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# Sernova Corp

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*The Path To A Regenerative Medicine Cure*

## BIOInvestor Forum
## October 13th – 15th , 2020

# Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of applicable Canadian securities laws. Forward-looking statements in this presentation are statements that are not historical facts and are generally, but not always, identified by the words “expects”, “plans”, “anticipates”, “believes”, “intends”, “estimates”, “projects”, “potential” and similar expressions, or that events or conditions “will”, “would”, “may”, “could” or “should” occur. Forward-looking statements include statements about subsequent clinical activity, including enrolment of patients and continuing results therefrom, and the potential benefits, safety and efficacy of the Cell Pouch for various indications, including type 1 diabetes (T1D).

While Sernova considers these assumptions to be reasonable, these assumptions are inherently subject to significant scientific, business, economic, competitive, market and social uncertainties and contingencies. Additionally, there are known and unknown risk factors that could cause Sernova’s actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements contained in this presentation. Results in early-stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. Readers should not place undue reliance on these statements, or the scientific data presented and should refer to the risk factors identified in the company’s continuous disclosure filed on SEDAR.com. Sernova expressly disclaims any intention or obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise.

# Sernova: Innovator & Leader

## Publicly traded, clinical-stage RM therapeutics solution innovator & leader:

- Cell therapy therapeutics solution **platform** treating chronic diseases & enhancing daily QOL
- **Integrated RM therapeutic solution** (Cell Pouch™ + therapeutic cells or tissue + immune-protection)
- Broad platform application potential: **multiple large market indications**
- **Cell Pouch** overcomes current barriers associated with therapeutic cells survival & function by forming **organ-like environment** for the cells to **produce missing proteins, hormones**, etc.
- **Diabetes lead program** & 1st company with RM therapeutic product showing insulin production & early clinical efficacy indicators for type 1 diabetes (T1D). **Active US Phase I/II clinical trial**.
- **Pre-Clinical proof-of-concept** demonstrated for **hemophilia A & thyroid disease**

# Sernova's Platform Approach

## Integrated RM Therapeutic Solution for Treatment of Chronic Diseases


### Cell Pouch

Implantable proprietary medical device that provides vascularized environment for therapeutic cells

### Therapeutic Cells

Human cells (donor / stem) & tissues that produce & release missing proteins or hormones into the bloodstream

