are organized groups of cells that have the full complement of glucose-regulating functions and hormones in normal pancreatic tissue. The contents of islets maintain glucose within a healthy range, not too high and not too low, and can regulate blood glucose constantly. Tight control of blood glucose, with a normal HbA1c, can decrease the risk of side effects from diabetes and improve quality of life.

Pancreas

## Sernova's Cell Pouch System™

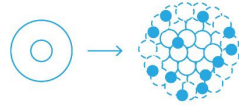
Evotec is manufacturing pancreatic islet-like clusters (ILCs) that mimic the function of human islets. Sernova's Cell Pouch, in combination with Evotec's ILCs, operates similarly to native pancreatic tissue that globally controls blood glucose, resulting in a commercial-scale potential 'functional cure' for insulin-dependent diabetes.



# Sernova and Evotec's Cell Therapy Commercial Approach for the Treatment of Type 1 Diabetes

## The Evotec iPSC-Based Manufacturing Process

The Evotec induced pluripotent stem cell (iPSC)-based manufacturing process allows for the commercial-scale production of best-in-class pancreatic islet-like cell clusters (ILCs). These ILCs can be cryopreserved, and as a result, can be shipped around the world, differentiating them from others in the industry. In combination with Sernova's Cell Pouch System™, these technologies offer a potential 'functional cure' for patients suffering from insulin-dependent diabetes.

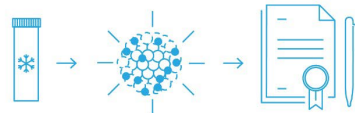


- 1 Using Good Manufacturing Practices, the iPSCs are differentiated (developed) into the target pancreatic islet-like clusters.



- 3 Storage or shipment of islet clusters (frozen).

- 2 Controlled freezing (cryopreservation), essential for making cells commercially viable on a large scale. Extensive quality control.



- 4 Thawing of cells to patient-ready form. Additional assurance that cells meet the rigorous standards set forth for cells to be transplanted into patient.

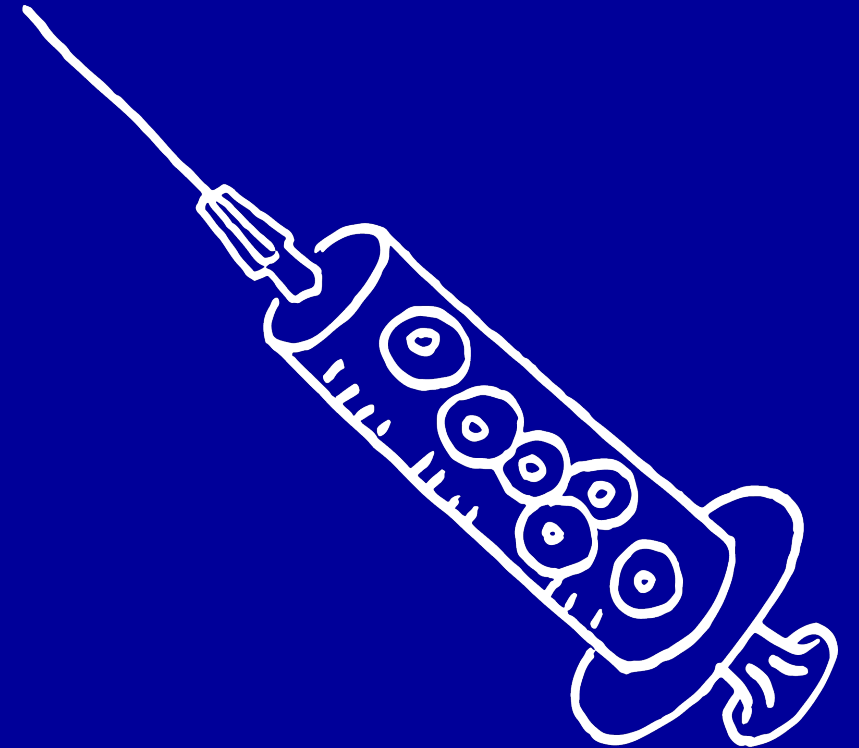
- 5 Temperature-controlled shipping for patient transplant.

