Sernova Corp.

Canada, USA, Germany / Biotechnology
TSX, Canada; OTCQX, US; FSE, Germany
Bloomberg: SVA CN
ISIN: CA81732W1041

Initiating coverage

RATING	**BUY**
PRICE TARGET	**CAD 3.80**
Return Potential	420.5%
Risk Rating	High

PIONEERING A POTENTIAL CELL-BASED CURE FOR TYPE I DIABETES

Sernova Corp (Sernova) is a Canadian, clinical-stage biotech company developing cell therapeutics towards 'functional cures' for chronic debilitating diseases based on its proprietary Cell Pouch System™ technology platform. The Cell Pouch device is unique. Once implanted deep under the skin of the abdomen, it creates an "organ-like" vascularised tissue matrix environment where therapeutic cells can thrive upon transplant. The ultimate goal in the lead type 1 diabetes indication (T1D) is curing the disease. The first generation product (1G – Cell Pouch + donor cells + immunosuppression) in phase 1/2 for T1D showed (I) In cohort 1, the first five patients achieved insulin independence for periods of ~6 months to >~3.5 years, and (II) in cohort 2 with a larger Cell Pouch (>50% more capacity), the first assessed patient demonstrated persistent serum C-peptide levels after only one islet transplant. This is a remarkable result as in cohort 1 using the smaller device this happened only after the 2nd implant. The company will publish a further update during Q4 2023. The supply of donor cell islets is scarce. Therefore, Sernova is developing a 2nd generation product which replaces donor cells with induced pluripotent stem cell-derived islets. Sernova's strategic partner, Evotec, will produce an unlimited supply of best-in-class insulin-producing islets. We anticipate this programme will start patient enrolment for phase 1/2 clinical trials in 2025. Long-term immunosuppression use has risks (e.g. cancer). Sernova is thus developing a preclinical 3G product using conformal coating (CC) technology licensed from the University of Miami (and others) that could provide optimal immunoprotection and ultimately lead to a cure for all T1D patients. The recent CC progress update was encouraging. We believe this combination product candidate could enter phase 1/2 clinical studies in 2026. An additional Cell Pouch-based preclinical programme in postoperative hypothyroidism is also scheduled to enter the clinic in H2 2024. If successful, the four combination product candidates could reach the market by 2028-2032 and we project combined sales potential of >USD15bn. We anticipate that positive news flow from the pipeline, particularly from the ongoing phase 1/2 T1D study, CC progress details at the upcoming IPITA conference on 26-29 October 2023, and the initiation of the hypothyroidism phase 1/2 study planned for 2024 will add substantial value to Sernova and act as catalysts for the stock. Based on our SOTP valuation model, we initiate coverage of Sernova with a Buy rating and a CAD3.80 (USD2.80; €2.60) price target.

FINANCIAL HISTORY & PROJECTIONS

	2019/20	2020/21	2021/22	2022/23E	2023/24E	2024/25E
Revenue (CAD m)	0.00	0.00	0.00	0.00	40.00	0.00
Y-o-y growth	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
EBIT (CAD m)	-5.26	-6.94	-24.75	-38.80	0.80	-34.40
EBIT margin	n.a.	n.a.	n.a.	n.a.	2.0%	n.a.
Net income (CAD m)	-5.32	-6.97	-24.42	-37.40	1.30	-34.30
EPS (diluted) (CAD)	-0.03	-0.03	-0.09	-0.12	0.00	-0.11
DPS (CAD)	0.00	0.00	0.00	0.00	0.00	0.00
FCF (CAD m)	-4.94	-6.86	-14.76	-29.70	5.99	-30.78
Net gearing	-124.4%	-99.3%	-7.9%	-46.9%	-131.2%	-144.3%
Liquid assets (CAD m)	3.95	27.87	49.78	20.00	25.91	20.06

RISKS

Risks include, but are not limited to development, regulatory, competition and financing risks.

COMPANY PROFILE

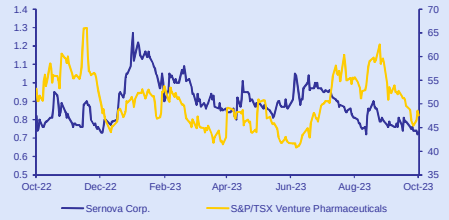
Sernova is a Canadian, clinical-stage biotech company focusing on the R&D of cell therapeutics towards potential 'functional cures' to treat chronic debilitating diseases. Sernova's core technology platform is the Cell Pouch System™, an implantable device containing immune-protected cells designed to create a natural environment where therapeutic cells can thrive. The company has a lead diabetes drug candidate in phase 1/2 clinical development, and preclinical programmes for hypothyroidism and haemophilia A.

MARKET DATA

As of 18 Oct 2023	
Closing Price	CAD 0.73
Shares outstanding	303.33m
Market Capitalisation	CAD 221.43m
52-week Range	CAD 0.72 / 1.27
Avg. Volume (12 Months)	172,266

Multiples	2021/22	2022/23E	2023/24E
P/E	n.a.	n.a.	168.0
EV/Sales	n.a.	n.a.	n.a.
EV/EBIT	n.a.	n.a.	234.2
Div. Yield	0.0%	0.0%	0.0%

STOCK OVERVIEW



COMPANY DATA

As of 31 Jul 2023	
Liquid Assets	CAD 31.04m
Current Assets	CAD 32.00m
Intangible Assets	CAD 0.37m
Total Assets	CAD 33.20m
Current Liabilities	CAD 9.92m
Shareholders' Equity	CAD 23.27m

SHAREHOLDERS

Evotec AG	5.3%
Management and Directors	9.0%
Freefloat and others	85.7%

Analyst: Christian Orquera, Tel. +49 (0)30 - 80 93 96 90

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INVESTMENT CASE

Sernova's organ-like, exchangeable proprietary Cell Pouch System™ overcomes the main causes of cell islets' poor survival: inflammation/fibrosis and hypoxia due to lack of oxygen The company has developed a unique Cell Pouch device that is implanted deep under the skin of the abdomen. Once implanted, a tissue matrix with tiny blood vessels that provide oxygen and nutrient supply form in the Cell Pouch over 4-6 weeks, after which therapeutic cells (i.e. pancreatic cell islets for type 1 diabetes – T1D) are implanted into the device chambers. Its "open architecture" is designed to create an "organ-like" natural environment where transplanted therapeutic cells can thrive, avoiding fibrosis and hypoxia. Importantly, if a problem arises, such as an adverse reaction or cell failure, the Cell Pouch can easily be removed and replaced with a new one, which is a great advantage over the traditional portal vein procedure where cells lodge in the liver.

The company's technology bundle addresses the three critical challenges in reaching curative cell therapy results in T1D patients Based on the Cell Pouch and two other licensed technologies, Sernova will address the three main obstacles that must be overcome to achieve curative results with cell therapy: (I) poor survival of the transplanted cells. This is solved with the Cell Pouch. (II) short supply of the required islets from cadaveric human donors and their poor and variable quality. This will be addressed by a second generation product (2G) using stem cell-derived cells in partnership with the leading German biotech Evotec; and (III) prevention of immune attack on foreign transplanted cells. This will initially be managed in the first (1G) and second (2G) generation products with immune suppression therapy. A third generation (3G) product will use a novel immune protection technology (i.e. islets conformal coating, licensed exclusively from the University of Miami) to overcome this problem and achieve long-lasting efficacy. We expect the later generation products will replace the earlier generation products over time.

1G product (10-channel Cell Pouch + implant of donor islets + immunosuppression) for T1D patients with hypoglycaemia unawareness shows excellent results in phase 1/2 in the US The first cohort of this study is underway and published very positive interim results at the 59th European Association for the Study of Diabetes (EASD) Conference on 5 October 2023: (I) Five out of the six patients participating in the first cohort using an 8-channel Pouch achieved insulin-independence for periods ranging from ~6 months to >~3.5 years; the sixth patient completed the islet transplant recently and will be assessed in the near future. (II) In the second cohort with a larger, optimised 10-channel Pouch (>50% more transplant capacity) in 7 patients, 5 out of 6 patients recruited so far have received at least the first of 2 planned islet transplants. One of these patients (#2) reached the stage where evaluation was possible, demonstrating persistent fasting and glucose-stimulated serum C-peptide levels after only one islet transplant. This is a remarkable result, as in the first cohort patients started being C-peptide positive only after the second implant. The company will publish a further update during Q4 2023. We expect the company to meet with the FDA in late 2024 or in early 2025 to discuss the results of the phase 1/2 study and the design of a potential phase 3 study. Assuming a successful phase 3 study, approval and launch could occur in 2028. We estimate US sales potential for the T1D indication of USD551m three years after launch.

2G product (10-channel Cell Pouch + Evotec's induced pluripotent stem cell islets + immunosuppression) – we project peak sales of ~USD4.1bn in the US In 2022, the company entered an exclusive collaboration with Evotec, that will secure an unlimited supply of best-in-class off-the-shelf cell islets for a 2G product with improved performance for T1D patients with hypoglycaemia unawareness. As part of the collaboration, Evotec invested ~USD21m (CAD27m), to acquire a 5.3% stake in Sernova. Evotec is a leader in the cell-based therapy industry with >100 people working in this segment. The product candidate is in late-stage pre-clinical development. We anticipate that patients will be enrolled in a phase 1/2 clinical study of the 2G product in 2025. We project that the phase 1/2 study will take ~1.5 years and a pivotal phase 3 study and registration ~3.5 years. We estimate a potential product approval and market launch in 2030 and peak sales three years after launch of USD4.1bn.

Curative 3G product (10-channel Cell Pouch + induced pluripotent stem cell islets + conformal coating immunoprotection) – we estimate USD9.8bn revenue potential in the US Sernova has exclusive, worldwide commercial rights to a preclinical conformal coating (CC) immune protection technology and an agreement to further develop it with the University of Miami and the inventor and leading international expert in immunoprotection and diabetes immunoengineering, Dr Alice Tomei. CC allows for islet encapsulation in a thin capsule capable of conforming to the islet shape and size. This unique feature allows close contact of the islets with the vascularised environment within the Cell Pouch, and normal diffusion of nutrients and other small molecules (i.e., glucose, insulin, and other proteins or hormones), leading to optimal glucose-stimulated insulin secretion without delay. The recent preclinical results obtained in diabetic rats are encouraging. The performance of the optimised CC formulation has been enhanced by the addition of a mild immune response agent, resulting in sustained normal blood glucose levels and complete insulin independence. Assuming positive results, we think it is likely that Sernova will be able to submit an IND filing and initiate phase 1/2 studies in the US in 2026. Furthermore, we assume that the phase 1/2 study will take ~2 years and a pivotal phase 3 study and registration ~4 years. We estimate a potential product approval and market launch in 2032 and peak sales five years after launch of USD9.8bn.

T1D market to show a healthy growth dynamic in the period 2023-2032 – Sernova has a competitive position vs Vertex and CRISPR The global T1D market was valued at USD7.6bn in 2022 and is expected to grow at a CAGR of 7.6% to reach USD13.6bn by 2030 (source: SNS Insider, 2023). Only a few companies within the regenerative medicine and cell/gene therapy space are comparable with Sernova. The most relevant are Vertex Pharmaceuticals and CRISPR Therapeutics, and they have both drug candidates in phase 1/2 clinical development. We believe Sernova has developed an implantable Cell Pouch that enables unmatched vascularisation and islet grafting. With this powerful device, the company, together with its world-class partners Evotec and the University of Miami, can generate robust and very competitive combo drug candidates for curing T1D.

Preclinical Cell Pouch programme in postoperative hypothyroidism (PH) represents USD1.4bn revenue potential Sernova's PH product candidate entails taking healthy tissue from each patient's thyroid gland and placing it into the Cell Pouch to avoid hypothyroidism after surgery. The company has conducted preclinical studies in mouse models demonstrating proof-of-concept and plans to file the IND in H1 2024. The product would then enter the clinic in H2 2024. Assuming successful clinical development, we project potential product approval and market launch in 2030. We conservatively project the product candidate will achieve peak sales of USD1.4bn five years after market launch.

Expanding the executive team enhances Sernova's product development, commercialisation and deal-making capabilities The addition of: (1) Cynthia Pussinen as the new CEO brings >25 years of experience in Big Pharma and the cell therapy industry. This includes C-suite executive and senior management positions at high-profile companies such as Spark Therapeutics/Roche (CTO), Ipsen Biomeasure & Biosciences (President & CEO) and Pfizer (Head of R&D). She has led the development, licensing and commercialisation of >15 products, including the first approved gene therapy Luxturna. Dr Philip Toleikis, former President & CEO who has led the company since 2009 through its development, remains on the Board and transitions to the CTO role; and (2) Dr Modestus Obochi, a seasoned dealmaker and strategic leader with >25 years of experience at leading pharma and biotech companies such as Pfizer and Baxter, has joined the team as Chief Business Officer to propel deal execution.

Sernova's shares are significantly undervalued in our view. We initiate coverage with a price target of CAD3.80 and a Buy recommendation In our valuation, we focus on the most advanced drug candidates – The Cell Pouch applied to T1D and PH. Our proprietary risk-adjusted sum-of-the-parts valuation model suggests fair value for Sernova of CAD3.80 (USD2.80; €2.60) per share. Over the next 12-18 months, we expect the achievement of relevant milestones in the two lead indications to significantly reduce pipeline risk and act as a catalyst for share price appreciation. We initiate coverage with a Buy recommendation.

SWOT ANALYSIS

STRENGTHS

- **Experienced management team** Ms Cynthia Pussinen (Chief Executive Officer), Dr Philip M. Toleikis, PhD, (Chief Technology Officer), Mr David Swetlow (Chief Financial Officer), and Dr Modestus Obochi, PhD, (Chief Business Officer) accompanied by Mr Frank Shannon (VP Clinical Development and Regulatory Affairs) and Mr Chris Barnes (VP Investor Relations) are all highly qualified executives with over 150 years of combined experience in the pharmaceutical, biotech and other high-tech industries.
- **Innovative Cell Pouch technology has generated a best-in-class device** The Cell Pouch™ device, implanted under the skin on the abdomen, has a unique "open architecture" designed to create an "organ-like" natural environment where transplanted therapeutic cells can thrive. In our view Sernova's pouch is the best device in the industry, having achieved unmatched vascularisation and engraftment of transplanted therapeutic islet cells without fibrosis in preclinical and ongoing phase 1/2 studies.
- **Excellent performance of the Cell Pouch which enabled T1D patients with severe hypoglycaemia unawareness to achieve insulin independence in phase 1/2 studies for >~3.5 years – the longest period so far** In the first cohort of the ongoing study, all of the five patients who had already undergone the procedure with an 8-channel Pouch achieved insulin independence for periods ranging from ~6 months to >~3.5 years.
- **Partnership deals with Evotec and AstraZeneca (AZN) have further validated the Cell Pouch's potential** In 2022, the company entered an exclusive collaboration with Evotec, which will provide an unlimited supply of best-in-class off-the-shelf cell islets for a 2nd generation product in T1D with improved performance. As part of the collaboration, Evotec invested ~USD21m (CAD27m) to acquire a 5.3% stake in Sernova. In addition, the company established a preclinical research collaboration with heavyweight AZN in May 2023 to explore potential use of the Cell Pouch for a next wave of cell therapies in additional indications beyond T1D. Two partners of the calibre of Evotec and AZN confirm the potential of the product.

WEAKNESSES

- **Small size compared with large dominant competitors** With a market cap of ~CAD 220m, Sernova is small compared to the big T1D players such as Vertex, Eli Lilly, Novo Nordisk, Sanofi, Merck, Astra Zeneca, Boehringer Ingelheim, Johnson & Johnson, Novartis, Takeda and Bayer.
- **Limited financial latitude** The company had cash resources of CAD31.0m at the end of 9M 22/23. These funds will finance operations into approx. Q4 2024. The early-stage pipeline will still require several years of funding before product candidates can be approved and generate revenue and profits. The lead drug candidate, the 1G product (Cell Pouch + implant of donor islets + immunosuppression) for T1D is at an advanced stage of phase 1/2 development and could achieve potential approval in 2028 at the earliest.

OPPORTUNITIES

- **Progress in the ongoing phase 1/2 clinical trials in T1D patients and the initiation of two further phase 1/2 studies may create significant shareholder value** Sernova will provide an update on the ongoing T1D study in H2 2023, providing important efficacy data. The company also plans to start a phase 1/2 programme for thyroid disease in 2024 and a phase 1/2 study of a 2nd generation product using Evotec islets in T1D with patient enrolment in 2025.
- **Additional upside from further pipeline product candidates** There is robust preclinical evidence for the use of conformal coating to immunoprotect transplanted therapeutic islets. This preclinical technology would enable the development of a ground-breaking curative 3G product in T1D. Sernova also has a preclinical programme for Haemophilia A. These new product generations/indications hold out the prospect of significant additional market potential.
- **Potential development deals with pharmaceutical companies** We believe management is considering licensing certain rights to its programmes, including options for upcoming product generations with a large pharmaceutical company once solid data from the ongoing phase 1/2 T1D study becomes available in 2024. A deal of this type will validate the product's potential, provide attractive non-dilutive funding in the form of upfront and milestone payments, and attract attention from the industry potentially leading to further co-development deals in other indications.

THREATS

- **Development and regulatory risks** Development of the Cell Pouch-based lead drug candidates for T1D, postoperative hypothyroidism and Haemophilia A may progress more slowly than expected or fail to show efficacy and safety in clinical trials. For example, the 1G product (Cell Pouch + implant of donor islets + immunosuppression) for T1D may not demonstrate efficacy in the ongoing phase 1/2 trials or in the future pivotal phase 3 trials. Also, the preclinical core technologies iPSC islets (mass production) from Evotec and conformal coating (immunoprotection) from the University of Miami, which are needed for the development of the 2G and the curative 3G products, may not perform as desired. Moreover, even if Sernova achieves good results in clinical trials, there is still a risk that the regulatory agency (FDA) will not approve the products or may request further trials.
- **Competitive risks** Sernova's Cell Pouch-based pipeline, particularly for the lead indication in clinical stage for T1D, may face competitive pressure. Several pharmaceutical and biotech companies, including Vertex Pharmaceuticals (phase 1/2), CRISPR Therapeutics (phase 1/2), Sigilon Therapeutics/Eli Lilly (advanced-preclinical) and the four players Novo Nordisk, TheraCyte, Procyon Technologies and Adocia with programmes in early to mid preclinical stage are developing new therapies for treating T1D. Any unexpected breakthrough by one or more competitors could hit Sernova's potential revenues.
- **Financing risks** Sernova's cash runway extends into Q4 2024. If the company does not manage to obtain a non-dilutive source of funding (e.g. licensing of rights or options to some of its programmes), it will need to raise funds in 2024. According to our projections, Sernova will need to finance further development of its R&D portfolio until profitability is reached by 2028 or 2029. Delays or negative results from clinical trials or a difficult financing environment could impede the raising of additional capital.

VALUATION

Biotechnology valuation is notoriously difficult since there is a high risk in developing the R&D pipeline, which leads to uncertainty in projecting cash flows. We have assessed Sernova's fair value based on a sum-of-the-parts methodology (SOTP). We believe this is the most appropriate valuation method for the company because it reflects the implicit risk-adjusted value of every product candidate in the R&D pipeline. Development risks, including clinical and regulatory risks, are considered, as are market size and the expected timing of cash flows post-approval for each project.

We have used a risk-adjusted NPV model for the three product generations of the Cell Pouch-based product candidate in type 1 diabetes (T1D), as well as the Cell Pouch-based product candidate in postoperative hypothyroidism. We believe that the Cell Pouch also has value in the Haemophilia A indication. However, this indication is still at an earlier preclinical stage (up to 2 years from entering the clinic), embedding significant development risk. We thus regard it as upside to our valuation.

During the forecasting process, we adjusted our sales projections and resulting cash flows for estimated success probabilities to obtain risk-adjusted expected values. We base our probability coefficients on statistical sector studies, such as *DiMasi et al.*, and on our own estimates. In this instance, we have derived a 48% probability of success for the 1G in the T1D indication (phase 1/2, has demonstrated achievement of insulin independence in humans), a 38% success probability for the 2G and 20% for the 3G in the T1D indication (preclinical), and a 38% success probability in postoperative hypothyroidism (preclinical).

Additionally, using First Berlin methodology, which takes company-specific risk factors into account, we have derived a cost of equity (COE) of 17.0% for Sernova Corp. Based on a debt ratio of 0.0%, we arrive at a WACC estimate of 17.0%, which we have used to discount projected cash flows. Including projected proforma net cash of USD49.4m, we value Sernova at USD933.2m, which implies a fair value of USD2.80 (CAD3.80; €2.60) per share on a proforma fully diluted basis. Using our ten-factor risk analysis, we set a High-risk rating for Sernova. The main risk factors that we have identified are development, regulatory, competition and financing.

Table 1: "Sum-of-the-parts" valuation model

Cell Pouch-Based Compound	Project[1)]	Present Value	Patient Pop (K)	Treatment Cost (USD)	Market Size (USDM)	Market Share (%)	Peak Sales (USDM)	PACME Margin[2)] (%)	Discount Factor (%)	Year of market launch
1G product	T1D - US	USD 41.6M	400K	225,000	90,000.0M	0.5%	550.7M	24%	17%	2028
2G product	T1D - US	USD 230.3M	400K	225,000	90,000.0M	3.5%	4,088.8M	24%	17%	2030
3G product	T1D - US	USD 482.3M	1,600K	120,000	192,000.0M	3.5%	9,769.9M	24%	17%	2032
1G product	Hypothyroidism-US	USD 197.4M	150K	225,000	33,750.0M	3.0%	1,401.5M	22%	17%	2030
PACME PV		USD 951.6M			405,750.0M		15,810.9M			
Costs PV[4)]		USD 97.1M								
NPV		USD 854.5M								
Milestones PV		USD 29.3M								
Net cash (proforma)		USD 49.4M								
Fair Value		USD 933.2M								
Share Count (proforma)		330,400K								
Price Target		USD 2.80								
Price Target		CAD 3.80	(based on CAD-USD exchange rate of 0.74)							
Price Target		EUR 2.60	(based on EUR-USD exchange rate of 1.06)							

1) A project typically refers to a specific indication or, where necessary or relevant, a combination between indication and geographic market

2) PACME (Profit After Costs and Marketing Expenses) reflects the company's profit share on future revenues. This share may be derived in the form of royalties (outsourced marketing/manufacturing) or operating EBITDA margin (in-house model), or some mix of both (depending on the specific parameters of partnership agreements)

3) Remaining market exclusivity after the point of approval

4) Includes company-level R&D, G&A, Financing Costs and CapEx; COGS and S&M are factored into the PACME margin for each project

Source: First Berlin Equity Research

Assessment of our SOTP valuation

We estimate Sernova is worth USD933m. We believe this value is quite conservative when considering the M&A transaction of a comparable competitor. In September 2019, speciality pharma heavyweight Vertex Pharmaceuticals acquired Sernova's peer Semma Therapeutics for USD950m, which at the time had a preclinical-stage cell-based pipeline in T1D. The acquired technology and two preclinical programmes are now the base for Vertex's position in T1D regenerative medicine.

There were two further takeover transactions in the T1D cell-therapy space. However, we believe the target companies were acquired at a discount. Following pipeline delays or setbacks, they had financial problems and were close to insolvency:

- In July 2022, Vertex acquired therapeutic cell specialist ViaCyte for USD320m, bringing another treatment option to the company. We believe the acquirer was interested in the complementary technologies and the highly skilled scientific staff of the troubled target. None of the clinical-stage programs has progressed since then.
- In June 2023, Eli Lilly acquired therapeutic cell specialist Sigilon for USD34.6m and up to USD310m if certain milestones are met. Following a setback in Sigilon's lead candidate, Sigilon had difficulty raising funds and was on the verge of bankruptcy (for more details, see the T1D competitive environment chapter).

PRODUCTS – DETAILED ANALYSIS

Estimation of price, sales potential and product value

Pricing of curative therapies Gene and cell therapies are considered breakthroughs for patients with devastating and costly diseases, as they are expected to provide lasting treatment effects and effectively cure the disease with a single administration. As a result, cell and gene therapy treatments approved in recent years have commanded very high reimbursement prices, particularly in the US. In the core US market, approved gene therapies have focused on rare diseases resulting from gene mutations and they have achieved high prices in the range USD850k-3.5m, with a rising pricing trend over time. Approved cell therapies are also commercialised at high prices in the range USD373k-475k, although the level is more modest than for gene therapies. Table 2 provides an overview of the 10 gene and cell therapies approved in the US in the last 6 years.