### Immune Protection

Technologies to protect therapeutic cells from immune system attack

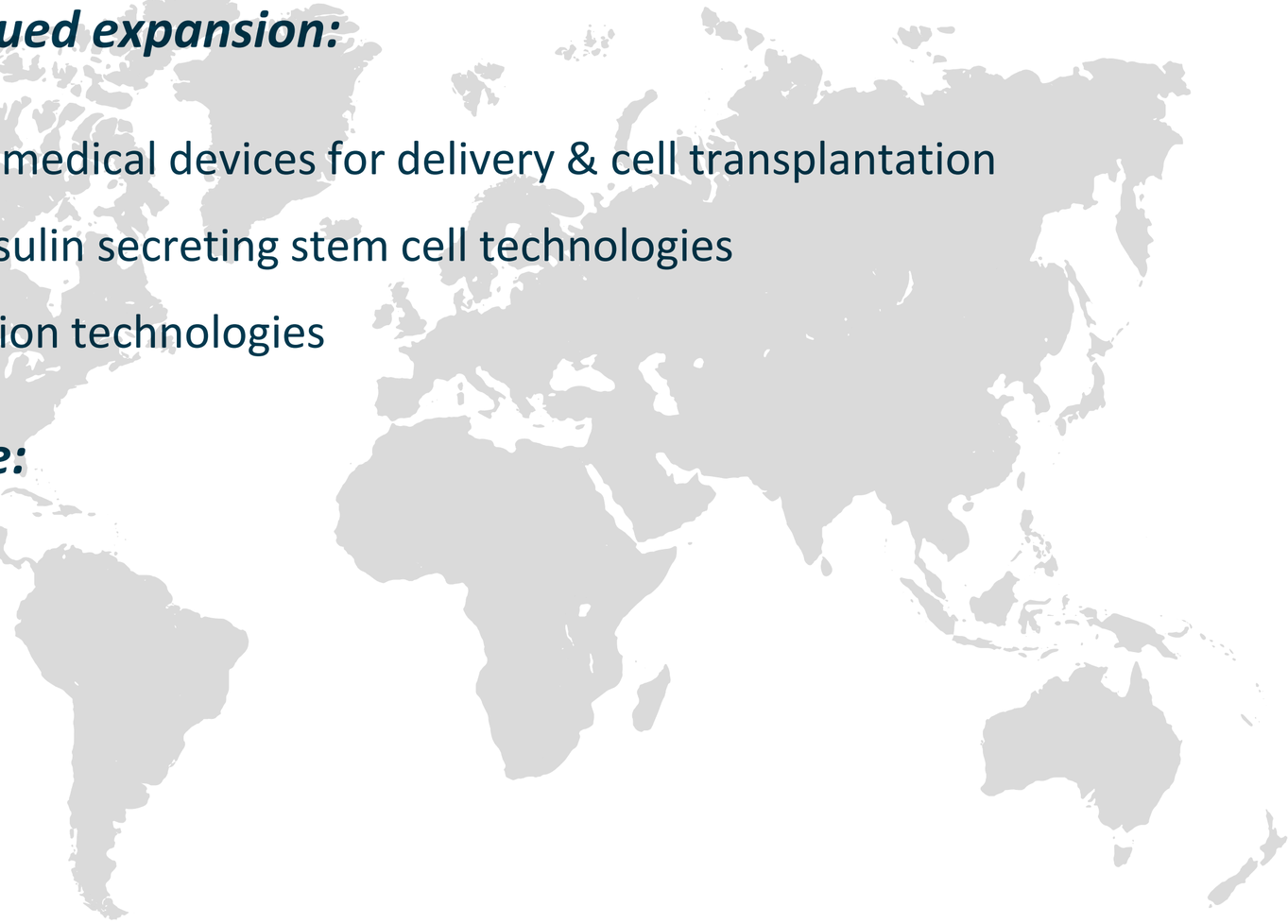
# Worldwide IP / Patent Portfolio

***International patents & patent applications portfolio in multiple patent families with broad application & continued expansion:***

- Composition & use of medical devices for delivery & cell transplantation
- Glucose responsive insulin secreting stem cell technologies
- Local immune protection technologies

***Broad geographic coverage:***

- North America
- South America
- Europe
- Asia



# Sernova Pipeline

| CELL POUCH CANDIDATE | PRE-CLINICAL | PHASE I | PHASE II | PHASE III | DEVELOPMENT STAGE | INDICATION |
|---|---|---|---|---|---|---|
| HUMAN DONOR ISLETS, SYSTEMIC IMMUNE PROTECTION | | | | | PHASE I/II INITIATED DEC 2018 | HYPOGLYCEMIA UNAWARENESS |
| LOCALLY IMMUNE-PROTECTED STEM CELL DERIVED CELLS | | | T1D | | ANTICIPATED 2ND APPROVAL FOR DIABETES | ALL INSULIN DEPENDENT DIABETIC PATIENTS |
| CORRECTED PATIENT CELLS | | | Hemophilia A | | PRE-CLINICAL | SEVERE HEMOPHILIA A PATIENTS |
| ALLOGRAFT IMMUNE-PROTECTED CELLS | | | | | EARLY DEVELOPMENT | BROADER HEMOPHILIA A PATIENTS |
| THYROID CELLS | | | Thyroid | | PRE-CLINICAL | THYROIDECTOMY PATIENTS FOLLOWING HYPERTHYROIDISM |

# Diabetes Market Opportunities

| | IP Status | 2020 Potential Patient Population (before market access considerations) | | | Potential Commercial Opportunity | | |
|---|---|---|---|---|---|---|---|
| | *Device / Method Patent* | *T1D Severe HU with Human Donor Islets* | *T1D Severe HU with iPSC* | *All T1D with iPSC* | *T1D Severe HU with Human Donor Islets* | *T1D Severe HU with iPSC* | *All T1D with iPSC* |
| **U.S.** | ✓ Granted | ~0.65 K Total Transplants | ~240 K Patients | ~1.6 M Patients | $65 – 130 M (per year) | $5 – 9.5 B (in total) | ↑ ? |
| **EU5** | ✓ Granted | ~0.5 K | ~195 K | ~1.3 M | $40 – 75 M | $3 – 6 B | ↑ ? |
| **APAC** *CHN & JPN only* | ✓ Granted | ~3.0 K | ~1.0 M | ~7.3 M | ~$225 M | ~$15 B | ↑ ? |
| **Total** | Sernova has a global IP portfolio across all key markets | ~4.2 K Transplants | ~1.4 M Patients | ~10.2 M Patients | $340 – 450 M (per year) | $24 – 31 B (in total) | ↑ ? |

