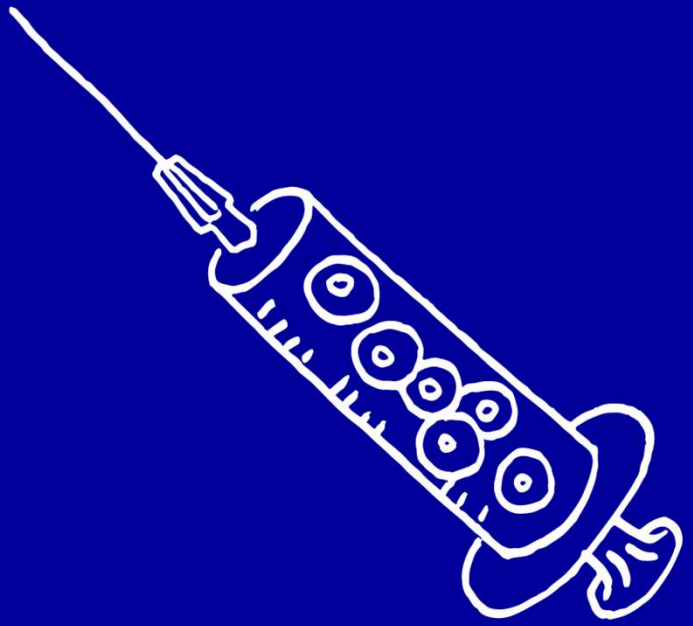
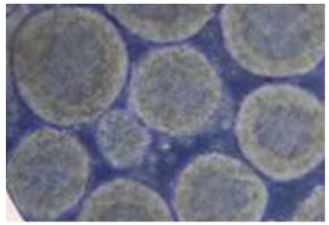
#RESEARCHNEVERSTOPS

In vivo-testing of Evotec iPSC-derived islet-like clusters in the Sernova Cell Pouch™



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

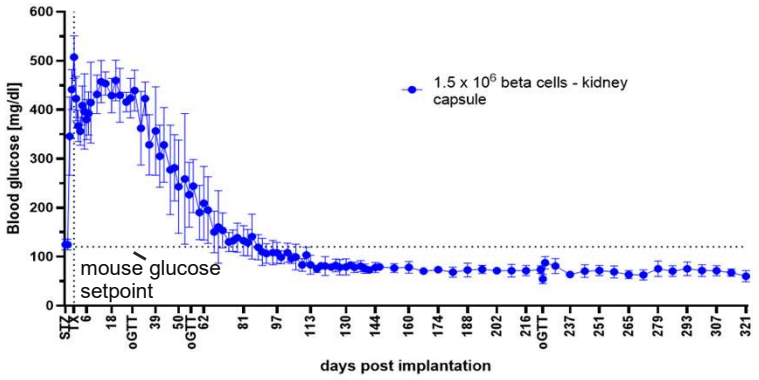
Robust, durable normalization of glycemic control in diabetic mice



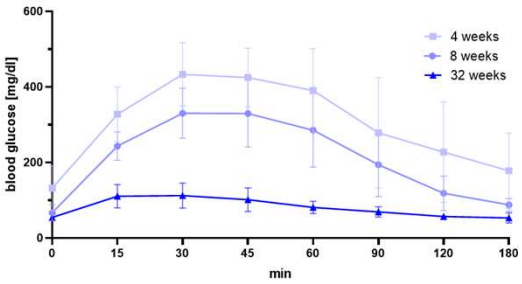
Evotec GMP manufacturing site near Modena/Italy

- 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

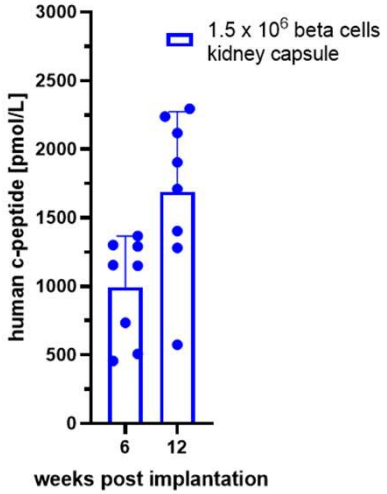
Efficient normalization of random fed glucose by kidney capsule-implanted ILCs



oGTT at weeks 4, 8 and 32 post ILC implantation



Circulating hC-peptide



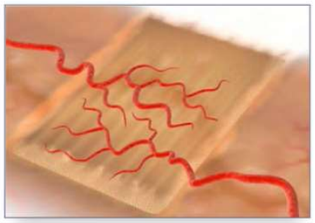
Combining high quality iPSC-derived ILCs with a clinically proven device