Table 2: Overview of pricing level for approved gene and cell therapies in the US

Product	Indication	Producer	Type of treatment	Approval	Price
Luxturna	inherited form of vision loss	Spark Theraputics	Gene therapy	2017	USD 850,000
Zolgensma	certain spinal muscular atrophy cases	Novartis	Gene therapy	2019	USD 2,100,000
Zynteglo	transfusion-dependent beta thalassemi	Bluebird Bio	Gene therapy	2022	USD 2,800,000
Skysona	cerebral adrenoleukodystrophy	Buebird Bio	Gene therapy	2022	USD 3,000,000
Hemgenix	haemophilia B	CSL Behring	Gene therapy	2022	USD 3,500,000
Tecartus	blood cancer - B-cell lymphoma	Kite Pharma	CAR-T cell therapy	2021	USD 373,000
Abecma	blood cancer - multiple myeloma	Bristol Myers/Bluebird	CAR-T cell therapy	2021	USD 419,500
Breyanzi	blood cancer - B-cell lymphoma	Bristol Myers	CAR-T cell therapy	2022	USD 410,300
Yescarta	blood cancer - B-cell lymphoma	Gilead	CAR-T cell therapy	2022	USD 424,000
Kymriah	blood cancer - B-cell lymphoma	Novartis	CAR-T cell therapy	2022	USD 475,000

Source: First Berlin Equity Research, companies

In our view, a price of USD200-400k is realistic for Sernova's Cell Pouch therapy in T1D in the US Sernova has conducted an independent survey of physicians and insurance companies in the US to explore the potential pricing of Cell Pouch therapy for T1D. These market participants see a price in the range of USD200-400K per patient per course of treatment. Based on our analysis of prices for recently approved gene and cell therapies, we think this price range is realistic.

Potential development of 1-3G products in T1D in the EU represents upside to our valuation For the time being, we assume Sernova will focus its development strategy on the highly lucrative US market and do not include the EU in our financial model, providing potential future upside.

Background, and target population statistics on type 1 diabetes (T1D) T1D, also known as insulin-dependent diabetes, is an autoimmune disease. It occurs when the immune system mistakenly attacks and destroys the insulin-producing beta cells in the pancreas, leading to a severe deficiency of insulin. Based on studies conducted in northern Europe, T1D can cut life expectancy of the affected patients by up to 11-18 years. According to the WHO, statistics from the International Diabetes Federation and the CDC's National Diabetes Statistics Report for 2022, there are ~60m people with diabetes in Europe and ~37m in the US. The CDC estimated that there were 1.6m people diagnosed with T1D in the US in 2020. Based on an estimated prevalence of T1D in diabetes patients of ~5-10%, we arrive at ~3-6m T1D patients in Europe. As referenced by Frier, T1D patients suffer from hypoglycaemia about twice a week and from severe hypoglycaemic events 1-1.7 times per year. Impaired awareness of hypoglycaemia (IAH), a dangerous condition in which too much insulin leads to an abnormally low glucose level of <70 mg/dL, is present in 25-40% of patients with T1D, which represents ~400k-640k patients in the US and 750k to 2.4m patients in Europe.

1G product for T1D patients with hypoglycaemia unawareness in the US: 10-channel Cell Pouch + implant of donor islets + immunosuppression We expect that the ongoing phase 1/2 study of the 1G product in the US will be completed in H1 2024. We anticipate the company will meet with the FDA to review the results and discuss the design of a potential phase 3 study in late 2024 or in early 2025. We have assumed that management will decide to conduct a phase 3 study despite the small target population additionally limited by the scarce supply of donor islets. We believe it is a major advantage that the FDA is familiar with the benefits of the Cell Pouch in the 2G and 3G products thereby allowing for their faster approval. Assuming Sernova conducts a successful phase 3 study, we estimate approval and launch would occur in 2028.

We have conservatively assumed a target population of 400k T1D patients with hypoglycaemia unawareness and a list price per treatment course per patient of USD300k coupled with ~25% discounts to insurance providers, equating to an average ex-factory therapy price of USD225k in the US. In our view Sernova's 1G Cell Pouch product is far superior to Prime Therapeutics' recently approved T1D cell therapy drug Lantidra (donislecel), with islets implanted at the liver through the portal vein. The peer's product is expected to be commercialised at an average annual cost of >USD300k (source: Prime Therapeutics).

We project that this segment will grow at a CAGR of 3% to 2040. Considering the limited supply of donor islets, we expect the 1G product will achieve a penetration rate of only 0.5%, leading to peak sales of USD551m three years after market launch. We anticipate a short life cycle for this product due to a strong cannibalisation effect by the 2G and 3G products. We see the 1G as a door-opener at the FDA and among clinics, allowing for faster adoption of the follow-up products.

Table 3: Assumed parameters for the 1G product in T1D patients in the US (currency: USD)

1G product T1D - US	Present Value	Patient Pop	Treatment Cost	Market Size	Market CAGR	Market Share	Peak Sales	PACME Margin	Discount Factor	Launch year
Parameters	$41.6M	400K	$225,000	$90,000M	3%	0.5%	$551M	24%	17.0%	2028

Source: First Berlin Equity Research

We thus assume that Sernova will out-license the product to a pharmaceutical partner following successful phase 1/2 trials. We anticipate the company will obtain a double-digit USD million milestone payment and an attractive net PACME royalty rate of 24% of sales. The partner will conduct the pivotal phase 3 study, commercialisation and bear the marketing expenses. It will also obtain a licensing option for the more valuable 2G and 3G products after the corresponding phase 1/2 studies. Sernova's royalties will roughly equate to its profit on the product. These assumptions are in accordance with metrics we have observed in the industry.

2G product for T1D patients with hypoglycaemia unawareness in the US: 10-channel Cell Pouch + implant of iPSC islets + immunosuppression Sernova's partner Evotec is at the late stage of pre-clinical development and optimisation of manufacturing to bring induced pluripotent stem cell islets (iPSC islets), also known as islet-like clusters (ILCs) into the clinic. We project that following IND filing Sernova will be enrolling patients for the phase 1/2 clinical of the 2G product in 2025. In addition, we assume that the phase 1/2 study will take ~1.5 years and a pivotal phase 3 study and registration ~3.5 years. We project a potential product approval and market launch in 2030.

Similarly to the 1G product, we assume a target population of 400k T1D patients with hypoglycaemia unawareness at the same therapy list price of USD300k and an average ex-factory price of USD225k in the US. However, due to the unlimited islet supply and ease of logistics, we anticipate a higher penetration rate of 3.5% for the 2G product, leading to peak sales of USD4.1bn three years after market launch. We anticipate that this product will replace the 1G product over time.

Table 4: Assumed parameters for the 2G product in T1D patients in the US (currency: USD)

2G product T1D - US	Present Value	Patient Pop	Treatment Cost	Market Size	Market CAGR	Market Share	Peak Sales	PACME Margin	Discount Factor	Launch year
Parameters	$230.3M	400K	$225,000	$90,000M	3%	3.5%	$4,089M	24%	17.0%	2030

Source: First Berlin Equity Research

Curative 3G product for T1D patients in the US: 10-channel Cell Pouch + implanted iPSC islets + immunoprotection Sernova's partner, Dr Tomei and her team at the University of Miami, are currently working on improving the conformal coating technology to achieve optimal immunoprotection in preclinical models. Results achieved so far are encouraging, and we think it is likely that the team will be able to complete the CC preclinical development and upscale the manufacturing process during 2024 and 2025, enabling an IND filing and initiation of phase 1/2 studies in 2026. Furthermore, we project that the phase 1/2 study will take ~2 years and a pivotal phase 3 study and the registration ~4 years. Assuming successful results, we project a potential product approval and market launch in 2032.

Given that this product will not need immunosuppression, has a safer profile and is curative, we expect it to be offered to a broader target population of 1.6m T1D patients, requiring a larger and more expensive phase 3 study. Therefore, we assume that the licensing partner of the 1G and 2G products will finance this study. Due to the sizable target population and the potential extensive burden to the healthcare system, we have assumed a lower therapy list price of USD160k and an average ex-factory price of USD120k in the US. Our estimated price is very conservative for a curative therapy and would promote the achievement of faster reimbursement as well as broader product adoption. We expect the 3G product to achieve a penetration rate of 3.5%, leading to peak sales of USD9.8bn five years after market launch. We anticipate that this product will replace the 1G and 2G products over time.

Table 5: Assumed parameters for the 3G product in T1D patients in the US (currency: USD)

3G product T1D - US	Present Value	Patient Pop	Treatment Cost	Market Size	Market CAGR	Market Share	Peak Sales	PACME Margin	Discount Factor	Launch year
Parameters	$482.3M	1,600K	$120,000	$192,000M	3%	3.5%	$9,770M	24%	17.0%	2032

Source: First Berlin Equity Research

1G product for the treatment of postoperative hypothyroidism: 10-channel Cell Pouch + implant of own healthy tissue from thyroid gland Hypothyroidism is a medical condition characterised by the underproduction of thyroid hormones by the thyroid gland. According to the US American Thyroid Association (ATA), 20m Americans currently suffer from thyroid disease, and 12% of Americans will develop thyroid disease in their lives. The ATA also estimates that ~150k thyroidectomies (partial or total surgical removal of the thyroid gland) are conducted annually in the US and that most of these patients will be diagnosed with benign disease after surgery, which requires daily hormone replacement therapy. Sernova's 1G product entails taking healthy tissue from each patient's own thyroid gland and placing it into the Cell Pouch to avoid hypothyroidism after surgery. The company has successfully conducted preclinical studies in mouse models demonstrating proof-of-concept and plans to file the IND in H1 2024. The 1G product would enter the clinic in H2 2024. We have assumed that the phase 1/2 study would take ~1.5-2 years and a pivotal phase 3 study and registration ~4 years. We project a potential product approval and market launch in 2030. Based on ATA statistics we see the ~150k patients p.a. undergoing thyroidectomy as the target population. We estimate an average ex-factory price of USD225k in the US, similar to the 1G product in the T1D indication. We conservatively project the 1G product will achieve a 3% penetration rate, leading to peak sales of USD1.4bn five years after market launch.

Due to limited funding, we assume that the company will license the product to a pharmaceutical partner after the successful completion of the phase 1/2 study, receiving a double-digit USD million amount and a net royalty rate of 22% upon commercialisation. We assume the US partner will fund phase 3 development expenses.

Table 6: Assumed parameters for the 1G product in postoperative hypothyroidism in the US (currency: USD)

1G product Hypothyroidism-US	Present Value	Patient Pop	Treatment Cost	Market Size	Market CAGR	Market Share	Peak Sales	PACME Margin	Discount Factor	Launch year
Parameters	$197.4M	150K	$225,000	$33,750M	3%	3%	$1,402M	22%	17.0%	2030

Source: First Berlin Equity Research

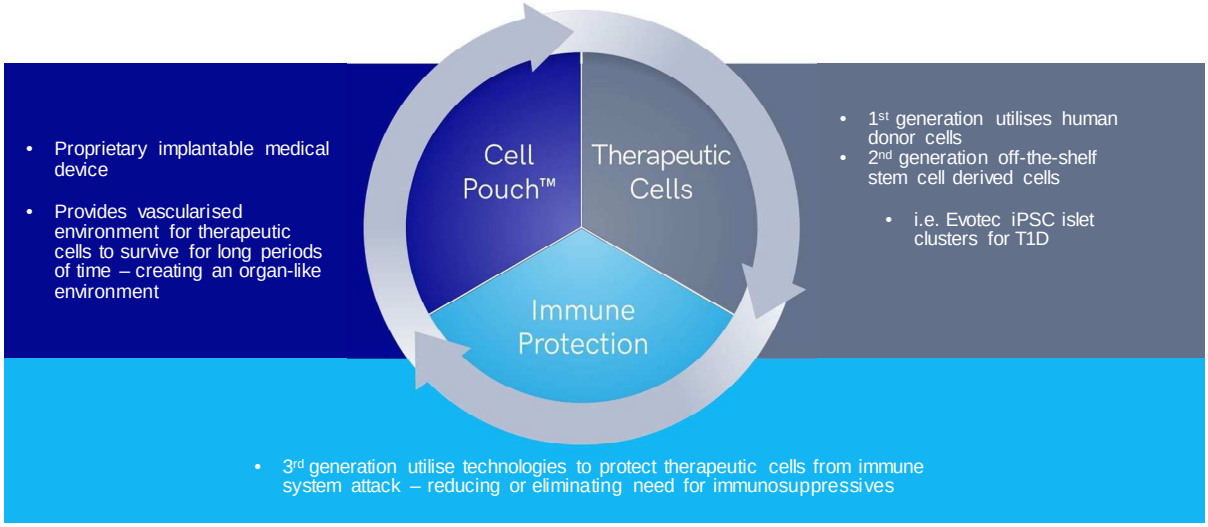
COMPANY PROFILE

OVERVIEW

Sernova Corp – a leading player in regenerative medicine Founded in 2006 and headquartered in London, Ontario, Canada, Sernova Corp is a leading clinical-stage biotech company focused on research and development in cell therapeutics for insulin-dependent type 1 diabetes (T1D) and other diseases with high unmet medical needs. Using cell therapy promises to halt and reverse diseases through restoration of key missing cells which produce critical proteins, hormones or other factors to ultimately provide a functional cure for patients. The Cell Pouch is a small biocompatible, flexible medical device implanted deep under the skin of the abdomen, designed to create an "organ-like" natural environment where transplanted therapeutic cells can thrive. In 2009, Dr Toleikis, an expert in the development of disruptive medical technologies, joined Sernova as CEO and with his team developed and patented the Cell Pouch and associated technologies. His goal was to drive the development of the Cell Pouch System™ using human derived cells (donor and/or stem cell derived islets) as a potential treatment for diabetes through commercialisation. Under his leadership, Sernova refined the technology and conducted preclinical studies in animal models, successfully demonstrating that the system supports the survival, function, and long-term engraftment of therapeutic cells, as well as its safety and efficacy. From 2012 to 2016, the company conducted the pilot proof-of-concept phase 1/2 study in three patients with T1D at the University of Alberta in Canada, demonstrating the safety and feasibility of the therapy using human cadaveric derived islets.

Sernova's technology bundle addresses the three critical challenges on the path to curative cell therapy outcomes in T1D patients The three main obstacles to overcome to achieve curative results with cell therapy are (I) the typically poor survival of the transplanted cells in the new environment in harmony with the rest of the body, this is solved with the Cell Pouch; (II) the scarce supply of needed islets from cadaveric human donors and their poor and variable quality; this will be addressed by a 2nd generation product (2G) through stem cell derived cells (i.e. islet cells in partnership with the leading German biotech Evotec); and (III) immune attack on the foreign transplanted cells. This has initially been managed in the 1st generation (1G) product through immune suppression therapy, but a third generation (3G) product will use a novel immune protection technology (i.e. conformal coating technology to encapsulate the islets – licensed from the University of Miami) to finally overcome this problem and offer a long-lasting curative result.

Figure 1: Technology platform to address the three key cell therapy shortcomings



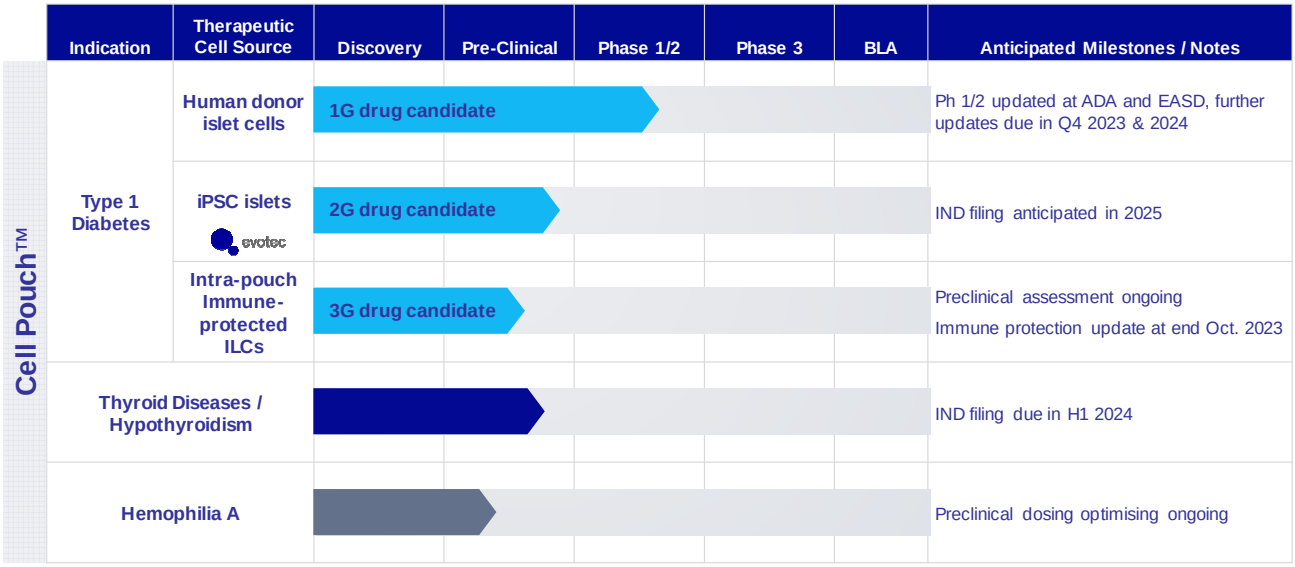
Source: First Berlin Equity Research, Sernova Corp

The 1G Pouch-based lead programme for type 1 diabetes (T1D) in phase 1/2 clinical development has recently presented excellent interim results Based on the valuable findings from the Canadian pilot study, the company expanded the clinical trials program in the US. In 2018, the company initiated a US single-arm phase 1/2 clinical study led by Dr Piotr Witkowski at the University of Chicago to evaluate T1D patients with severe hypoglycaemia unawareness following the transplant of islets into the Cell Pouch System supported by immunosuppression (https://classic.clinicaltrials.gov/ct2/show/NCT03513939):

- The study is underway with its first cohort of participants. Very positive interim results were presented at the 59th European Association for the Study of Diabetes (EASD) Conference on 5 October 2023. Five out of the six patients participating in the first cohort using an 8-channel Pouch achieved insulin independence for periods ranging from ~6 months to >~3.5 years. The sixth patient completed the islet transplant recently and will be assessed in the near future.
- In the second cohort investigating a larger, optimised 10-channel Pouch (>50% greater transplant capacity) in 7 patients, 5 out of 6 patients recruited so far have received at least the first of 2 planned islet implants. One of these patients (#2) demonstrated persistent fasting and glucose-stimulated serum C-peptide levels after only one islet transplant. This is a remarkable result. Unfortunately, this patient's second islet transplant was contaminated with the fungus Candida albicans (most likely from the donor) and these islets had to be explanted to prevent a systemic infection. This patient achieved insulin independence after receiving a very small supplemental islet transplant via the portal vein. Patient #1 developed neutropenia due to immunosuppressive medicine and requires time to recover from the immunosuppressive therapy. Patients #3, #4 and #5 are recovering after the first transplant and await assessment in the near future. The company will publish further updated data from the second cohort during Q4 2023.

Two programmes in preclinical development for thyroid disease and haemophilia A In addition to T1D, Sernova is exploring the application of its technology platform for other diseases that could benefit from cell therapy, including thyroid disease and haemophilia A. The company is actively engaged in preclinical trials to assess the safety and efficacy of these programmes. We give an overview of the company's pipeline in Figure 2 below.

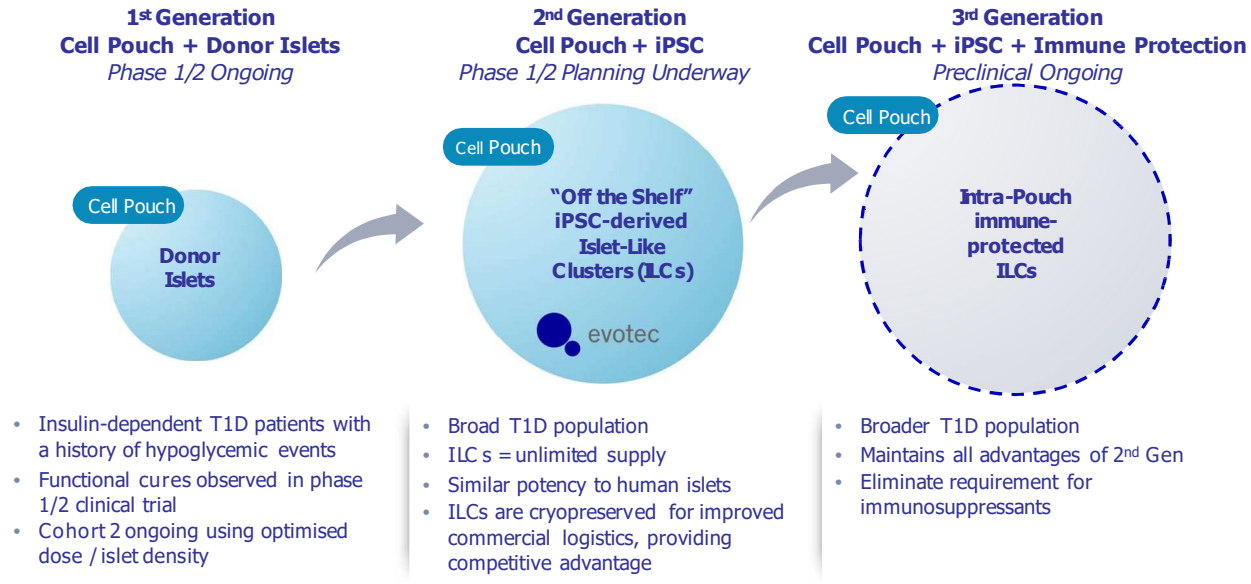
Figure 2: Snapshot of the R&D pipeline focusing on diabetes, thyroid disease and haemophilia A



Source: First Berlin Equity Research, Sernova Corp

Development strategy focused on the lead T1D programme – end goal is functional cure The company has a clear development strategy for the pipeline. The first and core development priority is completing the ongoing US phase 1/2 clinical study (2nd cohort) of the 1G product, which entails using cadaveric donor islets transplanted into the new optimised 10-channel Cell Pouch System supported by immunosuppression in seven T1D patients with severe hypoglycaemia unawareness. The study is expected to be completed in 2024. Subsequently, management will discuss the design of the pivotal phase III study with the FDA. In parallel, the company is advancing the development of the 2G product entailing the 10-channel Pouch System + stem cell-derived pancreatic islets (IPSC) engineered and produced by Evotec + immunosuppression. This product is at an advanced preclinical stage and we anticipate clinical studies to begin in 2025. In addition, the company will continue developing the conformal coating technology licensed from the University of Miami until preclinical development is complete. Subsequently, the company will launch a phase 1/2 clinical study of the 3G product using the 10-channel Pouch system + IPSC islets + conformal coating immunoprotection, which has the potential to cure T1D. We give an overview of the three product generations in Figure 3 below.

Figure 3: Cell Pouch development strategy in T1D with successive product generations until functional cure



Source: First Berlin Equity Research, Sernova Corp

Second development priority The second priority is completing the preclinical development of the 1G product for patients with hypothyroid disease (insufficient hormone production) due to thyroidectomy (surgical removal of all or part of the thyroid gland). The 1G product entails taking healthy tissue from each patient's own thyroid gland and placing it into the Cell Pouch to avoid hypothyroid after the surgery. The company has successfully conducted preclinical studies in mouse models and expects the 1G product to enter the clinic in 2024.

Third development priority The completion of preclinical development for the 1G product targeting Haemophilia A, a rare bleeding disorder, is the third priority. A blood sample of cells is taken from the patient (autologous), the defective clotting factor VIII is genetically corrected using a lentiviral vector-mediated gene transfer procedure, multiplying and placing them within the implanted 10-channel Cell Pouch (ex-vivo procedure). So far, the conducted preclinical studies in mouse models have achieved promising results. We expect the 1G product to enter the clinic by 2025 or 2026.

Partnership with AstraZeneca (AZN) to explore potential use of the Cell Pouch in further indications Under the preclinical research collaboration announced in May 2023, AZN will test the Cell Pouch in combination with AZN's novel therapeutic cells to create a next wave of cell therapies for various indications. AZN will lead and fund the related research and development efforts. This agreement validates and leverages the potential of Sernova's Cell Pouch.