*HU* = Hypoglycemia Unawareness  *Hypolgly.* = Hypoglycemia

# RM Diabetes Competitive Landscape

| | Clinical Efficacy Data: Therapeutic C-peptide Levels Measured in Bloodstream | Device Vascularization Islet Engraftment Demonstrated in Humans | Local Immune Protection Technology | Financial Metrics (USD Millions) | |
|---|---|---|---|---|---|
| Sernova Corp | ✓ Phase I/II initiated late 2018 in T1D patients with HU[1]; initial data demonstrates bloodstream C-peptide in T1D patient after 90-days post implant & other efficacy indicators[2] | ✓ Interim data demonstrated highly vascularized tissue chambers in human patients & abundant surviving islets robustly producing insulin [7] | ✓ Immuno-suppression is needed under current clinical trial regiment[1]. Local immune protection technologies secured. | $48 M | As of October 2020 Sernova's market cap |
| ViaCyte Regenerating Health | ✗ PEC-Direct initiated Phase I/II in 2017 in high risk T1D patients; initial data released in 2019 demonstrated cells produce sub-therapeutic C-peptide[3]<br>✗ PEC-Encap initiated Phase I/II in 2014, paused due to poor engraftment & restarted in 2019[4] | ✓ PEC-Direct vascularizes directly[8] & is verified in human trial[4];<br>✗ PEC-Encap has surface diffusion[8] but their trial was "paused" due to low levels of engraftment[9] – to date human vascularization data is lacking | ✗ PEC-Direct program requires long-term immunosuppression[8];<br>? PEC-Encap program may not require immunosuppression[8] – to date human validation has not been demonstrated | $240 M | November 2018, ViaCyte raised $80 M Series D financing at an undisclosed valuation[9]; in total ViaCyte has raised ~$240 M to date[14] |
| semma THERAPEUTICS | ✗ Expected to enter the clinic by 1H of 2020 for hypoglycemia unawareness; a broader trial for adult T1D patients is planned for 2020 H2[5] | ✗ Pre-Clinical PoC data in pigs demonstrated the vascularization capability of stem cell encapsulating device[5] – to date human vascularization data has not been generated | ? Semma's proprietary delivery system is designed to protect cells from the immune system[5] though human validation is lacking to date | $950 M | August 2019, Vertex acquired Semma for a $950 M cash payment[15] |
| sigilon therapeutics | ✗ Expected to enter the clinic by 1H of 2020 for hemophilia A using Shielded Living Therapeutics™ (SLTx™)[6] | ✗ In experimental animal models, SLTx™ resisted fibrosis for up to 12 months[10] – to date human vascularization data has not been generated | ? Sigilon believes SLTx™ will negate the need for immunosuppression[12] though human validation is lacking to date | $195 M | March 2020, Sigilon announced $80.3 M Series B financing at an undisclosed valuation[12]; in total Sigilon has raised ~$195 M to date[14] |

1.ClinicalTrials.gov; 2. Company Press Release; 3. Company Press Release; 4. JDCA; 5. Company Press Release; 6. Company Press Release; 7. Company Press Release; 8. Company Website; 9. Company Press Release; 10. Company Website; 11. Company Website; 12. Company Press Release; 13. Capital IQ; 14. Pitchbook Estimate; 15. Company Press Release
HU: Hypoglycemia Unawareness; T1D: Type 1 Diabetes.

# Therapeutic Cells

## Therapeutic Cell Options

- **Human donor cells** enable early safety / efficacy testing in the clinic for indications & patients with unmet needs & advanced disease (i.e. diabetes HU patients). Supply is limited; however, they enable **Cell Pouch validation** in preparation for stem cell technologies.
- **Stem cell derived cells** enable expanded availability to an **unlimited supply of cells** for large market opportunities (i.e. all T1D patients & other indications)

## Stem Cell Derived Technologies

- **Exclusive worldwide license** to a diabetes stem cell derived technology unlocking potential access to all T1D subjects & 30% of TD2 who convert to insulin use
- **Big Pharma collaboration** on other best in class stem cell derived technologies to advance **partnering opportunities**

# Immune Protection

- **Transplanted therapeutic cells must be protected from a natural immune system attack** response.
- While established systemic transplantation immuno-suppression (anti-rejection) drugs can be effective, **local immune protection (LIP) is optimal**. LIP alternatives present different opportunities & challenges.
- **Multiple approaches** under consideration to **optimize indication match, therapeutic solution delivery** & benefit, & eliminate the need for drugs & their associated side effects.

| IMMUNE PROTECTION APPROACH | SYSTEMIC (S) or LOCAL (L) | DEVELOPMENT PROFILE | | | | | SERNOVA ACTIVITY |
|---|---|---|---|---|---|---|---|
| | | Proof of Concept | Clinic Entry Timing | Side Effects | Development Risk Profile | Regulatory Complexity | |
| Immuno-suppression drugs | S | Proven | Achieved | Medium | Low | Low | In clinic |
| Immuno-protected macro device | L | Failed | Achieved | Medium | High | Medium | Never pursued |
| Cell encapsulation (conformal coating) | L | Proven | Near term | Low | Low | Low | Moving toward clinic |
| Cell tolerance (gene editing) | L | TBD | Mid term | Under Evaluation | Under Evaluation | Medium | Under evaluation |

