



# **SERNOVA CORP.**

**MANAGEMENT'S DISCUSSION AND ANALYSIS**

**FOR THE THREE AND NINE MONTHS ENDED**

**JULY 31, 2022 AND 2021**

Dated September 14, 2022

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## **SERNOVA CORP.**

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The following management's discussion and analysis (MD&A) explains the consolidated operating results, financial position, and cash flows of Sernova Corp. (Sernova, the Company, We, Us, or Our) for the three and nine months ended July 31, 2022, and 2021. This MD&A should be read in conjunction with the Company's most recent Annual Information Form (AIF); its unaudited interim condensed consolidated financial statements for the three and nine months ended July 31, 2022, and 2021; and its audited consolidated financial statements and related notes for the years ended October 31, 2021, and 2020, which have been prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (IASB).

The Company's accounting policies under IFRS are set out in *Note 3 – Significant Accounting Policies* of the audited consolidated financial statements for the years ended October 31, 2021, and 2020. All amounts are in Canadian dollars. The information in this report is dated as of June 27, 2022, unless otherwise noted.

### **FORWARD-LOOKING STATEMENT**

This MD&A contains "forward-looking statements" that reflect the Company's current expectations and projections about its future results. When used in this MD&A, the use of words such as "estimate", "project", "potential", "belief", "anticipate", "intend", "expect", "plan", "predict", "may", "could", "should", "will", "consider", "anticipate", "objective" and the negative of these words or such variations thereon or comparable terminology, are intended to identify forward-looking statements and information. Forward-looking statements are, by their nature, not guarantees of the Company's future operational or financial performance and are subject to risks and uncertainties and other factors that could cause the Company's actual results, performance, prospects, or opportunities to differ materially from those expressed in, or implied by, these forward-looking statements. No representation or warranty is intended with respect to anticipated future results or that estimates or projections will be sustained.

The Company's statements of "belief" concerning its technologies and product candidates are based primarily upon results derived to date from the Company's research and development programs. The Company also uses the term "demonstrated" in this MD&A to describe certain findings that it makes arising from its research and development (R&D), including any preclinical and clinical studies that the Company has conducted to date.

Specifically, this MD&A contains forward-looking statements which include, but are not limited to, statements regarding:

- the Company's corporate strategy and strategic objectives;
- the availability of various forms of external financing to fund the Company's ongoing liabilities and commitments;
- the expected benefits to patients with the Cell Pouch™ transplanted with therapeutic cells or tissue;
- the conduct of preclinical studies and clinical trials of our Cell Pouch System™ for the treatment of insulin-dependent diabetes, hypothyroid disease, hemophilia A and other clinical indications, and the Company's ability to conduct its clinical studies;
- the expected benefits to patients of our Cell Pouch diabetes, hypothyroid disease and hemophilia A cell therapy programs;
- the expected benefits to patients with type 1 diabetes (T1D) implanted with the Cell Pouch and human donor islets and or induced pluripotent stem cells (iPSC)
- the Company's intention to protect therapeutic cells within the Cell Pouch from immune

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attack using local immune protection technologies such as conformal coating, gene-editing, tolerance, or using a systemic anti-rejection regimen or a combination thereof and the expected benefits therefrom;

- the expected benefits of any next generation Cell Pouch System technologies;
- successful development up to an IND submission and beyond combined with the expected benefits of using iPSC derived islet clusters in combination with the Cell Pouch and ancillary technologies within the Evotec Collaboration (defined hereafter);
- the Company's intentions and ability to secure academic and pharmaceutical / medtech collaborations to develop and implement partnering strategies and manage partnerships;
- the Company's intention and ability to use human autograft cells or tissues or human donor allograft cells or xenogeneic cells for treatment, and the intention to use human stem cell-derived cells (i.e. iPSCs), considered unlimited cell sources for our Cell Pouch and Cell Pouch System for the potential treatment of various diseases;
- the Company's intention and ability to obtain regulatory clearance for clinical trials and marketing approval of the Cell Pouch or Cell Pouch System for the treatment of insulin-dependent diabetes, hemophilia A, thyroid disease, and other diseases;
- the Company's intentions and ability to obtain Orphan Drug (for rare diseases), Fast Track, Breakthrough Technology, Regenerative Medicine Advanced Therapy (RMAT), Accelerated Approval or Priority Review in the US, and similar regulatory designations in North America, Europe or other jurisdictions abroad, and the related impact on timeline estimates to conduct clinical trials or obtain marketing approval for the Company's products;
- the Company's expectations that Sernova's technologies are unique and may become a standard of care in therapeutic cell transplantation if they prove to be safe and effective in clinical trials;
- the Company's expectations with respect to the research and development of Sernova's products, clinical trials, and commercialization of our products;
- the Company's sales and marketing strategy for our technologies including Cell Pouch or Cell Pouch System and associated technologies;
- the Company's intentions regarding the development and protection of Sernova's intellectual property;
- the Company's intentions with respect to obtaining licenses for technologies compatible with the Cell Pouch System;
- the Company's intention to develop next-generation Cell Pouch or Cell Pouch System related technologies;
- the Company's ability to secure cGMP manufacturing facilities for its cell therapy programs;
- sufficient availability of Cell Pouch product for the conduct of preclinical studies, clinical trials, and following marketing approval for commercial use;
- the direct and indirect impact of the novel coronavirus (COVID-19) and variants and any other further global health emergencies on our business and operations, including supply chain, manufacturing, research and development costs, clinical trials including patient enrollment, contracted service providers and employees; and
- the Company's general business and economic events.

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In developing the forward-looking statements in this MD&A, the Company has applied several material assumptions, including the availability of financing on reasonable terms, the ability to form and maintain strategic alliances with other business entities, and general business and economic conditions.

Forward-looking information is based on the reasonable assumptions, estimates, analysis, and opinions of management made in light of its experience and perception of trends, current conditions, and expected developments, as well as other factors that management believes to be relevant and reasonable in the circumstances at the date that such statements are made, but which may prove to be incorrect. We believe that the assumptions and expectations reflected in such forward-looking information are reasonable.

Key assumptions upon which the Company's forward-looking information are based include:

- the Company's ability to manage its growth effectively;
- the expected benefits to patients of our technologies including Cell Pouch and Cell Pouch System cell therapy programs;
- the absence of material adverse changes in our industry or the global economy;
- trends in our industry and markets;
- the Company's ability to comply with current and future regulatory standards;
- the Company's ability to protect its intellectual property rights;
- the Company's continued compliance with third-party license terms and the non-infringement of third-party intellectual property rights;
- the Company's ability to attract and retain key personnel; and
- the Company's ability to raise sufficient equity or debt financing to support continued growth and operational needs.

There are a number of important factors that could cause Sernova's actual results to differ materially from those indicated or implied by forward-looking statements and information, including but not limited to: early-stage development and scientific uncertainty, lack of product revenues and history of losses, additional financing requirements and access to capital, patents and proprietary technology, dependence on collaborative partners, licensors, contract research organizations (CROs), contract manufacturing organizations (CMOs) and others, government regulations, hazardous materials and environmental matters, rapid technological change, competition, reliance on key personnel, status of healthcare reimbursement, potential product liability and volatility of share price, absence of dividends, fluctuation of operating results and the impacts of the continuing novel coronavirus (COVID-19) pandemic or related outbreaks. Such risks are further described under "**RISK FACTORS AND UNCERTAINTIES**" in this MD&A or under "*RISK FACTORS*" in our AIF. Potential investors, and other readers are urged to consider these factors carefully in evaluating these forward-looking statements and information and are cautioned not to place undue reliance on them. Sernova has no responsibility, nor does it intend, to update these forward-looking statements and information unless as otherwise required by law.

Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this MD&A or as of the date otherwise specifically indicated herein. Due to risks and uncertainties, including the risks and uncertainties associated with COVID-19 and as described elsewhere in this MD&A, actual events may differ materially from current expectations. The Company disclaims any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise.

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This MD&A has been prepared to help investors understand the financial performance of Sernova in the broader context of the Company's strategic direction, the risks and opportunities as understood by management, and some of the key metrics that are relevant to the Company's performance. This MD&A has been reviewed and approved for filing by the Company's Audit Committee and the Board of Directors. The Company's Audit Committee consists of three independent Directors, who are all considered to be "financially literate" as defined in NI 52-110.

#### **ABOUT SERNOVA**

Sernova is a clinical-stage regenerative cell therapeutics company focused on development and commercialization of our proprietary technologies, including Cell Pouch implantable device technologies and immune-protected therapeutic cells, herein termed Cell Pouch System. The Cell Pouch System is a technology platform being developed for the treatment of and a potential 'functional cure' for chronic debilitating diseases including type 1 diabetes (insulin-dependent diabetes or T1D), thyroid disease, and rare diseases such as hemophilia A. The Cell Pouch is a scalable, implantable, medical device, designed to create a highly vascularized organ-like environment for the transplantation and engraftment of therapeutic cells, which then release proteins and / or hormones into the microvasculature for the long-term treatment of various chronic diseases. The therapeutic cells used for therapeutic purposes may be autograft cells or tissues (self-cells / tissues) or allograft cells (non-self, donor cells) or allograft cells derived from sources known to provide a virtually unlimited supply of cells such as human stem cell-derived cells or from a xenogeneic (non-human) source. Furthermore, the therapeutic cells may be unmodified or may be genetically modified to produce their therapeutic product.

Our preclinical and clinical research studies to date support the safety and biocompatibility of the Cell Pouch and long-term survival and function of therapeutic cells transplanted into the vascularized Cell Pouch chambers. Our data demonstrates that, following implantation of the Cell Pouch deep under the skin or in other locations in the body, vascularized tissue incorporates through pores in the device forming fully enclosed vascularized tissue chambers. Upon transplantation of therapeutic cells into these vascularized chambers a natural tissue matrix forms around the cells along with microvessels to the cells, enabling them to engraft (survive and function). Thus, an anticipated benefit of the Cell Pouch is formation of a natural environment for the therapeutic cells that provides for enhanced long-term therapeutic cell survival and function. We believe this is due in part to the therapeutic cells living in a natural tissue matrix within close contact of microvessels.

We believe our unique approach in providing a natural environment for therapeutic cells and its ease of use may provide an opportunity for Sernova's technologies including the Cell Pouch System to become the standard of care in therapeutic cell transplantation for multiple diseases if they continue to demonstrate safety, tolerability and clinical benefit in preclinical and clinical trials.

As noted in our latest AIF, filed under the Company's SEDAR profile at [www.sedar.com](http://www.sedar.com) on March 28, 2022, our research activities during the past three years have focused on the development of the Cell Pouch System platform as a potential new treatment for various therapeutic indications including T1D, hemophilia A, thyroid disease and additional chronic debilitating and rare diseases. We have also entered into strategic collaborations and acquired, in-licensed or obtained an exclusive option to in-license related technologies to expand and support our research efforts. Earlier history of the corporate development of the Company and its business is also available on SEDAR.

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## **RECENT QUARTER HIGHLIGHTS**

### ***R&D HIGHLIGHTS***

June 2022: Updated interim data from our ongoing US Phase 1/2 Cell Pouch Clinical Trial was presented on June 6<sup>th</sup>, 2022, as an oral podium presentation “*Modified Approach for Improved Islet Allotransplantation into Prevascularized Sernova Cell Pouch™ Device: Preliminary Results of the Phase I/II Clinical Trial at University of Chicago*” at the American Diabetes Association (ADA) 82nd Scientific Sessions, held in New Orleans, LA. Key observations included the following:

- surgical implantation of the Cell Pouch continues to be generally well tolerated with a favorable safety profile;
- the first three patients with long standing T1D and serious hypoglycemia events (SHE), presented positive serum C-peptide values confirming active insulin production after islet transplantation into the Cell Pouch;
- a supplemental marginal dose islet transplantation via the portal vein was sufficient to allow those three patients to achieve and maintain insulin independence, ranging at the time of presentation from 3 months to over 2 years;
- the insulin independent patients have HbA1c in the normal range; and
- immunosuppression for three additional patients on the study who did not maintain optimal levels has been resolved, enabling those patients to receive further protocol-defined islet transplants.

Other key findings from the interim clinical update:

- decreasing the concentration of islet suspensions transplanted to Cell Pouch resulted in greater stimulated C-peptide

Based on the data, we believe implementing a higher capacity Cell Pouch will optimize patient outcomes from future transplantation procedures.

May 2022: We announced entering into an exclusive global strategic partnership with Hamburg, Germany based Evotec SE (NASDAQ:EVO | FSE:EVT), the leading developer of iPSC cell technologies for therapeutic applications, for the development and commercialization of an iPSC-based beta cell replacement therapy (Evotec Collaboration). The Evotec Collaboration is a transformative partnership for Sernova that will combine our proprietary Cell Pouch System, which has demonstrated Phase 1/2 clinical proof-of-concept using human donor islets, and related technologies with Evotec's best-in-class iPSC-based beta cells (islet-like clusters). We believe incorporating Evotec's insulin-producing, ethically derived islet-like clusters into Sernova's Cell Pouch platform creates the potential to provide a 'functional cure' for millions of people suffering from diabetes using an off-the shelf cGMP manufactured, scalable product.

### ***CORPORATE HIGHLIGHTS***

September 2022: We announced the appointment of Daniel Mahony, Ph.D. to our Board of Directors, effective September 30<sup>th</sup>, 2022. Dr. Mahony is Entrepreneur-in-Residence at Evotec and is also responsible for managing Evotec's equity investment portfolio. Dr. Mahony brings over 25 years of global healthcare investment, management and research experience covering biotechnology, medical technology, and healthcare service sectors.

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September 2022: We closed the second and final tranche of Evotec's strategic investment private placement with the effective exercise of an unconditional common share purchase warrant for 2,709,800 common shares at a price of \$2.50 per share for total proceeds of \$6,774,500.

June 2022: On June 2<sup>nd</sup>, 2022, trading of the Company's common shares commenced on the Toronto Stock Exchange (TSX:SVA) with its graduation from the TSX Venture Exchange (TSXV). Concurrently, the Company voluntarily delisted its common shares from the TSXV.