## The Patient Experience

Patients with insulin-dependent diabetes face an extreme burden of constant blood glucose checks, multiple daily insulin injections, and the risk of a potentially life-threatening complication of the inability to recognize the symptoms of low blood sugar. Sernova has developed the Cell Pouch System as a cutting-edge solution that allows for natural vascularization and free exchange of nutrients, oxygen, and hormones. In combination with Evotec's pancreatic islet-like clusters, operating similarly to native pancreatic tissue that controls blood glucose, the result is a commercial-scale potential 'functional cure' for insulin-dependent diabetes.



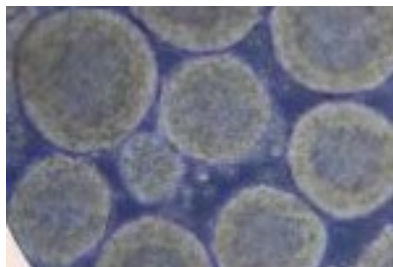
*In vivo-testing of Evotec  
iPSC-derived islet-like  
clusters in the Sernova  
Cell Pouch<sup>TM</sup>*





# iPSC-derived islet-like clusters (ILCs) with long-term antidiabetic efficacy

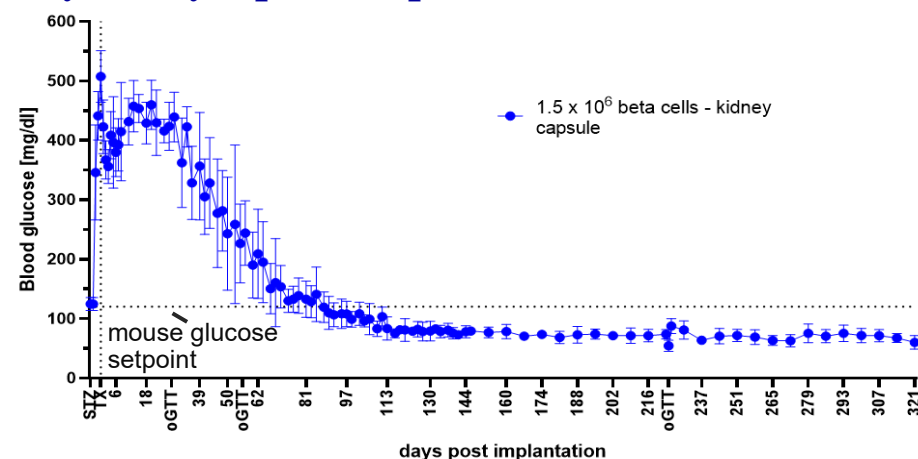
Robust, durable normalization of glycemic control in diabetic mice



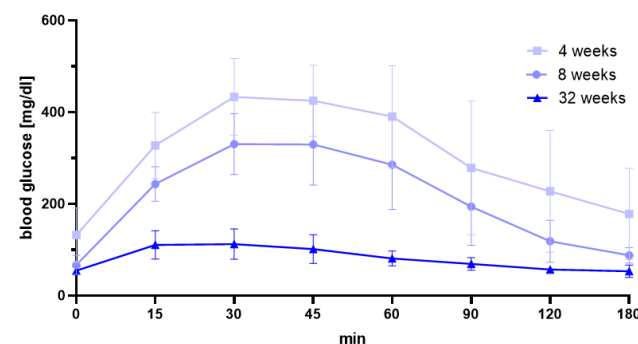
Evotec GMP manufacturing site near Modena/Italy

- We have developed a scalable, GMP-compatible process for ILC manufacturing from a GMP iPSC line
- Drug product with completed endocrine differentiation and optimized beta cell fraction
- We target an immature (KCl responsive) beta cell state for a short manufacturing process and high product resilience
- Manufacturing involves a cryopreservation step, and is currently implemented at Evotec's GMP manufacturing site