# Immune Protection

**Conformal Coating Technologies:**

- Sernova's proprietary cellular conformal coating technology - developed and optimized with years of research
- It consists of a thin biocompatible porous polymer hydrogel coating surrounding therapeutic cells (islets, stem cells)
- Proven to allow for physiological transfer of insulin and glucose unlike other encapsulation technologies
- Sernova is preparing for use within its Cell Pouch for islets, stem cell derived cells for multiple applications
- The potential to eliminate the need for anti-rejection medications significantly increases the number of treatable patients for Sernova's clinical products

**Gene-Editing Technologies:**

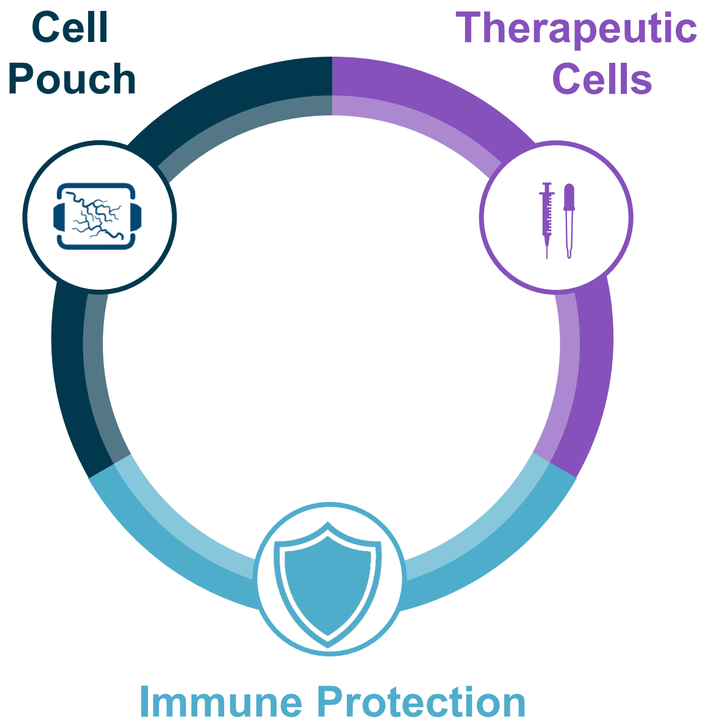
- Sernova entered in a collaboration to evaluate the potential of Sernova's pluripotent stem cell-derived pancreatic islet beta cells, and hemophilia cells engineered with AgeX's UniverCyte technology, to evade human immune detection.
- UniverCyte uses a modified form of HLA-G, a potent immunomodulatory molecule, which in nature protects an unborn child from their mother's immune system. AgeX's modified HLA-G has the potential to allow for long-term, stable and high expression of the immunomodulatory effect.
- The complementary combination of technologies could enable the transplantation of therapeutic cells in patients with T1D in an off-the-shelf manner using Sernova's Cell Pouch, without human leukocyte antigen (HLA) tissue matching or concurrent administration of immunosuppressive medications

# Strategic Development Approach

| Device | Therapeutic Cells | Immune Protection |
|---|---|---|
| Sernova Proprietary Cell Pouch | Human Donor | Immuno Suppression Drugs (systemic) |
| | Stem Cell Derived (iPSC / EPS) | Cell Encapsulation *Conformal Coating* (local) |
| | Human Tissue | Cell Tolerance *Gene Editing* (local) |

Development + Testing Cycle

## Sernova Integrated RM Therapeutic Solution Portfolio




Systematic stepwise “building-block” process deployed to:

- minimize unknown variable interdependencies
- de-risk development outcomes

vs. “all-in-one” failures by other RM cell therapy companies

# Diabetes… Hope for a Functional Cure

***The Reality:*** Diabetes is one of the most prevalent diseases & pervasive medical problems impacting society & everyday quality of life (QOL) today

- ***463 million affected worldwide and nearly 10% of these individuals have T1D****(1)*
- ***T1D represents a potential commercial opportunity of $30B+ for Sernova***

***The Hope:*** A functional cure for everyone suffering from diabetes

***The Problem:*** Lack of integrated RM therapeutic solution

***The Future:*** Blockbuster potential for Sernova's platform which could establish a new standard of care for diabetes treatment & management. Potential to be the biggest therapeutic advancement in diabetes treatment since insulin discovery 100 years ago.