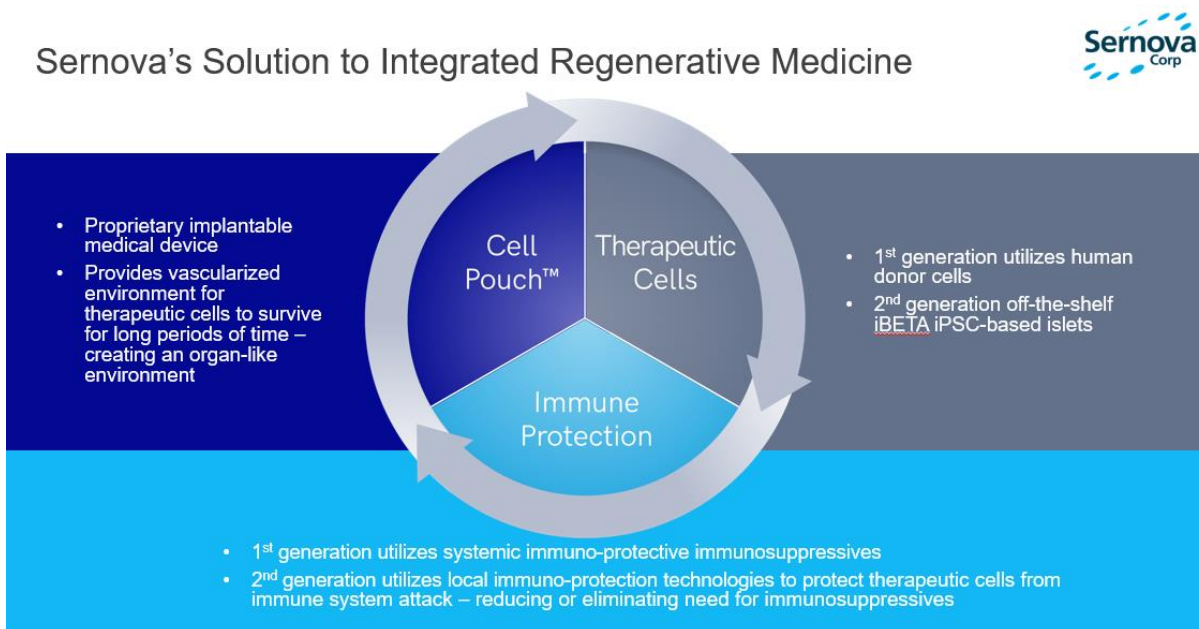
May 2022: Concurrent with entering into the Evotec Collaboration noted above, Evotec made a strategic equity investment commitment totaling approximately \$27 million of proceeds for the Company. The first tranche of 12,944,904 common shares at a price of \$1.57 per share for gross proceeds of \$20,323,500 was closed.

May 2022: We announced engaging New York based LifeSci Communications, a global life science and medical technologies-focused communications and marketing agency. LifeSci Communications will assist Sernova to expand and elevate its profile through strategic communications and public relations. Sernova is also working with affiliate LifeSci Advisors LLC, a leading investor relations consultancy firm serving life science companies, providing institutional investor communications and capital markets outreach services in support of the Company's U.S. capital markets objectives.

April / May 2022: We presented Sernova's vision and progress at a number of investment and healthcare industry conferences including: Alliance of Regenerative Medicine's Cell Gene Therapy Meeting on the Med in Barcelona, Spain; Roth Capital's Canada Corporate Access Day in New York, NY; the JDRF-NIH-FDA Beta Cell Replacement Workshop in Bethesda, MD; and the H.C. Wainwright Global Investment Conference in Miami Beach, FL.

## BUSINESS OVERVIEW

### *Sernova Cell Pouch System: A Platform Technology Approach*



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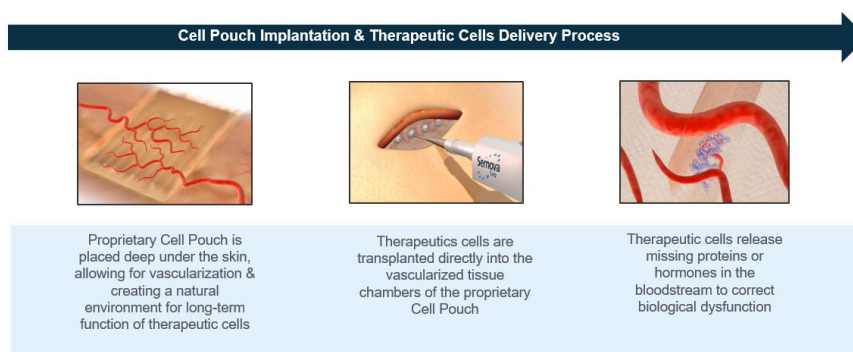
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Sernova's patented Cell Pouch System is designed to take into consideration the biological requirements of therapeutic cells. This is achieved through the establishment of an organ-like environment defined as a vascularized tissue matrix for therapeutic cells, which develops within the device chambers following implantation. Our novel approach seeks to provide local protection for therapeutic cells from immune system attack within the Cell Pouch or through systemic immune protection medications. We believe this unique approach of encouraging vascularized tissue incorporation into the device also helps prevent the issue of fibrosis that has plagued implantable cell therapy devices with differential designs and provides a biologically suitable environment for the engraftment and function of therapeutic cells.

The Cell Pouch is designed to be scalable to match the required cell dose for each clinical application. Our research demonstrates that following Cell Pouch implantation deep under the skin or in other locations, vascularized tissue chambers develop within the device. In long-term preclinical studies, it has been shown that the Cell Pouch maintains a stable, vascularized tissue environment prior to transplantation of therapeutic cells, which we believe is key for maintaining long-term survival and function of therapeutic cells. We believe Sernova's approach also addresses the potential issues of other competing implantable devices wherein therapeutic cells are pre-inserted prior to the device being implanted into the body which may result in hypoxia, ischemia, and cell death (resulting in poor engraftment). These issues relate to the lack of an integrated vascularized tissue environment into which cells are transplanted.

## Biologically Compatible Delivery Process



We have demonstrated in a series of ISO 10993 biocompatibility studies, multiple animal studies, a pilot human clinical trial and our ongoing US Phase 1/2 clinical trial that the Cell Pouch is biocompatible and safe. Long-term studies in several animal models have demonstrated that following transplant, insulin-producing islets become well-supported with microvessels, as occurs in their natural pancreatic environment. An anticipated benefit of the Cell Pouch is enhanced short and long-term therapeutic cell survival and function, which we believe is due in part to cells being transplanted into a natural tissue matrix within close contact of microvessels. For diabetes, as an example, this close vessel proximity enables islets to continuously monitor blood glucose levels and produce the appropriate amount of insulin into the bloodstream. We believe the Cell Pouch platform technologies may achieve this ideal therapeutic / microvessel connection through interaction with the local tissue environment. Our preclinical studies have shown that islets transplanted into the Cell Pouch can control blood glucose levels in small and large animal models of diabetes over extended periods. We have also observed encouraging preclinical results in other therapeutic cell applications, such as hemophilia A with



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corrected patient cells gene-edited to produce factor VIII, the missing protein preventing blood clotting, and hypothyroid disease with patient transplanted thyroid tissue with the goal to replace the function of the removed thyroid gland.

The cells transplanted into the Cell Pouch may be protected from immune system attack, when required, by systemic medications, through mechanisms that provide tolerance of the immune system to transplanted cells or through other local Cell Pouch immune protection technologies such as microencapsulation or conformal coating of cells. Microcapsules surrounding the cells have tiny pores, which have been shown to provide a means to allow nutrient and protein exchange within the local vascularized environment while preventing immune system attack. Conformal coating is a proprietary technology forming a cross-linked polymer coating around cells using a ‘shrink wrap’ approach that may also provide protection from immune system attack and has been shown to allow natural glucose and insulin flow in and out of cells, respectively. Sernova is also evaluating gene editing technologies for our stem cell-derived programs and other approaches such as development of immune system tolerance to transplanted cells that may provide an alternative method of cellular immune protection. These approaches alone or in combination are anticipated to reduce or eliminate the requirement of anti-rejection medications targeted to our therapeutic cell applications across a range of disease indications.

Thus, we believe our technology platform approach and its minimally invasive implantation approach through placement deep under the skin may provide an opportunity for the Cell Pouch System to become the standard of care for the treatment of multiple diseases with the goal of a ‘functional cure’.

**Pipeline – Life Cycle Iterations and Multiple Indications**



Product Candidate	Therapeutic Cell Source	Immune Protection	Indication	Discovery	Pre-Clinical	Phase 1/2	Phase 3	BLA
Cell Pouch System	Human donor islet cells	Immunosuppressives	Type 1 Diabetes Insulin-dependent Type 2 Diabetes	[Progress bar: Discovery to Phase 1/2]				
	Human donor islet cells	Local immune protection		[Progress bar: Discovery to Pre-Clinical]				
	Stem cells Evotec	Local immune protection		[Progress bar: Discovery to Pre-Clinical]				
Cell Pouch System	Corrected patient cells	Autologous cells	Hemophilia A - Severe	[Progress bar: Discovery to Phase 1/2]				
	Allograft immune protected stem cells	Local immune protection	Hemophilia A - All patients	[Progress bar: Discovery to Pre-Clinical]				
Cell Pouch System	Thyroid cells	Autologous cells	Thyroid Diseases / Hypothyroidism	[Progress bar: Discovery to Phase 1/2]				
	Allograft immune protected stem cells	Local immune protection	Thyroid Diseases / Hypothyroidism	[Progress bar: Discovery to Pre-Clinical]				

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#### ***Development of the Cell Pouch System Platform for the Treatment of Diabetes / T1D***

The goals of our T1D program are to provide people with T1D the ability to better control their diabetes, an improved quality of life, the reduction of debilitating disease side effects and complications, and ultimately a 'functional cure' to this disease.

According to the International Diabetes Federation (IDF), there are approximately 537 million people worldwide with diabetes, and nearly 10% of these individuals have T1D (insulin-dependent) diabetes (<https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html>) where the cells in the pancreas that control blood sugar levels through controlled release of insulin and have stopped functioning or have died allowing blood sugar levels to rise resulting in short and long term debilitating effects of the disease. In particular, the market for people with diabetes who suffer from hypoglycemia unaware events represents a significant subpopulation of diabetic patients that could be addressed by Sernova's products – subject to receiving marketing approval from regulatory authorities following completion of clinical studies. The subset of people with T1D and hypoglycemia unawareness, affects about 17% of people with T1D according to diabetesnet.com.

The primary treatment for T1D to help control blood sugar level is insulin injections by needle or insulin pump. The life of a person with diabetes is consumed with the constant attempt to control blood sugar levels to minimize both the acute effects of hypoglycemia and severe long-term effects of diabetes, which include heart and kidney disease, blindness, and amputations. There is a critical need to improve the treatment of diabetic people and to improve the quality of life of these individuals. Sernova believes its Cell Pouch System may provide a significant improvement in the quality of life of these individuals as well as an improvement in the potential efficacy and reduction of diabetes-related side effects in these people relative to the current standard of care of insulin by needle injection or pump. The goal of the cell therapy approach for T1D is to replace the insulin-producing cells of people with diabetes. The new islets are transplanted into a retrievable vascularized device to produce insulin as well as the other regulatory hormones to improve the quality of life of patients with the ultimate goal to return blood sugar regulation to the normal healthy state.

Our most advanced development program involves the clinical development and validation of the Cell Pouch System for the treatment of people with T1D who suffer from unstable diabetes and life-threatening severe hypoglycemia events. The current cell therapy is transplantation of donor islets in the portal vein of the patient's liver. This first-generation cell therapy approach involves the transplantation of pancreatic donor islets, often from multiple donors, into a patient's portal vein in which islets lodge in the microvasculature of the liver. Life-long systemic immunosuppressive drugs are required to inhibit rejection of the transplant. A portal vein islet transplant is the only cell therapy treatment approach possible for this population of people with diabetes and is only occasionally offered to reduce the occurrence of severe hypoglycemic episodes in these patients. Portal vein islet transplant is categorized as an experimental procedure by regulators, including the United States Food and Drug Administration (USFDA), and may only be administered under a clinical trial protocol.

It is encouraging that islet cell transplantation, even into the portal vein in humans, when considered a first step proof-of-concept for diabetes cell therapy treatment has shown some positive outcomes for diabetic patients. These positive effects demonstrate the potential of a cell therapy treatment approach for diabetes.

Despite the positive effects, there are a number of issues with portal vein delivery of either donor islets or stem cell derived technologies that we believe could be improved with Sernova's technologies. For example, following islet infusion with portal vein delivery, there is a significant reduction in the number of surviving islets due to an immediate blood-mediated inflammatory reaction (IBMIR), which may

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damage and destroy a substantial proportion of the islet cells infused into the portal vein. Due to IBMIR, often islets from multiple donor organs are required to achieve blood sugar control. Paradoxically, while a small dose of islets into the portal vein may be safe, undesirable portal vein hypertension, thrombosis, and liver steatosis (fatty liver) may occur following multiple cell transplants, which are typically required to achieve efficacy. This limits the number of doses of cells that can be infused into the portal vein during a patient's lifetime. A further shortcoming of portal vein transplant is that infusion of cells into the portal vein is not easily amenable to technologies such as glucose-responsive insulin-producing stem cell-derived cells, or xenogeneic cells being developed to overcome the limited supply of donor islet cells as these cells are not retrievable if there is a safety issue. The only way to explant liver infused cell technologies is to remove the liver, requiring a liver transplant, which becomes a life-threatening issue due to the lack of donor organs.

As noted in Table 1 below, we believe the Cell Pouch System can alleviate a number of important issues with portal vein transplantation. With the Cell Pouch System, the therapeutic cells live within a tissue matrix integrated with microvessels, similar to the islets' natural microenvironment rather than being subjected to a constant flow of blood with immune-reactive cells, which is believed to lead to IBMIR. We believe Cell Pouch transplant may eliminate the portal infused inflammatory response enabling improved islet survival and to potentially lower the number of islets or other sources of insulin-producing cells that need to be transplanted. Consequently, in improving the cell therapy placement, fewer donor pancreata (a marginal islet cell dose) than what is currently used for portal vein transplantation is anticipated to be required. In addition, known side effects of multiple infusions into the portal vein along with the costs of treating them are expected to be eliminated with the use of Sernova's Cell Pouch System, especially as we develop glucose responsive stem cell-derived technologies (see Table 1).