IP protection The Cell Pouch System is the result of >15 years of R&D which includes the characteristics, design and size of the device to optimise it through the achievement of "organ-like" properties. This IP is protected by one core published patent, unpublished patent updates, and trade secrets. We have identified the core patent held by Sernova which protects its entire Cell Pouch System until approximately September 2030 in the core US market (US10034963B2) and selected European/Asian countries (sources: Sernova's MDA filings and Google Patents archives https://patents.google.com/patent/US10034963B2/en). In addition, Sernova has protected every relevant technology advance by a patent re-filing to cover the new findings and features. Therefore, the company has many unpublished new patents and updates covering the following four main categories offering protection well beyond 2030:

1. Methods and devices for cellular implantation: 45 Sernova-owned patents issued and pending in 17 countries/ regions
2. Methods and compositions for generating pancreatic progenitors and functional beta cells from hPSCs: 39 patents issued and pending in 39 countries/regions
3. Conformal coating of cells for immunoisolation: 12 Sernova-owned patents issued and pending in 8 countries/ regions
4. Conformal coating of cells for immunoisolation: 15 patents pending, in-licensed from the University of Miami, in 15 countries/regions

LISTING ON CANADIAN TSX, US OTC, AND ON GERMAN EXCHANGES

Capital market listings enabled Sernova to finance R&D Sernova Corp was first listed on the Toronto Stock Exchange Venture (TSXV) under the symbol TSXV:SVA through the reverse merger with the public biotech company Pheromone Sciences Corp in 2006. Shortly thereafter, the shares also began trading on the US OTCQX Best Market under the symbol US:SEOVF. To expand its exposure to European investors, Sernova also registered the shares for trading in Germany on all main German Stock Exchanges including the Frankfurt Stock Exchange's XETRA trading platform in February 2021. mwb Wertpapierhandelsbank AG was appointed as designated sponsor. In June 2022, the Canadian TSXV listing was replaced with one on the primary Canadian market for senior issuers of the Toronto Stock Exchange (TSX), which should expand its access to investors and increase stock liquidity (trading volume). During FY 2021/22, the company raised funds totalling CAD36.5m, of which CAD27.1m from a private placement with the partner Evotec, and CAD9.4m from the exercise of warrants and options. The remaining outstanding warrants expired in Q1 2023. Therefore, there is no further potential dilution from warrant conversion.

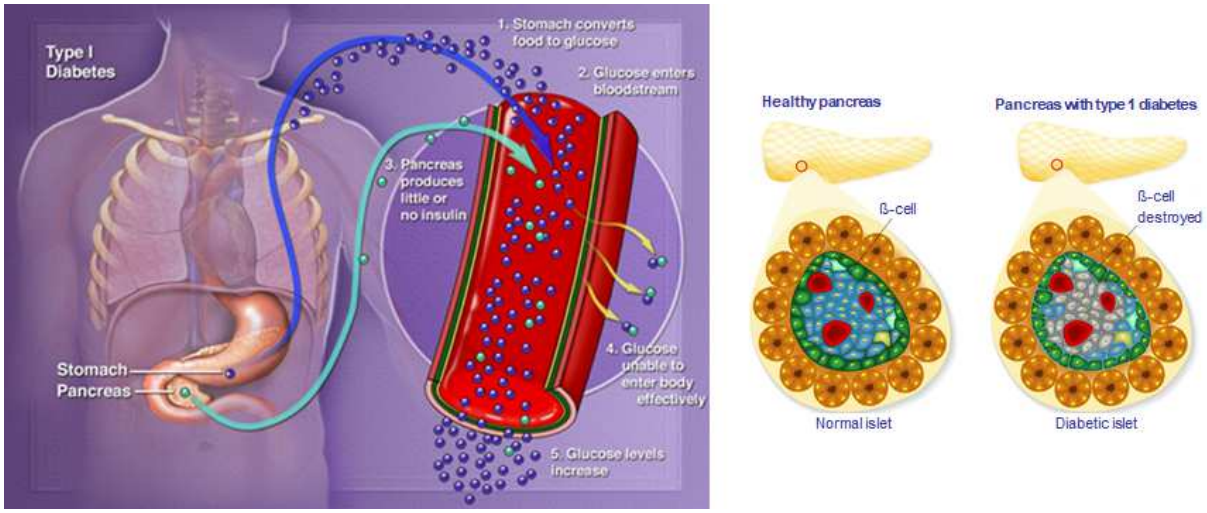
Potential dilution As of 31 July 2023, the company had 303.3m shares outstanding; the company's cash and marketable securities positions amounted to CAD 31.0m and management is guiding that these funds can finance the company until approx. Q4 2024. Sernova also has in place its "Incentive Plan" first implemented in 2015 and last updated on 30 June 2021, through which the company can issue options equivalent to a maximum of 38.7m shares. This plan is split into (A) fixed share options (Options) equating to 32.9m shares and (B) Deferred Share Units (DSUs) equating to 5.8m shares. As of 31 July 2023, the company has 30.1m options outstanding with an average exercise price of CAD0.92 and 5.5m DSUs.

TYPE 1 DIABETES (T1D)

T1D IS A DISEASE WITH HIGH UNMET MEDICAL NEED

Description of Diabetes mellitus… Diabetes mellitus is a chronic disease characterised by high levels of glucose (sugar) in the blood (i.e. levels > 250 mg/dL). It occurs when the pancreas either doesn't produce enough insulin, the hormone that regulates blood sugar, or cannot effectively use the insulin it produces. This leads to an inability to properly metabolise glucose and results in elevated blood sugar levels (known as hyperglycaemia). Insulin production is particularly relevant after meals, when carbohydrates (carbs) are broken down into glucose to be absorbed into the bloodstream. There are two main types of diabetes. Type 1 diabetes (T1D), also known as insulin-dependent diabetes, is an autoimmune disease. It occurs when the immune system mistakenly attacks and destroys the insulin-producing beta cells in the pancreas, leading to a severe deficiency of insulin (see Figure 4 below). Type 2 diabetes (T2D) occurs primarily due to insulin resistance, inadequate insulin production or because the insulin produced does not work effectively. T2D is the most common form of diabetes, accounting for 90-95% of all diagnosed diabetes cases in the US. Several factors can contribute to the development of T2D, including genetic predisposition, lifestyle factors (e.g. obesity, sedentary lifestyle, and poor diet), and age (sources: US Centers for Disease Control and Prevention; Cleveland Clinic, Mayo Clinic).

Figure 4: Type 1 diabetes



Source: First Berlin Equity Research, University of California San Francisco, European Biotechnology Magazine

…and T1D T1D is often diagnosed in childhood or adolescence and is therefore also known as juvenile diabetes. However, T1D can develop at any age. Recent studies show that >40% of prevalent cases are adults >40 years old (Green et al., 2021). The exact cause of T12 is not fully understood, but it is believed to involve a combination of genetic predisposition, environmental factors (e.g. toxins) and certain viral infections (e.g. mumps and Coxsackie viruses). It is not directly linked to lifestyle or diet choices. If left untreated or not properly managed, T1D can lead to serious short-term complications such as hyperglycaemia (shortage of insulin/blood glucose level too high at >125 mg/dL while fasting and >180 mg/dL 2 hours after a meal), hypoglycaemia (too much insulin/abnormal low glucose level of <70 mg/dL), seizures and the potentially life-threatening condition diabetic ketoacidosis (DKA - the body breaks down fat for energy, which causes the body to release ketones and the blood to turn acidic), as well as long-term complications including cardiovascular diseases, nerve damage (neuropathy), kidney damage (nephropathy), eye damage (retinopathy) and diabetic foot ulcers (5-13% of diabetic patients) & amputations. Based on studies conducted in northern Europe, T1D can cut the life expectancy of the affected patients by up to 11-18 years (source: Green et al., 2021).

Prevalence of T1D There is no epidemiologically accurate information on the prevalence and incidence of T1D in the world. In general, this condition is estimated to affect ~5-10% of all cases of diabetes. Based on a meta-analysis conducted by Mobasseri et al., 2020, the prevalence of T1D in Europe and the US may amount to 12.2 per 10k. The authors conclude that the incidence and prevalence of T1D are growing worldwide. According to the WHO, statistics from the International Diabetes Federation and the CDC's National Diabetes Statistics Report for 2022, there are ~60m people with diabetes in Europe and ~37m in the US. The CDC estimated that there were 1.6m people diagnosed with T1D in the US in 2020. We cannot find accurate statistics for the number of T1D patients in Europe. Applying the general ~5-10% prevalence estimates of T1D among diabetes patients to the 60m diabetic population in Europe equates to ~3-6m T1D patients in the region.

Healthcare burden According to a study published in JAMA Internal Medicine in 2020, the average annual healthcare expenditure for a patient with diabetes in the US was estimated to be ~USD9,600. This includes direct medical costs, such as insulin, supplies, doctor visits, hospitalisations, and indirect costs associated with productivity loss. In Europe, the healthcare cost per diabetic patient p.a. ranges from about USD1k in most of the Eastern European countries to ~€3-12k in the Western European countries (e.g. Germany USD4.6k, France USD4.9k, UK USD5.3k, Sweden USD6.6k, Norway USD9.1k and Switzerland USD11.9k; source: Statista, 2019). The lifetime diabetes-related cost of care is estimated at ~USD125k based on a 3% discount rate (not discounted: USD211k - source: Zhuo et al., 2014).

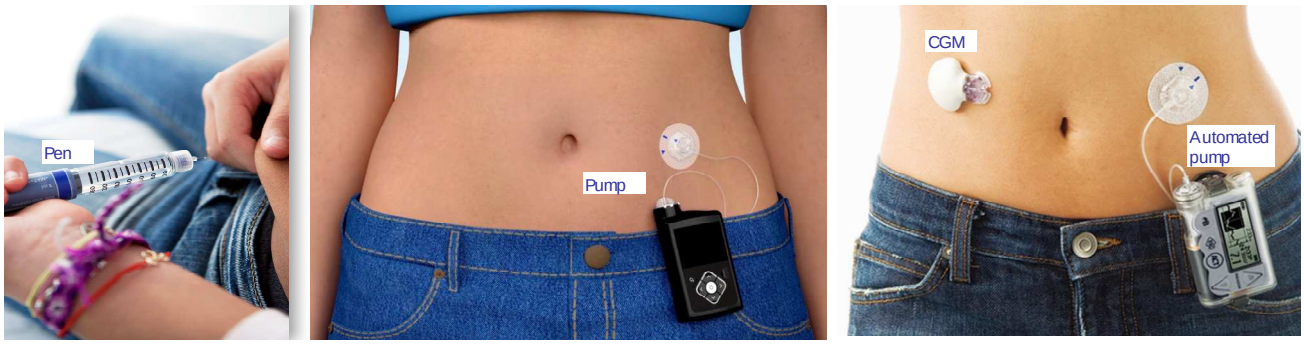
Diagnosis The diagnosis of T1D is made upon the appearance of typical symptoms such as thirst, frequent urination, unexplained weight loss, extreme fatigue, increased hunger, and blurred vision. The doctor will primarily evaluate the presence of symptoms, followed by the conduct of the following laboratory tests: (I) Blood Glucose Test to measure the level of glucose in the blood in two settings: a) a random test at any time without fasting, where a blood sugar level of ⩾200 mg/dL (11.1 mmol/L) suggests diabetes and b) a test after fasting for at least 8 hours, where a blood sugar level <100 mg/dL (5.6 mmol/L) is healthy, a level from >100 and <125 mg/dL (5.6 to 6.9 mmol/L) is considered prediabetes, and >125 mg/dL (7 mmol/L) on two separate tests indicate that the patient has T1D; (II) The Glycated Haemoglobin (A1C) Test provides an estimate of average blood glucose levels over the past 2-3 months. It measures the percentage of red blood cells, and more specifically their haemoglobin protein, which has glucose attached to it. A higher A1C level suggests poorer blood glucose control; an A1C level of ⩾ 6.5% on two separate tests represents a confirmation of T1D; (III) Antibody Testing: Since T1D is an autoimmune disease, specific antibodies associated with the destruction of insulin-producing beta cells may be present in the blood. Antibody tests, such as the glutamic acid decarboxylase antibody (GADA) test, insulin autoantibody (IAA) test, or others, can be conducted to detect these antibodies and discard T2D. In addition, the doctor may conduct further controls, such as a urine test to check for ketones (sources: Mayo Clinic, Cleveland Clinic).

TREATMENT OF T1D

Treatment and main approaches There is no cure for T1D, and standard-of-care treatment focuses on maintaining optimal blood sugar control and preventing disease complications by replacing the insulin the body cannot produce. The therapeutic treatment for T1D is tailored to specific symptoms and disease severity and it is usually combined with exercise, diet control (particularly carbs and sugar) and a healthy lifestyle. The main treatment options for T1D include:

- Insulin Therapy: People with T1D require lifelong insulin therapy. Insulin can be delivered via syringes, pen injectors (pre-loaded with insulin), and in certain cases pumps (about the size of a smartphone – see Figure 5 below) attached to the body by a tiny cannula that delivers insulin continuously under the skin to meet the required levels. There are various formulations of insulin, including rapid-, short-, intermediate- and long-acting insulin, to suit patients' needs. The type, dosage and timing of insulin administration may vary based on individual needs and blood glucose levels, but multiple injections per day may be necessary. Studies have shown that 3-4 insulin injections daily provide the best blood glucose control and can prevent or delay further long-term complications (source: American Diabetes Association).
- Blood Glucose Monitoring: Regular monitoring is essential to assess the effectiveness of insulin therapy and the necessity of adjustments if the insulin levels are too high or too low. This is typically done using a blood glucose metre, a flash glucose monitoring system, or a continuous glucose monitoring system (CGM – a device that checks glucose levels on a minute-to-minute basis by using a small sensor inserted just under the skin – see Figure 5 below).
- Artificial Pancreas Device Systems (APDS – see Figure 5 below): APDS are advanced therapeutic devices that automatically adjust insulin delivery to T1D patients to manage their blood glucose levels more effectively. These devices combine an insulin pump with a CGM and software with an algorithm capable of assessing the CGD data and delivering the required insulin amount through the pump. These devices have become standard of care for patients with severe hypoglycaemia.

Figure 5: Insulin therapy for T1D with pen (left), pump (middle) and APDS (right)



Source: First Berlin Equity Research, Sernova Corp, Medtronic Inc

Challenges of T1D management In a healthy body, the pancreas has a finely tuned mechanism for releasing insulin into the bloodstream that consists of a slow, continuous release of insulin throughout the day, regardless of food intake (also known as basal or background insulin), accompanied by large bursts of insulin after meals that slowly subside over 2 to 3 hours (bolus insulin). Basal insulin keeps blood glucose levels stable during periods of fasting, such as between meals and overnight, and it accounts for about 50% of a body's daily insulin needs. The goal of insulin therapy in T1D is to mimic the natural pattern of insulin release by a healthy pancreas. Therefore, standard insulin therapy comprises a 50/50 combination of short-acting insulin shots after meals with long-acting insulin shots to keep glucose blood levels stable throughout the day and night, adjusted to match the body's needs. However, the risk of hypoglycaemia can never be entirely eliminated due to various factors, including inaccuracies in insulin dosing, missed meals, unplanned physical activity, alcohol consumption, etc. Therefore, hypoglycaemia remains a main side effect of insulin administration (sources: Bethel et al., 2005; Ramchandani et al., 2010; US CDC).

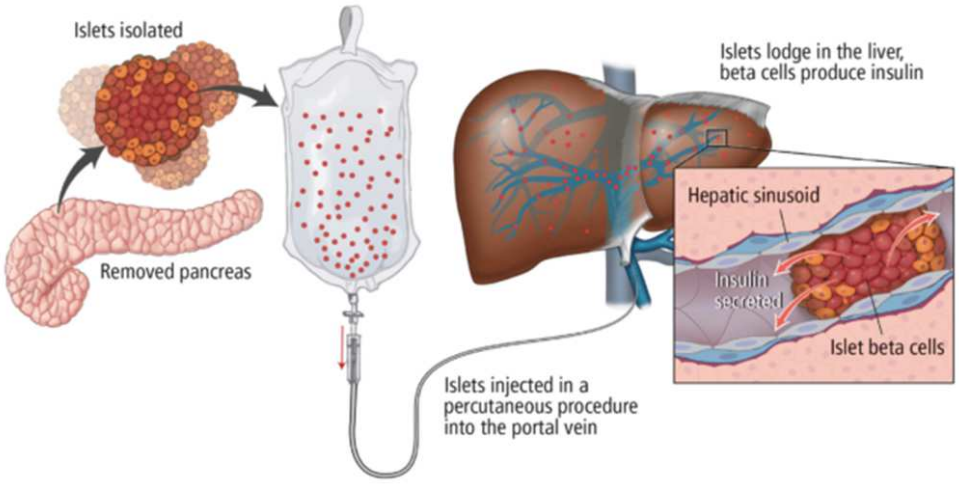
T1D patients with hypoglycaemia unawareness (IAH) have a higher mortality risk As referenced by Frier, T1D patients suffer from hypoglycaemia about twice a week and from severe hypoglycaemic events 1-1.7 times per year. In some cases, the body adapts over time to these low blood glucose levels and adjusts its response by lowering the threshold for releasing the required hormones (e.g. glucagon, catecholamine, adrenalin) that trigger the typical hypoglycaemia warning signs (e.g. sweating, trembling, hunger, and palpitations) until the glucose level is dangerously low. This condition is called impaired awareness of hypoglycaemia (IAH). IAH is present in 25-40% of patients with T1D and represents a 3-6 fold higher risk of severe hypoglycaemic events due to the lack of immediate appropriate corrective therapy. Presently, one of the major risk factors for the development of IAH is the duration of T1D. IAH can lead to many severe morbidity forms, including seizures, loss of consciousness, coma, cardiac arrhythmias, and is associated with an increased risk of mortality (sources: Farrel et al., 2021; Martín-Timón et al., 2015; McCall et al., 2012; Frier et al., 2007).

Extreme blood sugar swings make it difficult to control Brittle T1D Brittle T1D, also referred to as labile diabetes, is characterised by extreme swings in blood glucose levels. These patients frequently experience unpredictable episodes of both hyperglycaemia and hypoglycaemia even when they are closely following their treatment plans. This relatively rare condition affects a small percentage of people with T1D. In the US, it is estimated to affect <80k people. The cause of brittle T1D is unknown, but it is often associated with stress, depression and other psychological issues (sources: Cleveland Clinic; US National Organisation of Rare Diseases –NORD; Prime Therapeutics).

Is immunosuppression a therapeutic alternative to avoid beta-cell destruction by the immune system in T1D? Several recent studies have investigated the potential of immunosuppression in avoiding beta cell destruction in T1D patients. The results were mixed. In some cases, there was no difference in insulin dose compared with placebo; in some cases treated patients showed a less rapid decline in C-peptide levels vs placebo and also some reduction in daily insulin dose, suggesting a beneficial effect of immunosuppression on beta cell maintenance. However, in many cases the benefits were only temporary, and there were insulin-free periods in <5% of patients. Moreover, there are safety concerns about administering high-dose immunosuppressive agents (source: Couri et al., 2018).

Lantidra, a recently approved implanted islet cell therapy for patients with T1D and severe hypoglycaemia in the US On 28 June 2023, the US FDA approved the cell therapy Lantidra (donislecel), a procedure consisting of infusing cadaveric donor pancreatic islets through a catheter into the portal vein, in the liver, of the T1D patient (see Figure 6 overleaf). Once the islet cells are infused, they lodge into the liver's small vessels (capillaries). Lantidra consists of 400 mL of transplant medium in an infusion bag containing up to 1cc of packed islet tissue and is administered along with immunosuppressive therapy. It has been approved for the treatment of adult patients with T1D and repeated episodes of severe hypoglycaemia that cannot be controlled by other means (e.g. artificial pancreas device). The procedure was developed by the start-up CellTrans Inc in cooperation with the University of Illinois in Chicago (UIC). According to CellTrans' marketing & medical drug management advisor Prime Therapeutics, the anticipated annual cost of Lantidra will be >USD300k.

Figure 6: Islet cell therapy procedure in patients with T1D and severe hypoglycaemia



Source: Cleveland Clinic Foundation - CCF

The FDA Advisory Committee assessed an overall favourable benefit-risk profile for Lantidra, with 12 members voting yes and 4 voting no The efficacy and safety of Lantidra was tested in two non-randomised, single-arm studies in a total of 30 patients with T1D and hypoglycaemic unawareness. The phase 1/2 study had 9 patients and the phase 3 study 21 patients (https://classic.clinicaltrials.gov/ct2/show/NCT00679042). The composite primary efficacy endpoint was the number of patients achieving the goal of A1C ⩽ 6.5% and absence of severe hypoglycemic events for one year after a patient's last transplant over the two studies. Overall, 19 patients (63%) met the composite efficacy endpoint and 20 (67%) were insulin independent one year after transplantation. In addition, 8 of 12 (67%) evaluable patients met the composite efficacy endpoint as well as insulin independence six years after transplantation. However, the FDA saw the efficacy analysis as difficult to interpret due to the combination of a substantial quantity of missing data and the inclusion of a significant proportion of patients who had already met or nearly met the primary endpoint at baseline.

The safety analysis from the two studies showed that most serious adverse events were associated with immunosuppression (infection: 87%, malignancy: 37%) and the infusion procedure (liver laceration/hematoma, haemorrhage, and intra-abdominal bleeding: 13%; elevation of portal pressure 7%). Overall, 90% of the patients had at least one serious adverse reaction. Other adverse reactions were acne (87%), anaemia (83%), nausea (83%), fatigue (80%), abnormal loss of weight (73%), diarrhoea (73%), headache (63%), increased transaminases (63%), and vomiting (60%). Also, two patients died, one due to fulminant sepsis from an infection at 20 months post-transplant and one from severe dementia at 9 years post-transplant. The 4 no-voting panellists had concerns regarding (I) the side effects of long-term immunosuppression (e.g. gastrointestinal diseases, hypertension, anaemia, severe infections, cancer) and (II) the design and patient selection for the trials, particularly the lack of control group (sources: clinical trials.gov; the product labelling text at the FDA - https://www.fda.gov/media/169920/download; Pullen, 2021; Prime Therapeutics, 2021).

Lantidra and other portal vein infusion therapies have shortcomings… CellTrans Inc is a spin-off of the University of Illinois in Chicago, one of multiple universities with the required expertise for conducting islet cell transplantation and a member of the Clinical Islet Transplant Consortium (CITC). The CITC was established by the US National Institutes of Health (NIH) to evaluate more rigorously the risks and benefits associated with islet transplantation for T1D patients. The CITC has conducted 9 islet cell transplantation studies in T1D patients in the US (CIT02 through CIT08) and one in Nordic countries (CIT01). The key challenges of the procedure are:

1. The low availability of pancreas donors,
2. the safety primarily associated with immunosuppression and the portal vein infusion procedure,
3. partial long-term success (i.e. survival) of transplanting islets.

Similar to the CellTrans studies, the CITC's tested procedures have achieved encouraging results but with the same shortcomings. We take as an example the US uncontrolled, non-randomised phase 3 trial (CIT-07) in 48 patients with T1D of >5 years duration and IAH with persistent severe hypoglycaemic events (SHEs). The primary endpoint was success in controlling the glucose level measured with an HbA1c level of <7.0% after one year and freedom from SHEs. The results were as follows:

- After one year, 42 of 48 subjects (87.5%) achieved the primary endpoint. Importantly, only 25 patients (52.1%) achieved insulin independence at the end of year 1, and 20 patients (42%) remained insulin independent at the end of year 2. These results suggest partial engraftment and a declining trend of islets function (i.e. survival) over time. Several studies (e.g. Yan et al., 2022, Delaune et al., 2017) have shown that portal vein delivery negatively impacts the survival of transplanted islets and is associated with the early death of about 50-70% of them. The main reasons are hypoxia in connection with low oxygenation of the portal vein, the instant blood-mediated inflammatory reaction, inflammatory cytokines and the natural liver immune system. As a result, it has been observed that only 10% of patients remain insulin independent for > 5 years, and the majority of patients have to restart insulin use due to an islet function decline over time.
- At the end of year 1, 30 serious adverse events occurred in 21 patients, of which 22 were due to the transplant procedure and/or immunosuppression and 8 were due to nonstudy-related causes. Procedural bleeding requiring transfusion and/or surgery occurred in 5 of 56 portal vein cannulations (sources: Hering et al., 2016: https://classic.clinicaltrials.gov/ct2/show/NCT00434811; NIH NIDDK Central Repository for CIT-07 study - Clarke, 2023).

We therefore see substantial room to improve this pioneering procedure by addressing the three main shortcomings discussed above.