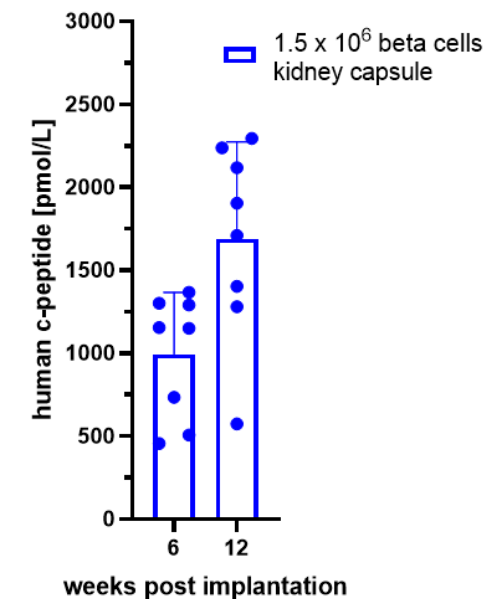
## Efficient normalization of random fed glucose by kidney capsule-implanted ILCs



## oGTT at weeks 4, 8 and 32 post ILC implantation



## Circulating hC-peptide



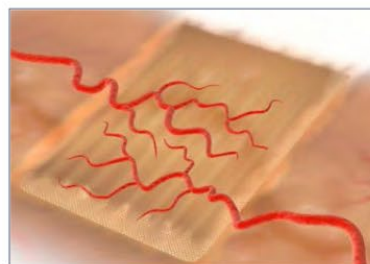
# Combining high quality iPSC-derived ILCs with a clinically proven device

## Evotec ILCs with Sernova Cell Pouch™

- The Sernova Cell Pouch™ is a pre-implanted, vascularized device providing an optimal environment for therapeutic cell function<sup>1</sup>
  - Accessible/retrievable implantation site
- Sernova has promising clinical data with isolated human islets in the Cell Pouch™
- Evotec and Sernova collaborate to develop a combination of ILCs in the Cell Pouch™ for diabetes cell therapy
- Initial patient population will be immunosuppressed patients with T1D

### Cell Pouch Containing Therapeutic Cells

Biologically compatible delivery process – allows natural vascularization



Proprietary Cell Pouch is placed deep under the skin, allowing for vascularization & creating a natural environment for long-term function of therapeutic cells



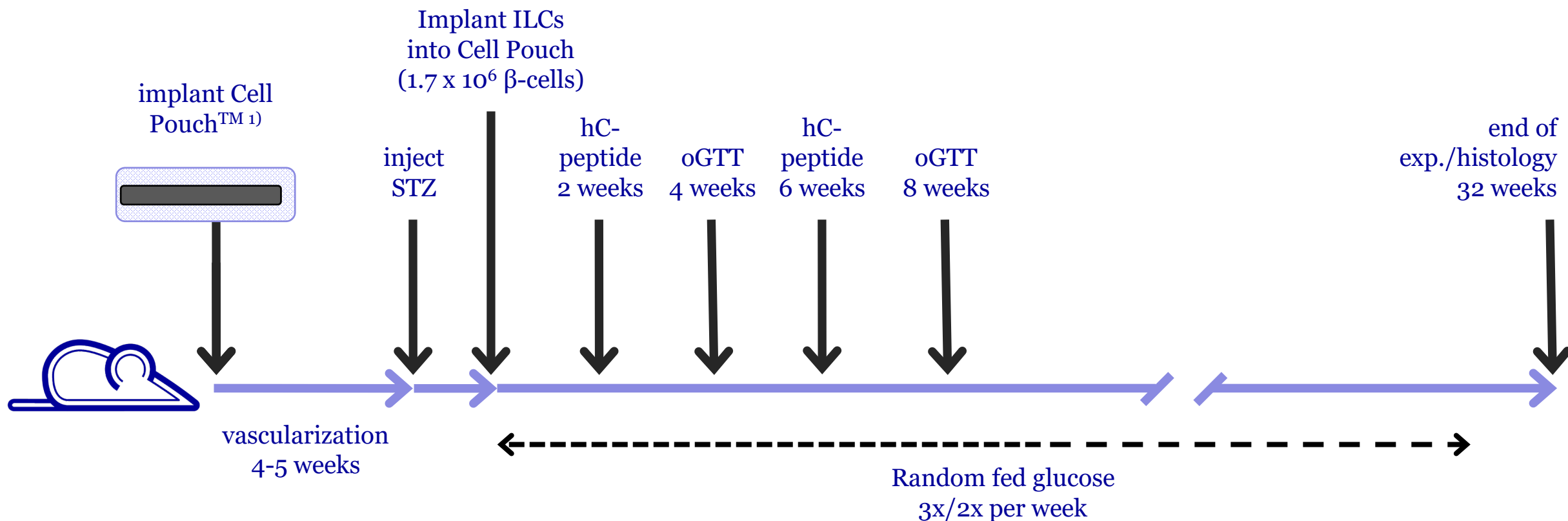
Therapeutic cells are transplanted directly into the vascularized tissue chambers of the proprietary Cell Pouch