*(1) source: International Diabetes Federation*

# Diabetes Clinical Progress Summary


- Completion of first-in-human proof-of-concept study for diabetic condition HU
- Clinical protocol & regulatory package development for US Ph I / II clinical trial for diabetic HU condition (T1D Study)
- FDA IND clearance to commence T1D Study
- T1D Study funding grant awarded by JDRF

- Prominent diabetes clinical investigator Dr. Witkowski joins T1D Study
- UChicago IRB approval obtained
- Clinical Trial & Consulting Services (CTI) engaged as T1D Study CRO
- Medtronic contracted for T1D Study CGM
- T1D Study patient screening & recruitment initiated, 1st patient enrolled

- Cell Pouch implantation into first T1D Study patient
- Human islet cells transplantation into Cell Pouch in first T1D Study patient
- T1D Study positive early safety & efficacy indicators observed
- Enduring level of fasting C-peptide in bloodstream observed

- Positive DSMB Review & Recommendation for Continuation of Ph I/II clinical trial
- Positive Efficacy Endpoint – Survival of Endocrine Tissue
- Ongoing T1D Study patient enrollment, treatment & follow-up

# Diabetes First Clinical Indication: HU

**Hypoglycemia unawareness (HU), the most critical unmet need in diabetes, affects 15% of T1D patients (~240 K patients in the US alone)**

- clinically defined as a complication of diabetes in which the **patient is unaware of a deep drop in blood sugar**
- **patients do not experience hypoglycemia warning symptoms** (palpitations, anxiety, excessive sweating, light headedness)
- **harmful effects: diabetic ketoacidosis (DKA), coma & death**

**1st study population for Sernova's integrated RM therapeutic solution for lead indication of insulin-dependent diabetes**

# US Ph I/II Study Design

## US Ph I/II Safety, Tolerability, Efficacy Study

***Study Design:*** Company-sponsored IND. Open-label, single-arm study. Human donor islets are transplanted into the Cell Pouch after implantation & stable anti-rejection medication activity has been established.

***Primary Objective:*** To demonstrate the safety & tolerability of islet transplantation into the Cell Pouch for the treatment of HU in T1D subjects with a history of severe hypoglycemic episodes.

***Secondary Objectives:*** To establish islet release criteria that accurately characterize the islet product & are predictive of clinical transplant outcomes into the Cell Pouch, demonstrated through defined efficacy measures:

- Survival of endocrine tissue in the Cell Pouch
- Proportion of subjects with a reduction in severe hypoglycemic events
- Proportion of subjects with a reduction in HbA1c >1mg%
- Over 20 additional endpoint analyses will occur

***Status:*** Study Active & Ongoing

- IND allowance by FDA & protocol approved by IRB
- Multiple subjects implanted & transplanted
- Positive early findings announced
- Patient enrolment & recruitment ongoing

# US Ph I/II Case Study Early Findings

## US Ph I/II Safety, Tolerability, Efficacy Study

### Safety Findings (90 days post-transplant)

*Incidence & severity of adverse events associated with Cell Pouch were monitored:*

- **No incidences of AEs** determined to be probable or highly probable to the Cell Pouch
- **Cell Pouch well-tolerated & safe** during the implant & the time of transplant
- **No reactions** to the Cell Pouch implant
- Cell Pouch **well-incorporated with vascularized tissue** & deemed suitable to receive the islet transplant

***WHY IS THIS IMPORTANT?***

Demonstrated Cell Pouch safety is a prerequisite for its use in multiple therapeutic indications

***CONCLUSION: S*afety findings met the first measure of the primary endpoint**

# US Ph I/II Case Study Early Findings

## US Ph I/II Safety, Tolerability, Efficacy Study

## First Patient Observed Data Presented by Clinical Investigator*

## Early Efficacy Findings

| Islet Transplant Status: | Before | 3 Mo. After |
|---|---|---|
| **Bodyweight** | 83kg | 73kg |
| **Hemoglobin A1C** | 6.5 | 5.6 |
| **Daily Use Of Long Acting Insulin Tresiba** | 14U | 8U |
| **Daily Use Of Short Acting Insulin** | 15 – 16 | 14 – 15 |
| **Severe Hypoglycem. Events** | 4 per week | 1 per week |

*presented at IPITA Q3 2019 in Lyon, France

*90-day post-transplant glucose tolerance test (i.e. patient given a high sugar drink) was administered over several hours:*

- showed **increase in blood levels of C-peptide**
- showed **increase in blood levels of insulin**

