The Path to a Regenerative Cure
Our Mission

Sernova’s goal is to improve the quality of life of people living with chronic diseases using a regenerative medicine approach.
Sernova’s Approach

A Total Regenerative Medicine Solution for the Therapeutic Treatment of Chronic Diseases

Cell Pouch™
- Implantable
- Scalable
- Medical device

Therapeutic Cells
- Produce and release missing proteins

Immune Protection
- Protect therapeutic cells from immune system attack

Cell Pouch

Therapeutic Cells

Immune Protection

Cell Pouch™

Therapeutic Cells

Immune Protection
Programs Overview

**Diabetes (Type 1)**
Phase 1/2 Clinical Trial in hypoglycemia unawareness

**Hemophilia**
Corrected patient clotting (Factor VIII)

**Thyroid**
Correct hypothyroid following surgical removal
Cell Pouch™
Human Clinical Evaluation
Type 1 Diabetes: 1st Clinical Indication

“Hypoglycemia unawareness” affects about 10% of Type 1 Diabetes patients

- Clinically defined as a complication of diabetes in which the patient is unaware of a deep drop in blood sugar levels
- Failure to control the symptoms of hypoglycemia (Palpitations, Anxiety, Excessive Sweating, Light Headedness)
T1D: Current Treatment Options

Insulin discovered in London, Ontario, in 1921
- Patent licensed by Novo Nordisk

Islet donor transplants through portal vein delivery have been used as a treatment for Type 1 Diabetes since the Edmonton Protocol in the 1990s

However, more can be done to progress the viability of islet transplantation

- Survival of Islets
- Transplant Rejection
- Alternative transplant site
- Avoid risks around portal vein transplantation
- Low number of cells available
- Unlimited supply of cells to treat all diabetic subjects
Sernova’s Cell Pouch™
First-in-Human Safety Study (Canada)
T1D: First-in-Human Study

**Study Design**
- Diabetes subjects with hypoglycemia unawareness
- Open-label; single-arm
- Donor islet transplantation 2-24 weeks post Cell Pouch™ implantation
- Primary endpoint - Safety post Cell Pouch™ implantation and 1-month post islet transplantation

**Cell Pouch™ and Islet Safety 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 are well-vascularized
  - Islet safety successfully met
  - Islets show evidence of insulin, somatostatin, & glucagon
  - Cell Pouch™ and islet biocompatibility met
  - Proof of islet protection from immune system attack
T1D: First-in-Human Study

Cell Pouch™ Clinical Histology
Insulin staining islets with microvessels
Cell Pouch Small Islet Dose: Insulin Independence

**Pepper AR, Shapiro AMJ. Transplantation, 2015**
Approximately 20 days with full islet mass, and 40 days with a marginal mass to fully reverse diabetes in mice. Results comparable to kidney capsule.

Glucose levels rise upon Cell Pouch™ removal

200 islets/mouse

Islets in tissue Matrix with microvessels

*Insulin staining*
Phase I/II Study (USA)
Phase I/II  U.S. Study

Safety, Tolerability and Efficacy Study of Sernova’s Cell Pouch™ for Clinical Islet Transplantation

Study design: Open-label, single-arm study of Sernova’s implanted Cell Pouch with islets. Islets are transplanted into the Cell Pouch after implantation and stable antirejection medication activity

Primary Objective: To demonstrate the safety and tolerability of islet transplantation into the Cell Pouch for the treatment of T1D in subjects with hypoglycemia unawareness and a history of severe hypoglycemic episodes

Secondary Objectives: To establish islet release criteria that accurately characterize the islet product and are predictive of clinical transplant outcomes into the Cell Pouch, which will be 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

Status: US IND Cleared by FDA and IRB and patient enrolment initiated; Medtronic Minimed, Northridge, CA CGM is supplying patients in Sernova’s U.S. regenerative medicine clinical trial of its Cell Pouch.

Next step: Ongoing safety and efficacy results
Phase I/II U.S. Study Timeline

**Primary Endpoint:**
Initial Topline Safety Readout

**1st Islet Dose Transplant**

**Cell Pouch™ Implantation**

**Imuno Suppression Introduced**

**Small (sentinel) Pouches Removed**

**Secondary Endpoints:**
- Survival of Endocrine Tissue & Identification of Hormones
- Reduction in hypoglycemic events
- Reduction in HbA1c

**1st Islet Dose Transplant**

**Day0**

**Day180**

**Day365**

**2nd Islet Transplant**
(increase dose)

**Safety**

**Efficacy**
First Observed Data
Presented at IPITA
July 2019
Primary Endpoint-Safety Measures

Patient Number 1: First Observed Data

Safety- incidence and severity of adverse events determined to be probable or highly probable to the Cell Pouch™

1. No incidences of AEs, determined to be probable or highly probable to the Cell Pouch™
2. Cell Pouch™ well-tolerated and safe during the implant and the time of transplant
3. No reactions to the Cell Pouch™ implant
4. Cell Pouch™ was well-incorporated with vascularized tissue and deemed suitable to receive the islet transplant

This first patient observed safety data met the first measure of the primary endpoint
Secondary Objectives / Endpoints