Therapeutic cells are responsive to endogenous regulation and release missing proteins or hormones into the bloodstream to correct biological dysfunction

# Testing the ILC + Cell Pouch™ combination in diabetic mice

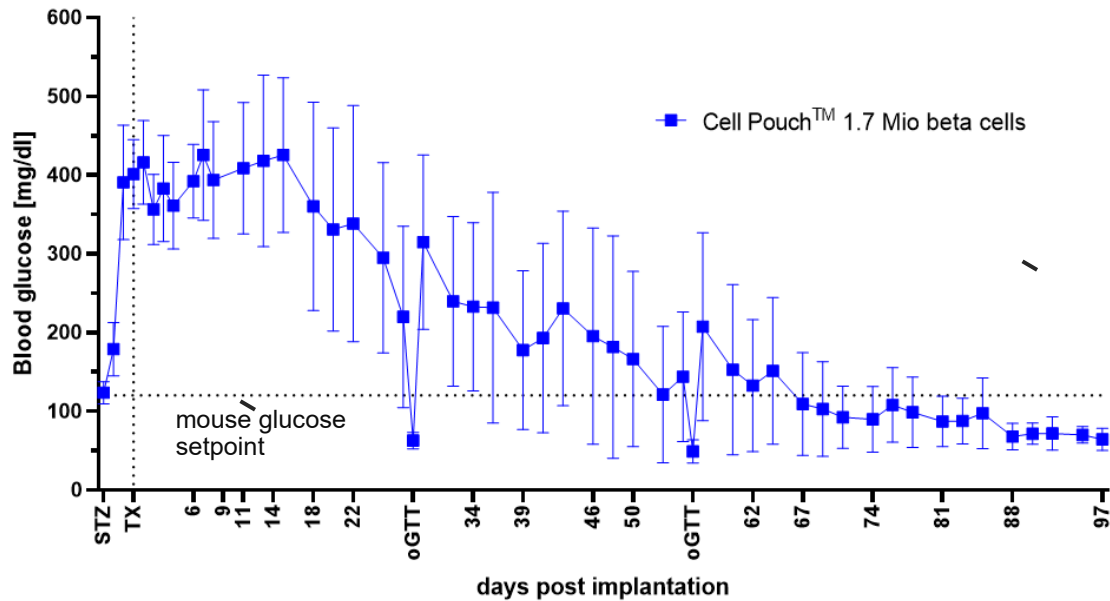
Sentinel-size Cell Pouch™ in STZ-diabetic NSG mice with ILCs containing  $1.7 \times 10^6$  beta cells



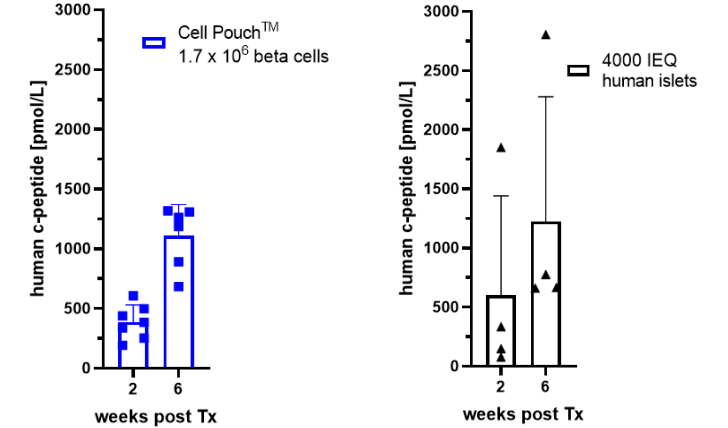
# Excellent anti-diabetic activity of ILCs in the Cell Pouch™