Evotec ILCs with Sernova Cell Pouch™

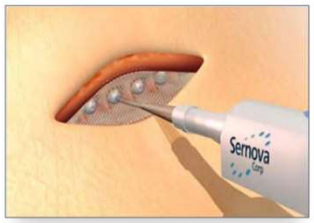
- The Sernova Cell Pouch™ is a pre-implanted, vascularized device providing an optimal environment for therapeutic cell function[1]
  - Accessible/retrievable implantation site
- Sernova has promising clinical data with isolated human islets in the Cell Pouch™
- Evotec and Sernova collaborate to develop 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



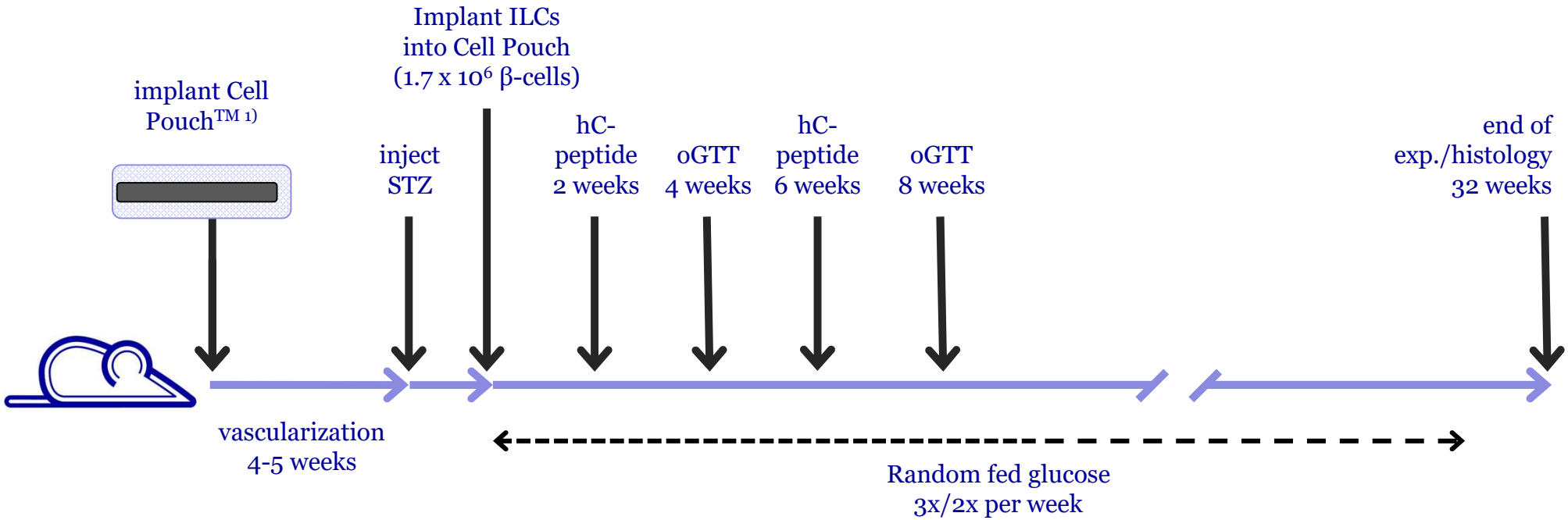
Therapeutics cells are transplanted directly into the vascularized tissue chambers of the proprietary Cell Pouch