Table 1. Potential Benefits of the Cell Pouch Islet Transplant over the Portal Vein Islet Transplant

<b>Characteristics</b>	<b>Cell Pouch</b>	<b>Portal Vein Transplant</b>
Smaller islet dose to achieve efficacy	Yes	No
Tissue matrix to house islets	Yes	No
Improved vascularization of islets	Yes	No
Retrievable site	Yes	No
Safe site for stem cell-derived cells	Yes	No
Minimally invasive site	Yes	No
Elimination of liver-associated toxicities	Yes	No
Elimination of IBMIR	Yes	No
Local immune protection of cells	Yes	No

While infusion of glucose responsive stem cell derived technologies into the portal vein may appear to be a solution to the limited supply of donor islets, the issues with portal vein transplant including IBMIR and the inability to retrieve the cells, if required, still remain.

With the encouraging initial results of portal vein islet transplantation, there is a need to develop a more suitable and retrievable environment for therapeutic cells. We believe an implantable and retrievable medical device that becomes highly vascularized when implanted into an appropriate area of the body for the placement and function of therapeutic cells, including donor islets and stem cell-derived technologies is a feasible and more sustainable approach. Sernova's Cell Pouch is a minimally invasive,

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retrievable device for the placement and long-term survival and function of therapeutic cells for the production of needed missing protein(s) or hormone(s) into the bloodstream.

Importantly, the Cell Pouch technologies are specifically and uniquely designed to be biocompatible featuring pores that incorporate with vascularized tissue to form fully enclosed chambers with central void spaces for placement of therapeutic cells. A serious problem that may be encountered with other implanted therapeutic medical devices is the development of unwanted fibrosis in which the body treats the device as foreign and walls off the device with scar tissue resulting in starving of the cells of oxygen and nutrients. We believe the unique design of the Cell Pouch device prevents the formation of scar like fibrotic tissue following implantation for the long-term survival and function of therapeutic cells.

As a novel approach beyond portal vein infusion of islets, we believe that islets (donor or stem cell-derived) transplanted into the Cell Pouch may provide a better means to optimize cell therapy for the treatment of diabetes. The data gained from our current clinical study using donor islets is being used to provide a basis for advancement of glucose-responsive immune-protected stem cell-derived cells for transplant into the Cell Pouch. We believe stem cell-derived islets have the potential to treat millions of people suffering from T1D.

Sernova's Cell Pouch technologies are designed and patented to take into consideration the biological requirements of therapeutic cells. In long-term preclinical evaluation, the Cell Pouch has been shown to maintain a stable, vascularized tissue environment prior to the placement of these transplanted therapeutic cells.

An independent preclinical study published in the journal "*Transplantation*" (Transplantation 2015 Nov; 99 (11):2294-300) demonstrated that the Cell Pouch with islets provided insulin independence for the length of the study (100 days) in a small animal model of diabetes using a marginal transplanted islet mass where over 95% of the animals achieved insulin independence. This study supports the concept that the Cell Pouch may require a smaller than initially anticipated dose of cells (marginal islet dose) resulting in a lower overall Cell Pouch cell density to achieve efficacy, one of the parameters being investigated and optimized in human clinical evaluation to achieve glucose control in patients with diabetes.

We have manufactured our Cell Pouch at a U.S. medical device contract-manufacture facility in compliance with ISO13485, EU Medical Devices Regulation MDR 2017/745, United States Food and Drug Administration Quality System Regulations (QSR) 21 CFR 820 and Canadian Medical Device Regulation (CMDR). We are manufacturing additional sizes of the Cell Pouch that will enable us to further optimize islet dosing and dose density which we believe may lead to enhanced patient outcomes with the Cell Pouch System, including our current Phase 1/2 T1D study with donor islets and in preparation for next step studies with the Evotec iPSC beta cell technology.

To validate our Cell Pouch System technologies in preparation for clinical evaluation for T1D, in addition to safety studies of the Cell Pouch alone we successfully transplanted donor islets into our Cell Pouch, to treat insulin-dependent diabetes in multiple small and large animal models (syngeneic, autograft and allograft) of diabetes. These studies in part provided proof of concept of the Cell Pouch System to support clinical evaluation of our Cell Pouch with donor islets.

Based on the encouraging preclinical results with donor islets, we conducted a first-in-human proof-of-concept (POC) clinical study for the treatment of human diabetes subjects with hypoglycemia unawareness. Patients received donor islets, protected by the standard of care immunosuppressives for a first in human Canadian safety study, cleared by Health Canada. The approach of using human donor islets in the Cell Pouch has enabled Sernova to understand the behaviour of transplanted insulin-

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producing cells in the Cell Pouch in humans as an initial step to the development of an immune-protected stem cell product to treat the larger treatable population of patients with diabetes.

This safety and tolerability Canadian clinical study demonstrated initial encouraging results for the Cell Pouch alone and with transplanted islets.

In summary, our first-in-human clinical results showed the following important findings:

- the biocompatibility and a favorable safety profile of the Cell Pouch in these subjects; and
- the islets within the Cell Pouch, as shown by independent histological analysis, were well-vascularized, living within a natural tissue matrix, and able to make insulin, glucagon and other key hormones important in the control of blood glucose levels and hypoglycemic events.

We believe such revascularization of islets and islet metabolic function within Sernova's implantable medical device for therapeutic cells in humans in this patient population is an important step forward in the regenerative medicine field.

While donor islets provide a first Cell Pouch System therapeutic cell source and potential product to treat patients with the most significant unmet need, those with severe hypoglycemic events, our goal is to have and enable the Cell Pouch System to offer treatment to the broader general patient population of millions of people with diabetes. Consequently, we have been searching for ethically derived advanced iPSC beta cell technologies that have the potential to be successfully commercialized. Accordingly, over the past several years Sernova established collaborations with several global pharmaceutical companies to assess the potential of their proprietary iPSC cell technologies. We demonstrated with the proprietary assets of multiple parties that ethically derived iPSC stem cell-derived beta cells can provide long-term insulin independence in small animal models of diabetes when transplanted into the Cell Pouch. We believe ethically derived induced pluripotent stem cells - iPSCs - are superior to progenitor embryonic stem cell-derived cells.

We chose Evotec's iPSC technology for this transformative component of our cell therapy therapeutics platform based on multiple scientific, regulatory, manufacturing capabilities, business and commercial factors. We believe the Evotec Collaboration secures a virtually unlimited supply of ethically derived advanced iPSCs and eliminates the limitation of a restrictive supply of donor islets for our current clinical programs and on eventual product commercialization, which we believe broadens and strengthens the appeal for business development and or M&A opportunities for our cell therapy platform and the Company overall. Evotec's iPSCs in combination with the Cell Pouch and immune protection technologies is a priority in our future clinical development plans and product pipeline.

#### ***Type 1 Diabetes Phase 1/2 US Clinical Trial for Patients with T1D and Severe Hypoglycemia Unawareness***

With the encouraging results and learnings from our first Cell Pouch clinical trial, we initiated a second clinical study - "*A Safety, Tolerability and Efficacy Study of Sernova's Cell Pouch™ for Clinical Islet Transplantation*" - to further address the safety, tolerability as well as function of the Cell Pouch with therapeutic cells. The primary objective of the study is to demonstrate the safety and tolerability of islet transplantation into the Cell Pouch. The secondary objective is to assess efficacy through a series of defined measures. This clinical study is lending to our understanding of the relationship between the dose and dose density of islets in the Cell Pouch and safety and efficacy measures in patients with long standing T1D and hypoglycemia unawareness as we progress our development of a cell therapy approach to the treatment of T1D for all patients with diabetes. Continuous glucose monitoring (CGM),

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mixed meal tolerance tests and daily insulin use are used to track the function of the cells transplanted into the Cell Pouch and to assess efficacy measures at multiple time points during the course of the clinical trial. CGM used in this study supports the analysis of mean glucose concentration, mean glucose variability, the number and duration of hyper and hypoglycemic episodes as well as total duration of hypoglycemia.

Following a peer review of the new clinical protocol, Sernova was awarded up to US\$2.45 million (approximately \$3.1 million) grant under an agreement with JDRF. The grant is supporting our Cell Pouch Phase 1/2 diabetes clinical trial, which is being conducted at the University of Chicago in collaboration with Principal Investigator Dr. Witkowski, M.D., Ph.D., Director of the University of Chicago's Pancreatic, and Islet Transplant Program, who is a leading expert in diabetes and islet transplantation and a published diabetes researcher and surgeon with a longstanding record in both basic science and clinical research pertaining to islet cell and abdominal organ transplantation.

This clinical trial is a Phase 1/2 non-randomized, unblinded, single-arm, company-sponsored trial to evaluate the safety and efficacy of the Cell Pouch as a potential treatment for diabetic patients with hypoglycemia unawareness (US Phase 1/2 Cell Pouch Clinical Trial).

Patients eligible for the study have long standing T1D, severe hypoglycemic unawareness and a history of severe hypoglycemic events despite optimized medical care, and lack the ability to produce insulin from their pancreas, as shown in a glucose tolerance test by the lack of necessary blood levels of C-peptide, a quantitative biomarker of islet insulin production. The trial is designed to enroll seven (7) patients who are implanted with therapeutic Cell Pouches, and small sentinel pouches. Following the development of vascularized tissue chambers within the Cell Pouch, enrolled patients are stabilized on immunosuppression and activated on the donor transplant list. Upon receipt of a suitable donor pancreas and following isolation of islets, a relatively small dose of purified islets under strict release criteria is transplanted into the Cell Pouches.

A sentinel pouch, also transplanted with islets, is removed at approximately 90 days following transplant for an early assessment of islet function within the Cell Pouch. In our US Phase 1/2 Cell Pouch Clinical Trial, subjects are followed for safety, tolerability and efficacy measures for approximately six months post-transplant. At that time, a decision is made with regards to the transplant of a further second small islet dose with subsequent safety and efficacy follow-up. Patients are then followed for approximately one year and thereafter may receive a protocol-defined marginal dose portal vein top-up dose of islets. The goal of providing several doses is to help us understand the relationship between dose and efficacy level as well as islet dose density in the Cell Pouches required to achieve maximum efficacy. These learnings resulted in the Company manufacturing somewhat larger Cell Pouches that can provide up to 50% more islets spread at a lower cell density to provide the individual islets increased vascularization and access to systemic blood sugar levels. Subjects who complete the study protocol are followed up longer term by Dr. Witkowski.

We believe these preliminary findings from our clinical investigator support the safety, viability, and efficacy of the Cell Pouch System approach following protocol mandated islet transplants for the treatment of diabetic patients with severe hypoglycemia unawareness and the inability to produce their own insulin. Following removal of a sentinel device transplanted with islets and independently assessed by a pathologist, healthy abundant islets intimately associated with blood vessels housed in a natural tissue matrix were observed, showing the ability to produce insulin. Of significant importance, observations have been reported reflective of early diabetes improvement indicators in the most advanced trial patients: fasting and glucose-stimulated blood levels of C-peptide (a biomarker of insulin produced by cells), reduction in the number of severe hypoglycemic events, reduction in HbA1c, and

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other parameters. These indicators were further improved with the protocol mandated supplemental portal transplant following which subjects became insulin independent. We believe these indicators suggest a potential normalizing response of the Cell Pouch's therapeutic cells to the body's varied need for insulin production.

We believe these preliminary findings are an important achievement in the regenerative medicine therapeutics field and a first for an implanted prevascularized device with islet cells, transplanted deep under the skin. These encouraging results using human donor islets in our Cell Pouch in subjects with hypoglycemia unawareness represents an important advance of our stepwise approach toward our goal of developing and optimizing a treatment for all T1D patients employing immune protected stem cell-derived iPSC islet clusters within our Cell Pouch.

We believe the Cell Pouch can be used with a variety of cell sources, such as glucose-responsive insulin-producing cells derived from stem cells, addressing the limited availability of donors and allowing the extensive treatment of insulin-dependent diabetes and we have demonstrated this in several pharmaceutical collaborations in small animal models of T1D. Using our extensive learnings of human donor islets within the Cell Pouch, Sernova is using knowledge gained as we develop iPSC beta cell technologies including our licensed intellectual property from the University Health Network (UHN) in Toronto, Ontario and our recently announced iPSC beta cell technology from Evotec to provide an immune-protected cell-based therapeutic for all people with insulin-dependent diabetes.

On January 15, 2021, we announced that Dr. Piotr Witkowski presented interim data from our US Phase 1/2 Cell Pouch Clinical Trial study at the American Society of Transplant Surgeons (ASTS) 21st Annual State of the Art Winter Symposium in a peer-reviewed abstract entitled "*Islet Allotransplantation Into Pre-Vascularized Sernova Cell Pouch – Preliminary Results from The University of Chicago*". Dr. Witkowski reported Sernova's Cell Pouch transplanted with insulin-producing cells in patients with T1D continues to show persistent islet function and clinically meaningful improvement in measures of glucose control.

Data from two transplanted patients who are furthest in the study and who have received a second islet transplant were focused on. Importantly, these patients showed defined clinical benefit with a clinically meaningful reduction in daily injectable insulin requirement, along with the following additional clinical benefit indicators:

- absence of life-threatening severe hypoglycemic events;
- sustained blood levels of C-peptide (a biomarker for insulin produced by cells in the Cell Pouch);
- reduction in HbA1c (a measure of long-term glucose control); and

improvement in overall Continuous Glucose Monitoring (CGM) measured glucose control parameters (i.e., blood glucose 'Time in Range'). (CGM used in this study supports the analysis of mean glucose concentration, mean glucose variability, number and duration of hyper and hypoglycemic episodes as well as total duration of hypoglycemia.)

On February 18, 2021, we announced that an independent Data Safety Monitoring Board (DSMB) completed its second planned annual review of our US Phase 1/2 Cell Pouch Clinical Trial and did not raise concerns regarding safety and recommended continuation of the study.

On April 6, 2021, President and CEO Dr. Toleikis as an invited presenter delivered an update on Sernova's Regenerative Cell Therapeutics Platform and our diabetes program at the 2021 Cell and Gene Therapy Meeting on the Med virtual conference.

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On June 5, 2021, Dr. Piotr Witkowski presented new preliminary data from our US Phase 1/2 Cell Pouch Clinical Trial at the American Transplant Congress (ATC) 2021 Virtual Connect conference. Dr. Witkowski's presentation entitled "*Islet Allograft Transplantation Into The Pre-Vascularized Sernova Cell Pouch™ Device - Preliminary Results Of The Phase 1/2 Prospective, Open-Label, Single-Arm Study At University of Chicago*".