Rapid normalization of glycemic control with human islet-like potency

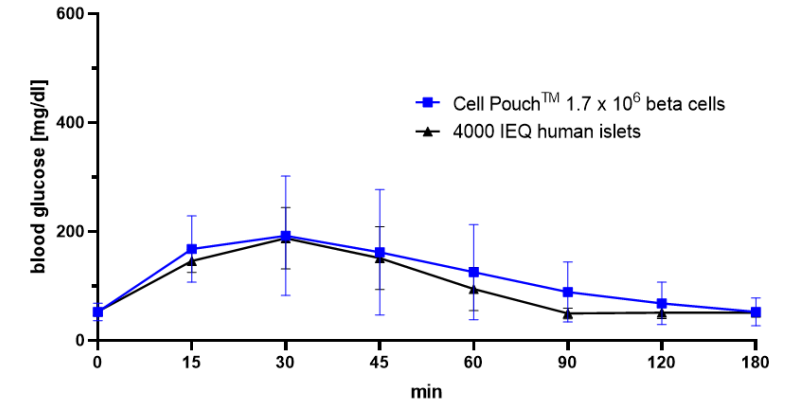
## Efficient normalization of random fed glucose



## Robust circulating hC-peptide levels



## Efficient glucose clearance and no hypoglycemia in oGTT (8 week timepoint)

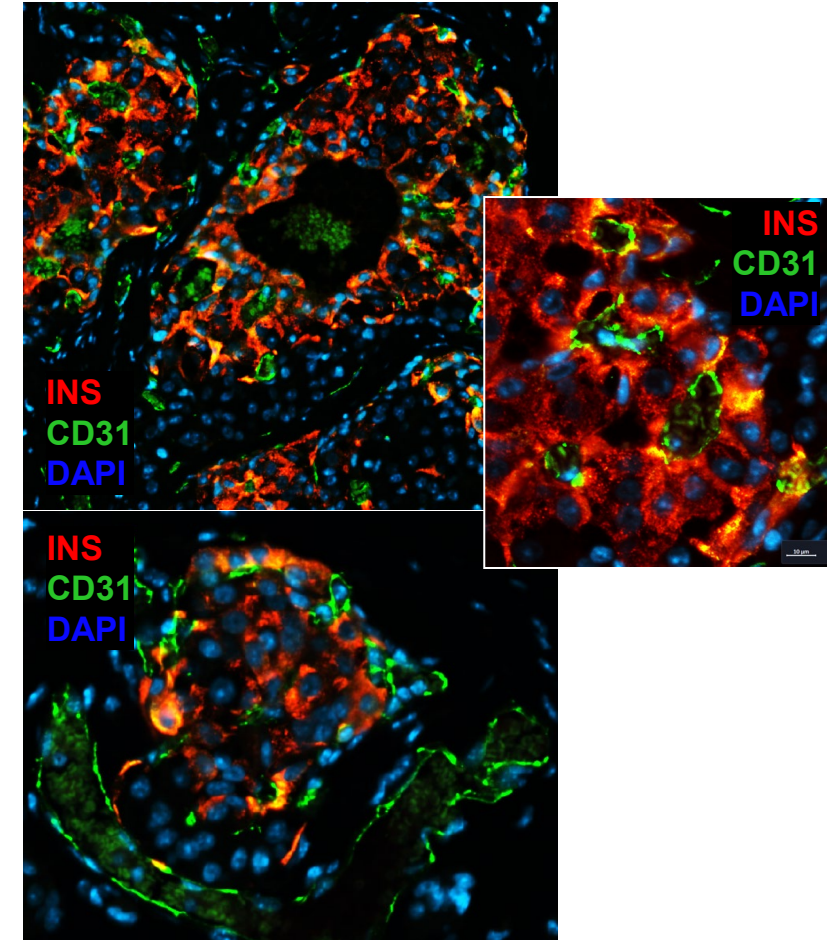
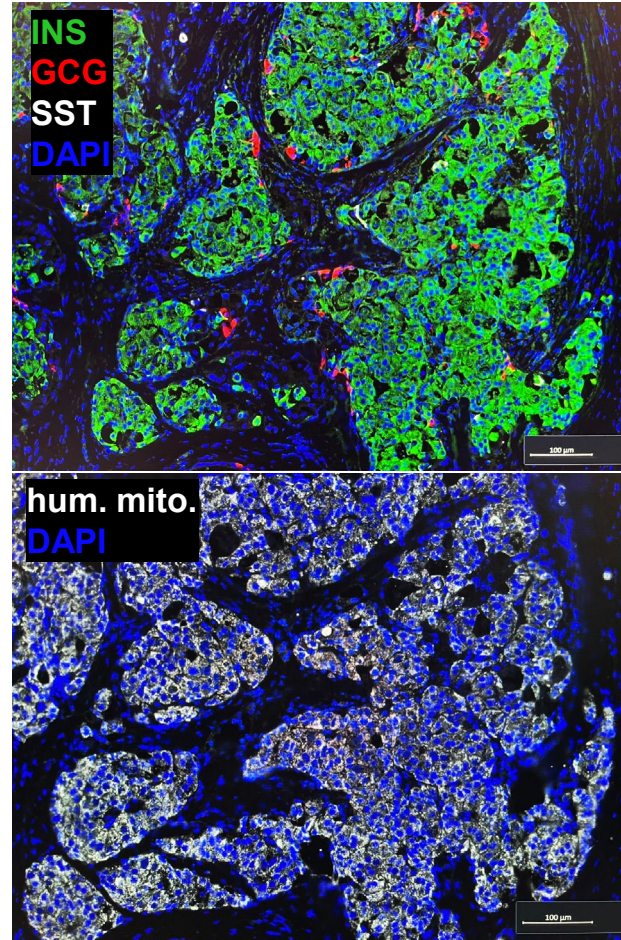