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

1 https://sernova.com/

Testing the ILC + Cell Pouch™ combination in diabetic mice

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



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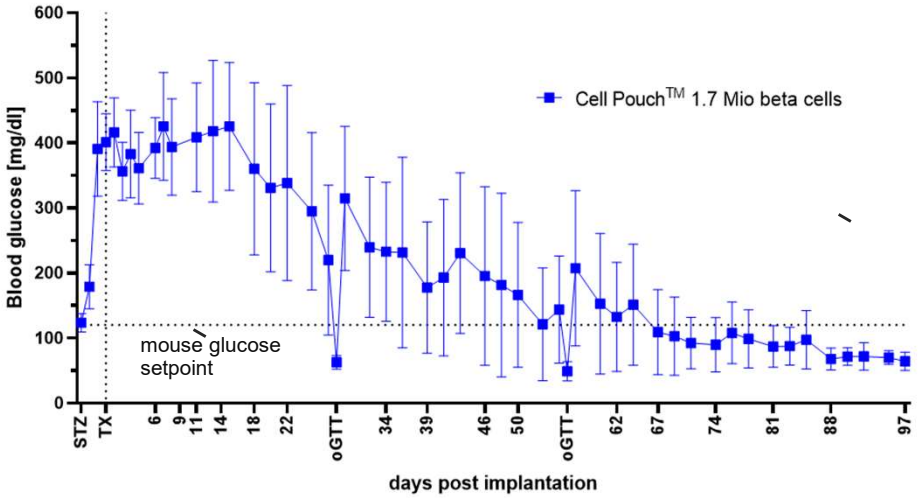
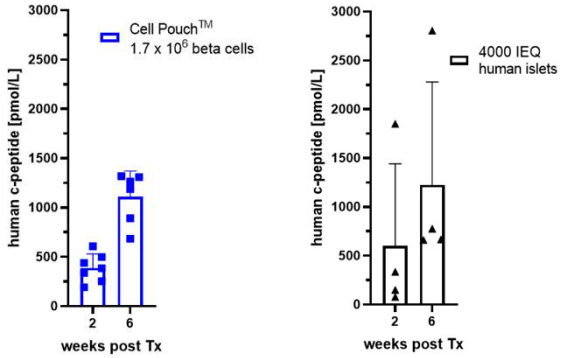
Excellent anti-diabetic activity of ILCs in the Cell Pouch™

Rapid normalization of glycemic control with human islet-like potency

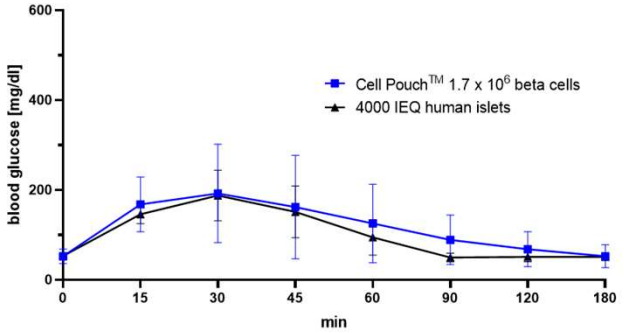
Efficient normalization of random fed glucose



Robust circulating hC-peptide levels



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



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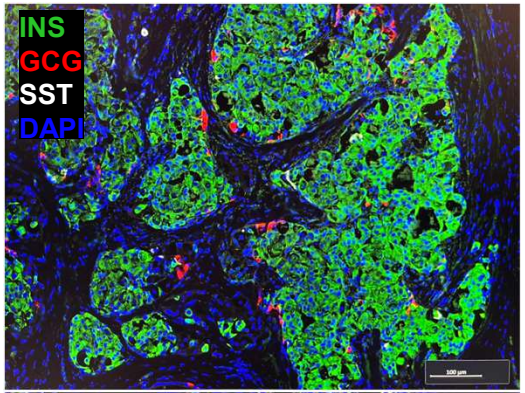
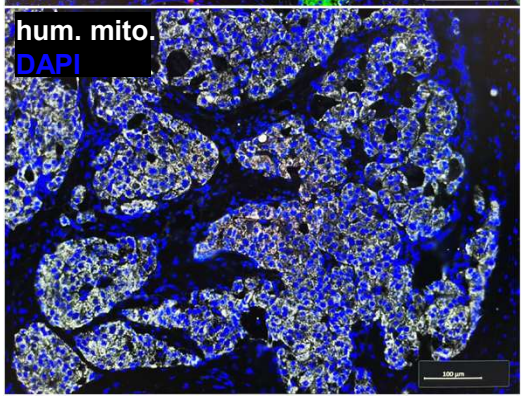
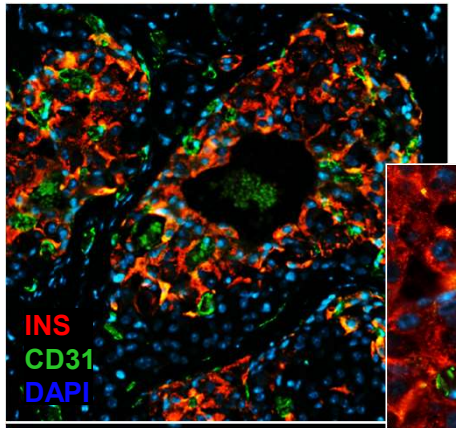
High β-cell fraction and dense vascularization of ILCs in the Cell Pouch™