Lantidra opened up the regulatory path for superior cell islet therapies in the future

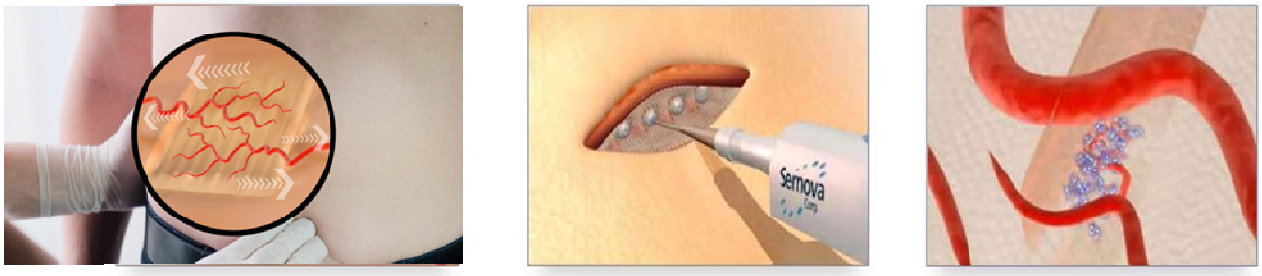
FDA approval of allogeneic islet therapy as a biologic rather than a transplant was a major challenge for CellTrans. The first Biologics License Application (BLA) was submitted in 2017 and triggered a substantial number of questions from the FDA, particularly on the manufacturing process. Donor islets vary in quality depending on the donor, making it difficult to ensure uniform quality of the final product, which is a typical characteristic of a drug. It took about 3 years of educating the FDA and strengthening certain manufacturing processes and documentation before resubmission in 2020. Following a positive review from an FDA advisory committee in April 2021, the first islet cell therapy was approved in June 2023. This approval paves the way for future islet-based products like those from Sernova.

SERNOVA'S TECHNOLOGY BUNDLE APPLIED TO T1D

1G PRODUCT USING TECH 1: THE CELL POUCH SECURES LONG-TERM SURVIVAL OF TRANSPLANTED CELL ISLETS

The organ-like, exchangeable pouch overcomes the main causes of cell islets' poor survival – inflammation/fibrosis and hypoxia due to lack of oxygen The Cell Pouch is a rectangular microporous device about the size of a business card made of polypropylene plastic membranes. Its body is divided into several parallel cylindrical chambers. For the T1D application it has 8 or 10, which are prefilled with solid plugs comprised of polytetrafluoroethylene (PTFE). The device is designed to be implanted under the fat layer of the abdominal skin at the level of the deep subcutaneous muscle during a minor surgical procedure. After implantation, the Pouch undergoes an initial vascularisation period over 4-6 weeks. Thereafter, the PTFE plugs are removed and the therapeutic cells, in this case pancreatic cell islets, are implanted into the resulting void space. The Pouch's unique "open architecture" allows tissue and tiny blood vessels that provide oxygen and nutrient supply to form within and around the device. Essentially the Pouch integrates into the body's own tissues as if it were an additional organ, which may also help prevent local inflammation and fibrosis that typically occurs with other implantable devices. The implanted cell islets settle in an oxygen- and nutrient-rich natural environment so that they can grow and function optimally like the cells of the original organ, sensing the body's needs, and releasing the required hormones (e.g. insulin, glucagon and somatostatin) into the bloodstream. The Pouch becomes a "tissue-engineered pancreas" that is intended to be a long-term solution. However, if a problem arises, such as a negative reaction or cell failure (e.g. they stop working), the Cell Pouch can be easily removed and replaced with a new one. This is a major advantage over the traditional portal vein procedure, where the infused cell islets lodge in a difficult-to-reach location such as the liver and their removal would require liver transplant. We give an overview of Sernova's Cell Pouch System in Figure 7 below.

Figure 7: Cell Pouch containing therapeutic cells allows for natural vascularisation



The proprietary Cell Pouch is placed deep under the skin, allowing for vascularisation & creating a natural environment for long-term function of therapeutic cell islets

About 4 weeks later, therapeutic cell islets are transplanted directly into the vascularised tissue chambers of the proprietary Cell Pouch

Therapeutic cells are responsive to endogenous regulation and release missing proteins or hormones (e.g. insulin) into the bloodstream to correct biological dysfunction

Source: First Berlin Equity Research, Sernova Corp,

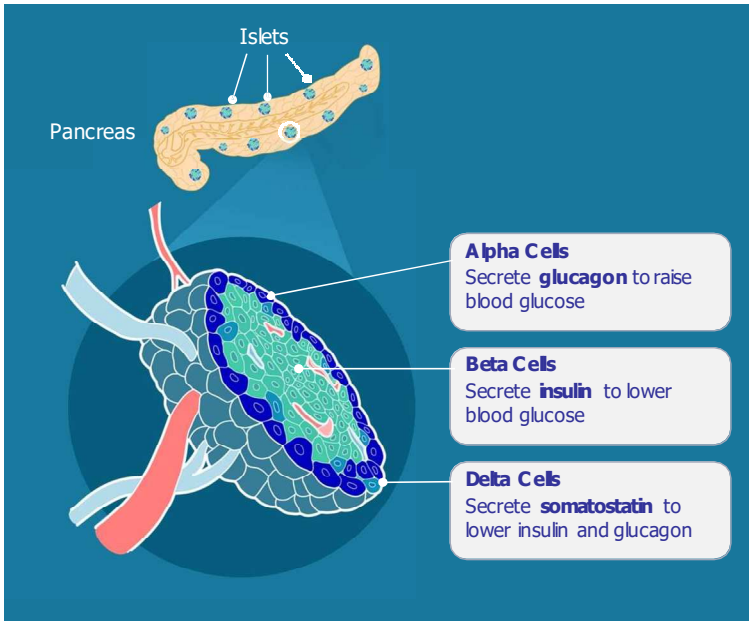
Why is islet transplant a superior therapeutic approach to insulin injection? Pancreatic islets, also known as islets of Langerhans, are tiny clusters of several types of cells scattered throughout the pancreas. Altogether, they play a crucial role in the endocrine function of the pancreas, producing various hormones that regulate the body's blood glucose levels. The main three islet cell types and their functions are:

- **Beta cells:** These are the most common type of cells in the islets, making up about 52-75% of the total. Beta cells produce insulin, the hormone that regulates blood glucose levels by allowing cells in the body to take in and store glucose.

- **Alpha cells:** Making up about 30-40% of islet cells, alpha cells produce glucagon, a hormone that raises blood glucose levels by triggering the conversion of stored glycogen into glucose in the liver.
- **Delta cells:** These cells, which comprise ⩽10% of islet cells, produce somatostatin. Somatostatin inhibits the release of several other hormones, including insulin and glucagon, helping to regulate their secretion (sources: Bru-Tari et al., 2021; Da Silva-Xavier; 2018, Chao et al., 2012).

Although the autoimmune attack in T1D is primarily directed at beta cells, research has shown that alpha and delta cells may also be affected over the course of the disease, albeit to a lesser extent. Still, the dysfunction of alpha and delta cells in T1D patients has been shown to exacerbate hyperglycaemia or lead to severe hypoglycaemia (sources: Yosten, 2018, Panzer et al., 2022). Therefore, insulin therapy can only lower blood glucose, but it struggles to properly regulate the right level of glucose due to lack of glucagon and somatostatin. Islet transplant represents the complete approach capable of supplying all three key types of cells required for proper blood glucose management (see Figure 8 below).

Figure 8: Advantages of pancreatic islets transplant over insulin injection



Source: First Berlin Equity Research, Sernova Corp,

Preclinical animal studies for T1D with scaled-down pouches demonstrated long-term insulin independence with a success rate of up to 95% In a first pilot animal study conducted at the University of Western Ontario in 2012, a mini-pouch prototype was implanted into the abdomen of 13 female Lewis rats. After four weeks, the investigators induced diabetes in 10 of them by injection of the beta-cell-specific toxin streptozotocin. Once diabetes was confirmed, they implanted purified rat cell islets. The rats were administered insulin for about two weeks until their implanted islets grafted and started producing insulin. 7 of the 10 rats became insulin independent and their blood glucose level was normal at about 8 mmol/L (normal level is ⩽11.1 mmol/L) until the pouches were extracted at day 100 when the rats became hyperglycaemic (>18 mmol/L) and stayed so through the end of the study on day 120. The remaining 3 rats showed poor islet engraftment and their glucose blood level was >14 mmol/L, with the procedure showing a promising 70% success rate in achieving insulin independence. The investigators believe that the main reasons for the failure in the 3 rats were related to variations in the islets transplanted quantity and the surgical procedure. The device proved to be safe in all 13 diabetic and non-diabetic rats (source: Kriz et al., 2012).

A further animal study led by one of Sernova's scientists, Dr Pepper, conducted at the Canadian University of Alberta in 2015, compared the engraftment of transplanted islets into the Cell Pouch of 20 rats vs islets injected in the same subcutaneous space, but without device, in 6 rats, to demonstrate the value of the device. The Cell Pouch group showed an excellent result. 19 of the 20 rats became insulin independent by 40.5 ± 5.0 days after islet transplantation, equating to an outstanding success rate of 95%. These rats stayed insulin-independent in the long term throughout the study (100 days). In contrast, none of the 6 rats without a device was insulin independent. We believe the superior success rate of the Pouch in this study is related to (I) the investigator's greater experience with the device, (II) an improved version of the device (e.g. size, diameter) and (3) the implant of an optimised islet dose, which led to better engraftment, albeit with a slight delay in insulin independence (source: Pepper et al., 2015; Sernova).

Canadian first-in-human phase 1/2 study of the Pouch using donor islets in T1D patients demonstrated safety and provided valuable insights to optimise the density of cell islets population The pilot proof-of-concept phase 1/2 study in T1D patients was conducted under the leadership of Dr Shapiro at the University of Alberta in Canada from 2012 until 2016 (https://classic.clinicaltrials.gov/ct2/show/NCT01652911). This was an open-label, single-arm, non-randomised study investigating cell islets implanted into the Cell Pouch supported by immunosuppression. The primary endpoint was safety, although secondary endpoints looked for signs of efficacy. The investigators implanted the Cell Pouch in T1D patients between 2 and 12 weeks prior to implant of different quantities of islets into the device to study the dynamics of Pouch vascularisation and its relationship with different quantities of implanted islets (i.e. cell density in the device). The study design envisaged the treatment of up to 20 patients, but the company stopped after the third patient produced measurable results. While the procedure and the device met the primary endpoint (safety), the preliminary efficacy results obtained did not meet expectations. The islets largely did not produce enduring plasma C-peptide during the initial engraftment period, resulting in measurable C-peptide in all 3 subjects only within the initial 24 hours, turning C-peptide negative afterwards. Encouragingly, histological analysis showed that the islets in sections of the device were functioning and producing insulin, glucagon and somatostatin. Dr Shapiro concluded that the research team may have transplanted too many islets, thereby overwhelming the device's capacity to provide the required oxygen and nutrients. Based on the data analysis, Sernova recalculated a more optimal cell density to populate the device and fine-tuned the procedure, including the optimal place in the abdomen to implant the pouch; these findings were used in the next study (source: Gala-Lopez et al., 2016, Sernova).

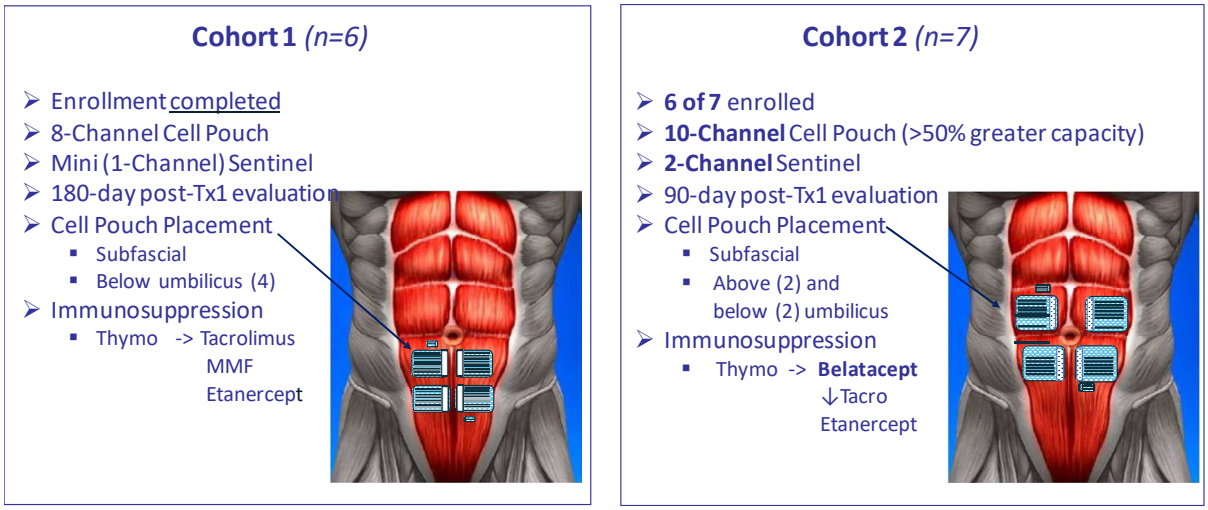
US phase 1/2 clinical study of the Cell Pouch using donor islets for T1D – first cohort initiated in 2018 Based on the valuable findings from the Canadian pilot study, the company expanded the clinical trial programme to the US. A number of modifications were made to the surgical procedure, islet purity, etc. The new procedure included two successive small islet transplants in an 8-channel Pouch followed by the infusion of a small dose of islets through the portal vein. In 2018, the company initiated the first cohort of a US single-arm phase 1/2 clinical study led by Dr Piotr Witkowski at the University of Chicago to evaluate 6 T1D patients with severe hypoglycaemia unawareness following islets transplanted into the Cell Pouch System supported by immunosuppression (https://classic.clinicaltrials.gov/ct2/show/NCT03513939). The company used this study approach to gain further knowledge of islets engraftment depending on islet density within the device and optimise the required dose further.

The findings from the first cohort were used to define an optimised dosing regimen and shorter dosing periods for the second cohort Based on the preliminary results obtained until 2022, Sernova was able to establish an accurate threshold for optimal islet dose and density and make procedural changes to improve the transplant process that have been implemented in the 2nd cohort. The key study design changes for the 2nd cohort are:

- Expansion from the existing 8 to a new, slightly larger 10-channel Cell Pouch, which provides >50% more space for the islets to graft according to their optimal density. The new size resulted in a small change in the placement of the Cell Pouch (see figure 9 below).
- Performance of only two density-optimised implants in the Pouch, potentially eliminating the need for topping up in the portal vein. This will depend on availability of the target optimal dose of islets; unlike Sernova's iPSC derived technology in which optimal islet dose can be accurately measured and implanted, the dose of isolated islets from donor pancreata is not predictable.
- Shortening of the interval between islets implants from 6 to 3 months.
- Improved immunosuppression therapy by administering the less toxic Belatacept instead of Tacrolimus, which also enabled lower doses of the drug Mycophenolate mofetil (MMF). This regimen is intended to prevent rejection of the cell islets.
- The company will study up to 7 T1D patients and will additionally engage a patient recruitment agency to expedite the enrolment of study patients.

Figure 9 below provides an overview of the main features of the study design of the two cohorts:

Figure 9: Overview of the multi-cohort phase 1/2 T1D and hypoglycaemia unawareness study

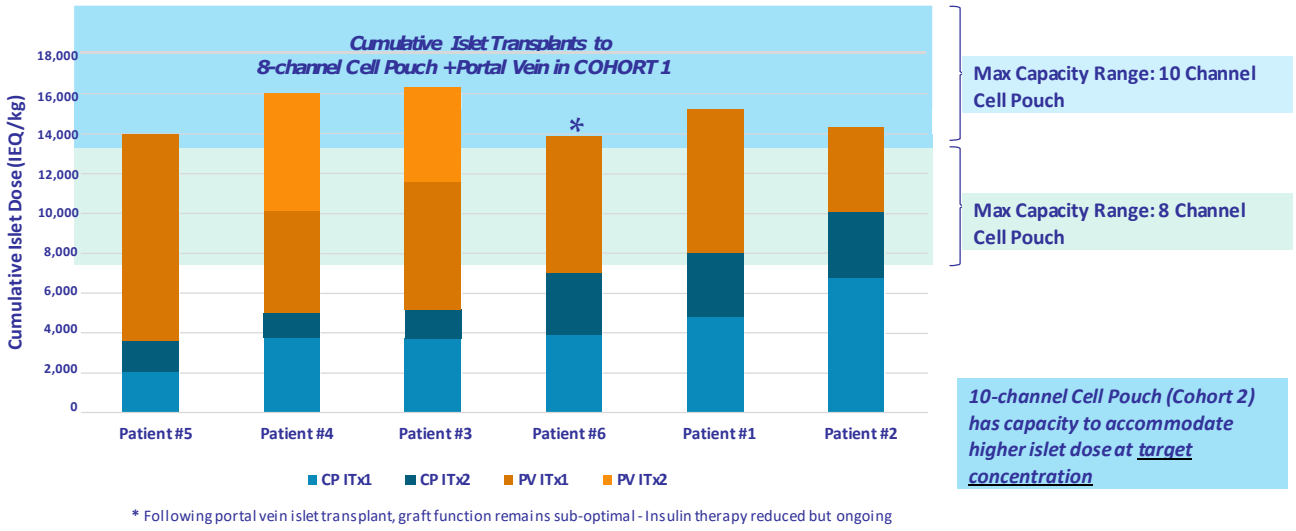


Source: First Berlin Equity Research, Sernova Corp

Positive interim results from the first cohort of the ongoing phase 1/2 study using a 8-channel Cell Pouch – 5 out of 6 T1D patients achieved insulin independence for ~6 months to > ~3.5 years The first cohort of this study published very positive interim results at the American Diabetes Association (ADA) 83rd Scientific Sessions on 24 June 2023 and at the 59th European Association for the Study of Diabetes (EASD) Conference on 5 October 2023. A clear safety profile for the Cell Pouch was confirmed across all patients. Efficacy performance was as follows: Three of the six patients (#1, #2 and #3) exhibited positive stimulated and fasting serum C-peptide through to 12 months after the 2nd transplant into the Cell Pouch. Unfortunately, the other three patients (#4, #5 and #6) developed donor-specific antibodies against the islets (immune rejection) because the

patients were not optimally compliant with their immunosuppression therapy. Therefore, no C-peptide levels were detectable in these patients. However, two of the three patients (#4 and #5) had surviving functional islets in the Cell Pouches. All six patients received a supplemental islet transplant via the portal vein as planned. The cumulative amount of islets measured in each patient varied widely. The reason for this could be the variability and difference in the yield of donor islet pancreas. Overall, five of the six patients in the first cohort who used an 8-channel Pouch achieved insulin independence (their blood glucose / haemoglobin A1c values were in the non-diabetic range of ⩽6.5%) over periods ranging from ~6 months to > ~3.5 years. Patient #6 completed the islet transplant recently and will be assessed in the near future. An overview of the cumulative dosing results for the six patients is provided in Figure 10 below. This Figure also shows that the 10-channel Cell Pouch used in cohort 2 provides sufficient capacity to accommodate an optimal target range of islet dose that allowed insulin independence to be achieved in cohort 1.

Figure 10: Cumulative islet transplant doses in cohort 1



Source: First Berlin Equity Research, Sernova Corp

Excellent results from the second cohort of the phase 1/2 study – 6 out of 7 T1D patients enrolled in record time, one patient already showed persistent serum C-peptide levels after the first islet transplant At the recent EASD conference, the company presented a promising preliminary update from the second cohort with optimised 10-channel Pouch. 6 of 7 patients have been recruited to date and have received at least the first of 2 planned islet implantations. One of these patients (#2) reached the stage where evaluation was possible. Remarkably, this patient showed persistent fasting and glucose-stimulated blood C-peptide levels, which indicate insulin production after only one Cell Pouch Islet Transplant (CPITx1). In the first cohort, patients started being C-peptide positive only after the second implant. This is excellent news and suggests that Sernova's islets dose and density optimisation measures were right. Unfortunately, this patient's second islet transplant (CPITx2) was contaminated with Candida albicans fungus (most likely from the donor) and the CPITx2 islets and Pouches had to be explanted to prevent a systemic infection. Considering that the islets transplanted into the first two Pouches at CPITx1 were unaffected and functioning well, the company decided to administer a very small additional dose of islets via the portal vein. This patient has been insulin-independent since day 30 of the portal vein transplant. Patient #1 developed neutropenia due to immunosuppressive medicine and needs time to recover from the immunosuppressive therapy. Patients #3, #4 and #5 are recovering from the first transplant and are awaiting evaluation in the near future. Patient #1 developed persistent neutropenia (lower-than-normal level of neutrophils, a type of white blood cell that plays a key role in the body's defence against bacterial infections)

due to immunosuppressive medicine requiring recovery of neutrophil levels. Enrolment of patient #1 is scheduled for the coming weeks. The company will publish further updated data from the second cohort during Q4 2023.

Figure 11: Status of cohort 2

Patient	Cell Pouches	Cell Pouch Islet Tx 1	Cell Pouch Islet Tx 2	Clinical Details
#1	Yes	Yes	Awaiting	Persistent neutropenia, immunosuppression stopped for 3 months. The body rejected the graft and there was no C-peptide. Options are being considered.
#2	Yes	Yes	Yes	Excellent response to CPITx1; contaminated donor islets at CPITx2 which had to be explanted. A modest supplemental dose led to insulin independence.
#3	Yes	Yes	No	Recovering after CPITx1
#4	Yes	Yes	No	Recovering after CPITx1
#5	Yes	Yes	No	Recovering after CPITx1
#6	Yes	Awaiting	No	Awaiting CPITx1

Source: First Berlin Equity Research, Sernova Corp

The ongoing phase 1/2 study could be completed by H1 2024 – if Sernova decides to conduct a phase 3 study, we project a potential drug approval and market launch in 2028 We expect the company to meet with the FDA in late 2024 or in early 2025 to discuss the results of the phase 1/2 study and design of a potential phase 3 study. Depending on the outcome of this meeting, we believe management will decide whether it is worthwhile to proceed with a phase 3 study. Not only does this product have a small target population, but it would also be limited by the scarce supply of donor islets. However, we believe it would be a major advantage that the FDA is familiar with the Cell Pouch, which will benefit the 2G and 3G products and allow for faster approval. Assuming Sernova conducts a successful phase 3 study, approval and launch could occur in 2028.

Cell Pouch manufactured under GMP Sernova's Cell Pouch is manufactured under GMP by an FDA-inspected US-based contract manufacturer (CMO), whereby all configurations are produced in a Class VII Clean Room. This type of facility typically provides air cleanliness levels of a maximum of 10,000 particles (⩾0.5µm) per cubic foot and a minimum of 60 air changes per hour. The device has an established 2-year shelf-life based on real-time stability testing. It complies with ISO 13485, the EU Medical Device Regulation (MDR 2017/745), the US FDA Quality System Regulations (QSR – 21 CFR 820) and the Canadian Medical Device Regulation (CMDR). The CMO has conducted all package integrity and ship testing procedures in accordance with its Quality System, as required for clinical trials and potential future commercialisation.

Figure 12: Cell Pouch GMP manufacturing

GMP manufactured in a Class VII clean room


Cell Pouch packaged ready for clinical trials


Package integrity testing completed


Ship testing completed

Source: First Berlin Equity Research, Sernova Corp

2G PRODUCT ADDING TECH 2: EVOTEC'S IPSC CELLS WILL SECURE UNLIMITED SUPPLY AT THE HIGHEST QUALITY

Shortcoming of cadaveric islet cell transplant A pancreatic islet cell transplant requires that the islet cells are isolated from the pancreas of a deceased donor (brain dead or without a beating heart) obtained through an anonymous multi-organ donation. Access to this procedure is typically limited by the availability of pancreas from deceased donors for islet isolation, which would be exacerbated if the procedure were to become more widespread. Although science has made great strides, allogeneic islet transplantation is still hampered by the limited number of islet donors and the required lifelong immunosuppression, which causes a variety of adverse effects. As a result, several studies are seeking new and improved methods for expanding pancreatic islet-cell cultures in the lab to increase the supply of these cells.