# High $\beta$ -cell fraction and dense vascularization of ILCs in the Cell Pouch™

Histological graft analysis – 32 weeks post-implantation

- Abundant endocrine cells with high beta cell fraction detectable
  - Alpha and delta cells are observed at lower frequencies
- ILC cells are embedded in host-derived connective tissue
- Excellent intra-graft vascularization, likely contributing to strong graft functionality<sup>1)</sup>





# Excellent anti-diabetic activity of an ILC/Cell Pouch™ combination

## Summary

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- We have set up a scalable GMP manufacturing workflow from GMP iPS cells to ILCs, yielding a high beta cell fraction drug product
  - ILCs are cryopreserved at a late intermediate stage
  - Endocrine differentiation is complete – no post-implantation variability of cell composition
  - Immature beta cells to ensure a cost-effective manufacturing process, improved cell shipping and post-implantation survival
  - ILCs deliver rapid onset of physiological function, and human islet-like potency on a per-beta-cell basis after maturation is complete
- The Evotec ILC/Sernova Cell Pouch™ combination delivers excellent graft integration, vascularization and potent anti-diabetic function
  - Cell implantation in the Cell Pouch™ also ensures retrievability
- The project is at GMP manufacturing stage and on track for clinical testing in humans in 2024



Upcoming Catalysts

# Upcoming Catalysts

## Anticipated Milestones and Data

2023

- Immune protection update
- US Phase 1/2 T1D second cohort patient enrollment update
- US Phase 1/2 T1D first cohort clinical update
- US Phase 1/2 T1D second cohort clinical update
- FDA interactions regarding potential US Phase 3 design for donor islets / Cell Pouch

H1 2023

H1 2023

Q2 2023

Q4 2023

Q4 2023

2024

- IND filing with Cell Pouch and Evotec islet clusters
- Phase 1/2 initiation of Cell Pouch with Evotec islet clusters

H1 2024

H2 2024

*Note – dates above are based on calendar year*



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