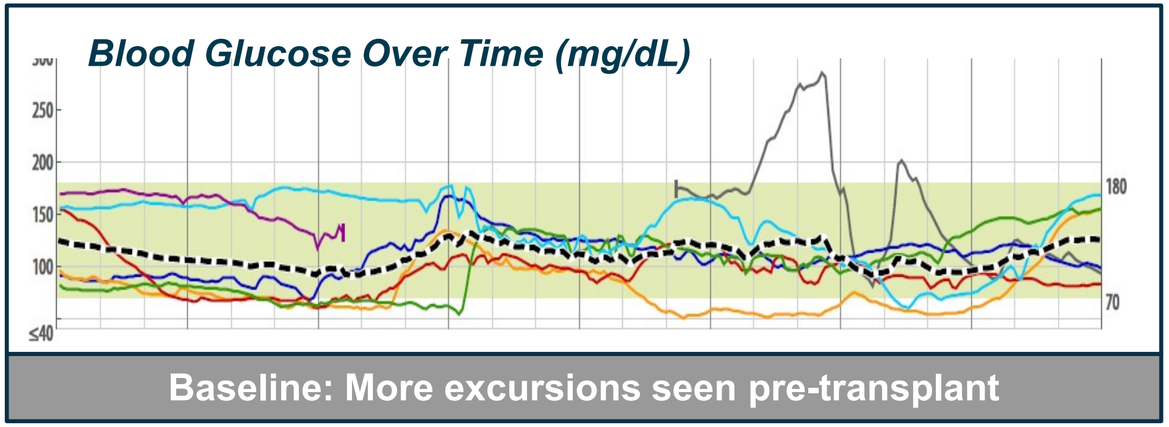
***WHY IS THIS IMPORTANT?***

C-peptide is a biomarker confirming insulin production by cells

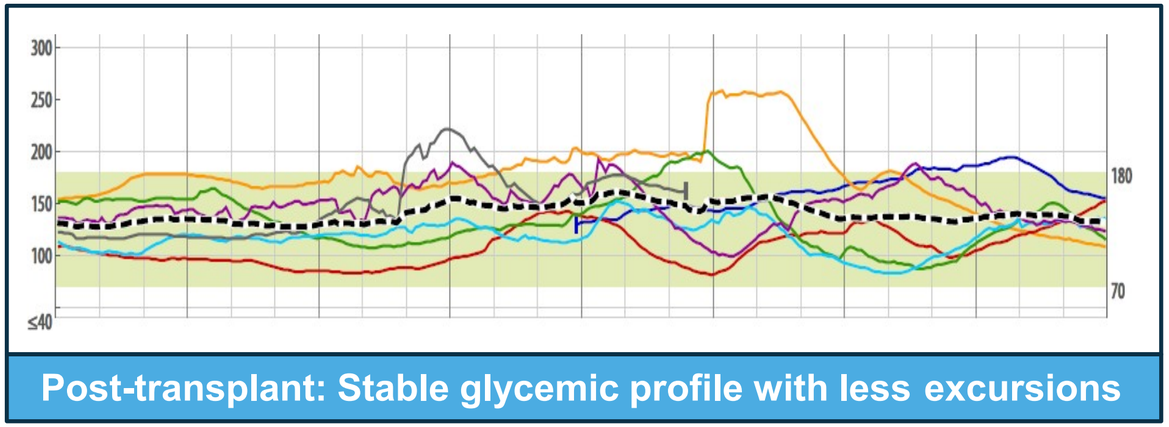
***SUBSEQUENT FINDING*: Enduring blood levels of fasting C-peptide & ongoing evidence of islet engraftment & durable therapeutic effect detected post-second Cell Pouch islet dose**

# US Ph I/II Case Study Early Findings

## Improvement in *ALL* CGM Parameters



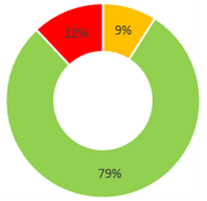

**Baseline: More excursions seen pre-transplant**




**Post-transplant: Stable glycemic profile with less excursions**

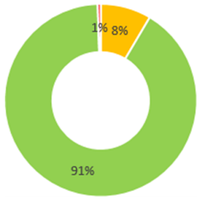
**BASELINE CGM**

More excursions, hyper/hypo events
Less time in range




**CGM POST CELL POUCH ISLET TRANSPLANT**

Less excursions, hyper/hypo events
More time in range




Medtronic

- Time above 180 mg/dL
- Time in Range of 70-180 mg/dL
- Time below 70 mg/dL

| Parameter | Baseline | Post-transplant |
|---|---|---|
| High Glucose Value (mg/dL) | 285 | 231 |
| Low Glucose Value (mg/dL) | 50 | 66* |
| # Glucose Excursions | 15 | 3 |
| # High Excursions | 7 | 2 |
| # Low Excursions | 8 | 1 |
| Standard Deviation | 37 | 31 |

* Lowest excursion was 66mg/dL and this occurred only once.