In addition to the continued confirmation of ongoing safety and tolerability in all 6 currently enrolled patients, Dr. Witkowski provided further updates on the longest treated study patients. These patients have continued to show defined clinical benefit associated with ongoing efficacy indicators including:

- reduction / elimination in the need for daily injectable insulin;
- continued improvement, i.e. reduction/elimination, in Severe Hypoglycemic Events (SHE);
- persistent detection of fasting and stimulated C-peptide in patients' bloodstream;
- reduction in HbA1c; and
- continued improvement of glucose control determined through patient blinded Continuous Glucose Monitoring (CGM) and measured by reduction of Time Above Range (TAR) and increase of Time in Range (TIR).

On June 28, 2021, Dr. Piotr Witkowski and the Clinical Trial Team for our US Phase 1/2 Cell Pouch Clinical Trial presented additional data and patient observations from the ongoing study at the American Diabetes Association's 81st Scientific Sessions. Data was delivered in a poster presentation entitled "*Persistent graft function after allotransplantation into pre-vascularized Sernova Cell Pouch™ device: Preliminary results from the University of Chicago*." Dr. Witkowski confirmed continued safety and tolerability in all six enrolled study patients. In addition, the two longest-treated patients continue to demonstrate clinical benefit in line with previously established key T1D efficacy indicators including reduction in HbA1c, reduction or elimination of severe hypoglycemic events, reduction or elimination of daily injectable insulin, detection of C-peptide in the patients' bloodstream, and improvement in glucose control as measured by CGM. The remaining patients are advancing through the study at different stages and their progress continues to be evaluated.

The most advanced patient has successfully completed the study protocol. Data from this patient supports the long-term safety of Sernova's Cell Pouch and, importantly, the patient then remained insulin independent (no requirement for injectable insulin) for approximately 15 months - with optimal glucose control.

On October 12, 2021, Dr. Toleikis provided a corporate update presentation at the Alliance of Regenerative Medicine (ARM) Cell and Gene Meeting on the Mesa virtual event.

On December 16, 2021, we announced that Dr. Piotr Witkowski would release updated interim data from our US Phase 1/2 Cell Pouch Clinical Trial study on January 13<sup>th</sup>, 2022, at the American Society of Transplant Surgeons (ASTS) 22<sup>nd</sup> Annual 'State of the Art' Winter Symposium from his peer-reviewed abstract entitled "*A Modified Approach for Improved Allograft Transplantation into the Pre-vascularized Sernova Cell Pouch*". Due to COVID-19 concerns, the ASTS conference was subsequently postponed to July 2022.

On January 10, 2022, with the postponement of the 2022 ASTS meeting, we reported on the highlights of Dr. Witkowski's updated interim data for our US Phase 1/2 Cell Pouch Clinical Trial as follows:

- ongoing safety and tolerability of Cell Pouch has been maintained in all study patients;
- islet transplantation to the Cell Pouch resulted in the establishment of new, measurable islet function documented by detectable levels of stimulated C-peptide in the first three patients, who



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completed the protocol-defined course of transplants;

- a supplemental, single intraportal islet transplant was sufficient for the first two patients to achieve and maintain sustained ongoing insulin independence and freedom from severe hypoglycemic events for over 21 and 2 months, respectively;
- the third transplanted patient recently completed their course of Cell Pouch transplants and a supplemental intraportal islet infusion, with favorable improvements in glucose control, near-normal levels of C-peptide, an absence of severe hypoglycemic events and reductions in daily insulin use; and
- the other three enrolled study patients are progressing through the study protocol, as planned. All have received Cell Pouch implants and are at various stages of protocol-defined islet transplants and follow-up.

Recruitment, screening and enrollment finalization of the 7<sup>th</sup> study patient under the active protocol for our US Phase 1/2 Cell Pouch Clinical Trial continues and remains a top priority.

The preliminary results to-date for our US Phase 1/2 Cell Pouch Clinical Trial are encouraging and are providing important information on the behaviour of our device with donor islets in real life situations in our study patients. As the therapeutic benefit of Sernova's Cell Pouch with donor islets for T1D continues to be demonstrated and validated, we progress in our ongoing pursuit of developing and commercializing a 'functional cure' for people with T1D using Sernova's Cell Pouch System technologies.

On March 17, 2022, we announced that after having completed its third annual review of our ongoing US Phase 1/2 Cell Pouch Clinical Trial, the DSMB recommended continuation of the clinical study according to the study plan.

On June 6, 2022, the Research Team from Dr. Piotr Witkowski's laboratory at the University of Chicago for our US Phase 1/2 Cell Pouch Clinical Trial presented updated positive data from the ongoing study at the American Diabetes Association's 82nd Scientific Sessions in New Orleans, LA. Updated data was presented in an oral podium presentation, "*Modified Approach for Improved Islet Allotransplantation into Prevascularized Sernova Cell Pouch™ Device: Preliminary Results of the Phase I/II Clinical Trial at University of Chicago*" [Abstract 306-OR].

The presented data reviewed the six patients who lived with long-standing insulin-dependent T1D and hypoglycemia unawareness prior to study treatment that underwent both Cell Pouch implantation and islet transplantation. Graft function was measured by blood glucose, patient insulin usage, and C-peptide, a widely used measure of islet function. The first three patients achieved complete and sustained insulin independence. Three additional patients on study did not maintain optimal immunosuppression, however this was resolved enabling those patients to receive further protocol-defined islet transplants.

Key highlights included:

- the first three patients have been insulin independent for over 2 years, 6 months, and 3 months, respectively;
- those first three patients with islets transplanted into the Cell Pouch subsequently presented positive serum C-peptide values confirming active insulin production by the Cell Pouch islet grafts; and
- the Cell Pouch was well tolerated with implant durations exceeding 35 months.

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Key findings from the interim clinical update:

- surgical implantation of the Cell Pouch was found to be generally well tolerated with a favorable safety profile;
- all patients who had favorable immunosuppression achieved complete insulin independence:
  - first three transplanted patients presented positive serum C-peptide values confirming active insulin production after islet transplantation into the Sernova Cell Pouch;
  - supplemental marginal dose islet transplantation via the portal vein was sufficient to allow those three patients to achieve and maintain insulin independence for over 2 years, 6 months, and 3 months, respectively; and
  - insulin independent patients have HbA1c in the normal range: 5.0, 5.2, and 5.2%, respectively.
- Dr. Witkowski further optimized outcomes in the ongoing clinical trial:
  - replacing patients' own plasma with serum as the islet suspension medium;
  - decreasing the concentration of islet suspensions transplanted to Cell Pouch resulted in greater stimulated C-peptide; and
  - the Cell Pouch implantation procedure was optimized with two shorter incisions to minimize infection risk and enhance healing.

Based on study data, we believe implementing a higher capacity Cell Pouch System would optimize patient outcomes.

Further trial information may be found at <https://www.clinicaltrials.gov/ct2/show/NCT03513939>.

#### ***Development of the Cell Pouch System for the Treatment of Postoperative Hypothyroidism***

The goals of our thyroid transplant program are to provide people with hypothyroid disease improvement in the natural thyroid hormone feedback loop, an improved quality of life and ultimately a 'functional cure' to this disease.

According to the American Thyroid Association (ATA), 20 million Americans currently live with thyroid disease, and 12% of Americans will develop a thyroid condition during their lifetime. The thyroid gland produces and secretes thyroid hormones that regulate the body's metabolism and is thus essential for life. The development of new treatments for patients with unsatisfactory control of the thyroid hormones feedback loop may satisfy this unmet medical need. We believe that thyroid tissue transplanted into an implanted Cell Pouch offers a novel approach that could improve the quality of life and outcomes of patients experiencing postoperative hypothyroidism. Sernova's first approach in the treatment of hypothyroid disease is to transplant remaining healthy thyroid tissue of patients following thyroidectomy into the pre-implanted vascularized Cell Pouch. The goal is to retrieve the natural feedback system for release of thyroid hormones.

The thyroid gland affects all critical body functions including heart rate, energy levels, and the rate at which energy is produced from nutrients. Its essential functions include control of how quickly the body uses energy, makes proteins, and sensitivity to other hormones, principally through the production of thyroid hormones, mainly triiodothyronine (T3) and thyroxine (T4).

Hypothyroidism is a condition where the thyroid gland does not produce sufficient hormones thereby upsetting the normal balance of chemical reactions. If left untreated, hypothyroidism can cause health

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problems such as obesity, joint pain, infertility, heart disease, and eventually death. Common causes are autoimmune disease, radiation treatment, and surgical removal of the thyroid (thyroidectomy). Patients may undergo surgical reduction (thyroid lobectomy) or complete removal of the thyroid gland (thyroidectomy) for treatment of several disorders such as thyroid nodules, which are reported to occur in up to 65% of patients (PMID: 19041821); Grave's Disease (a type of hyperthyroidism); and or large multinodular goiters. Thyroidectomy is also commonly performed for cancer diagnosis or treatment.

Hypothyroidism inevitably occurs after total thyroidectomy and may also occur in up to 10% of people after thyroid lobectomy (Johner, A. et al, *Ann of Surg One* 2011; 18(9):2548-2554). The American Thyroid Association estimates that about 150,000 thyroidectomies are performed in the US yearly, and most individuals undergoing a thyroid operation will be diagnosed with benign disease after their operation.

Following thyroidectomy, patients require daily hormone replacement therapy with T4. Published research indicates up to 50% of thyroxine users do not achieve adequate hormone levels (Okosieme, OE et al. *Expert Opin Pharmacother* 2011; 12(15):2315-2328). Moreover, it is evidenced that patients treated adequately with T4 still experienced several symptoms, including deficits in cognition and mood, ability to focus, and general mental well-being (Kansagra, S. et al. *Laboratory Medicine* 2010; 41(6):338-48.). In addition, long-term thyroid hormone administration may be associated with significant morbidity, and thus may result in many associated healthcare costs.

Results of our preclinical research are being used as a foundation for anticipated clinical trials using the Cell Pouch in combination with thyroid-hormone producing cells with the goal to preserve thyroid function and improve patient quality of life.

In this regard, Sernova has conducted preclinical research with our Cell Pouch for the treatment of postoperative hypothyroidism. To advance this platform technology, in collaboration with Dr. Sam Wiseman, BSc, MD, FRCSC, FACS, Professor, Faculty of Medicine, University of British Columbia and in part funded by a Transplant Venture Grant awarded by the Transplant Research Foundation (TRF) of British Columbia, we have assessed healthy human thyroid tissue transplanted into a previously implanted Cell Pouch in a preclinical model, in preparation for a clinical program. Our initial approach in the treatment of postoperative hypothyroid disease is to auto-transplant healthy thyroid tissues of patients undergoing thyroidectomy into the pre-implanted vascularized Cell Pouch, to reduce the burden and risks of postoperative hypothyroidism. The overall aim of the program is the evaluation of the survival and function of thyroid tissue after implantation into the Cell Pouch to establish proof-of-concept of this novel approach.

On April 30, 2019, we announced a collaboration with the University of British Columbia for development of a Cell Therapy-based program for the treatment of hypothyroidism under the direction of Dr. Sam Wiseman BSc, MD, FRCSC, FACS of the University of British Columbia, thyroid surgeon and researcher, and the Director of Research in the Department of Surgery at Providence Healthcare in Vancouver, BC, Canada.

On April 14, 2021, we announced the appointment of Dr. Sam Wiseman to Sernova's Scientific Advisory Board.

On April 28, 2021, Sernova hosted a virtual Thyroid Disease key opinion leader (KOL) event, led by internationally renowned expert Dr. Sam Wiseman, that highlighted the potential of our novel Cell Pouch cell therapy approach for the potential treatment of thyroid disease.

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On January 27, 2022, we announced the publication of a peer reviewed preclinical study demonstrating positive results of a novel Cell Pouch System cell therapy approach to treat hypothyroidism and potentially avoid lifelong dependence on thyroid medication following surgical removal of the thyroid gland. The journal article entitled “*Subcutaneous transplantation of human thyroid tissue into a pre-vascularized Cell Pouch™ device in a Mus musculus model: Evidence of viability and function for thyroid transplantation*” by lead author, Dr. Wiseman, a leading surgeon and internationally renowned expert in the management of thyroid and parathyroid disease, was published in the scientific journal, *PLOS ONE*, January 20, 2022 edition. In this study, thyroid tissue from patients undergoing surgery for treatment of benign disease was transplanted into Sernova Cell Pouches that had been previously implanted into laboratory mice. The aim of the study was to investigate the long-term survival of human thyroid tissue in the Cell Pouch and evaluate the ability of these thyroid transplants to release thyroid hormones into the bloodstream. The study confirmed that the human thyroid tissue transplanted into the Cell Pouch survived and released human thyroglobulin into the bloodstream, with no adverse effects for the three-months duration of the study. Thyroglobulin was used as a biomarker efficacy measure in this study as it is the precursor of thyroid hormones.

The results to date from this collaboration have been encouraging and support the potential of transplanted thyroid tissue to provide clinical benefit for the treatment of hypothyroidism.

We are completing documentation including clinical protocol and other required supporting information in support of a Phase 1/2 clinical study. We are preparing an independent market assessment of the hypothyroid indication for this initial and next generation stem cell-derived technology. Documentation has been submitted to the regulatory authorities to determine how the product will be regulated, whether through the device or combination product process. To add to our already completed preclinical studies, we initiated a final study to mimic the clinical trial design approach.

Our goal is to file the regulatory documentation and to seek regulatory authorization to initiate a company sponsored first-in-world clinical trial for thyroid patients with significant unmet need requiring a cell transplantation approach for anticipated regulatory clearance to initiate the trial in 2023.

#### ***Development of the Cell Pouch System for the Treatment of Hemophilia A***

The goals of our hemophilia program are to provide people with hemophilia A improvement in the natural production of factor VIII (FVIII) in their bloodstream from FVIII corrected cells within the Cell Pouch, to reduce bleeds associated with this disease, an improved quality of life and ultimately a ‘functional cure’ to this disease.

Hemophilia A is a rare, serious genetic bleeding disorder caused by missing or defective clotting factor VIII in the bloodstream. A cellular genetic deficiency in FVIII results in a reduced ability for blood to clot naturally resulting in increased bleeding, even in circumstances where small blood vessels naturally break and heal such as in joints, resulting in inflammatory arthritic type symptoms and joint damage. To counteract this reduction in blood clotting, patients require frequent blood transfusions which put them at risk of acquiring blood-borne infections, such as HIV, hepatitis B and hepatitis C. The alternative is taking infusions of FVIII up to three times a week to maintain a blood level of FVIII that can reduce the bleeding.