Stem cells – an ideal potential source of pancreatic islet cells One promising approach to obtain cell islets for transplant is to differentiate stem cells in the lab into cell islets in sufficient number and optimal functional state. Stem cells represent the beginning of life. All cells and tissues of the human body originate from these cells as they have the unique ability to develop into many kinds of cells or tissues. They are found in various tissues in the body, and their origin determines their capabilities. Some of the primary sources of stem cells are:

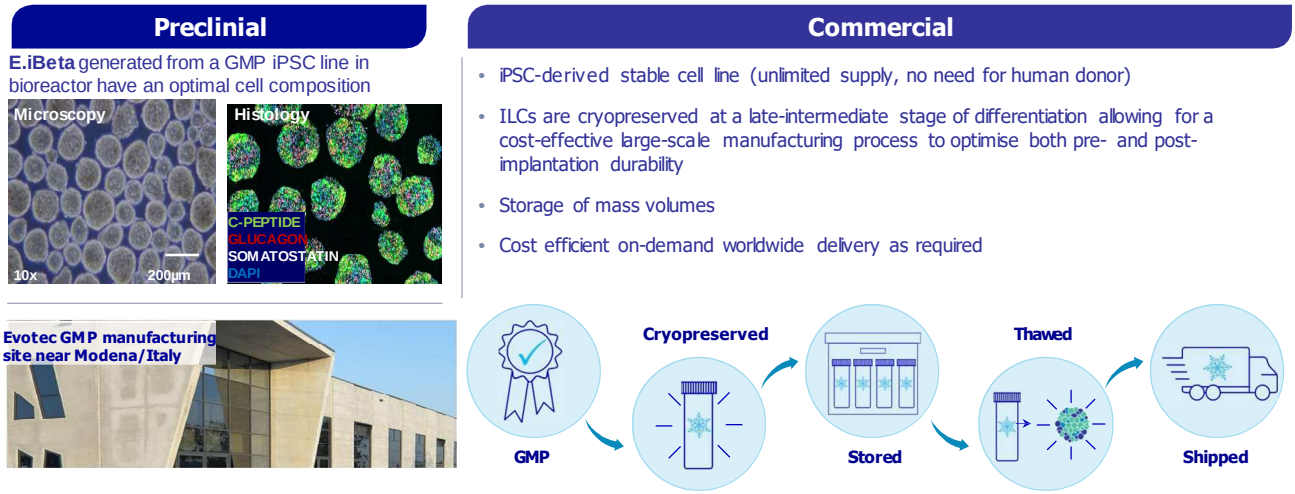
- **Embryonic Stem Cells (ESCs)** ESCs come from embryos that are 4 to 7 days old. At this stage, an embryo is called a blastocyst. These stem cells are pluripotent, meaning they can divide into more stem cells or become any type of cell in the body. This versatility makes ESCs very attractive for their potential to regenerate or repair diseased tissue and organs. However, research using ESC's is controversial due to ethical reasons and is prohibited in several European countries (e.g. Germany, Austria, Italy, and Portugal)
- **Adult Mesenchymal Stem Cells (MSCs)** MSCs are found in small quantities in most adult tissues, such as the bone marrow, fat or muscle, as well as in umbilical cord blood, the placenta and the amniotic fluid in birthing women. They have a more limited ability than ESCs to generate various cells and tissues of the body.
- **Induced Pluripotent Stem Cells (iPSCs)** iPSCs are adult somatic cells, typically taken from skin or blood, that have been genetically reprogrammed back to an embryonic stem cell-like state where they regain pluripotency. This breakthrough process was discovered by Shinya Yamanaka and his team at Kyoto University in 2006, for which he won the Nobel Prize in Medicine in 2012. iPSCs are generated by introducing a specific set of genes, such as OCT4, SOX2, KLF4, and c-MYC – also known as the OSKM or Yamanaka factors, into the somatic cells, resetting and forcing them to express genes and factors important for maintaining the defining properties of ESCs. Recent research has discovered further alternative gene choices to improve reprogramming efficiency for therapeutic use (source: Brower et al., 2015).

Shortcomings of stem cells in therapeutic use Stem cells are already in use to treat several types of diseases, mostly blood-related disorders such as leukaemia. Given that stem cells are characterised by their ability to proliferate extensively, one of the most challenging tasks when incorporating them into clinical practice is directing and controlling their division and differentiation potential. For example, if their growth is left uncontrolled, this could potentially lead to tumour formation. Therefore, optimisation of the in vitro differentiation process is essential to minimise the formation of unwanted cell types and validate a technology for clinical use. In addition, if the stem cells are not generated from the patient cells (allogenic), this will lead to immune rejection. Another relevant challenge is ensuring a safe (contaminants-free) and consistent manufacturing process in accordance

with GMP. Scientists consider pluripotent iPSCs and ESCs promising, ideal candidates for differentiation into pancreatic cell islets in therapeutic applications. Differentiation protocols, cell culture methods and immunoprotection technologies are being developed to optimise their production (source: Ebrahimi et al., 2021; Borges et al., 2022; Mayo Clinic).

Partnership with the leading German biotech specialist Evotec AG to develop a first-in-class cell therapy for insulin-dependent diabetes patients In May 2022, Sernova entered into an exclusive global strategic partnership with Evotec, which will develop iPSC-based beta cells for the treatment of insulin-dependent diabetes to pair with the Cell Pouch for a second generation product (2G). Evotec has a unique platform for GMP-compliant generation of iPSC cell lines that can produce an unlimited supply of various cell types such as cell islets. The company's iPSC platform can thus manufacture off-the-shelf islet-like clusters that mimic human islet cells in a scalable bioreactor format with comprehensive quality control procedures to the highest standards. Evotec's E.iBeta generated iPSC cell islets, also known as islet-like clusters (ILCs), exhibit optimal cell composition (i.e. beta, alpha and delta cells) capable of producing the key hormones insulin, glucagon and somatostatin, with no pre- or post-implantation variability of cell composition. Importantly, the developed manufacturing workflow includes ILCs cryopreservation at a late-intermediate stage of differentiation, allowing for ILCs storage until cells need to be shipped for implantation. This cost-effective manufacturing process also optimises both pre- and post-implantation shelf-life and quality, offering a major advantage over competing cell therapies in development. Evotec is a leader in the industry with >100 people dedicated to developing iPSC-based cells for drug discovery and cell therapy applications.

Figure 13: Evotec's iPSC cell islets microscopic and histological overview, the GMP manufacturing plant (left) and its commercial competitive advantage (right)

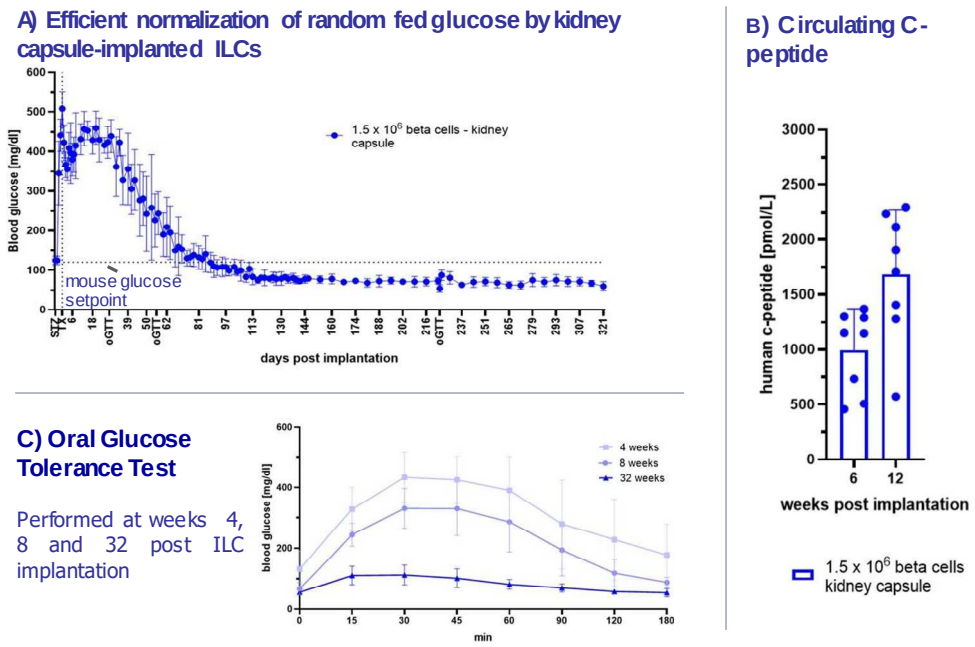


Source: First Berlin Equity Research, Sernova Corp

Evotec's €20m investment in Sernova validates potential of the 2G product In connection with the agreement, Evotec made a strategic equity investment of €20m/~CAD27m (CAD20m at CAD1.57 p/s on 16 May 2022 and CAD7m at CAD2.50 p/s on 31 August 2022) in Sernova. In the light of Evotec's thorough due diligence, this deal underscores the company's high interest and commitment to the promising 2G product. The preclinical development is being jointly funded until the Investigational New Drug (IND) Application is approved. Evotec will contribute to cell manufacturing until commercialisation and will decide on joint funding of clinical development in the future. Sernova has an option for an exclusive global license on the 2G product, which it can exercise upon filing the IND. The profits from commercialisation will be shared between the two companies depending on their contribution to clinical development.

Evotec's E.iBETA preclinical programme has generated well-functioning iPSC islet cells that produced long-term blood glucose normalisation in diabetic mice The E.iBETA cell programme has generated excellent preclinical data, which was presented at the 4th International Pancreas and Islet Transplant Association (IPITA) / Harvard Stem Cell Institute (HSCI) / Juvenile Diabetes Research Fund (JDRF) Summit (IPITA/HSCI/JDRF) on 23 April 2023. Evotec's iPSC cell islets, transplanted into the Cell Pouch of streptozotocin-induced diabetic mice, had the ability to normalise blood glucose levels over the planned testing period of 320 days. Moreover, standard deviation of the blood sugar level in blood also declined over time which shows that the maturing ILCs controlled sugar levels very tightly (see Figure 14A). Evotec also measured the level of the insulin marker C-peptide 6 12 weeks post implant of the ILCs into the mini pouch. This showed a normal level as the ILCs matured (see Figure 14B). Similarly, Evotec conducted oral glucose tolerance tests (OGTT) to investigate how well the mice were processing a larger amount of sugar 4, 8 and 32 weeks post ILCs implant, also showing normally improving performance over time and no hypoglycaemia (see Figure 14C). Remarkably, the company also conducted an additional mouse study implanting human donor primary islets (4,000 islet equivalence – IEQ) to compare their performance to the implanted ILCs on the basis of C-peptide and OGTT. These tests showed similar results over time which demonstrated the ILCs' equipotency to human primary islets (data not disclosed).

Figure 14: Evotec's iPSC cell islets blood glucose normalisation in diabetic mice, also demonstrated with glucose tolerance test and C-peptide test in blood



Source: First Berlin Equity Research, Sernova Corp

The 2G product using 10-channel Cell Pouch + Evotec iPSC islets +immunosuppression is set to enter clinical development in 2025 Evotec is at the late stage of preclinical development & optimisation of chemistry, manufacturing and control (CMC) efforts to bring the ILCs into the clinic. We project that the 2G product will file for IND and start the phase 1/2 clinic study in 2025. In addition, we have assumed that the phase 1/2 study will take ~1.5 years and a pivotal phase 3 study and the registration ~3.5 years. We project a potential drug approval and market launch in 2030 (see Figure 15 overleaf).

Figure 15: Sernova and Evotec's 2G product is due to start phase 1/2 study in 2024

Source: First Berlin Equity Research, Sernova Corp

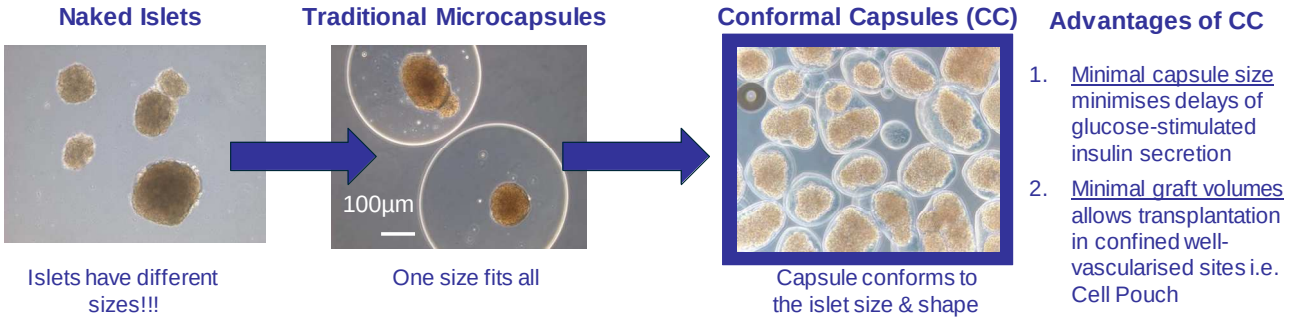
3G PRODUCT ADDING TECH 3: IMMUNOPROTECTION TECHNOLOGY WILL ALLOW CURATIVE RESULTS

Immunosuppression – a transitory solution until immunoprotection is market-ready A key shortcoming of systemic immunosuppression use is that it may expose the patient to undesirable adverse effects. Immunosuppression administration involves potential short-term risks of infection (e.g. MRSA and sepsis), acute organ dysfunction and death, and long-term risks of malignancies (i.e. cancer) and secondary autoimmune diseases. Therefore, Sernova is exploring new technologies to protect the transplanted islet cells.

Cell microencapsulation for islets immunoprotection, while promising, has shortcomings… Microencapsulation of islets represents a promising bioengineering approach to eliminate the need for toxic immunosuppression by surrounding transplanted allogeneic islets with a semipermeable, biocompatible material that prevents immune cells and cytotoxic molecules from recognising and destroying the islets while allowing the passage of nutrients, oxygen, and hormones. Microencapsulation typically consists of enclosing the cells with an alginate hydrogel, agarose gel, or another biocompatible material. This technology has been shown in studies with small and large diabetic animal models to protect the graft from attack by the host immune system and to prolong islet cell survival without immunosuppression, but none has yet demonstrated long-term efficacy in large animal models and humans. A major shortcoming of microencapsulation is that the total volume of the implant increases after microencapsulation. The average diameter of the islets is about 150µm. The diameter of the capsules is 500-1000µm or >3 times that of the original islets and the total volume of the microcapsules is thus estimated to be >27 times that of the islets. Due to the large size of the islets and the large volume of a few litres required to achieve curative results, they would only fit in the abdominal cavity, a site with poor oxygen tension and graft survival that does not permit graft retrieval. Also, due to the large capsule sizes, glucose sensing and glucose-regulated insulin secretion is delayed. This problem is exacerbated in the abdominal cavity. Therefore, this technology, besides being suboptimal, has the additional problem that the encapsulated islets would by no means fit in Sernova's Cell Pouch at doses that would be expected to provide efficacy (sources: Stock et al., 2022, Dimitrioglou et al., 2019; Krishnan et al., 2014; Teramura et al., 2010).

…that are overcome by conformal coating technology As an alternative, conformal coating allows for encapsulation of the islets in a thin polyethylene glycol (PEG) hydrogel capsule that is a few tens of micrometres thick regardless of the size of islets and capable of conforming to the islet shape and size. These unique features allow close contact of the transplanted islets with the vascularised environment (i.e. tissue within the Cell Pouch), an easier diffusion of nutrients, small molecules and biomolecules (i.e., glucose, insulin, and other proteins or hormones), leading to optimal glucose-stimulated insulin secretion without delay (source: Stock et al., 2022; Dr Alice Tomei webinar at https://youtu.be/U57fkmsBT7k).

Figure 16: Conformal coating enables the encapsulation of cell islets with a uniformly thick layer that only marginally increases their volume



Source: First Berlin Equity Research, Tomei et al., 2014

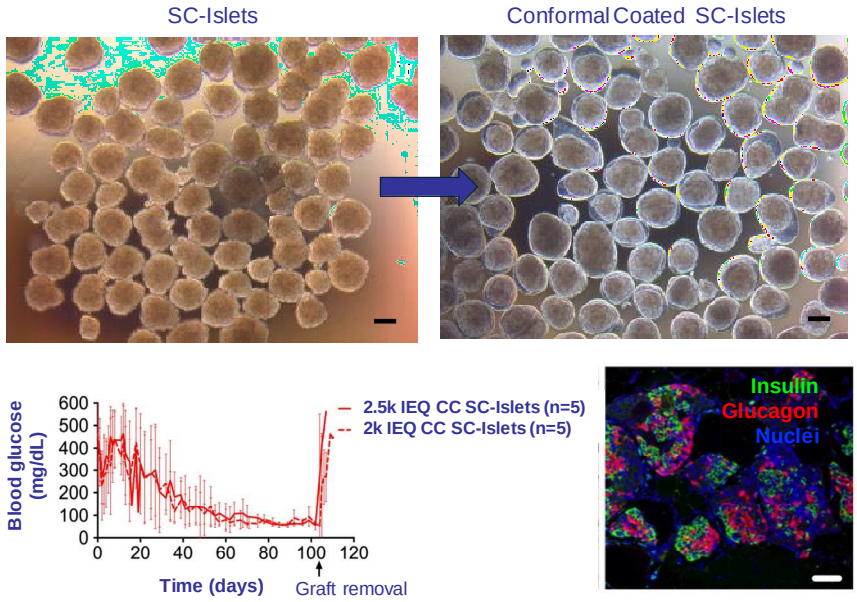
Acquired IP and licensing agreement with the University of Miami secured access to conformal coating technology In June 2020, Sernova acquired from the US company Converge Biotech Inc, a spinoff of the University of Miami, all IP related to conformal coating cell encapsulation technology, including issued patents, patent applications, and know-how. We have identified 6 conformal coating patents assigned to Converge Biotech, two of which were co-owned by the University of Miami. Therefore, in August 2020, Sernova broadened its IP by licensing exclusive, worldwide commercial rights to conformal coating immune protection technologies and closing a two-year agreement for further development of the technology with the University of Miami. The majority of patents and technologies were primarily developed by Dr Jeffrey Hubbell, Eugene Bell Professor of Tissue Engineering at the University of Chicago and leading international researcher in immunoengineering, and Dr Alice Tomei, a leading international expert in immunoprotection and diabetes immunoengineering of the renowned Diabetes Research Institute (DRI), a designated Center of Excellence at the University of Miami Miller School of Medicine. Dr Tomei is one of the original inventors of the conformal coating technology, which has been developed and optimised over >12 years. Under the renewable agreement, Sernova has committed to fund up to USD1.4m (CAD1.9m), of which USD0.9m (CAD1.2m) had already been spent by 30 April 2023.

Substantial progress achieved with the CC technology, but there is still optimisation work to be done until it can reach the clinic Dr Tomei's team has conducted substantial preclinical efforts in-vitro and in-vivo to improve the conformal coating (CC) technology. CC has already been demonstrated to be by far superior to existing microencapsulation technologies, solving size, volume and insulin delay problems, showing that CC is suitable for use in the Cell Pouch. Over the past five years, the team has tested further alternatives on the coating composition and the process to improve existing shortcomings in the performance related to immune protection and overall grafting efficiency (sources: Manzolli et al., 2018; Stock et al., 2022, DeToni et al., 2022). The main achievements were:

- Manzolli et al showed that an improved CC hydrogel composition using an additive to PEG as viscosity enhancer led to diabetes reversal in 100% of mice tested (immune protection issue solved). However, a) inflammation was seen around the area and b) reduced islets engraftment efficacy (probably due to islets exposure to low pH in the coating process).
- Stock et al tested further CC hydrogel compositions in mice, rats and primate models. The team removed the viscosity enhancer that was immunogenic and conducted partial cross-linking of the hydrogel base polymer to generate the required viscosity from immunoprotection. It also conducted process variations, sorting out the pH issue and increasing encapsulation throughput by 5x. The test in the different animal models showed an improved dose-dependent efficacy and even an encouraging diabetes reversal in mice (see Figure 17 overleaf). However,

(a) in rats, diabetes reversal happened only in 1 of 3 animals, and (b) in primates, only a slight improvement of higher C-peptide level was achieved. This showed that larger animals are more complex models and that the environment of the transplanted islets is likely also important, and the CC composition needs further improvements, particularly related to immune isolation, which would need to be demonstrated in animal models before it can enter human trials.

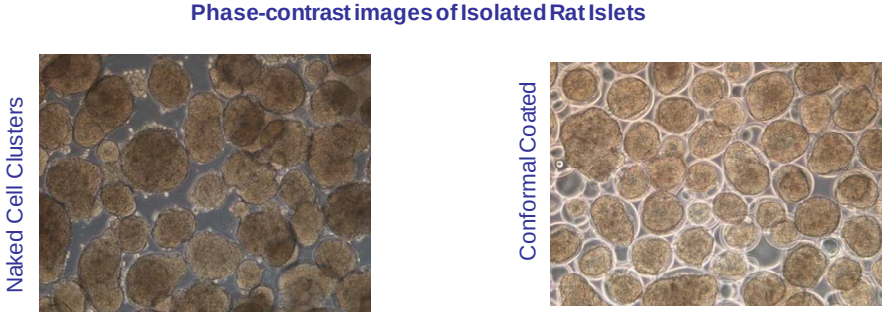
Figure 17: Conformal coated stem cell derived islets reverse T1D in mice for >80 days and regulate blood glucose to human levels



Source: First Berlin Equity Research, Sernova Corp and Stock et al., 2019

Encouragingly, in further in-vivo validation experiments in rats, uniform islet coating was achieved… Dr Tomei's team has conducted additional preclinical efforts in rats to improve the CC technology. The latest CC formulation tested in rats resulted in a uniformly thick layer with only a marginal increase in volume (see figure 18).

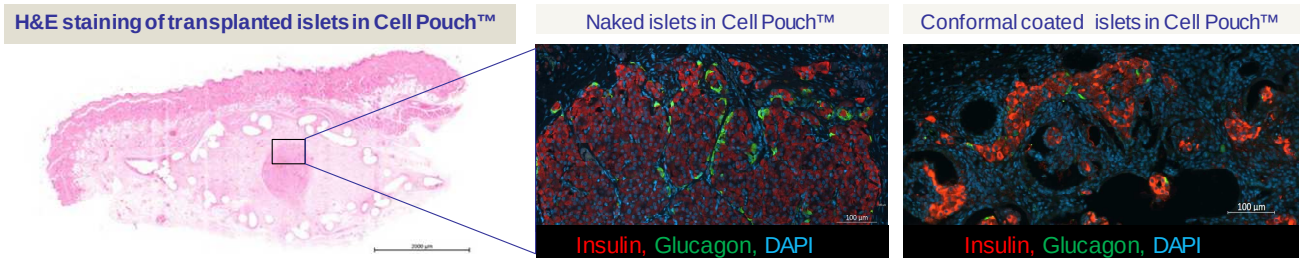
Figure 18: Conformal coating enables the encapsulation of cell islets with a uniformly thick layer that only marginally increases their volume



Source: First Berlin Equity Research, Sernova Corp

…whereas the most recent optimised formulation of CC islets implanted in the Cell Pouch was functioning well Haematoxylin and eosin (H&E)–stained images revealed islet grafts with CC islets integrated into the host tissue of rats (Figure 19, left). Immunofluorescence staining showed grafts with abundant insulin- and glucagon-positive cells (Figure 19, right). This investigation showed that CC human islet graft performance is roughly equivalent to naked human islet graft.

Figure 19: CC islets implanted in the Cell Pouch of rats model showed positive engraftment and encouraging functional results without previous issues of a fibrotic reaction



Source: First Berlin Equity Research, Sernova Corp

The performance of the CC formulation has been further enhanced by the addition of a mild immune response agent. Ongoing work, including preclinical validation and upscaling of production, is progressing well On 7 September, Sernova gave a positive development update, and Dr Tomei will present the details at the 2023 IPITA-IXA-CTRMS Joint Congress in the US on 26-29 October (https://www.sandiego2023.org/). The latest CC formulation is administered in combination with a mild, single selective immune response agent. It is our understanding that this agent may have a very benign safety/toxicity profile compared with immunosuppressants and may have a complementary mode of action to CC, providing complete direct and indirect protection against T-cells. In a syngeneic rat model of T1D, islets protected with the CC + mild immune response agent and transplanted into the pre-vascularised Cell Pouch regulated insulin production and achieved sustained normal blood glucose levels and complete insulin independence. Dr Tomei's team is also conducting characterisation assays and scaling up processes to manufacture sufficient coated cells for clinical applications and preparing final safety and toxicology studies.

We anticipate IND filing in 2026 Based on the leading expertise of the team which has already overcome important hurdles so far, we think it likely that they can complete CC testing and manufacturing upscaling during 2024 and 2025, enabling an IND filing and initiation of phase 1/2 studies in 2026. Furthermore, we have assumed that the phase 1/2 study will take ~2 years and a pivotal phase 3 study and the registration ~4 years. We project a potential product approval and market launch in 2032.

Figure 20: Sernova's 3G curative product consisting of Cell Pouch+Evotec's iPSC islets+conformal coating immunoprotection

Source: First Berlin Equity Research, Sernova Corp

Gene editing technology aims to provide a next-generation immunoprotection solution for the longer term Gene editing is a revolutionary technology which is advancing rapidly and therefore holds the promise of potentially treating or curing many genetic diseases. While the path to developing gene-edited drugs and obtaining their approval still involves multiple challenges that need to be addressed (e.g. off-target effects, immune response, long-term safety, reversibility), this technology will play a relevant role in regenerative medicine in the future. Therefore, Sernova is evaluating gene editing technologies as an additional therapeutic cell local immunoprotection approach. The company's goal is to engineer ex-vivo transplantable, immune-protected therapeutic cells.