To establish islet release criteria that:

1. Accurately characterize the islet product and
2. Are predictive of clinical transplant outcomes into the Cell Pouch™, which will be 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
First Observed Data Presented by Clinical Investigator

<table>
<thead>
<tr>
<th></th>
<th>PREISLET TRANSPLANT</th>
<th>3 MONTHS POST TRANSPLANT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BODYWEIGHT</strong></td>
<td>83 KG</td>
<td>73 KG</td>
</tr>
<tr>
<td><strong>HEMOGLOBIN A1C</strong></td>
<td>6.5</td>
<td>5.6</td>
</tr>
<tr>
<td><strong>DAILY USE OF LONG ACTING INSULIN TRESIBA</strong></td>
<td>14 U</td>
<td>8 U</td>
</tr>
<tr>
<td><strong>DAILY USE OF SHORT ACTING INSULIN</strong></td>
<td>15-16</td>
<td>14-15</td>
</tr>
</tbody>
</table>

- **90 Day Post-Transplant Glucose Tolerance Test**
  
  Patient is given a high sugar drink. C-peptide and insulin response is measured over several hours.
  
  - Showed increase in blood levels of C-Peptide
  - Showed increase in blood levels of Insulin and a typical insulin response

![Graph showing glucose levels over time](image)
First Observed Data Presented by Clinical Investigator

**CONTINUOUS GLUCOSE MONITOR: IMPROVEMENT IN ALL GLUCOSE PARAMETERS SEEN POST TRANSPLANT**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Post Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest Sensor Glucose Value (mg/dL)</td>
<td>285</td>
<td>231</td>
</tr>
<tr>
<td>Lowest Sensor Glucose Value (mg/dL)</td>
<td>50</td>
<td>66</td>
</tr>
<tr>
<td># Glucose Excursions</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td># High Excursions</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td># Low Excursions</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Standard Deviation (Variability)</td>
<td>37</td>
<td>31</td>
</tr>
</tbody>
</table>

**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

**Performance**

**Cell Pouch™ for Islet Transplantation**

![Graph showing time above 180 mg/dL, time in range of 70-180 mg/dL, and time below 70 mg/dL for Baseline and Post Transplant CGM.]
Summary

At this early observed timepoint, the transplanted Cell Pouch showed the following improvements relative to baseline:

- **90-day improvement in Hemoglobin HbA1c**
- **90-day reduction in use of daily long acting insulin**
- **Continuous Glucose Monitor Assessment**
  - Improvement in all glucose control parameters measured by continuous glucose monitoring
  - Reduction in severe hypoglycemic events
  - 87.5% reduction in overall hypoglycemic events
  - Time below 70mg/dL: 12% control versus 1% post-Cell Pouch Islets
- **90-day Glucose Tolerance Test**
  - Showed typical insulin release curve
  - Showed C-Peptide blood levels
Additional Programs
Next Generation: Treatment of all people with diabetes

**Immune Protected Cell Pouch™**
(No Need for Immuno-suppression)\(^1\)

\(^1\) Immune protection technology not disclosed yet

- All Type 1 diabetic patients and 30% of Type 2 diabetes who convert to insulin use

**Immune Protected Cell Pouch™ with Pluripotent Stem Cells**

- Unlimited supply of cells
- Worldwide exclusive rights to UHN (University Health Network) diabetes stem cell technology
- CCRM (Center for Commercialization of Regenerative Medicine) successfully conducted tech transfer, optimize cell production process and produce cells for testing within the Cell Pouch
- Robust cell production process has been developed where cells consistently reach or exceed release criteria
- Local Immune Protection Technologies
  - Stem cell derived technology
  - Purified islets
Hemophilia Program

Patient Population
• Hemophilia A ≈ 20,000 NA/EU

Hemophilia Therapy
• Factor VIII Gene corrected cells within Cell Pouch – produce constant therapeutic Factor VIII levels
  o Patient corrected cells (autologous)
  o Stem cell derived technology and local immune protection (allograft)

Therapeutic Goals:
• Improved efficacy with prophylactic treatment reduced cost; improved patient QOL; reduction of disease side effects

Sernova’s Product Approach
• Corrected own patient cells into the Cell Pouch (Horizon 2020 Grant)
  o Status: Corrected patient cells survive and produce Factor VIII in hemophilia model
• Treatment for all patients
  o Stem cell releasing Factor VIII product
  o Status: in development

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
Hypothyroid Disease Program

Patient Population
2% of the population. 150,000 thyroidectomies performed in the US each year

Thyroid Therapy (Current Standard of Care)
Oral – Intravenous – Others

Targeted Thyroid Disorders (Thyroidectomy)

Therapeutic Goals:
Improved efficacy with prophylactic treatment reduced cost; improved patient QOL; reduction of disease side effects

Sernova’s Product Approach
• Thyroidectomy patient cells transplanted into the Cell Pouch
  o Status: Preclinical assessment: Corrected patient cells survive and produce thyroid hormone

Sernova’s Cell Pouch™ 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
International Patent Protection

International (North/South American, Europe, Asia) patents and patent applications portfolio in 10 patent families:

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