According to a publication by the Alliance for Regenerative Medicine ([ARM](#)), the estimated annual cost of treatment for hemophilia A represents an average of US\$200,000 per patient.

We believe that the therapeutic potential to have a constant release of FVIII from a hemophilia A patient’s own genetically corrected cells placed within the implanted Cell Pouch would be a very

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significant advancement in the treatment of hemophilia A and a disruptive approach to the current standard of care treatment for hemophilia A. Corrected cells placed in an implanted Cell Pouch could release FVIII at a rate expected to reduce disease-associated hemorrhaging and joint damage. The continuous delivery of FVIII could also reduce or eliminate the need for multiple weekly infusions, which is the current standard of care using plasma-derived or recombinant, genetically engineered FVIII for the prophylactic treatment of hemophilia A. This approach is analogous to that used for CAR T-cell therapy as a validated therapeutic approach where a patient's own cells are collected from a blood sample and modified, scaled-up and placed back into the body to treat disease.

Sernova's approach to the cell therapy treatment of hemophilia A involves obtaining a blood sample from the patient and correcting the genetic defect in certain isolated cells so the cells produce the required FVIII. The cell numbers are then expanded for placement into our Cell Pouch, that has been previously implanted into the patient. We believe the therapeutic potential to have a constant release of FVIII from a hemophilia A patient's own genetically corrected cells in the Cell Pouch would be a significant advancement in the treatment of hemophilia A and other diseases that can be treated with genetically engineered cells. Sernova's therapeutic approach could reduce or eliminate the need for patients to take expensive life-long infusions of FVIII to reduce or prevent the deleterious effects of this disease.

In the development of this novel technology multi-year product development and proof-of-concept studies have been conducted and successfully completed by Sernova and a European team of experts collectively forming the HemAcure Consortium (HemAcure Consortium). The aim of the HemAcure Consortium three-year project was to develop a permanent, safe, therapeutic solution for those living with hemophilia A in the form of a novel ex vivo gene therapy, cell-based approach within Sernova's proprietary Cell Pouch. This combination therapy strives to replace missing clotting human FVIII in the patient's own Blood Outgrowth Endothelial Cells (BOECs) transplanted into the Cell Pouch. These corrected cells function to release FVIII into the bloodstream restoring the ability for blood clotting to occur preventing uncontrolled bleeding. The HemAcure Consortium was funded by a €5.6 million (approximately \$8.5 million) European Commission Horizon 2020 grant (Horizon 2020 Grant) to develop a Good Manufacturing Practices (cGMP) compliant human cell product to enable the completion of safety and efficacy studies in the Cell Pouch as part of a regulatory package in preparation for human clinical testing.

On May 19, 2020, the HemAcure Consortium presented the scientific results of the consortium's HemAcure Hemophilia Cell Therapy Program research, noted above, at the 23rd American Society of Gene & Cell Therapy (ASGCT) Annual Meeting. The results support the potential of using genetically corrected cells from a patient's own BOECs transplanted into the Cell Pouch to replace missing clotting human FVIII in patients with hemophilia A.

The following are the highlights of the results presented in the peer-reviewed abstract entitled "*Combined Gene and Cell Therapy for the Treatment of Hemophilia A within an Implantable Therapeutic Device*":

- BOECs were safely isolated and grown from a small sample of circulating peripheral blood of volunteer hemophilia A patients unable to express the required FVIII for clotting;
- to regain the function of the BOECs' ability to produce clotting FVIII, techniques were successful in safely inserting the gene responsible for the correction and production of human FVIII into the patient's BOECs, and these corrected cells were safely multiplied to increase their number;
- tests were conducted to ensure the safety, and the newly corrected BOECs produced enough

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human FVIII both in the laboratory and in an initial preclinical animal model deficient of FVIII. FVIII blood levels reached up to 10%, a therapeutically relevant level of FVIII;

- to further test cell dose-response, in the preclinical model of hemophilia A, animals originally unable to clot their blood were implanted with a Cell Pouch and in separate groups transplanted with two different doses of human BOECs corrected for the ability to produce human FVIII;
- to assess the safety of the combined product, the Cell Pouch and corrected human FVIII BOECs derived from the volunteer participants with hemophilia A were examined using histological analyses. Importantly, histology showed healthy tissue represented by the presence of stromal growth and new blood vessel formation within the Cell Pouch;
- further histological investigation of the transplanted Cell Pouch sections demonstrated long-term survival of human FVIII BOECs present within the vascularized Cell Pouch achieved through co-staining for blood vessels (von Willebrand Factor stain) and the presence of the patients corrected human cells (HLA-ABC stain) in a preclinical animal model;
- in both experimental doses, human FVIII was detected in circulating peripheral blood up to 4 months following transplantation, with more human FVIII present in peripheral blood using the higher dose of corrected BOECs; and
- data further confirmed functional clotting improvement in the blood at the four months' time point where FVIII BOECs transplanted into the hemophilia A mouse model restored the animal's FVIII activity at a therapeutic level in the Cell Pouch.

During December 2021, the results of the HemAcure Consortium's study were published in a journal article entitled "*Efficient and Safe Correction of Hemophilia A by Lentiviral Vector-Transduced BOECs in an Implantable Device (Sernova's Cell Pouch™)*" in the scientific journal *Molecular Therapy: Methods & Clinical Development*, Volume 23.

We believe these published results demonstrate the potential of our Cell Pouch System to provide a novel approach for the treatment of hemophilia A using an ex vivo gene therapy, cell-based technology that could lead to improved efficacy and quality of life of people suffering from hemophilia A.

The proposed hemophilia A therapy is paving the way for future human clinical testing in hemophilia A patients using Sernova's Cell Pouch transplanted with genetically corrected FVIII releasing cells developed by the HemAcure Consortium team.

We are evaluating a next step preclinical dose optimization study to maximize release of Factor VIII in Cell Pouch using the hemophilia A mouse model with human corrected cells. Completion of this work will provide guidance on next steps in clinical development.

#### ***Developing the Cell Pouch for the Treatment of Additional Disorders and Rare Diseases***

We are exploring the potential use of our technology for the treatment of other rare disease indications to further expand the application of our Cell Pouch™ and cell therapy platform technologies further.

On January 28, 2021, we provided a Collaborations Update highlighting Sernova had multiple active research collaborations with major pharmaceutical companies. In this regard, Sernova is deploying its in-house cell therapy expertise and proprietary Cell Pouch technologies in combination with proprietary therapeutic cell assets designated by the pharmaceutical collaborators to conduct proof of concept studies for additional potential clinical indications. These collaborations with leaders in the pharmaceutical industry build upon our business strategy to develop a portfolio of therapeutic technologies to realize the full potential of Sernova's cell therapy regenerative medicine platform. We

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### **MANAGEMENT'S DISCUSSION AND ANALYSIS**

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believe collaborating / partnering with multiple pharmaceutical and life science companies will not only expand our therapeutic treatment potential but also provides a de-risked approach for Sernova as we develop our technologies and bring new therapies to patients with the goal to provide people with a 'functional cure' for multiple chronic and rare diseases. To date we have obtained encouraging results assessing various stem cell-derived technologies for a number of clinical indications and we are continuing to advance select collaborations with the goal of achieving long-term development partnerships.

#### ***Local Immune Protection & Other Complementary Technologies***

We believe that therapeutic cell encapsulation and other advanced technologies such as gene-editing of cells may protect therapeutic cells from immune system attack within the Cell Pouch vascularized environment while providing the means to enable close association of therapeutic cells with the required microvessels and tissue matrix. Such approaches may enable long-term survival and function of therapeutic cells within the Cell Pouch for the treatment of multiple disease indications while also allowing the reduction or elimination of immunosuppression medications and their associated side effects.

Consequently, development of cellular local immune protection technologies is an important pillar for our cell therapy therapeutics platform. During the 2020 fiscal year, we secured by acquisition and licensing local immune protection technologies for our Cell Pouch cell therapy platform.

Our approach of protecting cells in a safe manner, locally within the Cell Pouch tissue matrix, may represent a competitive advantage as a biologically compatible approach, which may accelerate the development of our therapeutic programs. We continue to evaluate additional immune protection technology approaches. We believe we are well-positioned to advance our total regenerative medicine cell therapy therapeutics platform to multiple clinical applications and broader patient populations.

#### ***Cellular Conformal Coating Approach***

The goal of our conformal coating program is to provide patients with protection of transplanted therapeutic cells without the need for life long antirejection medication. This would be accomplished by providing a cellular local immune protection of their transplanted cells, resulting in an improved quality of life.

In June 2020, we acquired an innovative cellular local immune protection technology from Converge Biotech, Inc. Pursuant to an asset purchase agreement, we acquired all intellectual property for a conformal coating cell technology (Conformal Coating Technology), including issued patents, patent applications and know-how. This technology acquisition provides a pivotal component required for our regenerative medicine therapeutics platform and could accelerate our first-to-market strategy for T1D and significantly expand the number of treatable patients suffering from chronic diseases.

The Conformal Coating Technology consists of a thin proprietary cross-linked polymer coating layer designed to surround therapeutic cells with the goal to protect them from an auto-response attack by one's own immune system post cell transplantation into the body.

The advantages and potential benefits of Conformal Coating Technology are anticipated as follows:

- provides protection of the therapeutic cells from immune system attack locally within the Cell Pouch chambers, potentially avoiding the need for life-long immunosuppression medications that are currently required following cell transplantation;

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- enables close contact of the transplanted therapeutic cells with the vascularized tissue matrix within the Cell Pouch chambers to enable more intimate interactions;
- enables the diffusion of small molecules and biomolecules (i.e. glucose, insulin, and other proteins or hormones), to provide a physiological glucose-stimulated insulin response without delay that occurs with other encapsulation technologies; and
- due to the improved diffusion of biomolecules relative to other encapsulated technologies, it may require a smaller load of therapeutic cells to achieve the desired therapeutic effect in comparison to standard microcapsules.

In August 2020, we announced entering into an exclusive, worldwide license with the University of Miami (UMiami) for the commercial rights to novel complementary conformal coating immune protection technologies, which enables Sernova to broaden the intellectual property and technology scope of its immune protection conformal coating technologies.

In September 2021, we announced a collaboration with the UMiami and Dr. Alice Tomei, a leading international expert in immunoprotection and diabetes management from the renowned Diabetes Research Institute at the University of Miami Miller School of Medicine, to validate our Conformal Coating Technology in combination with therapeutic cells in Sernova's Cell Pouch for T1D. Under the terms of the agreement, the Company has committed to fund a one-year budget of up to US\$833,154 (approximately \$1,052,357). Technology optimization and further preclinical validation work is progressing as expected. Dr. Tomei is one of the original inventors of the Conformal Coating Technology that has been developed and optimized over 12 years with her dedicated team. This important collaboration is multifaceted in nature and designed to advance for the first time locally immune protected cells within the Cell Pouch with the goal of advancing these technologies into clinical trials without the need for life long immune suppression technologies. We believe successful development of this combination technology could meet an unmet need in a broader population of people with T1D who seek a 'functional cure' for their diabetes without the need to take life-long immunosuppression medications.

Subsequent to the collaboration announcement, in September 2021 we hosted an information session webinar "The Ultimate Combination of Two Proven Technologies as a Potential Functional Cure for Type 1 Diabetes and Other Chronic Diseases". The webinar featured Dr. Tomei, who spoke about the use of our Conformal Coating Technology as a technology approach for local cellular immune protection. The webinar is available at [https://www.sernova.com/investor/#News\\_Releases](https://www.sernova.com/investor/#News_Releases) or at <https://youtu.be/U57fkmsBT7k>.

Our R&D group has been working closely with Dr. Tomei's team to advance the collaboration as well as the scale up processes to manufacture sufficient coated cells for clinical applications. We have substantially increased our knowledge regarding the combination of conformally coated islets in the Cell Pouch and have gathered important information about the criteria needed to release the combined product for clinical use.

#### ***Gene Editing Approach***

In May 2020, we entered into a research collaboration with AgeX Therapeutics, Inc. (NYSE American: AGE) to investigate their UniverCyte gene-editing technology to generate transplantable, universal locally immune protected therapeutic cells for use in combination with our Cell Pouch to provide a total regenerative medicine cell therapy therapeutic solution for the treatment of T1D and hemophilia A. The goal of this collaboration is to evaluate the technology as a next-generation local immune protection



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approach for therapeutic cells or tissue transplanted into the Cell Pouch. The research collaboration was extended in 2022.

UniverCyte uses a novel modified form of HLA-G, a potent immunomodulatory molecule, to mask transplanted therapeutic cells from immune detection and attack. The research collaboration will evaluate whether Sernova's pluripotent stem cell-derived therapeutic cells engineered with the UniverCyte technology can evade human immune detection. Research will include UniverCyte modification of multiple cell types, including stem cell-derived islets, stem cell-derived human FVIII releasing cells as well as adult donor-derived FVIII releasing cells. We believe that the combination of these technologies could enable the transplantation of therapeutic cells in patients within an off-the-shelf manner using Sernova's Cell Pouch, without human leukocyte antigen (HLA) tissue matching or concurrent administration of immunosuppressive medications.

We may evaluate additional complementary technologies in the future to further broaden and enhance Sernova's technology platform and expand market penetration potential for our future product offerings.

#### ***Sernova's Access to Multiple Sources of Therapeutic Cells***

Our transplantation technologies may incorporate autologous cells, donor cells, or other sources of cells, including therapeutic cells derived from human stem cells or derived from xenogeneic sources, depending on the clinical indication under evaluation. As such, we continue to work with academic collaborators and industry partners to identify and secure the required cells for our therapeutic indications.

We are developing stem cell-derived technologies with the expectation to provide a virtually unlimited supply of cells for the treatment of diabetes to overcome the limited supply of human donor islets. Pursuant to our strategy of obtaining sources of supply for our therapeutic cell applications, the Company entered into a license agreement with the University Health Network in Toronto, Ontario, Canada. This license agreement gives us exclusive worldwide rights to certain patented and patent-pending technologies for the advancement of glucose-responsive insulin-producing stem cells for treatment of patients with insulin-dependent diabetes.