COMPETITIVE ENVIRONMENT IN T1D

THE TYPE 1 DIABETES MARKET

T1D market to show a healthy growth dynamic in the period 2023-2032 The global T1D market was valued at USD7.6bn in 2022 and is expected to reach USD13.6bn by 2030, expanding at a CAGR of 7.6% in the period (source: SNS Insider, 2023). Growth will be chiefly driven by the rising prevalence of T1D among the young population, increasing therapy demand, launches of new advanced drugs and geographic expansion of major key players. The US and Canada is the leading region in the global T1D market, representing >50% of the world market.

Large pharmaceutical companies control the T1D market The global T1D market is dominated by large pharma companies that have been continuously expanding their presence in this market for years. According to the Access to Medicine Foundation, there are three key pharmaceutical companies playing a key role in the global T1D and insulin market: Eli Lilly, Novo Nordisk & Sanofi. These are the largest global manufacturers of insulin, currently accounting for >90% of the market in volume and value. Still, other large pharmaceutical players such as Merck, Astra Zeneca, Boehringer Ingelheim, Johnson & Johnson, Novartis, Takeda and Bayer are also relevant players in this market.

KEY PEERS WITH CLINICAL-STAGE CELL-BASED CANDIDATES

There are only a few companies within the regenerative medicine and cell/gene therapy field truly comparable with Sernova in terms of strategy, technology, programme depth (including development stage), indication focus and risk profile. In first place, we have identified the private biotech company CellTrans Inc, the owner of the only FDA-approved cell therapy Lantidra (procedure consisting of infusing donor pancreatic islets through a catheter into the portal vein plus immunosuppression therapy – for more details, see the T1D current therapies chapter). In addition, there are two key leading regenerative medicine players developing products for T1D, thereby using innovative technologies to address the two main factors limiting the use of islet transplant, (1) short supply of donor islets and (2) side effects of immunosuppression. These two players are Vertex Pharmaceuticals and CRISPR Therapeutics, and they both have drug candidates in phase 1/2 clinical development. We see them as Sernova's closest competitors.

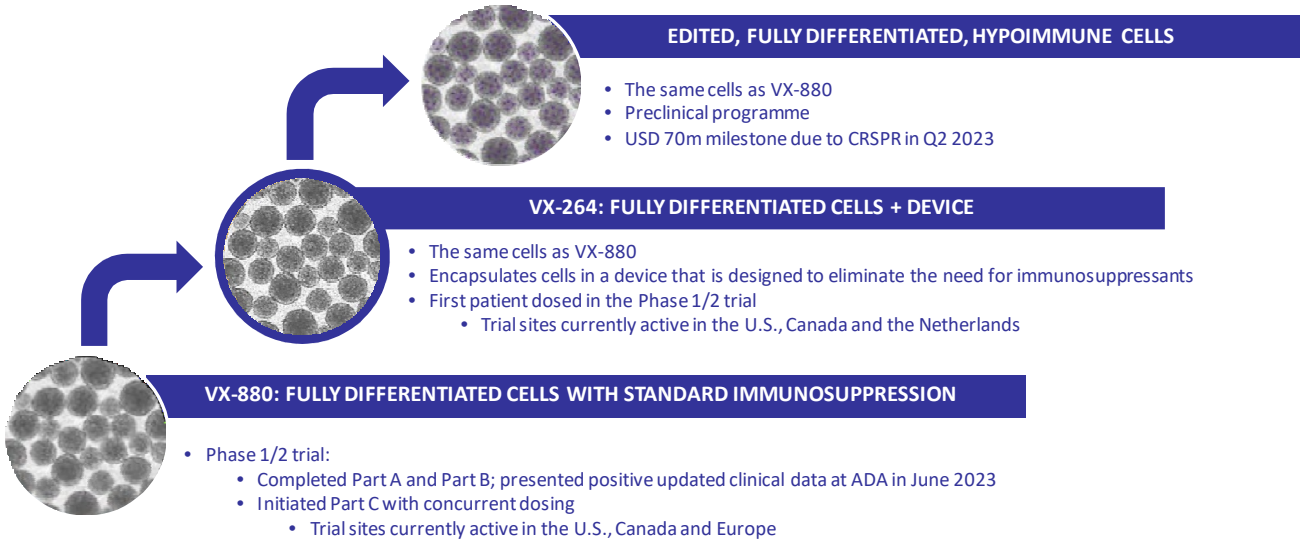
Vertex Pharmaceuticals (US) – a heavyweight in the biotech field Founded in 1989, Vertex is a global biotechnology company that focuses on the discovery, development, and commercialisation of specialty therapies, including cystic fibrosis (CF – rare inherited genetic disease), pain and T1D. The company currently has a monopolistic position in the CFTR-modulators segment, being the absolute leader with four commercialised products achieving a share of >75% in the CF market. Vertex reported group sales of USD8.9bn (+18% Y/Y) in 2022 and has a current market cap of ~USD90bn. The company entered the T1D field intending to dominate the market through the acquisition of two important smaller players in the T1D regenerative medicine field and a gene editing technology licensing deal:

(1) Vertex acquired the private biotech company Semma Theraputics for USD950m in 2019. Semma owned a technology to generate functional, insulin-producing stem cell-derived islets (iPSCs) in the laboratory which had shown preclinical proof-of-concept. In addition, Semma developed a semipermeable device made from two polyvinylidene fluoride membranes to be implanted subcutaneously. The device was designed to allow for vascularisation but impede entry of cells with a molecular weight >500 kDa such as immune cells and IgM antibodies. Vertex has taken the two acquired lead T1D programmes based on Semma's technologies, VX-880 (iPSCs islets + immunosuppression) and VX-264 (iPSCs islets +immunoprotecting device), into phase 1/2 clinical trials.

(2) Vertex acquired the private firm ViaCyte Inc focused on delivering novel stem cell-derived cell replacement therapies for USD320m in 2022. Viacyte had developed a human embryonic stem cell platform to generate insulin-secreting islet cells as well as a semipermeable pouch called Encaptra to be implanted subcutaneously. The first version of the device, VC-01, was tested in clinical trials in 2014. It proved to be safe but required immunosuppression, showed poor vascularisation and produced a host reaction against the implant leading to the death of most of the cells due to hypoxia. The improved version of this device, known as VC-02 or PEC-Direct, was designed as an open device with multiple large across-membrane pores to support vascularisation, thus requiring immunosuppression. In two small open-label clinical trials in 17 patients conducted in 2018-2021, cells achieved engraftment and insulin expression in 63% of devices at 3-12 months post-implant (source: Shapiro et al., 2021). In addition, ViaCyte had a development partnership with the gene-editing specialist CRISPR Therapeutics to jointly develop a drug for T1D. We will give more details about this product later on.

(3) Vertex licensed CRISPR Therapeutics' Crispr/Cas9 gene editing technology for use in its preclinical T1D cell-based programmes. The deal entitled CRISPR to receive an upfront payment of USD100m, up to USD230m in R&D milestone payments plus royalties on potential sales.

Figure 21: Overview of Vertex's T1D development strategy



Source: First Berlin Equity Research, Vertex Inc

VX-880 – iPSCs islets + immunosuppression for T1D patients with impaired hypoglycemic awareness and severe hypoglycemia VX-880 is Vertex's lead drug candidate using allogeneic, stem cell-derived islet cells delivered by an infusion into the portal vein in combination with immunosuppressive therapy. The ongoing phase 1/2 study in up to 17 patients entails three parts: (a) administers 50% of the targeted dose; (b) administers 100% of the targeted dose; and (c) concurrent dosing at full dose. The company reported data on six patients, whereas only two were in therapy for at least 1 year (i.e. 12 and 21 months); both patients achieved insulin independence with no severe hypoglycaemic events. One patient withdrew from the study.

VX-264 – iPSCs islets + immunoprotective device for T1D patients In March 2023, the FDA approved the initiation of the VX-264 phase 1/2 open-label study. By early August the first of projected 17 patients had been dosed.

CRISPR Therapeutics AG (Switzerland) Founded in 2013, CRISPR is a pioneering, development-stage, gene-editing company focused on developing drug candidates for serious diseases, including the rare genetic blood disorders sickle cell disease and beta-thalassemia (collaboration with Vertex who paid USD 900m upfront and may pay a further USD200m upon approval), immune-oncology (CAR-T cell therapy) and T1D, using its proprietary CRISPR/Cas9 platform. The company has a current market cap of ~USD3.9bn. In 2018, CRISPR and ViaCyte closed a partnership to jointly develop a drug candidate for diabetes, which resulted in the generation of VCTX210 (formerly PEC-QT).

VCTX210 – iPSCs islets + gene editing immunoprotection for T1D patients The lead programme started an open-label phase 1/2 clinical trial in up to 7 patients with T1D in January 2022. VCTX210 has been engineered through a combination of ViaCyte's embryonic stem cell line with CRISPR Therapeutics' gene editing technology to prevent their destruction by the patient's immune system, potentially eliminating the need to administer immunosuppressants.

Conclusions on the competitive environment Vertex and CRISPR are in our view two strong players with the currently most advanced regenerative medicine drug candidates for T1D offering a combo of iPSC cell islets implant + immunoprotection, either through macroencapsulation (closed device) or gene editing. Still, in the past, these technologies have shown some shortcomings, such as insufficient islet vascularisation, engraftment or dosing, and insufficient device immunoprotection accompanied by fibrosis. Even though the companies may in the meantime have improved their drug candidates and intend to fine-tune them during the phase 1/2 development process, these are quite challenging tasks. In addition, we see CRISPR cell and gene therapy applied to T1D as a complex and challenging endeavour which still needs time to bear fruits. We believe Sernova has developed an implantable Cell Pouch that enables unmatched vascularisation and islet grafting. The ease of access of the device implanted under the fat layer of the abdominal skin has the advantage that it can be removed at any time if needed (e.g., if the cells no longer function or an upgrade is sought), which is not the case with portal infusion to the liver. With this powerful device the company can generate robust and very competitive combo drug candidates for curing T1D, together with its world-class partners Evotec to produce high-quality iPSC islets and the University of Miami to make the conformal coating encapsulation for immunoprotection.

RELEVANT PEERS WITH CELL-BASED CANDIDATES IN LATE PRECLINICAL STAGE

We have identified five further biotech companies at the preclinical stage worthwhile keeping an eye on. Based on promising technologies, these second wave companies are developing drug candidates to cure T1D. The companies are Sigilon Therapeutics, TheraCyte, Procyon Technologies, Novo Nordisk, Technion and Adocia (see Table 7 below).

Table 7: Representative cell delivery systems in preclinical development

Company name	Device	Preclinical studies
Sigilon Therapeutics	Afibromer technology to generate the "Shielded Living Therapeutics"	Plans to start IND-enabling studies in H2 2023
TheraCyte	TheraCyte device	Tested in rodents and non-human primates
Procyon Technologies	Miniaturised electrochemical oxygen generator combined with immuno-isolating device	In discovery phase
Novo Nordisk	Electrospun nanofibrous device	Have been tested in immunocompetent mice
Technion	Bioengineered vascular bed	Have been tested in immunodeficient mice
Adocia	AdoShell	Have been tested in rats

Source: Wiley et al., 2022, Companies

Sigilon, Procyon and Adocia are the three major peers with preclinical products We believe the two most relevant players are Sigilon and Procyon, as reflected in attractive development agreements signed with leading T1D pharmaceutical companies. We also believe it is also important to watch the French biotech company Adocia.

Sigilon Therapeutics (US) Founded in 2016 as a spin-off from MIT, Sigilon has a platform to generate stem cell-derived cells such as iPSC islets which are then encapsulated in spheres using Sigilon's Afibromer technology. In the company's preclinical study with diabetic mice, encapsulated human ß-cells delivered to the peritoneal cavity immediately normalised blood glucose levels and maintained a normal level until their removal after 174 days. Sigilon's lead candidate SIG-001, which uses spheres harbouring allogeneic cells genetically engineered to express human factor VIII protein to treat the blood clotting disorder haemophilia, started a phase I clinical trial in 2020. However, the trial was placed on hold in July 2021 because of safety concerns. The third patient who received the highest number of cells developed antibodies to factor VIII. The company switched focus to its second lead candidate SIG-002 for T1D and later terminated the SIG-001 programme.

SIG-002 – iPSC islets + spheres encapsulation immunoprotection for T1D patients developed in partnership with giant Eli Lilly In 2018, Sigilon closed a partnership with the pharmaceutical giant and diabetes leader Eli Lilly. Lilly committed to an undisclosed equity investment in Sigilon, an upfront payment of USD63m and up to USD410m in development and commercialisation milestones. Under the terms of the partnership, Sigilon is to complete preclinical development of a lead candidate to IND at its own expense, while Lilly is to fund clinical trials and conduct commercialisation. Sigilon generated SIG-002 by using its Afibromer technology to encapsulate insulin-producing iPSC islets for the potential treatment of T1D. The drug candidate is set to start IND-enabling studies in H2 2023.

Lilly acquired Sigilon for USD 34.6m upfront; achievement of development milestones can expand the value of the deal to USD 310m The setback with SIG-001 put Sigilon under financing difficulties which ultimately led to it accepting the acquisition offer from its development partner Lilly in June 2023. Until then, the US private biopharmaceutical company was Sernova's last independent peer belonging to the first wave of most advanced regenerative medicine biotech players aiming to develop a cell therapy to cure T1D.

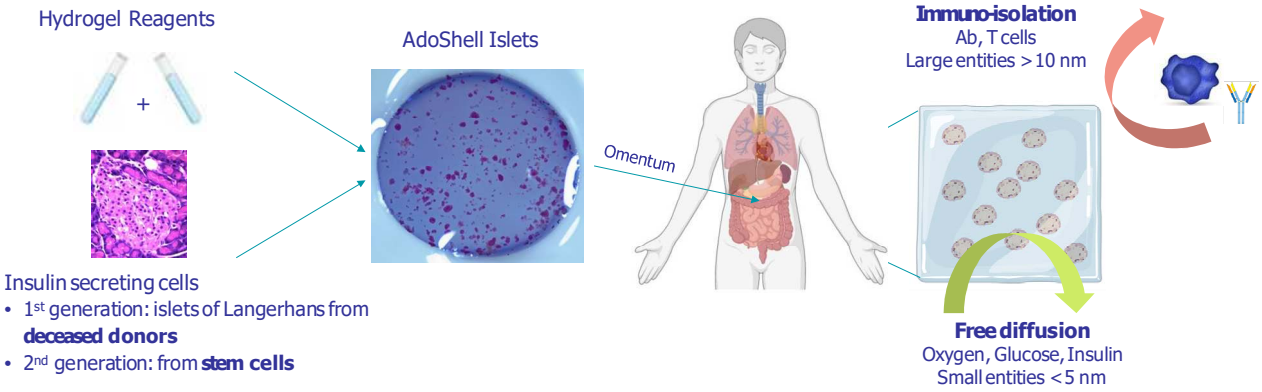
Procyon Technologies (US) Founded in 2016, Procyon is a startup biotech company spun off from the University of Arizona. The company developed a miniaturised electrochemical oxygen generator to be worn as a wristband. The generator is intended to provide oxygen via a delivery tube connected to cell clusters implanted in an immuno-isolated encapsulation device. One of the disadvantages of this device is that the implant needs to be in close proximity to the wristband, limiting the implant volume and likely also affecting hand movement. Therefore, the company plans to reduce the size of the oxygen generator to a size that will allow for implantation in other body sites (source: Wiley et al., 2022).

Partnership with the Danish drug maker Novo Nordisk In 2020, Procyon announced a collaboration to jointly develop a device for treating T1D with Novo Nordisk, a leading player in the diabetes segment. They intend to combine Procyon's expertise in oxygen-enabled implantable cell encapsulation devices with Novo Nordisk's expertise in stem cell-derived insulin-secreting cells. However, in our view this product still needs a few years until it is ready for IND filing.

Adocia SA (France) Founded in 2005, Adocia is a biopharmaceutical company that specialises in the development of innovative therapies for patients with diabetes, obesity and other metabolic disorders. Since its inception, the company has focused on developing novel formulations of insulin (e.g. ultra-rapid-acting insulin analogues and insulin delivery

systems) and other compounds to improve the treatment of diabetes. The company relies on four proprietary technology platforms (BioChaperone®, AdoShell®, AdOral® and AdoGel®) which it has used to develop its clinical-stage pipeline. AdoShell is an immunoprotective scaffold in preclinical investigation for transplantation of islets with the goal of curing T1D. According to Adocia, AdoShell ensures cell engraftment and long-term functionality in the absence of immunosuppression (see figure 22).

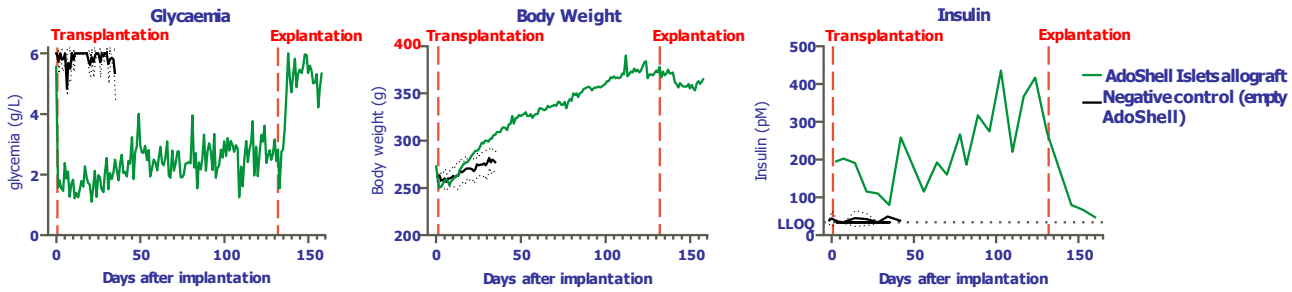
Figure 22: Adocia's immonoprotective scaffold for islets transplantation in T1D



Source: First Berlin Equity Research, Adocia SA

Preclinical study in diabetic rats Adocia's published data on its AdoShell immunoprotection technology is positive. The company reported that AdoShell enabled the achievement of glycaemia in a 132-day preclinical study in diabetic rats without the need of immunosuppression therapy. The company will give a presentation with an update of this study at the upcoming IPITA conference in October. The next development step for AdoShell is a proof-of-concept study in a large animal model, paving the way for a first in-human study. We believe the AdoShell technology looks promising, but it still has significant hurdles to overcome. We wonder how well AdoShell will be able to prevent direct as well as indirect activation of T-cells through antigens. This was one of the biggest challenges for Sernova's CC technology. In addition, the volume of islets encapsulated in AdoShell required for adequate insulin production can be quite large, and the only space that meets these requirements is the abdominal cavity, an environment with poor oxygen supply that does not support islet survival and engraftment well.

Figure 23: Preclinical study in diabetic rats in which glycaemia is controlled without immunosuppression during a 132-day study



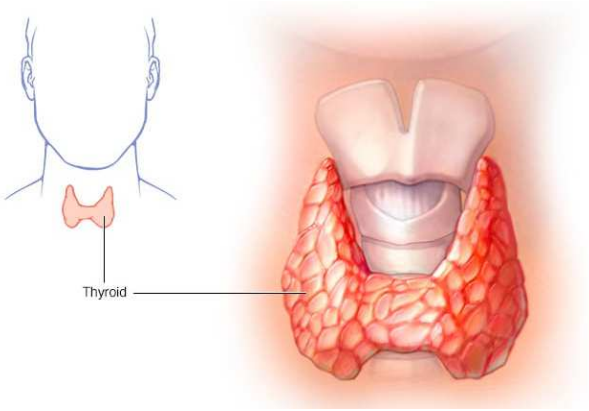
1. **Transplantation of AdoShell containing allogenic islets** in diabetic rat peritoneum at day 0
2. **Explantation** of the implant at day 132. Sacrifice of control group at day 35

Source: First Berlin Equity Research, Adocia SA

THE CELL POUCH APPLIED TO HYPOTHYROIDISM

Description of hypothyroidism Hypothyroidism is a medical condition characterised by the underproduction of thyroid hormones by the thyroid gland. The thyroid gland is a small butterfly-shaped gland located in the front of the neck (see Figure 24 below), and its hormones (mainly thyroxine, or T4, and triiodothyronine, or T3) play a critical role in regulating the body's metabolism. The thyroid gland affects all critical body functions, including heart rate, energy levels, and the rate at which energy is produced from nutrients. When the thyroid gland does not produce enough of these hormones, metabolism slows down, affecting the body. It can lead to a wide range of symptoms and complications such as fatigue, weight gain, dry skin, cold intolerance, constipation, muscle weakness, memory and concentration problems, depression, anaemia and cardiovascular disease. The causes of thyroid problems are largely unknown.

Figure 24: Thyroid gland



Source: Mayo Clinic

Prevalence in the US According to a recent study conducted by Wyne et al in 2022, the prevalence of hypothyroidism in the US has significantly increased over the past two decades; it amounted to ~11.7% as of 2019, affecting ~30m people age 18+. The American Thyroid Association (ATA) is more conservative in its projections, estimating that ~20m Americans have thyroid disease and up to 60% of these people are unaware of it.

Diagnosis and treatment For patients, it can be difficult to identify hypothyroidism because the symptoms can be easily confused with other conditions. Following a clinical examination, the way a doctor can diagnose hypothyroidism is a blood test called the thyroid stimulating hormone (TSH) test to measure the thyroid activity, sometimes followed by the T4 and T3 tests. For patients suspected of having Hashimoto's thyroiditis (an autoimmune form of hypothyroidism), doctors may order antibody tests targeting the thyroid (anti-TPO and anti-thyroglobulin). The most common therapeutic treatment for hypothyroidism is levothyroxine, a synthetic version of T4, the main hormone produced by the thyroid gland. Levothyroxine restores adequate hormone levels and reverses the symptoms of hypothyroidism, although patients must take the drug for life. According to Wyne et al., >78% of patients received this drug in 2019.

Thyroidectomy and its implications Thyroidectomy is a surgical procedure in which all or part of the thyroid gland is removed. The main reasons for conducting a thyroidectomy include management of thyroid cancers and benign (non-cancerous) diseases that include nodules, goitre, and hyperthyroidism. In the US, it is estimated that >150k thyroidectomies are performed each year and there were ~52k new cases of thyroid cancer in 2019, suggesting that thyroid surgeries are done largely to treat benign conditions (source: Duong et al., 2022). Some patients undergoing partial thyroidectomy and all patients undergoing total thyroidectomy will require lifelong daily thyroid hormone replacement therapy consisting

primarily of levothyroxine. A major challenge is finding the right dose so that the patient does not receive too much or too little of the hormone. As a result, many patients do not achieve the appropriate hormone level and experience several symptoms of hypothyroidism, including lethargy, weight gain, fatigue, and “brain fog” (sources: Hannoush et al., 2016; Okosieme et al., 2011).

Sernova’s autologous approach for the treatment of postoperative hypothyroidism The company’s strategy is to harvest healthy tissue from each patient’s own thyroid gland that has been removed during thyroidectomy and transplant this tissue into the pre-implanted vascularised Cell Pouch. The company anticipates that each patient’s own thyroid tissue will regain the natural ability to release thyroid hormones in the Cell Pouch, thereby curing the patient.

Preclinical development in collaboration with Dr Wiseman at the University of British Columbia Sernova’s preclinical activities regarding its Cell Pouch for the treatment of postoperative hypothyroidism have been conducted in collaboration with Professor Dr Sam Wiseman, Director of Research in the Department of Surgery at the University of British Columbia Faculty of Medicine in Vancouver, BC, Canada. He is an internationally recognised expert in the surgical treatment of thyroid disease and has also been a member of Sernova’s Scientific Advisory Board since 2021.

Study in mice showed the viability of human thyroid tissue transplanted into a pre-implanted Cell Pouch – the tissue survived and produced thyroglobulin Dr Wiseman studied the transplantation of healthy human thyroid tissue taken from three patients undergoing surgery for treatment of benign disease into a pre-vascularised Cell Pouch in a preclinical mouse model. The research team used nude laboratory mice from a strain with a genetic mutation that has an inhibited immune system due to a lack of T-lymphocytes. The results were published in a peer-reviewed journal in 2022 (see: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8775351/). The study confirmed that the human thyroid tissue transplanted into the Cell Pouch survived robustly and permanently released human thyroglobulin into the bloodstream with no adverse effects during the three-month study period. Thyroglobulin, a protein made by the thyroid gland to produce T3 and T4, was used as a biomarker efficacy measure in the study.