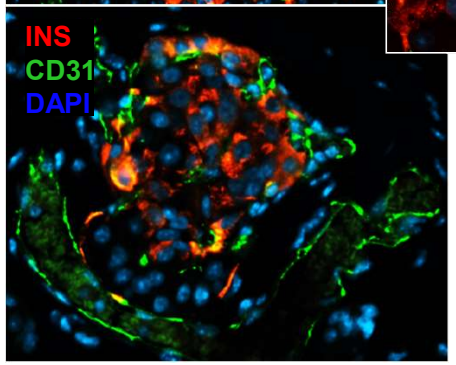
Histological graft analysis – 32 weeks post-implantation

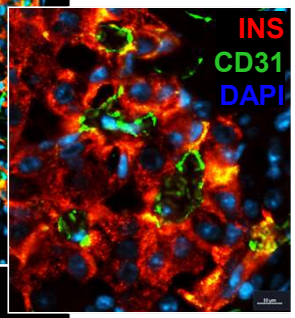
- Abundant endocrine cells with high beta cell fraction detectable
  - Alpha and delta cells are observed at lower frequencies
- ILC cells are embedded in host-derived connective tissue
- Excellent intra-graft vascularization, likely contributing to strong graft functionality[1)]











1 Vascularization staining data: Arash Memanejadian, Sernova Inc.

Excellent anti-diabetic activity of an ILC/Cell PouchTM combination

Summary

- 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

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Matthias Austen
SVP Cell Therapy

Matthias.Austen@evotec.eu

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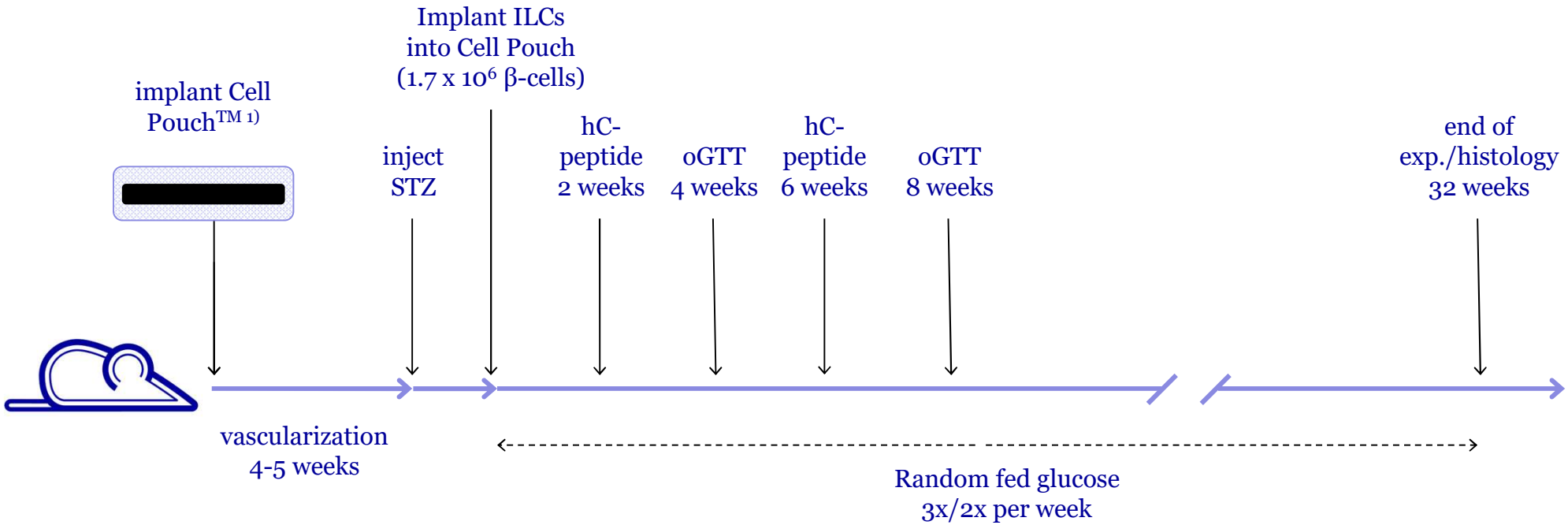

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