As mentioned above, Sernova is also expanding its collaborations with global pharmaceutical partners to evaluate various cell technologies using different approaches combining Sernova and partner technologies with the goal to create best-in-class therapeutics.

In addition, a collaboration with an international pharmaceutical company to study Sernova's Cell Pouch in a large animal diabetes model has been successfully conducted. The collaboration involved the study of safety, survival, and efficacy of locally immune protected xenogeneic therapeutic islets in our Cell Pouch in a proof-of-concept study.

We have demonstrated long-term insulin independence in several collaborations with global pharmaceutical partners using advanced iPSC stem cell-derived diabetes technologies within the Cell Pouch in accepted animal models of T1D. This work supported the concept of the Cell Pouch combined with an advanced stem cell source meant to provide an unlimited supply of therapeutic cells to treat a significant number of T1D subjects. These collaborations resulted in Sernova and Evotec coming to terms on an iPSC derived beta cell technology for Sernova.

Sernova plans to continue to establish and develop additional collaborations with pharmaceutical and medtech companies for its diabetes and other clinical indications with the end goal to have long-term licensing and or co-development relationships. In addition to pharmaceutical companies, Sernova has

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entered collaborations with various academic institutions relating to its Cell Pouch technologies for next-generation products.

#### ***Sernova Acquisitions, In-Licensing and Collaborations***

##### *Exclusive License Option for Leading Advanced iPSC Beta Cells for Replacement Therapy*

On May 16<sup>th</sup>, 2022, we entered into an exclusive global strategic partnership with Evotec, the global life science company and leading developer of iPSC cell technologies for therapeutic applications, to develop a best-in-class cell therapy treatment for people living with insulin-dependent diabetes. Together we will combine and leverage our respective technologies and scientific expertise to develop an implantable iPSC-based beta cell replacement therapy to provide an unlimited insulin-producing cell source to treat patients with insulin-dependent diabetes.

The Evotec Collaboration combines our Cell Pouch System, which has previously demonstrated Phase 1/2 clinical proof-of-concept using human donor islets, with complementary technologies and Evotec's iPSC-based beta cells for clinical development and commercialization. Incorporating Evotec's insulin-producing, ethically derived beta cells within our Cell Pouch platform creates the potential to provide a 'functional cure' for millions of people suffering from diabetes using a cGMP controlled and scalable off-the-shelf product.

With its long-standing beta cell development program, Evotec has demonstrated the ability to reliably produce high quality, stable, human iPSC-derived beta cells using its proprietary process for producing islet-like clusters in a quality-controlled scalable bioreactor process. These islet-like clusters have been demonstrated to be functionally equivalent to primary human islets in their ability to normalize blood glucose levels in *in vivo* models of T1D for approximately one year and ongoing.

After continued development and optimization of its iPSC technologies and evaluation of the existing and development landscape for implantable medical devices to be part of an iPSC treatment solution for the treatment of T1D, Evotec concluded the Cell Pouch and Cell Pouch System was the best fit for its field leading iPSC technologies for T1D. Similarly, based on data from other collaborations activities we've been working on, we concluded that Evotec had the ideal ethically derived iPSC beta cell technology with the greatest potential to become a commercial product.

The Evotec Collaboration provides Sernova with a worldwide exclusive option to license Evotec's iPSC-based beta cells for use in treating both type 1 and type 2 diabetes.

##### *Conformal Coating Technology Acquisition*

As noted above, Sernova completed its acquisition of cellular local immune protection technology from Converge Biotech, Inc. (Converge), as a strategic accelerator for expansion of Sernova's total regenerative medicine cell therapy therapeutics platform. Sernova acquired all intellectual property associated with the Conformal Coating Technology.

The Conformal Coating Technology consists of a thin proprietary coating layer that effectively cloaks coated therapeutic cells to protect them from an auto-response attack by a patient's own immune system following cell transplantation into the body. The technology was developed by Dr. Tomei and Dr. Hubbell. Dr. Tomei, of the renowned Diabetes Research Institute, a designated Center of Excellence at the University of Miami Miller School of Medicine, is a leading international expert in immunoprotection and diabetes immunoengineering. Dr. Hubbell is the Eugene Bell Professor of Tissue Engineering at the University of Chicago and a leading international researcher in immunoengineering.

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#### *Conformal Coating Technology In-License Expansion*

On August 4, 2020, Sernova announced it had entered into an exclusive, worldwide license with UMiami for the commercial rights to the novel conformal coating immune protection technologies, further developed by Dr. Tomei.

This exclusive worldwide license agreement broadens the technological scope of Sernova's immune protection conformal coating technologies and related intellectual property. Furthermore, it adds to the series of our recent strategic acquisitions and collaborations building on the Company's goal of protecting Sernova's therapeutic cells or tissues transplanted into Sernova's Cell Pouch from a detrimental auto-immune system response with the goal of eliminating the need for life-long immunosuppressive drugs in treated patients.

In addition to filing an international patent application following further encouraging research supporting the Conformal Coating Technology in islets and stem cell derived technologies at UMiami, a collaborative research plan advancing the Conformal Coating Technology in combination with therapeutic cells within Cell Pouch as well as the scale up of the Conformal Coating Technology has been developed in support of advancing the combined technologies towards the clinic.

#### *Conformal Coating Technology Collaboration*

On September 16, 2021, we announced a research agreement with Dr. Tomei and UMiami to validate our Conformal Coating Technology in combination with therapeutic cells in Sernova's Cell Pouch for T1D. This important collaboration is multifaceted in nature and designed to advance locally immune protected cells within the Cell Pouch into clinical use, without the need for immunosuppression medications. The work being conducted in this collaboration is well under way with the Sernova and UMiami collaboration teams.

The preliminary positive results reported to date in patients for T1D, implanted with Sernova's Cell Pouch and transplanted with islets, continue to validate our cell therapy therapeutics approach. These collaborations position Sernova's advancing cell therapies to include locally immune protected stem cell-derived cells as a leader in the development of a potential 'functional cure' for all patients with diabetes and other chronic diseases.

#### *Gene Editing Collaboration*

As noted above, during May 2020 Sernova announced a collaboration with AgeX Therapeutics, Inc. (AgeX), a biotechnology company developing therapeutics for human aging and regeneration, where Sernova would utilize AgeX's UniverCyte™ gene technology to generate immune-protected universal therapeutic cells for use in combination with Sernova's Cell Pouch for treatment of T1D diabetes and hemophilia A. Sernova's goal is to reduce or eliminate the need for immunosuppressive medications following Cell Pouch cell transplantation.

The research collaboration is evaluating whether Sernova's pluripotent stem cell-derived pancreatic islet beta cells engineered with AgeX's UniverCyte technology can evade human immune detection. 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. With a similar intent, pluripotent stem cell-derived or adult donor-derived human Factor VIII-releasing cells modified with AgeX's UniverCyte will be evaluated in Sernova's hemophilia A program.

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Under the terms of the agreement, Sernova is granted a time-limited, non-exclusive research license by AgeX. A commercial license for Sernova to utilize UniverCyte to engineer cellular products for therapeutic and commercial purposes may be negotiated between the companies pending successful study outcomes.

The UniverCyte technology aims to mask therapeutic cells derived from pluripotent stem cells or adult donors from human immune detection to allow for off-the-shelf cellular products without the need for immunosuppressant medications, which may have potent side effects, or HLA-matching between donor and patient. UniverCyte uses a novel, modified form of HLA-G, a potent immunomodulatory molecule, which in nature protects an unborn child from their mother's immune system. In almost all human cells, native HLA-G expression is silenced after birth. AgeX's modified HLA-G shows evidence of being resistant to this silencing, thereby potentially allowing for long-term, stable and high expression of the immunomodulatory effect.

This collaboration is allowing Sernova to further identify and evaluate technologies complementary to Sernova's Cell Pouch therapeutic platform and to expand Sernova's immune protection offerings with potential benefit over current immunosuppressive strategies for regenerative medicinal therapeutics. As of the date of this MD&A, the collaboration has been extended to continue the evaluation of the HLA-G technology with stem cell derived cells within Sernova's Cell Pouch. Success with the preclinical evaluation could lead to a licensing agreement and clinical evaluation of the technology in a diabetes stem cell derived program.

#### *Pharmaceutical and Life Sciences Company Collaborations*

The goal of our collaborations with pharmaceutical and life sciences companies is to establish new cell therapeutic products to provide potential 'functional cures' for a series of diseases involving replacement of missing proteins or hormones through the combination of Sernova and collaborator technologies. The collaborations may result in the in-licensing or out-licensing of technologies or co-development of therapeutic products. These collaborations may also result in other M&A activities between Sernova and the collaborator companies.

In this regard, Sernova is deploying its in-house cell therapy expertise and proprietary Cell Pouch technologies in combination with proprietary therapeutic cell assets designated by pharmaceutical or life science company collaborators. The research collaborations follow the ongoing clinical success of our Cell Pouch technologies in diabetes and reflect the value and evolving recognition of our technologies and cell therapy platform. These important partnerships with leaders in the pharmaceutical industry build upon our business strategy to develop a portfolio of products to realize the full potential of Sernova's regenerative medicine therapeutic platform by extending and broadening its application to new therapeutic areas and modalities. We believe partnering with multiple pharmaceutical companies not only will expand our therapeutic treatment potential but also provides a de-risked approach for us as we develop our technologies and bring new therapies to patients with the goal to provide people with a functional cure for multiple chronic and rare diseases.

We have shown in multiple research collaborations testing advanced glucose responsive stem cell-derived technologies in combination with Sernova's Cell Pouch that the combination achieved long-term insulin independence in small animal models of T1D. After comprehensive evaluation, we selected Evotec as our partner for iPSC beta-cell diabetes and an exclusive collaboration.

Research for non-diabetes indications through pharmaceutical company collaboration is continuing.

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#### ***Protection of Proprietary Intellectual Property***

As the pharmaceutical and biotechnology industries are very competitive, Sernova has filed international patent applications related to the Cell Pouch System to protect its intellectual property rights related to its therapeutic programs. Sernova has been successful at achieving patent claims in multiple countries around the world.

Our international patent portfolio currently consists of issued and pending patents in multiple families covering our platform and related enabling technologies in important markets in North America, South America, Europe, and Asia. We strive to obtain broad claims for our patents, including exclusivity of our Cell Pouch device and related technologies in combination with a wide range of therapeutic cell technologies including glucose-responsive insulin-producing stem cell-derived cells, and with our acquired local immune protection conformal coating intellectual property and that recently licensed from UMiami, for the treatment of a number of chronic diseases. We intend to continue to expand our patent and licensing portfolio, through inventions developed internally as well as through strategic in-licensing, to maximize the commercial potential of our platform technologies.

Sernova will continue to protect the commercial therapeutic applications of its discoveries and inventions. In addition, the Company has developed technologies, which it may elect to keep as trade secrets and not publicly disclose in patent applications.

#### ***Research and Development (R&D)***

Our R&D efforts focus principally on the development of our Cell Pouch System cell therapy platform in conjunction with various therapeutic cells and local immune protection technologies for the treatment of major and rare diseases in humans.

Our overall objective is to advance our medical technologies through the various stages of preclinical and clinical development and ultimately to provide commercial products to patients. The programs we undertake may involve internal preclinical and clinical development efforts in addition to third-party collaborations and corporate partnerships.

Our primary activities to achieve our overall objective and related goals include the following:

- conducting the series of clinical trials required to gain eventual marketing approval for the Cell Pouch System in countries that have a significant market opportunity. We are developing our first therapeutic product for the treatment of T1D and severe hypoglycemic events utilizing human donor islets;
- advancing a treatment that we believe could potentially treat millions of people with diabetes consisting of the Cell Pouch System using immune protected Evotec iPSCs and our owned, licensed or controlled technologies; and
- ongoing R&D activities related to our proprietary Cell Pouch in the following areas:
  - continuing our research and development of additional therapeutic indications such as hemophilia A and postoperative hypothyroid disease;
  - developing therapeutic cell sources for transplantation within our Cell Pouch, such as autologous cells (self-cells) and allogeneic cells (stem cell-derived cells) to treat patients with these chronic diseases;
  - identifying, evaluating and potentially in-licensing complementary technologies which may improve the safety and efficacy of cells within the Cell Pouch;
  - establishing research collaborations to assess alternative cellular immune protection

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technologies;

- developing acquired and in-licensed cellular local immune protection technologies;
- continuing to develop proprietary processing and supply of therapeutic cells;
- ongoing international development of our intellectual property portfolio and development of new and or licensing of intellectual property; and
- establishing partnerships with medical device (medtech) and or pharmaceutical companies as well as academic institutions for the development of our products and to advance our next-generation technologies.

**RESULTS OF OPERATIONS*****Selected Financial Information***

The selected financial information provided below is derived from the Company's unaudited interim condensed consolidated financial statements.

	<u>Three months ended July 31</u>		<u>Nine months ended July 31</u>	
	2022	2021	2022	2021
Research and development expenses	\$ 4,005,508	\$ 956,965	\$ 10,353,048	\$ 2,746,350
General and administrative expenses	1,905,441	679,816	5,948,886	1,732,330
Loss and comprehensive loss	5,831,492	1,630,998	16,210,114	4,790,196

For the three months ended July 31, 2022, we recorded a loss of \$5,831,492, an increase of \$4,200,494 / 258% compared to the same period in the prior year. The increase was driven by the combined effect of increased R&D and G&A costs. Approximately \$1.3 million or 32% of the total increase was primarily attributable to incremental non-cash share-based compensation expense associated with new stock option and DSU grants during the 2022 fiscal year first quarter and to a lesser extent stock option grants to new personnel since that quarter. The increase in other R&D and G&A costs from the comparative period are discussed in more detail below.

For the nine months ended July 31, 2022, we recorded a loss of \$16,210,114, an increase of \$11,419,918 / 238% compared to the same period in the prior year. Similar to the third quarter, higher R&D and G&A costs both had an impact on the year-to-date increase. Approximately \$6.0 million or 52% of the total increase is attributable to incremental non-cash share-based compensation expense associated with the aforementioned stock option and DSU grants.