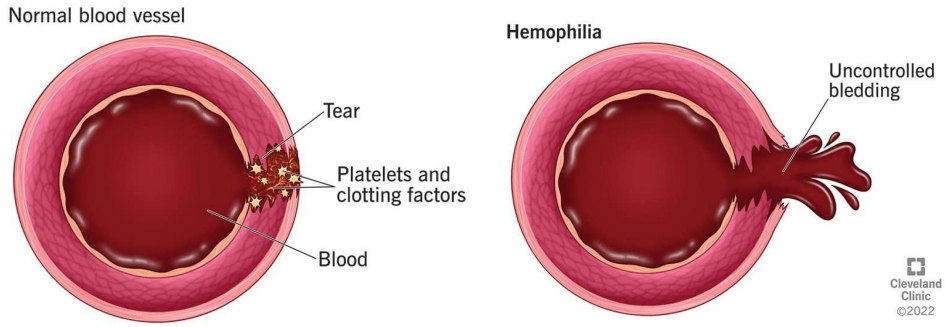
Proof-of-concept preclinical study in mice demonstrated that auto-transplantation of thyroid tissue into the Cell Pouch can compensate for removal of the thyroid gland The results of this animal study were published in January 2023. The research team implanted the Cell Pouch six weeks ahead of the total thyroidectomy. The thyroid gland was then removed and implanted in the Cell Pouch. The study design included a control group that received the Cell Pouch implant and had the thyroid removed but did not receive a thyroid transplant. The team monitored circulating thyroid hormones T3 and T4 weekly over several months. The treatment group saw T3/T4 levels drop after the surgery but recover to normal/close to normal levels after transplantation. In the control group, the level declined and remained below baseline until the end of the experiment. The findings further demonstrate the viability of the Cell Pouch for this new indication. New data from radio-isotope uptake imaging and histologic examination presented at the American Thyroid Association Annual Meeting 2023 confirmed the presence of healthy and functional thyroid tissues within the Cell Pouch six months after reimplantation.

The company is completing preclinical studies and preparing the dossier – IND or CTA submission in postoperative hypothyroidism set for H1 2024 Sernova is currently in discussions with Canadian and US regulatory authorities (Health Canada/FDA) to pre-determine how the product will be regulated in each jurisdiction to choose the most efficient regulatory pathway. The company plans to submit a clinical trial application (CTA) and/or an IND application in H1 2024 and initiate a clinical trial in patients with planned thyroidectomy for benign disease in H2 2024.

THE CELL POUCH APPLIED TO HAEMOPHILIA A

Description of Haemophilia A Haemophilia A is a rare, severe genetic bleeding disorder caused by a deficiency or dysfunction of clotting factor VIII. As a hereditary condition resulting from an F8 gene mutation in the X chromosome, it mainly affects males with an XY genotype. Women with an XX genotype are primarily carriers of the disease and are sometimes affected, usually in a mild form. The condition leads to prolonged or spontaneous bleeding, both externally and internally.

Figure 25: Haemophilia A



Source: Cleveland Clinic

Prevalence in the US According to a recent study by the US Centers for Disease Control and Prevention (CDC), the estimated prevalence of haemophilia A is 12 cases per 100k US males and there are about 30-33k people with the condition in the US. Haemophilia is classified as mild, moderate, or severe, depending on the level of clotting factor in the blood. Of all men with haemophilia, slightly more than 40% have the severe form of the disease.

Diagnosis and treatment Initial suspicion of haemophilia A often arises due to clinical symptoms such as bruising or excessive bleeding after minor injuries or surgery, spontaneous bleeding episodes without apparent cause, especially into joints or muscles and family history of bleeding disorders. The disease can be diagnosed through several blood tests, such as complete blood count (CBC), prothrombin time (PT) test & activated partial thromboplastin time test to see how quickly blood clots and specific clotting factor test(s). The main approach for the treatment of haemophilia A involves preventing life-threatening bleeding, including muscle and joint bleeding, through prophylactic infusions of factor VIII concentrates. This replacement therapy helps to replace the missing or deficient factor VIII, allowing the blood to clot more effectively. There are two types of clotting factor therapies (1) plasma-derived generated from human blood and (2) recombinant which is generated in a lab through the use of DNA technology. > 75% of haemophilia patients take a recombinant product. Replacement therapy still has shortcomings, such as immunogenicity (immune response against the product), which eliminates the therapeutic effect. The incidence of immune antibodies against factor VIII occurs in about 25–35% of patients with severe disease (source: Marchesini et al., 2021). The estimated annual cost of treatment with protein replacement therapy for haemophilia A amounts to an average of USD200k per patient (source: George et al., 2015). In 2017, the FDA approved Roche's coagulating-enhancing targeted therapy Hemlibra, which offers comparable or better efficacy than replacement therapy, at an annual list price of USD482k in the first year and USD448k after that (source: Fierce Biotech).

Gene therapy is also an emerging therapy approach for haemophilia A, aiming to provide a long-term or permanent solution to the disorder by addressing its genetic basis. In June, the FDA approved the first gene therapy for severe disease, Biomarin's Roctavian, which is priced at USD 2.9m. A second gene therapy candidate from Roche's subsidiary Spark Therapeutics, SPK-8011, is expected to enter phase 3 soon.

Sernova's approach for haemophilia A: Cell Pouch + ex-vivo gene therapy – support from HemAcure Consortium In this process a blood sample is taken from the patient to correct the genetic defect in certain isolated cells ex-vivo. Subsequently, these cells are expanded and transplanted into a Cell Pouch previously implanted in the patient. These cells are expected to achieve a constant release of factor VIII. To support this endeavour, Sernova formed the HemAcure Consortium, a European team of experts in this field. This Consortium was funded with a grant of €5.6m from the EU Horizon 2020 programme to conduct preclinical safety and efficacy studies for GMP-compliant cell therapy.

Preclinical study demonstrated safety and long-term improvement in blood clotting in haemophilia A mouse model The results were published in the scientific journal Molecular Therapy: Methods & Clinical Development in December 2021 (see: https://www.cell.com/molecular-therapy-family/methods/fulltext/S2329-0501(21)00172-8).
The research team isolated endothelial cells that line blood vessels and have been shown to produce factor VIII from haemophilia A patients, then inserted an altered human form of the F8 gene to correct the mutation using a lentivirus. Then they expanded the lentivirus-corrected blood outgrowth endothelial cells (BOECs) in a culture medium. Once the team determined in vitro that the BOECs were able to secrete factor VIII, they implanted them in three doses in pre-implanted, vascularised Cell Pouches of immunodeficient NSG laboratory mice with haemophilia A. All implanted BOECs in all doses proved to be safe, with no visible tumours in the mice. The efficacy was determined by a tail bleeding test comparing haemophilia A mice with and without BOEC implants after 4 months of the implant. The BOEC mice showed a substantial clotting increase reflected in a lower volume of blood recovered. Importantly, the level was similar to healthy NSG mice, confirming that a gene correction had been achieved through the BOEC implant in the Cell Pouch. These results were encouraging and demonstrated the viability of the procedure. Still, gene technology is a very complex field and there is substantial room for improvement particularly related to two critical points; (1) the vector to be used – so far a lentivirus – and; (2) the cell target to address before the programme is ready to enter human clinical trials.

FINANCIAL HISTORY AND OUTLOOK

Sernova's financial statements are prepared in accordance with International Financial Reporting Standards (IFRS). The company's financial year differs from the calendar year and runs from 1 November to 31 October of the following year.

FINANCIAL HISTORY

Income statement FY 2021/22 Sernova's financial statements are typical of a development-stage biotech company. The company is generating no revenues and is loss-making. In FY 21/22, OPEX increased substantially to CAD24.8m (FY 20/21: CAD6.9m), driven by the combined effect of higher R&D and G&A expenses. However, CAD7.2m or 41% of the total increase, is related to non-cash share-based compensation expense. Sernova's incentive plan has two components, (I) fixed share options (options) and (II) deferred share units (DSUs) which were established based on the company's philosophy and earlier work conducted by the independent compensation consultant Marsh & McLennan. The share-based expense figure booked in FY 21/22 was unusually high because it represented two fiscal years of "catch-up" stock options and DSU awards and initial grants for new employees, combined with a higher Black Scholes-based stock option valuation following the substantial share price appreciation in 2022 vs the level seen in 2020-2021.

G&A expenses rose YoY by CAD5.6m, or 242%, to CAD 7.9m (FY 20/21: CAD2.3m), with 65% of this increase coming from non-cash stock option compensation. Excluding these non-cash costs, G&A grew by 89% to CAD4.1m. The main reasons for the G&A increase were higher (1) personnel expenses due to staff expansion, (2) consulting/professional fees due to business development, the expansion of IR activities, and (3) up-listing to the TSX.

R&D expenses increased by CAD12.3m, or 264%, to CAD16.9m in 2022 (FY 20/21: CAD4.6m). Excluding the effect of the non-cash share-based compensation expense, R&D costs increased YoY by CAD8.7m or 191% to CAD13.2m. The higher R&D spending was chiefly related to development progress in (1) US phase 1/2 study of the 1G Cell Pouch programme in T1D, (2) preclinical activities of the 2G Cell Pouch using iPSC islets in cooperation with Evotec for T1D, and (3) expansion of the R&D team.

The EBIT loss widened to CAD-24.8m (2021: CAD-6.9m). The net financial result grew to CAD333k, chiefly thanks to higher interest income of CAD577k (FY 20/21: CAD71k) Sernova reported a net loss of CAD-24.8m (FY 20/21: CAD-7.0m), which equates to CAD-0.09 p/s (FY 20/21: CAD -0.03 p/s).

Table 9: Income statement 2021/22 vs 2020/21 and 9M 2022/23 vs 9M 2021/22 (KPIs)

in CAD'000	2021/22	2020/21	Delta	9M 2022/23	9M 2021/22	Delta
Revenue	**0**	**0**	n.a.	**0**	**0**	n.a.
General & Administrative	-7,857	-2,299	n.a.	-6,323	-5,949	n.a.
Research & Development	-16,897	-4,638	n.a.	-22,367	-10,353	n.a.
OPEX	-24,754	-6,937	n.a.	-28,690	-16,302	n.a.
EBIT	**-24,754**	**-6,937**	n.a.	**-28,690**	**-16,302**	n.a.
Net financial result	333	-29	n.a.	1,396	92	n.a.
Net income	**-24,421**	**-6,966**	n.a.	**-27,294**	**-16,210**	n.a.

Source: Sernova Corp

9M 2022/23 income statement – ongoing OPEX expansion due to development activity with focus on the Cell Pouch 1G and 2G programmes for T1D OPEX widened to CAD28.7m (9M 21/22: CAD16.3m) due to higher development expenses of CAD22.4m (9M 21/22: CAD10.4m) and G&A of CAD6.3m (9M 21/22: CAD5.9m). Incremental R&D spend

was chiefly directed at the 1G phase Cell Pouch 1/2 study that included a higher number of patients from the added second cohort and progress in the 2G Cell Pouch programme using iPSC islets. We note that 9M 21/22 R&D expenses included one-off share-based compensation of approximately CAD2.4m. The net financial result increased to CAD1.4m (9M 21/22: CAD92k) chiefly due to higher interest income of CAD1.2m and a foreign exchange gain of CAD217k (fluctuations in the CAD/USD exchange rate). The net result amounted to CAD-27.3m (9M 21/22: CAD-16.2m).

Balance sheet FY 21/22 and 9M 22/23 Following successful capital measures, Sernova's cash position including short-term investments increased to CAD 49.8m at YE 21/22 (YE 20/21: CAD27.9m), but fell to CAD31.0m at 9M 22/23 due to funding of ongoing operations. Based on the company's planned burn rate, management expect that the cash runway will reach into Q4 2024. Similarly, Sernova's equity position increased to CAD 47.6m at YE 21/22 (YE 20/21: CAD28.1m), dropping to CAD23.3m at 9M 22/23. The equity ratio (ER) declined to 70% at 9M 22/23 (YE 20/21 ER: 94%). Property, plant and equipment increased from CAD176k in YE 20/21 to CAD429k in 9M 22/23 chiefly due to purchase of laboratory equipment for R&D. Accounts payables/accrued liabilities increased from CAD1.4mat
YE 20/21 to CAD 4.6m at YE 21/22 and CAD 9.8m at 9M 22/23 and are also chiefly related to R&D and clinical trial expenses (i.e. cooperation with Evotec to develop the iPSC cells).

Table 8: Balance Sheet FY 2021/22, FY 2020/21 and H1 2022/23 (KPIs)

in CAD'000	2021/22	2020/21	Delta	9M 2022/23	2021/22	Delta
Cash	3,776	27,874	-86%	17,778	3,776	*371%*
Short-term investments	46,000	0	-	13,260	46,000	*-71%*
Account receivables & others	1,315	453	190%	961	1,315	*-27%*
Current Assets, Total	**51,091**	**28,327**	80%	**31,999**	**51,091**	*-37%*
Property plant and equipment	402	176	128%	429	402	*7%*
Intangible assets	517	717	-28%	367	517	*-29%*
Deposits	224	212	0	259	224	*16%*
Other LT assets	251	388	-35%	148	251	*-41%*
Non-Current Assets, Total	**1,394**	**1,493**	-7%	**1,204**	**1,394**	*-14%*
Accounts payable	4,600	1,358	239%	9,761	4,600	*112%*
Other current liabilities	140	117	19%	159	140	*14%*
Other LT liabilites	136	276	-51%	14	136	*-89%*
Total Liabilities	**4,876**	**1,752**	178%	**9,935**	**4,876**	*104%*
Equity	47,608	28,068	70%	23,268	47,608	*-51%*
Equity ratio	91%	94%	-	70%	91%	-

Source: Sernova Corp

Cash flow statement FY 2021/22 In FY 21/22, negative cash flow from operating activities increased to CAD-14.4m (FY 20/21: CAD-6.8m). The increase is chiefly related to higher operating expenses in connection with R&D. As is the case with most biotech companies, CAPEX plays a minor role at Sernova. The company's clinical trials are conducted by external Clinical Research Organisations (CROs), and the Cell Pouch and iSPC islets are produced by external partners (i.e. US GMP-certified contract manufacturer and Evotec). CAPEX rose to CAD329k in FY 21/22 from CAD17k in FY 20/21 chiefly due to purchase of laboratory equipment and cash flow from investing expanded to CAD46.3m in connection with the investment of funds in short-term marketable securities. In FY 21/22, cash flow from financing activities increased to CAD36.7m, of which CAD27.1m stemmed from a private placement with the partner Evotec and CAD 9.4m from the exercise of warrants and options. The remaining outstanding warrants expired in Q1 2023. Thus, net cash flow in FY 21/22 came in at CAD-24.1m (FY 20/21: CAD23.9m).

Table 11: Cash flow statement 2021/22 vs 2020/21 and 9M 2022/23 vs 9M 2021/22 (KPIs)

in CAD'000	2021/22	2020/21	Delta	9M 2022/23	9M 2021/22	Delta
Operating cash flow	-14,421	-6,844	n.a.	-18,988	-9,668	*n.a.*
Cash flow from investing	-46,341	-229	n.a.	32,605	-39,323	*n.a.*
Cash flow from financing	36,665	30,997	18%	385	24,134	*-98%*
Net cash flow	-24,098	23,925	n.a.	14,002	-24,856	*n.a.*

Source Sernova Corp

Cash Flow Statement 9M 2022/23 In 9M 22/23, operating cash flow rose significantly to CAD-19.0m (9M 21/22: CAD-9.7m) due to increased development activity. CAPEX declined to CAD99k (9M 21/22: CAD310k), and cash flow from investment amounted to CAD32.6m (9M 21/22: CAD-39.3m) due to the change in marketable securities. Financing cash flow was CAD385k, chiefly stemming from grant contribution receipts and research collaboration advances. In 9M 21/22, cash flow from financing amounted to CAD24.1m due to a capital increase (CAD20.3m), exercise of warrants/options (CAD3.8m) and grants receipts (CAD224k) less payments for lease liabilities (CAD126k). The net cash flow came in at CAD14.0m (9M 21/22: CAD-24.9m).

FINANCIAL OUTLOOK

Income statement Given that Sernova's lead drug candidate 1G Cell Pouch for T1D is still undergoing phase 1/2 development, we anticipate first revenues from its potential market launch by 2028. We have assumed the potential market launch of the 2G and 3G products as well as the 1G product in the second indication of hypothyroidism in the period 2030-2032.

We have assumed that the company will finance further pipeline development until a sustainable breakeven is achieved through a combination of raising funds from investors and upfront payments from licensing the drug candidates after successful phase 1/2 results. We project that the out-licensing of US rights for the 1G-3G products in T1D and the 1G in hypothyroidism will lead to upfront payments of CAD40m in FY 23/24E and a further CAD20m in FY 25/26E. We expect that Sernova's partners will finance and conduct the expensive phase 3 trials in the four programmes. For the time being, we have left potential development in the less lucrative regions of Europe and Asia out of our projections and leave this as upside.

Our FY 22/23 projections are the baseline for our projections going forward. Given that the expensive 1G phase 1/2 study with two cohorts is ongoing, we forecast OPEX of CAD38.8m in FY 22/23, above the previous year's level of CAD24.8m. We forecast a positive net financial result of CAD1.4m. We thus expect a net loss of CAD37.4m. Going forward, we project OPEX to increase slightly to CAD39.2m in FY 23/24 and decline to CAD34.4m in FY 24/25 once a partner takes over the expensive phase 3 trials for the lead product. Our scenario includes expenses for the preclinical ongoing R&D and the upcoming phase 1/2 trials of the 2G and 3G in T1D and 1G in hypothyroidism. We give an overview of our financial projections in Table 12 below.

Table 12: Income Statement KPIs FY 19/20-24/25E

in CAD'000	2019/20	2020/21	2021/22	2022/23E	2023/24E	2024/25E
Revenue	0	0	0	0	40,000	0
General & Administrative	-2,501	-2,299	-7,857	-8,600	-9,200	-9,400
Research & Development	-2,759	-4,638	-16,897	-30,200	-30,000	-25,000
OPEX	-5,260	-6,937	-24,754	-38,800	-39,200	-34,400
EBIT	**-5,260**	**-6,937**	**-24,754**	**-38,800**	**800**	**-34,400**
Net financial result	-62	-29	333	1,400	500	100
Net income	**-5,321**	**-6,966**	**-24,421**	**-37,400**	**1,300**	**-34,300**

Source: First Berlin Equity Research, Sernova Corp

Balance sheet We estimate the company will progressively spend cash in the clinical development of its pipeline and its operations in the period FY 22/23-24/25 (see Table 13). Given that current cash may reach until approximately Q4 23/24, we look for Sernova to raise non-dilutive funding of CAD60m from licensing deals in FY 23/24 and FY 25/26 and CAD40m from capital increases over the period 24/25-26/27 to extend the cash runway further. In our scenario, we project that the cash and other ST investments will decline from CAD49.8 at YE 21/22 to CAD20.1m at YE 24/25. As Sernova has done in the past, we assume that it will continue financing some of its personnel expenses with stock payments. With the above-mentioned capital measures, the company will be capable of adequately funding operations until the business model of Sernova becomes self-sustaining in FY 27/28 (assuming a successful launch of 1G Cell Pouch for T1D in FY 27/28). At that point, the company will generate enough cash to finance further organic growth. This will be reflected in a progressively growing cash position from 2028.

Table 13: Balance sheet KPIs FY 19/20-24/25E

in CAD'000	2019/20	2020/21	2021/22	2022/23E	2023/24E	2024/25E
Cash	3,949	27,874	3,776	6,801	25,915	20,056
Short-term investments	0	0	46,000	13,200	0	0
Account receivables & others	656	453	1,315	1,150	1,025	930
Current Assets, Total	**4,605**	**28,327**	**51,091**	**21,151**	**26,940**	**20,986**
Property plant and equipment	203	176	402	462	498	550
Intangible assets	917	717	517	317	117	0
Deposits	0	212	224	224	224	224
Other LT assets	0	388	251	124	24	24
Non-Current Assets, Total	**1,120**	**1,493**	**1,394**	**1,127**	**863**	**798**
Accounts payable	878	1,358	4,600	7,510	7,800	7,644
Other current liabilities	-	117	140	152	163	175
Other LT liabilites	703	276	136	109	87	70
Total Liabilities	**2,551**	**1,752**	**4,876**	**7,771**	**8,050**	**7,888**
Equity	3,174	28,068	47,608	14,506	19,752	13,895
Equity ratio	55%	94%	91%	65%	71%	64%

Source: First Berlin Equity Research, Sernova Corp

Cash flow statement We expect further product development activity will result in falling negative operating cash flows in the period 22/23 - 24/25. We forecast a negative operating cash flow of CAD-29.5m for 22/23, turning positive at CAD6.1m in 23/24 due to an upfront payment of CAD40m from licensing, before turning negative again at CAD-30.6m for 24/25. We expect Sernova to continue outsourcing the clinical development of its lead programmes to Clinical Research Organisations (CROs) and therefore see minor CAPEX investment in the range of CAD 150-180k p.a. in the forecasting period. Our cash flow from investing projections chiefly reflect divestment of marketable securities to increase liquidity. In 24/25 and 26/27 we have assumed capital increases of CAD25m and CAD15m respectively. We expect net cash flow to total CAD3.0m in 22/23 and provide an overview of our cash flow projections in Table 14 below. Going forward, we project that a potential approval and commercialisation of the 1G Cell Pouch for T1D in 27/28 will drive strengthening operating performance, having a positive impact on the company's free cash flow and net cash flow.

Table 14: Cash flow statement KPIs FY 19/20-24/25E

in CAD'000	2019/20	2020/21	2021/22	2022/23E	2023/24E	2024/25E
Operating cash flow	-3,939	-6,844	-14,421	-29,516	6,140	-30,625
Cash flow from investing	994	-229	-46,341	32,620	13,050	-160
Cash flow from financing	5,097	30,997	36,665	-79	-76	24,926
Net cash flow	2,152	23,925	-24,098	3,025	19,114	-5,859

Source: First Berlin Equity Research, Sernova Corp

NEWSFLOW

In our view, Sernova's stock price will be driven by news about its pipeline as well as by the achievement of financial milestones. We expect the company to make a number of announcements during the coming 12-18 months which will act as catalysts for the stock. These include:

Pipeline

- Update of the ongoing phase 1/2 study of the 1G Cell Pouch product for T1D patients in the US planned for Q4 2023. The final headline results of the phase 1/2 study and a meeting with the FDA to discuss the design of a phase 3 study should be due in H2 2024. The potential phase 3 study may start in early 2025.
- Details on progress of the development of the conformal coating technology for the 3G product in T1D will be presented at the IPITA-IXA-CTRMS Joint Congress in the US on 26-29 October 2023.
- Filing of the 1G Cell Pouch product for patients with hypothyroid disease in the US is planned for H1 2024. The phase 1/2 study should start in H2 2024.
- Filing of the 2G product for T1D patients in the US is planned for H1 2025; the phase 1/2 study should start in late 2025.

Financial results

The company publishes financial results and a "Management's Discussion and Analysis" (MDA) report on a quarterly basis. We expect the publication of financial results, including detailed updates on the business development and the R&D pipeline, as follows:

- FY 22/23 results and MDA report are due on 29 January 2024.
- Q1 23/24 results and MDA report are due on 18 March 2024.
- Q2 23/24 results and MDA report are due on 14 June 2024.

MANAGEMENT

MANAGEMENT BOARD

Management strengthened Sernova expanded its Management Board with two highly experienced executives: (1) On 5 September, the company announced that Cynthia Pussinen has been appointed as the new Chief Executive Officer. She brings extensive Big Pharma and biotech experience at the C-level and other senior positions to Sernova. Former President & CEO Philip Toleikis, PhD, remains on the Board, transitioning to the Chief Technical Officer role. (2) In July the company announced the appointment of Modestus Obochi, PhD, MBA, a seasoned dealmaker and strategic leader with 25+ years of biotech and pharmaceutical industry experience, as Chief Business Officer effective 8 September 2023. With the bolstered management team, the company wants to transition its focus from technology and drug development towards business development and commercialisation. This includes paving the way for partnering deals for the products after achieving the relevant development milestones.

Cynthia Pussinen, Chief Executive Officer, Member of the Board of Directors

Ms Pussinen joined Sernova as CEO on 5 September. Her expertise spans the drug development continuum from research through commercialization. She has led the development, licensure, commercialisation and/or subsequent delivery to patients, of more than 15 new medical therapies for patients globally, including Obizur® (Antihemophilic Factor (Recombinant), Porcine Sequence), Eraxis® (anidulafungin), Zmax® (azithromycin extended-release) and LUXTURNA® (voretigene neparvovec-rzyl), the first gene therapy approved in both the US and the EU. Most recently, Ms. Pussinen was the Chief Technical Officer for the commercial-stage gene therapy company Spark Therapeutics Inc, a fully integrated subsidiary of the Roche Group. Prior to joining Spark in 2021, Ms. Pussinen served six years as President and CEO of Ipsen Biomeasure and Ipsen Biosciences in the US, the R&D focused subsidiaries of Ipsen. She was instrumental in leading and executing the divestiture of Obizur® and its associated physical manufacturing infrastructure to Baxter. Ms. Pussinen was also the Executive Vice President, Technical Development, Operations & Supply Chain for Actinium Pharmaceuticals Inc and the Global Vice President and General Manager, Life Sciences and Specialty Chemicals for Honeywell International. Early in her career Ms Pussinen spent more than 18 years at Pfizer in a variety of increasingly responsible leadership roles across various functional areas. Ms Pussinen earned a Master of Science in R&D management from Rensselaer Polytechnic Institute and a Bachelor of Science in chemistry with a minor in engineering from the University of Connecticut. She is lean six sigma certified, recognised as a mentor through the Healthcare Businesswomen's Association (HBA), and was recipient of the WEST (Women in the Enterprise of Science and Technology) Giving Back award.