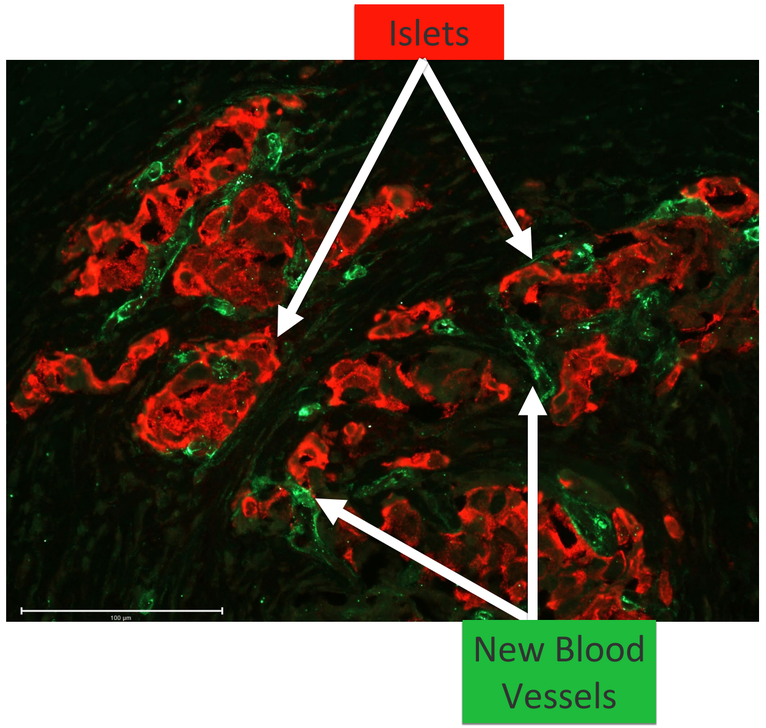
# US Ph I/II 90-Days Post Transplant

## Achievement of Secondary Endpoint

*"Survival of endocrine tissue in the Cell Pouch™ (defined by positive staining of islets during histological analysis) [ Time Frame: 90±5 days post-transplant for sentinel Cell Pouch™ ]"*

***Independent Pathologist reported:***

- **abundant viable, organized islet cells**
- **intimately associated with blood vessels**
- **within a collagen matrix**
- **islet cells strongly express insulin**




- Indicator of transplanted islet health in the therapeutic Cell Pouches remaining in the subject
- Ability to produce insulin and deliver to the bloodstream
- Previously demonstrated by reported findings of blood levels of both glucose-stimulated & fasting C-peptide plus other efficacy indicators

# Earlier First-in-Human Study

**First-in-World Successful Proof-of-Concept**

## Study Design

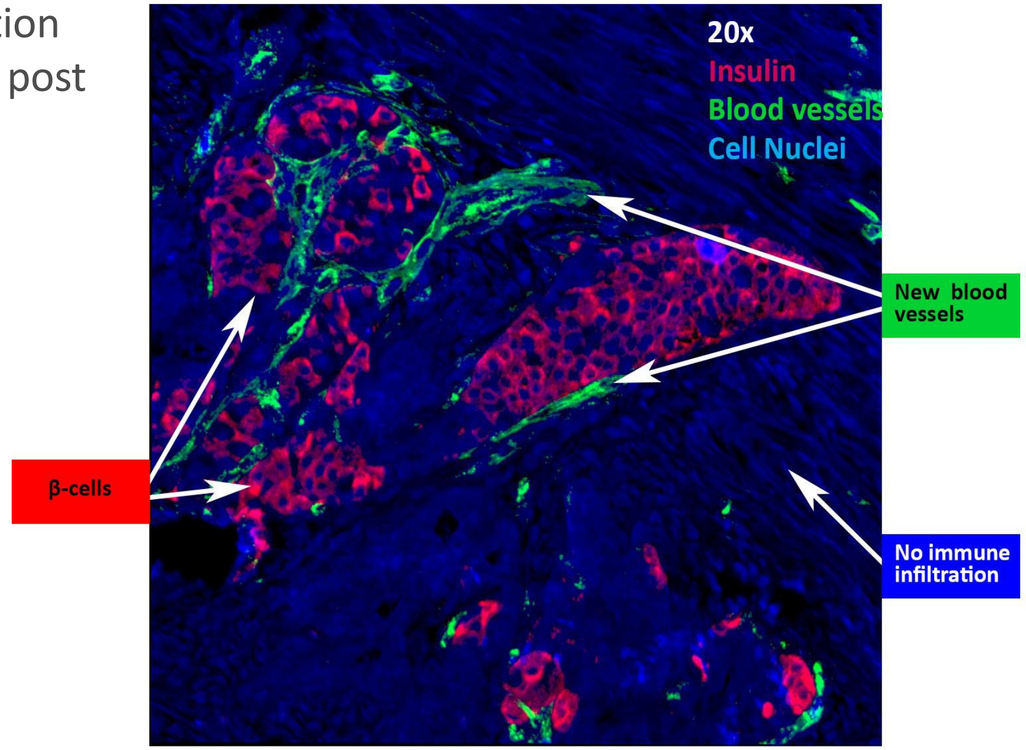
- T1D subjects with HU & a history of severe hypoglycemic episodes
- Open-label, single-arm
- Donor islet transplantation 2 – 24 weeks post Cell Pouch implantation
- **Primary Endpoint:** Safety post Cell Pouch implantation & 1-month post islet transplantation