The subject stock options and DSUs granted were based on the Company's established compensation philosophy and earlier work conducted by independent compensation consultant Marsh & McLennan. As the last grants occurred during fiscal year 2019, these new grants primarily represented two fiscal years of "catch-up" awards in combination with initial grants for new employees hired. With the grant of some stock option and DSU awards effectively delayed by up to two fiscal years, a portion of each were granted with immediate vesting during the first quarter to affect a similar vesting result as if the relevant awards had been granted more timely. Of the \$6.0 million incremental year-to-date non-cash share-based compensation expense amount noted above, approximately \$2.4 million related to the cumulative one-time non-cash expense for the portion of stock option and DSU awards granted with immediate vesting. Vesting aside, the magnitude of the relevant expense recognized for all stock options and DSUs granted was significantly compounded by an approximate 3.5 and 6 fold increase in the Black

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Scholes fair value of each stock option and DSU granted, respectively. This increase in fair value was driven by a 528% increase in the Company's share price since the last grant date in 2019. The fair value of the non-immediately vested stock options and DSUs will be recognized (i.e. expensed) over up to three years.

Excluding the significant effect of non-cash share-based compensation expense, the latest quarter's loss increased by 187% versus the comparative period. On a year-to-basis for the nine months ended July 31, 2022, our loss increased by 118% after non-cash share-based compensation expense exclusion. The increase is reflective of our continued growth and the advancement of our US Phase 1/2 Cell Pouch Clinical Trial, our Cell Pouch System platform and related technologies and initial costs associated with our new iPSC initiative and Evotec Collaboration. Components of both R&D and G&A costs and changes from period to period are further discussed below.

R&D and G&A costs can vary significantly between reporting periods due to differences in timing of expenditures as well as the level and status of specific research and corporate activities.

***Research and Development Expenses***

	<u>Three months ended July 31,</u>		<u>Nine months ended July 31,</u>	
	2022	2021	2022	2021
Personnel costs	\$ 440,255	\$ 255,848	\$ 1,275,008	\$ 821,435
Research and clinical development	2,469,269	477,690	5,024,101	1,777,374
Manufacturing costs	216,530	63,321	664,169	63,321
Patent fees and costs	88,673	210,673	301,194	456,927
Other costs	50,997	38,410	123,941	135,287
Amortization and depreciation	108,836	60,157	299,433	180,319
Share-based compensation	701,661	(10,479)	3,066,200	81,008
Total	4,076,221	1,095,620	10,754,046	3,515,671
Less: grants, contributions and tax credits	(70,713)	(138,655)	(400,998)	(769,321)
Net	\$ 4,005,508	\$ 956,965	\$10,353,048	\$ 2,746,350

For the three months ended July 31, 2022, the Company incurred net R&D expenses of \$4,005,508, a \$3,048,543 / 319% increase from the comparative period. Excluding the effect of the non-cash share-based compensation expense discussed above, the latest quarter's net R&D costs increased by \$2,336,403 / 242% compared to the same period in the prior year. The increase reflects the continued advancement of our US Phase 1/2 Cell Pouch Clinical Trial, advancement of our iPSC initiative and Evotec Collaboration and expansion of our R&D initiatives. Other significant contributory factors were higher personnel costs with the expansion of our R&D team and recruiting costs; higher clinical trial costs reflecting a greater number of study patients coupled with the protocol progression of all study patients; higher iPSC development cost recognition; and manufacturing costs for the initial production run of our new upsized 10 plug Cell Pouch and related testing. Lower grants, contributions and tax credits which predominately include cost recoveries related to our pharmaceutical company collaboration activities also had a negative impact on net R&D costs.

Excluding the effect of the non-cash share-based compensation expense, net R&D costs increased by \$4,621,506 / 173% for the nine months ended July 31, 2022 over the comparative period, with the same factors driving the increase as described above for the latest quarter.

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*General and Administrative Expenses*

	<u>Three months ended July 31,</u>		<u>Nine months ended July 31,</u>	
	2022	2021	2022	2021
Personnel costs	\$ 267,901	\$ 161,738	\$ 722,124	\$ 550,329
Consulting and professional fees	163,321	102,480	481,851	217,628
Director fees and expenses	75,323	66,302	223,364	163,780
Investor relations	272,368	137,350	625,409	443,097
Public company expenses	184,253	64,122	366,167	132,502
Insurance and other costs	189,757	35,623	415,557	123,984
Amortization and depreciation	7,780	1,056	22,944	2,142
Share-based compensation - DSUs	241,786	19,772	1,190,584	75,064
Share-based compensation - options	502,952	91,373	1,900,886	23,804
	<u>\$ 1,905,441</u>	<u>\$ 679,816</u>	<u>\$ 5,948,886</u>	<u>\$ 1,732,330</u>

For the three months ended July 31, 2022, total G&A expenses increased by \$1,225,625 / 180% from the comparative period. Approximately half of this increase was attributable to higher non-cash share-based compensation expense related to new stock options and DSUs granted during the first quarter of our 2022 fiscal year, as discussed above. Excluding the non-cash share-based compensation expense impact, G&A expenses increased by \$592,032 / 104%. This normalized increase reflects incremental costs related to: increased business development activities and professional services provided; higher public company expenses, driven by both the application fee for listing on the Toronto Stock Exchange (TSX) and escalated stock exchange annual sustaining listing fees due to the Company's significantly increased market capitalization; a significant increase in insurance costs, with program changes and an increase in premium rates; and higher personnel costs attributable to additional hires and recruiting costs.

Total G&A expenses for the nine months ended July 31, 2022 increased by \$4,216,556 / 243% from the comparative period. Higher non-cash share-based compensation expense, discussed above, accounted for 71% of this increase. Excluding non-cash share-based compensation, G&A expenses increased by \$1,223,954 / 75% over the comparative period. The increase was primarily attributable to the same factors noted above for the current quarter, coupled with incremental costs related to our uplisting to the TSX; and increased business development and conference related travel as COVID-19 pandemic related travel restrictions eased during the period.

Amidst the COVID-19 pandemic environment and related continued uncertainties ahead we continue to monitor and manage costs closely.



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**LIQUIDITY AND CAPITAL RESOURCES**

The selected financial information provided below is derived from the Company's unaudited interim condensed consolidated financial statements.

As at	July 31, 2022	October 31, 2021
Cash	\$ 3,017,859	\$ 27,874,198
Marketable securities	39,000,000	–
Total assets	44,585,972	29,820,344
Current liabilities	2,360,252	1,475,871
Non-current liabilities	173,488	275,979
Total liabilities	2,533,740	1,751,850
Share capital, warrants and contributed surplus	113,011,297	82,817,445
Deficit	(70,959,065)	(54,748,951)

The Company's unaudited interim consolidated financial statements have been prepared assuming the Company will continue as a going concern. As at July 31, 2022, the Company had working capital of \$40,732,332 (October 31, 2021 – \$26,851,474) and for the nine months ended July 31, 2022 had a negative cash flow from operations of \$9,680,235 (2021 - \$4,826,122), excluding grant contributions received in the amount of \$224,168 (2021 - \$871,799). The Company has experienced operating losses and net cash outflows from operations since its inception.

During the nine months ended July 31, 2022, capital expenditure investment increased to \$310,454 (2021 - \$15,992) as we expand and upgrade the equipment in our laboratory to support our R&D efforts.

We anticipate increased cash requirements for the next 12 months as we continue to advance our US Phase 1/2 Cell Pouch Clinical Trial, the Evotec Collaboration, accelerate development of our local immune protection technology assets, prepare for and initiate our first thyroid clinical trial, advance research collaborations and execute upon strategic initiatives. Some of the increased cash requirements anticipated for the US Phase 1/2 Cell Pouch Clinical Trial may be offset by additional milestone achievement draws against the Company's JDRF grant award.

Until such time as the Company's products are approved and available for sale and profitable operations are developed, its liquidity requirements and ability to continue as a going concern are subject to management's ongoing ability to successfully raise additional working capital and ultimately generate cash flow from the commercialization of its products. Failure to do so could have a material adverse effect on the Company's financial condition and financial performance. During the year ended October 31, 2021, we completed a \$23 million financing to augment our cash resources and the funding of our operating plan. During the three months ended July 31, 2022, we raised an additional \$20.3 million with the purchase by Evotec of 12,944,904 common shares of the Company at \$1.57 per share pursuant to a non-brokered private placement. Cash and marketable securities on hand of approximately \$42.0 million as at July 31, 2022 are anticipated to fund our operating plan for a period of at least 12 months. Subsequent to the July 31, 2022 quarter end, we raised an additional near \$6.8 million for the issuance of an additional 2,709,800 common shares to Evotec at a price of \$2.50 per share. Future financing will depend on many factors, including, but not limited to, market conditions that are not within the Company's control and the market acceptance of its products. No assurance can be given that any such additional financing will be available or that, if available, it can be obtained on terms favourable to the Company. See section "**RISKS AND UNCERTAINTIES**" and "**CAPITAL MANAGEMENT**,

## **SERNOVA CORP.**

### **MANAGEMENT'S DISCUSSION AND ANALYSIS**

**FOR THE THREE AND NINE MONTHS ENDED JULY 31, 2022, AND 2021**

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#### **FINANCIAL INSTRUMENTS AND RISKS” in this MD&A.**

If the going concern assumption was not appropriate for the consolidated financial statements, adjustments would be necessary to the carrying value of assets and liabilities, the reported expenses, and the classifications used in the consolidated statements of financial position. The consolidated financial statements do not include adjustments that would be necessary if the going concern assumption was not appropriate.

#### ***Financing Activities***

During the nine months ended July 31, 2022, the Company received proceeds of \$3,757,004 from the exercise of common share purchase warrants and stock options and the corresponding issuance of 9,179,088 common shares.

On May 16, 2022, the Company completed the first tranche of a non-brokered private placement as part of an exclusive global strategic partnership with Evotec, issuing a total of 12,944,904 common shares at a price of \$1.57 and 2,709,800 unconditional common share purchase warrants. The gross proceeds from this private placement were \$20,323,500, before deducting issuance costs totalling \$44,322.

Subsequent to the July 31, 2022 quarter end, the Company closed the second and final tranche of the Evotec private placement commitment pursuant to the effective exercise of an unconditional common share purchase warrant for 2,709,800 common shares at a price of \$2.50 per share for total proceeds of \$6,774,500. Additional proceeds of \$2,154,283 have also received from the exercise of other common share purchase warrants and the corresponding issuance of 7,157,947 common shares. All common share purchase warrants with expiry dates up to September 9, 2022, outstanding as at the July 31, 2022, were fully exercised by warrant holders.

During the nine months comparative period ended July 31, 2021, the Company received proceeds of \$8,548,522 from the exercise of common share purchase warrants and stock options and the corresponding issuance of 28,483,142 common shares. In addition, the Company issued 4,000,000 common share for the conversion of convertible debentures with outstanding principal of \$1,000,000, at the fixed conversion price of \$0.25 per common share. No additional consideration was received for the conversion into common shares. In accordance with terms of the convertible debentures, the Company elected and also issued 138,980 common shares as settlement for \$40,110 of interest accrued on the convertible debentures.

On March 1st, 2021, the Company completed a brokered bought deal offering (Offering) of 19,205,000 units, including the full exercise of the underwriters' 15% over-allotment option, at the issue price of \$1.20 per unit (2021 Units) for cash proceeds of \$23,046,000. Each 2021 Unit consists of a common share and one common share purchase warrant, with each common share purchase warrant being exercisable into one common share at a price of \$1.70 per share until March 1, 2023, subject to abridgment of the exercise period if the ten-day volume-weighted price of the Company's common shares exceeds \$3.05 per share. As consideration for services provided in connection with the Offering, the Company paid to the underwriters: a cash commission of \$1,452,981, a corporate finance fee of 384,100 2021 Units (Corporate Finance Fee Units) and 1,210,818 broker warrants (also referred to as compensation options), where each broker warrant upon exercise entitles the holder to purchase one 2021 Unit at \$1.20 until March 1, 2023 (Broker Warrant). The Corporate Finance Fee Units and Broker Warrants issued were valued at \$460,920 and \$2,350,924, respectively. Share issuance costs totalling \$258,837 were also incurred and paid. The value of the Broker Warrants was determined using the Geske Model with the following assumptions: volatility of 129%, a risk-free interest rate of 0.3%, an expected life of two years, a dividend yield of 0% and no forfeiture.

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**MANAGEMENT'S DISCUSSION AND ANALYSIS**  
**FOR THE THREE AND NINE MONTHS ENDED JULY 31, 2022, AND 2021**

**Common Shares**

	Number of Common Shares
Balance outstanding as at October 31, 2021	261,133,258
Issued in conjunction with a private placement	12,944,904
Issued upon exercise of stock options	237,500
Issued upon exercise of warrants	8,941,588
Balance outstanding, as at July 31, 2022	283,257,250
Issued upon exercise of warrants	9,867,747
Balance outstanding as at the date of this MD&A	293,124,997

**Warrants**

	Number of Warrants	Weighted Average Exercise Price
Balance outstanding as at October 31, 2021	46,144,142	\$ 0.93
Issued in conjunction with a private placement	2,709,800	2.50
Issued in conjunction with the exercise of broker unit warrants	100,000	1.70
Exercised	(8,941,588)	(0.41)
Balance outstanding as at July 31, 2022	40,012,354	1.15
Exercised	(9,867,747)	(0.90)
Balance outstanding as at the date of this MD&A	30,144,607	\$ 1.23

**SERNOVA CORP.****MANAGEMENT'S DISCUSSION AND ANALYSIS**

FOR THE THREE AND NINE MONTHS ENDED JULY 31, 2022, AND 2021

**Incentive Plan**

The Company has an incentive plan with two components: (i) a fixed Share Option Plan (Option Plan) and (ii) a Deferred Share Unit Plan (DSU Plan) (collectively the Incentive Plan).

	Number of Options	Weighted Average Exercise Price
Balance outstanding as at October 31, 2021	8,892,500	\$ 0.24
Granted	14,095,984	1.32
Exercised	(237,500)	(0.22)
Balance outstanding as at July 31, 2022	22,750,984	0.91
Granted	255,000	1.10
Balance outstanding as at the date of this MD&A	23,005,984	\$ 0.91
		Number of DSUs
Balance outstanding as at October 31, 2021		4,150,001
Granted		1,360,000
Balance outstanding as at July 31, 2022, and the date of this MD&A		5,510,001

The Company initiated its Incentive Plan in 2015, with the latest amendments thereto approved by shareholders of the Company on June 30, 2021. The aggregate maximum of 38,746,536 common shares allowable under the Incentive Plan consists of: (i) a maximum of 30,997,229 common shares reserved for the exercise of share options pursuant to the Option Plan and (ii) a maximum of 7,749,307 DSUs reserved under the DSU Plan component, representing 12.5% and 2.5% respectively of the then issued and outstanding common shares of the Company.