Philip M. Toleikis, PhD, Chief Technology Officer, Member of the Board of Directors

Dr Toleikis was appointed CTO of Sernova on 5 September 2023, after serving as the company's CEO since 2009. He is an expert in the development of disruptive medical technologies and the evolution of cell therapy therapeutics. Dr Toleikis has led the development of Sernova's integrated Cell Pouch System cell therapy platform with the vision of establishing a 'functional cure' for chronic diseases, such as diabetes, thyroid and rare diseases. He has contributed to Sernova's core IP development and secured in-licensing agreements, and the acquisition of Sernova's core technologies, including most recently iPSC stem cell-derived (Evotec) and cellular immune protection (University of Miami) technologies. Dr Toleikis has evolved and grown Sernova's international shareholder base; key banking, collaboration, strategic partner, pharma and institutional relationships; and

secured funds of >CAD 100m from equity capital, convertible debenture issuance, and non-dilutive research funding. Prior to joining Sernova, Dr Toleikis consulted for various pharmaceutical, medical device and combination product companies. Previously he was VP, R&D at Angiotech Pharmaceuticals Inc, which developed and partnered with Boston Scientific in commercialising one of the first drug-eluting coronary stents. Dr Toleikis is the author of over 100 issued patents, patent applications, and numerous scientific publications involving transplantation, metabolic, cardiovascular, oncology, and autoimmune disease. He obtained his PhD in the Department of Medicine, Pharmacology and Therapeutics from the University of British Columbia, his MSc at the University of Michigan, and BA at the University of Vermont.

David Swetlow, Chief Financial Officer

Mr Swetlow joined Sernova in 2019 as CFO. He brings over 20 years of experience as CFO and further financial leadership, board & advisory positions within the biotech and other high-tech industries. He held leadership roles predominantly for start-up acceleration and at high growth-stage companies, including multiple firms listed on the TSX and Nasdaq, such as QLT Inc, Protox Therapeutics Inc, and Xillix Technologies Corp. Mr Swetlow's biotech experience includes biopharmaceutical, medical device, and drug/device combination technologies and products. He served on the Board of Directors for the Saskatchewan Science Center and was a member of its Finance, Audit & Risk Committee from 2018 to 2021. Previously he also served on the council of CMC-Saskatchewan, the provincial institute of CMC-Canada (the Canadian Association of Management Consultants), as Public Representative appointed and re-appointed for three-year terms by the Brad Wall led provincial government. Before that, he was also a co-founding Director of the TSX Venture company OMNItech Capital Corp and served as Director and Audit Committee Chairman for successor companies One Person Health Sciences Incand HealthPricer Interactive Ltd. He has an entrepreneurial nature; he has thus also started and run a few businesses of his own during his career. Mr Swetlow holds a Bachelor of Business Administration degree from Simon Fraser University (SFU) and obtained his CA designation while at Deloitte.

Modestus Obochi, PhD, MBA, Chief Business Officer

Dr Obochi will join Sernova on 8 September 2023. He is a veteran dealmaker and strategic leader with over 25 years of biotech and pharmaceutical industry experience. Dr Obochi joins Sernova from the US contract development and manufacturing organisation (CDMO) Phlow Corp, where he served as Executive Vice President of Strategy and Business Development. In that role, he led the design, development, and execution of corporate strategy and business development plans. He also managed the due diligence, structuring, and negotiations of all transactions, including licensing deals, product acquisitions, partnerships, M&A, and strategic investments. Prior to his role at Phlow Corp, Dr Obochi held several executive-level commercial and business development roles at leading pharmaceutical companies including Pfizer, Hospira, and Baxter International, and has previously consulted for several biotechnology companies. Most notably, in these roles, Dr Obochi has helped corporations raise significant capital and has successfully structured and closed multiple strategic transactions worth over USD 5bn. Dr Obochi holds a PhD in Immunology from the University of British Columbia, Vancouver, and an MBA from the Beedie School of Business of Simon Fraser University, Vancouver. He has published over 30 manuscripts, including journal articles and symposia abstracts, and is an inventor on several patents, including one on cell transplantation.

Frank Shannon, VP of Clinical Development and Regulatory Affairs

Mr Shannon has been the VP of Clinical Development and Regulatory Affairs) of Sernova since 2021. He has a track record of >25 years of proven experience in clinical development and regulatory affairs. He has served in senior-level positions within the international medical device, pharmaceutical, and biologic industries, where he achieved commercial

goals through innovative risk management and execution strategies, to obtain marketing approval of products. Most recently, Mr Shannon served as VP of Clinical Development, Regulatory Affairs and Quality at Ripple Therapeutics, a spin-out of Interface Biologics where he has served in the same capacity since 2016. Prior to these appointments, he held various senior clinical/regulatory positions at Baxter International, St. Jude Medical, Boehringer-Ingelheim, Hoffmann-La Roche/Roche Laboratories, Inc, Genentech Canada, Inc., and Ciba-Geigy Canada, Ltd.

Christopher Barnes, VP Investor Relations

Mr Barnes has been VP Investor Relations of Sernova since 2021. He is a capital market specialist with > 25 years of experience. Most recently, he worked on capital markets in senior VP positions as an IIROC registered institutional sales person with three Toronto-based investment boutiques, including Fraser Mackenzie, Octagon Capital and Pace Securities covering accounts in Canada, the US and Europe. Previously, he was Director of investor relations for Extendicare Inc, a large North American nursing home company listed on the TSX and NYSE. Before that, he served as investor relations consultant at his own firm Barnes Capital Communications. Mr Barnes holds a bachelor's degree in English and Political Science from Laurentian University, plus he completed the Richard Ivey School of Business at University of Western Ontario, Strategic Investor Relations diploma.

BOARD OF DIRECTORS

Brett Whalen, Chairman

Mr Whalen has >20 years of investment banking and M&A expertise, primarily spending over 16 of those years at the wealth management firm Dundee Corporation (Dundee Corp). Most recently, Mr Whalen served as VP and Portfolio Manager of Goodman and Company (a division of Dundee) and was President and CEO of the CMP Group of Companies, where he managed over CAD 1bn of assets. Prior to that, he worked at Dundee Corp as an investment banker, where he was directly involved in completing approximately CAD 2bn in M&A deals and directly raised over CAD 10bn in capital globally. He has also held Board seats in several TSX-listed and privately held companies. He holds a BA (Honours) degree in Economics and Finance from Wilfrid Laurier University and is a CFA Charterholder.

Dr Daniel Mahony, Board Member

Dr Mahony currently serves as Chairman of Trellus Health plc, an AIM LSE-listed digital health company. Dr Mahony brings over 25 years of global healthcare investment, management and research experience covering biotechnology, medical technology, and healthcare service sectors. He was previously Entrepreneur-in-Residence at Evotec, where he was responsible for managing the company's equity investment portfolio. Prior to joining Evotec, he served as the Co-head of Healthcare at Polar Capital, where he launched the firm's healthcare investment business in 2007 and grew it to over USD 4bn of assets under management. Prior to Polar Capital, he was head of European healthcare research at Morgan Stanley, and analyst at ING Barings Furman Selz in New York, and a postdoctoral research scientist at DNAX Research Institute in California. Dr Mahony holds multiple industry leadership positions. He currently chairs the board of the BioIndustry Association (BIA), the industry trade association for UK life sciences, and holds non-executive directorships at the Wellcome Sanger Institute and Keepabl. In November 2022, Dr Mahony was appointed as the UK Life Sciences Investment Envoy by the UK Government. He was awarded a first-class honours degree in biochemistry from Oxford University and received his doctorate degree from Cambridge University.

James Parsons, Board Member

Mr Parsons is a life sciences industry consultant and director. He previously served as the CFO of Trillium Therapeutics Inc from 2011 to its acquisition by Pfizer in November 2021 for USD 2.2bn. Mr Parsons has a broad background in the life sciences industry across

therapeutics, diagnostics and device companies. He has extensive experience in strategic planning, financing, contract negotiation, investor relations, risk management, corporate governance and public company management. Mr. Parsons also serves on the board of directors of DiaMedica Therapeutics and is chair of their audit committee and serves on the board of Oncolytics Biotech Inc. He has a Master of Accounting degree from the University of Waterloo and is a Chartered Professional Accountant, Chartered Accountant (CPA, CA).

Dr Steven Sangha, Board Member

Dr Sangha has >25 years of experience in investment banking, business development, and asset management. Dr Sangha's extensive experience with Public Company Governance & Compliance, and finance has led him to successfully run a Private Fund Family Office. His interest in the biotechnology and mining industries has allowed positive growth for early-stage companies with his consummate efforts in assessment, development, and financial support. Dr Sangha holds a Doctorate of Dental Surgery (DDS) from the University of Western Ontario in London, Ontario, and a Bachelor of Pharmaceutical Science (BscPharm) from the University of British Columbia in Vancouver, British Columbia.

Bertram T. von Plettenberg, Board Member

Mr von Plettenberg presently works as an independent business consultant focusing on project development and management of active investments. Between 1999 and 2022, he worked as founding partner and CEO of CMF AG, Munich, Germany, a consulting and corporate finance firm dedicated to advisory work in the fields of general corporate management, restructurings, M&A, Venture Capital, and Private Equity, areas in which he had also worked before setting up CMF AG. He previously co-founded and co-managed one of the first leveraged buy-out funds in Germany and before, worked on M&A and investment banking assignments as a senior associate with The First Boston Company in New York. Mr von Plettenberg started his business career as a management consultant at Roland Berger & Partner, Munich, Germany, the leading German strategy consulting firm. He then went on to work in Zurich, Switzerland, at Bearbull AG in Private Wealth Management, also setting up the first German- and Swiss-registered fund for US public small-cap technology companies in collaboration with Hambrecht & Quist, San Francisco. Mr von Plettenberg studied law at ICADE, Madrid, Spain, and received an MBA from INSEAD, Fontainebleau, France.

SHAREHOLDERS & STOCK INFORMATION

Stock Information	
ISIN	CA81732W1041
WKN	A0LBCR
Bloomberg ticker	SVA CN
No. of issued shares	303.33m
Transparency Standard	TSX
Country	Canada
Sector	Healthcare
Subsector	Biotech

Source: Börse Frankfurt, First Berlin Equity Research

Shareholder Structure	
Evotec AG	5.3%
Management and Directors	9.0%
Freefloat and others	85.7%

Source: Sernova Corp.

INCOME STATEMENT

All figures in CAD '000	2019/20	2020/21	2021/22	2022/23E	2023/24E	2024/25E
Revenue	**0**	**0**	**0**	**0**	**40,000**	**0**
Cost of goods sold	0	0	0	0	0	0
Gross profit	0	0	0	0	40,000	0
General & Administrative	-2,501	-2,299	-7,857	-8,600	-9,200	-9,400
Research & Development	-2,759	-4,638	-16,897	-30,200	-30,000	-25,000
Total operating expenses (OPEX)	**-5,260**	**-6,937**	**-24,754**	**-38,800**	**-39,200**	**-34,400**
Operating income (EBIT)	**-5,260**	**-6,937**	**-24,754**	**-38,800**	**800**	**-34,400**
Net financial result	-62	-29	333	1,400	500	100
Non-operating income/expenses	0	0	0	0	0	0
Pre-tax income (EBT)	**-5,321**	**-6,966**	**-24,421**	**-37,400**	**1,300**	**-34,300**
Income taxes	0	0	0	0	0	0
Net income / loss	**-5,321**	**-6,966**	**-24,421**	**-37,400**	**1,300**	**-34,300**
Diluted EPS (CAD)	**-0.03**	**-0.03**	**-0.09**	**-0.12**	**0.00**	**-0.11**
Ratios						
EBIT Margin on Revenue	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
EBITDA Margin on Revenue	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Net Margin on Revenue	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Expenses as % of OPEX						
Sales & Marketing	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
General & Administrative	47.6%	33.1%	31.7%	22.2%	23.5%	27.3%
Research & Development	52.4%	66.9%	68.3%	77.8%	76.5%	72.7%
Y-Y Growth						
Revenue	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Operating income	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Net income/ loss	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

BALANCE SHEET

All figures in CAD '000	2019/20	2020/21	2021/22	2022/23E	2023/24E	2024/25E
Assets						
Current Assets, Total	**4,605**	**28,327**	**51,091**	**21,151**	**26,940**	**20,986**
Cash	3,949	27,874	3,776	6,801	25,915	20,056
Short-term investments	0	0	46,000	13,200	0	0
Accounts receivables	507	449	1,147	900	800	750
Other current assets	149	4	168	250	225	180
Non-Current Assets, Total	**1,120**	**1,493**	**1,394**	**1,127**	**863**	**798**
Property plant and equipment	203	176	402	462	498	550
Intangible assets	917	717	517	317	117	0
Deposits	0	212	224	224	224	224
Other LT assets	0	388	251	124	24	24
Total Assets	**5,726**	**29,820**	**52,485**	**22,278**	**27,802**	**21,784**
Shareholders' Equity & Debt						
Current Liabilities, Total	**1,848**	**1,476**	**4,740**	**7,662**	**7,963**	**7,819**
Accounts payable	878	1,358	4,600	7,510	7,800	7,644
Other current liabilities	-	117	140	152	163	175
Longterm Liabilities, Total	**703**	**276**	**136**	**109**	**87**	**70**
Other liabilities	703	276	136	109	87	70
Shareholders Equity	**3,174**	**28,068**	**47,608**	**14,506**	**19,752**	**13,895**
Total Consolidated Equity and Debt	**5,726**	**29,820**	**52,485**	**22,278**	**27,802**	**21,784**
Ratios						
Current ratio (x)	2.49	19.19	10.78	2.76	3.38	2.68
Quick ratio (x)	2.49	19.19	10.78	2.76	3.38	2.68
Net gearing	-124.4%	-99.3%	-7.9%	-46.9%	-131.2%	-144.3%
Book value per share (€)	0.02	0.11	0.17	0.05	0.07	0.05
Net debt	-3,949	-27,874	-3,776	-6,801	-25,915	-20,056
Equity ratio	55.4%	94.1%	90.7%	65.1%	71.0%	63.8%

CASH FLOW STATEMENT

All figures in CAD '000	2019/20	2020/21	2021/22	2022/23E	2023/24E	2024/25E
Net income	**-5,321**	**-6,966**	**-24,421**	**-37,400**	**1,300**	**-34,300**
Interest, net	62	29	-333	-1,400	-500	-100
Tax provision	0	0	0	0	0	0
Non-operating items	0	0	0	0	0	0
EBIT	**-5,260**	**-6,937**	**-24,754**	**-38,800**	**800**	**-34,400**
Depreciation and amortisation	225	220	440	447	414	225
EBITDA	**-5,035**	**-6,716**	**-24,314**	**-38,353**	**1,214**	**-34,175**
Derivative liability	0	0	0	0	0	0
Share based payments	683	218	7,451	4,550	4,000	3,500
Changes in w orking capital	863	518	2,947	3,087	426	-50
Cash interest net	-62	-29	333	1,400	500	100
Other adjustments	-389	-835	-839	-200	0	0
Operating cash flow	**-3,939**	**-6,844**	**-14,421**	**-29,516**	**6,140**	**-30,625**
CapEx	-5	-17	-341	-180	-150	-160
Free cash flow	**-4,945**	**-6,861**	**-14,763**	**-29,696**	**5,990**	**-30,785**
Other investments	2,000	-212	-46,012	32,800	13,200	0
Cash flow from investing	**994**	**-229**	**-46,341**	**32,620**	**13,050**	**-160**
Debt Financing, net	0	0	0	0	0	0
Equity Financing, net	4,533	31,025	36,510	0	0	25,000
Other financiing activities	564	1,093	155	-79	-76	-74
Cash flow from financing	**5,097**	**30,997**	**36,665**	**-79**	**-76**	**24,926**
Net cash flows	**2,152**	**23,925**	**-24,110**	**3,025**	**19,114**	**-5,859**
Cash, start of the year	1,797	3,949	27,874	3,776	6,801	25,915
Cash, end of the year	**3,949**	**27,874**	**3,776**	**6,801**	**25,915**	**20,056**

Y-Y Growth						
Operating Cashflow	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Free cashflow	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

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First Berlin Equity Research

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Anschrift:
First Berlin Equity Research GmbH
Friedrichstr. 69
10117 Berlin
Germany

Vertreten durch den Geschäftsführer: Martin Bailey

Telefon: +49 (0) 30-80 93 9 680
Fax: +49 (0) 30-80 93 9 687
E-Mail: info@firstberlin.com

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First Berlin Equity Research GmbH

Authored by: Christian Orquera, Analyst
All publications of the last 12 months were authored by Christian Orquera.

Company responsible for preparation: First Berlin Equity Research GmbH, Friedrichstraße 69, 10117 Berlin

The production of this recommendation was completed on 19 October 2023 at 15:21

Person responsible for forwarding or distributing this financial analysis: Martin Bailey

INFORMATION PURSUANT TO SECTION 85 (1) SENTENCE 1 OF THE GERMAN SECURITIES TRADING ACT [WPHG], TO ART. 20 (1) OF REGULATION (EU) NO 596/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL OF APRIL 16, 2014, ON MARKET ABUSE (MARKET ABUSE REGULATION) AND TO ART. 37 OF COMMISSION DELEGATED REGULATION (EU) NO 2017/565 (MIFID) II.

First Berlin Equity Research GmbH (hereinafter referred to as: "First Berlin") prepares financial analyses while taking the relevant regulatory provisions, in particular section 85 (1) sentence 1 of the German Securities Trading Act [WpHG], art. 20 (1) of Regulation (EU) No 596/2014 of the European Parliament and of the Council of April 16, 2014, on market abuse (market abuse regulation) and art. 37 of Commission Delegated Regulation (EU) no. 2017/565 (MiFID II) into consideration. In the following First Berlin provides investors with information about the statutory provisions that are to be observed in the preparation of financial analyses.

CONFLICTS OF INTEREST

In accordance with art. 37 (1) of Commission Delegated Regulation (EU) no. 2017/565 (MiFID) II and art. 20 (1) of Regulation (EU) No 596/2014 of the European Parliament and of the Council of April 16, 2014, on market abuse (market abuse regulation) investment firms which produce, or arrange for the production of, investment research that is intended or likely to be subsequently disseminated to clients of the firm or to the public, under their own responsibility or that of a member of their group, shall ensure the implementation of all the measures set forth in accordance with Article 34 (2) lit. (b) of Regulation (EU) 2017/565 in relation to the financial analysts involved in the production of the investment research and other relevant persons whose responsibilities or business interests may conflict with the interests of the persons to whom the investment research is disseminated. In accordance with art. 34 (3) of Regulation (EU) 2017/565 the procedures and measures referred to in paragraph 2 lit. (b) of such article shall be designed to ensure that relevant persons engaged in different business activities involving a conflict of interests carry on those activities at a level of independence appropriate to the size and activities of the investment firm and of the group to which it belongs, and to the risk of damage to the interests of clients.

In addition, First Berlin shall pursuant to Article 5 of the Commission Delegated Regulation (EU) 2016/958 disclose in their recommendations all relationships and circumstances that may reasonably be expected to impair the objectivity of the financial analyses, including interests or conflicts of interest, on their part or on the part of any natural or legal person working for them under a contract, including a contract of employment, or otherwise, who was involved in producing financial analyses, concerning any financial instrument or the issuer to which the recommendation directly or indirectly relates.

With regard to the financial analyses of Sernova Corp. the following relationships and circumstances exist which may reasonably be expected to impair the objectivity of the financial analyses: The author, First Berlin, or a company associated with First Berlin reached an agreement with the Sernova Corp. for preparation of a financial analysis for which remuneration is owed.

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- The author, First Berlin, or a company associated with First Berlin owns a net long or short position exceeding the threshold of 0.5 % of the total issued share capital of the analysed company;
- The author, First Berlin, or a company associated with First Berlin holds an interest of more than five percent in the share capital of the analysed company;

- The author, First Berlin, or a company associated with First Berlin provided investment banking or consulting services for the analysed company within the past twelve months for which remuneration was or was to be paid;
- The author, First Berlin, or a company associated with First Berlin reached an agreement with the analysed company for preparation of a financial analysis for which remuneration is owed;
- The author, First Berlin, or a company associated with First Berlin has other significant financial interests in the analysed company;

First Berlin F.S.B. Investment-Beratungsgesellschaft mbH (hereafter FBIB), a company of the First Berlin Group, holds a stake of under 0.5% of the shares in the company which has been covered in this analysis.

The analyst is not subject to any restrictions with regard to his recommendation and is therefore independent, so that we believe there is no conflict of interest.

With regard to the financial analyses of Sernova Corp. the following of the aforementioned potential conflicts of interests or the potential conflicts of interest mentioned in Article 6 paragraph 1 of the Commission Delegated Regulation (EU) 2016/958 exist: The author, First Berlin, or a company associated with First Berlin reached an agreement with the Sernova Corp. for preparation of a financial analysis for which remuneration is owed.

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INFORMATION PURSUANT TO SECTION 64 OF THE GERMAN SECURITIES TRADING ACT [WPHG], DIRECTIVE 2014/65/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL OF 15 MAY 2014 ON MARKETS IN FINANCIAL INSTRUMENTS AND AMENDING DIRECTIVE 2002/92/EC AND DIRECTIVE 2011/61/EU, ACCOMPANIED BY THE MARKETS IN FINANCIAL INSTRUMENTS REGULATION (MIFIR, REG. EU NO. 600/2014).

First Berlin notes that is has concluded a contract with the issuer to prepare financial analyses and is paid for that by the issuer. First Berlin makes the financial analysis simultaneously available for all interested security financial services companies. First Berlin thus believes that it fulfils the requirements of section 64 WpHG for minor non-monetary benefits.

PRICE TARGET DATES

Unless otherwise indicated, current prices refer to the closing prices of the previous trading day.

AGREEMENT WITH THE ANALYSED COMPANY AND MAINTENANCE OF OBJECTIVITY

The present financial analysis is based on the author's own knowledge and research. The author prepared this study without any direct or indirect influence exerted on the part of the analysed company. Parts of the financial analysis were possibly provided to the analysed company prior to publication in order to avoid inaccuracies in the representation of facts. However, no substantial changes were made at the request of the analysed company following any such provision.

ASSET VALUATION SYSTEM

First Berlin's system for asset valuation is divided into an asset recommendation and a risk assessment.

ASSET RECOMMENDATION

The recommendations determined in accordance with the share price trend anticipated by First Berlin in the respectively indicated investment period are as follows:

Category		1	2
Current market capitalisation (in €)		0 - 2 billion	> 2 billion
Strong Buy[1]	An expected favourable price trend of:	> 50%	> 30%
Buy	An expected favourable price trend of:	> 25%	> 15%
Add	An expected favourable price trend of:	0% to 25%	0% to 15%
Reduce	An expected negative price trend of:	0% to -15%	0% to -10%
Sell	An expected negative price trend of:	< -15%	< -10%

[1] The expected price trend is in combination with sizable confidence in the quality and forecast security of management.

Our recommendation system places each company into one of two market capitalisation categories. Category 1 companies have a market capitalisation of €0 – €2 billion, and Category 2 companies have a market capitalisation of > €2 billion. The expected return thresholds underlying our recommendation system are lower for Category 2 companies than for Category 1 companies. This reflects the generally lower level of risk associated with higher market capitalisation companies.

RISK ASSESSMENT

The First Berlin categories for risk assessment are low, average, high and speculative. They are determined by ten factors: Corporate governance, quality of earnings, management strength, balance sheet and financial risk, competitive position, standard of financial disclosure, regulatory and political uncertainty, strength of brandname, market capitalisation and free float. These risk factors are incorporated into the First Berlin valuation models and are thus included in the target prices. First Berlin customers may request the models.

RECOMMENDATION & PRICE TARGET HISTORY

Report No.:	Date of publication	Previous day closing price	Recommendation	Price target
Initial Report	Today	CAD0.73	Buy	CAD3.80

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