## Cell Pouch and Islet Safety Endpoints Met

- Safety successfully met for the Cell Pouch
- Cell Pouch histology assessed by independent pathologists blinded to the treatment:
  - Islets housed within a natural tissue matrix
  - Islets were well-vascularized
  - Islet safety successfully met
  - Islets show evidence of insulin, somatostatin & glucagon
  - Cell Pouch & islet biocompatibility met
  - Proof of islet protection from immune system attack

## Cell Pouch™ Clinical Histology

**Insulin staining islets with microvessels**



# Hemophilia A Program

**Benefits of Sernova's Cell Pouch with factor VIII releasing cells:**

- Reduce / eliminate factor VIII infusions
- Maintain constant blood levels of factor VIII
- Reduce joint bleeds
- Improve long-term efficacy
- Improve QOL

Therapeutic Benefits

**Estimated Market**

- **~20 K patients across North America & EU**
- **~$10 B orphan indication**

**Standard of Care**

- **Patients receive regular infusions of missing clotting factors (i.e. factor VIII)**
  - Infusions are highly expensive & burdensome
  - Select patients develop inhibitors, reducing the effectiveness of infusions

**Therapeutic Goals**

- **Improved efficacy with prophylactic treatment; reduced cost; improved patient QOL; reduction of side effects**

**Sernova Approach**

- **Gene corrected own patient cells into the Cell Pouch (EU5.6M Horizon 2020 Consortium Grant)**
- **Potential treatment for all patients**
  - Stem cell releasing factor VIII product

**Status**

- **Completed pre-clinical proof-of-concept**
  - Cell manufacturing process developed
  - Corrected patient cells survive & produce factor VIII in pre-clinical hemophilia model
- **Further development being scoped**

Horizon 2020
European Union Funding
for Research & Innovation

# Thyroid Disease Program

**Benefits of Sernova's Cell Pouch with Thyroid releasing cells:**

- Reduce / eliminate daily life long thyroid medications
- Recover natural feedback loop of thyroid hormones
- Reduce side effects from low thyroid hormone levels
- Improve long-term efficacy
- Improve QOL

**Therapeutic Benefits**

| | |
|---|---|
| **Estimated Market** | ➢ 150,000 thyroidectomies performed annually in US<br>➢ ~$2.2 B market opportunity |
| **Standard of Care** | ➢ Patients require lifelong thyroid hormone replacement therapy<br>➢ Various oral / IV / other therapies may also be needed depending on underlying condition |
| **Therapeutic Goals** | ➢ Improved efficacy with prophylactic treatment; improved patient QOL; reduction of side effects |
| **Sernova Approach** | ➢ Thyroidectomy patient healthy tissue isolated & transplanted into the Cell Pouch<br>➢ Patient cells survive within the Cell Pouch & produce thyroid hormone |
| **Status** | ➢ Completed pre-clinical proof-of-concept<br>➢ Clinical program under development |

# NEXT STEPS – Action Plan

**Platform Technology**

- Develop licensed/acquired local immune-protection technologies for therapeutic cells
- Advance local immune-protected diabetes stem cell technology in preparation for First-in-Man (FIM) study
- Expand existing strong worldwide multi-family patent portfolio

**Diabetes T1D**

- Complete T1D Study patient enrolment
- Continue T1D Study patient treatment & follow up
- Ongoing T1D Study safety & efficacy data evaluation
- Strategic pharma / medtech collaboration(s) expansion

**Hemophilia A**

- HemAcure study results conference presentation & publication
- Market & product positioning assessment
- Regulatory & Clinical plan development

**Thyroid**

- Complete Pre-Clinical studies
- Prepare & submit FIM regulatory package

# Management Team

## Dr. Philip Toleikis

**PRESIDENT & CEO**

- 20+ years experience in biotech management & product development in pharmaceutical & combination products.
- Previous Angiotech VP R&D (achieved $2 B market cap;  product revenue $200 M per year).

## David Swetlow CPA, CA

**CFO**

- 20+ years experience in life sciences (biopharma, combination products & devices) & high-tech industries, including Ondine, Protox, QLT, Xillix.
- Various senior management, board & advisory roles. Nasdaq & TSX experience.

## Delfina M. Mazzuca-Siroen

**SR. DIRECTOR & HEAD OF R&D / CLINICAL**

- 20+ years senior management roles in R&D, clinical, regulatory, product development.
- Biochemistry, translational cell biology, device & transplantation expertise.
- Publications & patents author / co-author.

## Board of Directors

- Frank Holler, Chair
- Jeffrey Bacha
- James Parsons, CPA, CA
- Deborah Brown
- Dr. Philip Toleikis

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