**COMMITMENTS AND CONTINGENCIES**

The Company was previously awarded a US\$2.45 million (approximately \$3.14 million) grant under an agreement with JDRF Therapeutics Fund LLC (JDRF). The grant supports a Phase 1/2 clinical trial of Sernova's Cell Pouch for treatment of patients with T1D. Pursuant to the agreement, the Company has committed to perform certain clinical trial activities and to use commercially reasonable efforts to introduce a diabetes product into the US market. No contributions relating to milestone achievements were earned during the three months ended July 31, 2022 or 2021, and US\$148,430 (\$189,872) was earned in aggregate during the nine months ended July 31, 2022 (2021 - US\$400,000 (\$500,014)). Remaining funding available to be earned under the JDRF grant award totals approximately US\$0.42 million (\$0.54 million) as at July 31, 2022. The Company is required to pay royalties to JDRF as a percentage of any future net sales received from such diabetes product or in certain future license or disposition transactions up to an aggregate maximum of four times the aggregate amount of JDRF grant funding received. A bonus amount equal to the total amount of grant funding received is also payable to JDRF on two aggregate net sales thresholds if they are achieved. Given the early and inconclusive stage of development of the diabetes product, the royalty is not probable at this time and therefore no liability has been recorded.

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## MANAGEMENT'S DISCUSSION AND ANALYSIS

FOR THE THREE AND NINE MONTHS ENDED JULY 31, 2022, AND 2021

In May 2022, the Company entered into an exclusive global strategic partnership with Evotec (NASDAQ:EVO | FSE:EVT) for the development and commercialization of an iPSC-based beta cell replacement therapy (“iPSC Program”) with the goal to provide an unlimited insulin-producing cell source to treat patients with insulin-dependent diabetes. The Company has committed to pay future milestone and royalty payments to Evotec pursuant to the occurrence of certain events as set forth in the Evotec collaboration agreement (the “Evotec Agreement”). Under the terms of the Evotec Agreement, the preclinical development program(s) will be jointly funded up to IND with the Company’s share of potential costs capped at a maximum of approximately US\$25 million. The Evotec Agreement is cancellable by the Company with notice, subject to certain terms and conditions. iPSC Program costs of US\$1,427,587 (\$1,885,832) and US\$1,940,870 (\$2,537,172) were incurred during the three and nine months ended July 31, 2022, respectively (2021 – \$nil).

The Company expects to pay certain future costs related to preclinical and clinical trial activities. Such payments are expected to include the cost of our clinical / R&D personnel and related overheads, for patient procedures performed and activities related to the US Phase 1/2 Cell Pouch Clinical Trial, CRO costs, additional Cell Pouch manufacturing, clinical trial insurance, and outsourced or lab work and testing, and may include travel and a portion of drug or procedure-related expenses or transplantation expenses not covered by patients’ insurance. We enter into contracts and agreements in the normal course of business, including for research and development activities, consulting, and other services. The majority of these contractual obligations are cancelable at any time by us, generally upon prior written notice to the service provider or vendor. In addition, the Company has minimum annual royalty payment obligations of approximately \$30,000 for third party licensing agreements.

Effective September 1, 2021, the Company entered into a two-year lease for both its existing office premises and lab facilities and additional office space at a rate of \$14,000 per month, with a 2% increase on the anniversary of the lease agreement. Under the terms of the lease, the Company has an option to extend the lease term for an additional 12 months, up to August 31, 2024.

The following table summarizes our significant contractual obligations as at July 31, 2022:

Contractual Obligations <sup>(1)(2)</sup>	Payment Due by Period				
	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
Operating lease obligations <sup>(3)</sup>	\$ 360,147	\$ 171,080	\$ 189,067	\$ –	\$ –
Purchase obligations <sup>(4)</sup>	5,001,787	3,662,646	1,339,141	–	–
	\$ 5,361,934	\$ 3,833,726	\$ 1,528,208	\$ –	\$ –

## NOTES

- (1) Contractual obligations in the above table do not include amounts in accounts payable and accrued liabilities on our statement of financial position as at July 31, 2022.
- (2) Contingent milestone and royalty payments under collaboration agreements noted above are not included in the table.
- (3) Includes operating lease obligations for laboratory and office facilities.
- (4) Purchase obligations include cancellable and non-cancellable contracts including agreements related to the conduct of our clinical trial, preclinical studies, and manufacturing activities.

**SERNOVA CORP.****MANAGEMENT'S DISCUSSION AND ANALYSIS**

FOR THE THREE AND NINE MONTHS ENDED JULY 31, 2022, AND 2021

**RELATED PARTY TRANSACTIONS**

During the three and nine months ended July 31, 2022, and 2021, there were no related party transactions other than for the payment of compensation to key management personnel of the Company in the ordinary course of business. Refer to Note 8 – *Related Party Transactions* in our interim condensed consolidated financial statements for further information.

**SUMMARY OF QUARTERLY RESULTS**

The following table presents unaudited selected financial information for the eight most recently completed fiscal quarters:

Fiscal Year		1 <sup>st</sup> Quarter	2 <sup>nd</sup> Quarter	3 <sup>rd</sup> Quarter	4 <sup>th</sup> Quarter
2022	Loss	\$ 5,458,935	\$ 4,919,687	\$ 5,831,492	
	Loss per share	0.02	0.02	0.02	
2021	Loss	\$ 1,492,232	\$ 1,666,966	\$ 1,630,998	\$ 2,175,343
	Loss per share	0.01	0.01	0.01	0.01
2020	Loss				\$ 1,030,536
	Loss per share				0.01

Compared to the quarters of fiscal year 2021, the loss for each completed quarter in fiscal year 2022 has increased significantly and is largely attributable to the non-cash share-based compensation expense recognized for the stock options and DSUs granted during the first quarter of the current fiscal year. With the last set of grants occurring in 2019, the December 2021 grants effectively encompassed two years of grants and were based on earlier work conducted by independent compensation consultant Marsh & McLennan. The magnitude of the expense recognized in the two most recently completed quarters was significantly compounded by an approximate 3.5 and 6-fold increase in the fair value of each stock option and DSU granted, respectively, due to a 528% increase in the Company's share price since the prior grants made in 2019. With the delay in granting some options and DSUs, a portion of each were immediately vested resulting in a large one-time incremental expense impact (\$2.4 million) on the results of the first quarter of the 2022 fiscal year.

Since the beginning of fiscal year 2021 and furthermore during the current 2022 fiscal year, quarterly losses have generally trended higher reflecting the ongoing overall growth of the Company and the advancement of our R&D programs and commensurate with increased study patient activities and support for our US Phase 1/2 Cell Pouch Clinical Trial. Initial start up costs associated with our new iPSC research initiative and Evotec Collaboration were also incurred during the recently completed fiscal year 2022 second quarter, and further research costs will be regularly incurred quarterly going forward until approximately the first quarter in fiscal year 2024.

Quarterly clinical trial costs have continued to trend up as expected due to additional patient enrollment, a corresponding increase in the number of patient protocol-based procedures performed, the conduct of individual patient trial procedures being more expensive the further a patient advances along the study protocol and associated with incremental clinical trial support activities internally and conducted by our study CRO and other service providers. Cell Pouch manufacturing development and production

**SERNOVA CORP.****MANAGEMENT'S DISCUSSION AND ANALYSIS****FOR THE THREE AND NINE MONTHS ENDED JULY 31, 2022, AND 2021**

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activities during the last quarter of fiscal year 2021 and each of the current fiscal year's completed quarters have significantly contributed to higher R&D costs in those particular quarters. Other factors contributing to up trending quarterly losses include increased costs for the addition of personnel and building core competencies internally to support our future activities.

It is important to note that historical patterns of expenditures cannot be taken as an indication of future expenditures. The amount and timing of expenditures, and therefore liquidity and capital resources, may vary substantially from period to period depending on the business and research activities being undertaken at any one-time and the availability of funding from investors and prospective collaborative partners. Grants earned and contributions recognized are also dependent on the completion of specific subsets of patient procedures or specific collaboration activities, which can vary significantly from quarter to quarter.

**OFF-BALANCE SHEET ARRANGEMENTS**

The Company does not have any off-balance sheet arrangements.

**CAPITAL MANAGEMENT, FINANCIAL INSTRUMENTS AND RISKS**

Refer to the Company's audited consolidated financial statements for the years ended October 31, 2021, and 2020 for a summary of and discussion on capital management, financial instruments and associated risks.

**CRITICAL ACCOUNTING POLICIES AND ESTIMATES**

The preparation of financial statements requires the Company to make judgments, estimates, and assumptions that affect the application of accounting policies, the reported amounts of assets, liabilities, and expenses, as well as the Company's ability to continue as a going concern. The estimates and assumptions made are continually evaluated and have been based on historical experience and other factors, including expectations of future events that are believed to be reasonable under the circumstances. Such estimates and assumptions are inherently uncertain, and actual results could differ materially from these estimates and assumptions. Revisions to estimates are recognized in the period in which the estimate is revised and may impact future periods.

The full extent to which the COVID-19 pandemic may directly or indirectly impact the Company's business, results of operations and financial condition, including our ability to finance our operations, expenses, clinical trials, and research and development costs, will depend on future developments that are evolving and highly uncertain, such as the duration and severity of outbreaks, including future waves or cycles, and the effectiveness of actions to contain and treat COVID-19. As events continue to evolve and additional COVID-19 or outbreak information becomes available, the Company's estimates may change materially in future periods.

Refer to the Company's audited consolidated financial statements for the years ended October 31, 2021 and 2020 for discussions on our accounting policies and significant estimates that are most important in assessing, understanding and evaluating our interim condensed consolidated financial statements.

**SERNOVA CORP.****MANAGEMENT'S DISCUSSION AND ANALYSIS****FOR THE THREE AND NINE MONTHS ENDED JULY 31, 2022, AND 2021**

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**INTERNAL CONTROLS OVER FINANCIAL REPORTING**

The Company's management is responsible for establishing and maintaining disclosure controls and procedures (DC&P), as defined in NI 52-109. Management has designed such DC&P to provide reasonable assurance that material information with respect to the Company is made known to them and information required to be disclosed by the Company in its annual filings, interim filings or other reports filed or submitted by it under securities legislation is recorded, processed, summarized and reported within the specified time periods and in compliance with applicable securities legislation and guidelines.

The Company's management is responsible for establishing and maintaining internal controls over financial reporting (ICFR), as defined in NI 52-109 and have designed such ICFR to provide reasonable assurance regarding the reliability of financial reporting for external purposes in accordance with IFRS.

There have been no changes in the Company's ICFR during the three months ended July 31, 2021, that have materially affected, or are reasonably likely to materially affect, the Company's ICFR.

**CHANGES IN ACCOUNTING POLICIES***New accounting standards adopted during the current period*

None

*New accounting standards and interpretations not yet adopted***IAS 1 Presentation of Financial Statements**

In January 2020, the IASB issued amendments to International Accounting Standard 1 *Presentation of Financial Statements* (IAS 1) to provide a more general approach to the classification of liabilities under IAS 1 based on the contractual arrangements in place at the reporting date. The amendments to IAS 1 are effective for annual reporting periods beginning on or after January 1, 2023. The Company is currently evaluating the potential impact of adoption.

In February 2021, the IASB issued amendments to IAS 1 and IFRS Practice Statement 2 *Making Materiality Judgements* in which it provides guidance and example to help entities apply materiality judgements to accounting policy disclosures. The amendments apply to annual reporting periods beginning on or after January 1, 2023, with earlier application permitted. The Company is currently evaluating the potential impact of adoption.

**IAS 8 Accounting Policies, Changes in Accounting Estimates and Errors**

In February 2021, the IASB issued amendments to International Accounting Standard 8 *Accounting Policies, Changes in Accounting Estimates and Errors* (IAS 8) in which it introduces a new definition of 'accounting estimates'. The amendments clarify the distinction between changes in accounting estimates and changes in accounting policies and the correction of errors. Also, the amendments clarify how entities use measurement techniques and inputs to develop accounting estimates. The amendments apply to annual reporting periods beginning on or after January 1, 2023, with earlier application permitted. The Company is currently evaluating the potential impact of adoption.



**SERNOVA CORP.****MANAGEMENT'S DISCUSSION AND ANALYSIS****FOR THE THREE AND NINE MONTHS ENDED JULY 31, 2022, AND 2021**

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**RISKS AND UNCERTAINTIES**

We are a clinical stage biotechnology company that operates in an industry that is dependent on several factors that include the capacity to raise additional capital on reasonable terms, obtain positive results of clinical trials, obtain positive results of clinical trials without serious adverse or inappropriate side effects, obtaining marketing authorization for products and ultimately market acceptance of its product.

An investment in our common shares is subject to several risks and uncertainties and being high risk in nature should be considered speculative. Several of the factors, risks and uncertainties are outside the control of the Company's management. Additional risks and uncertainties not presently known to us or that we believe to be immaterial may also adversely affect our business. An investor should carefully consider the risks described in our most recently filed AIF, as well as our other public filings with the securities regulators before investing in our common shares. If any of such described risks occur, or if others occur, our business, operating results and financial condition could be seriously harmed and adversely impacted, and investors could loss all or part of their investment.

For information on important risks and uncertainties that could impact our business, please refer to the "*RISK FACTORS*" section of our most recent AIF, and included or discussed in our other periodic public filings, such as previous Management's Discussion and Analysis, filed on SEDAR at [www.sedar.com](http://www.sedar.com).

**DIRECTORS AND OFFICERS**

Frank Holler	Director and Executive Chair of the Board
Jeffrey Bacha	Director and Compensation Committee Chair
James Parsons, CPA, CA	Director and Audit Committee Chair
Deborah Brown	Director and Nomination and Governance Committee Chair
Dr. Mohammad Azab	Director
Dr. Philip Toleikis	President, Chief Executive Officer, and Director
David Swetlow, CPA, CA	Chief Financial Officer

**ADDITIONAL INFORMATION**

Additional information relating to the Company can be found on SEDAR at [www.sedar.com](http://www.sedar.com).