First Take

Sernova Corp. (SVA.TO)

January 30, 2023

Price: C$1.12; Market Cap (M): C$328; *1/27/2023 Close*

Rating: Buy; Price Target: C$6.00

Joseph Pantginis, Ph.D. - (646-975-6968) / jpantginis@hcwresearch.com

Preclinical Data Suggest the Cell Pouch System Could be an Effective Treatment Option for Hypothyroidism

Preclinical study shows thyroid transplantation into the Cell Pouch can restore thyroid hormone production. This morning, Sernova announced results from a preclinical study related to its thyroid cell therapy program. We remind investors, an estimated 150,000 thyroidectomies are performed annually in the U.S. alone, and hypothyroidism represents a high unmet need indication with a significant market opportunity (approximately $2.2 billion). Thyroid hormone replacement (THR) is long-standing and effective therapy for hypothyroidism. The goal of THR is to replace thyroid hormones (TH) that are no longer produced (e.g., triiodothyronine (T3) and thyroxine (T4)). Despite thyroid hormone replacement being effective at compensating for gland loss, ongoing side effects are still very frequent. Using Cell Pouch implantation and hormone replacement via functioning thyroid tissue, the Sernova's THR strategy is to treat a broad population by 1) reducing and/or eliminating daily use of lifelong thyroid medications; 2) recover natural feedback loop of thyroid hormones described previously; 3) reduce side effects from low thyroid hormone levels thereby enhancing long-term efficacy; and critically 4) improving quality of life for hypothyroidism patients. In data announced today, the company reports that a thyroidectomy followed by an immediate transplantation into the Cell Pouch allows for reestablishment of production of T3 and T4 and the hypothalamic-pituitary-thyroid axis. More specifically, the preclinical animal study utilized a Cell Pouch that was pre-implanted for several weeks prior to a total thyroidectomy. In an experimental group, the thyroid gland of each subject was removed and transplanted into the pre-implanted Cell Pouch. These animals were then compared to control group that did not receive a transplant. Thyroid hormones were monitored over several months with weekly measurements of circulating thyroid hormones (e.g., T3, T4). Following thyroidectomy in the treatment group, the T3 and T4 levels initially fell but subsequently recovered to normal or near-normal levels following thyroid transplant into the Cell Pouch. In the control group, post-thyroidectomy T3 and T4 rapidly decreased and remained below baseline. We are encouraged by these data and believe if the Cell Pouch technology continues to have success in preclinical as well as clinical stages, it could represent a paradigm shifting treatment modality for very large populations of patients diagnosed with chronic diseases, including hypothyroidism, hemophilia, type 1 diabetes (more below). Additional data from this study are expected to be presented at a scientific conference later this year, and Sernova is engaged with regulatory authorizes to begin clinical development of this program. For additional details and analysis related to Sernova's thyroid hormone replacement program, refer to our initiation report: *Maybe Buh Bye to Insulin in T1D Patients? Initiating at Buy and $CDN 6 PT*.

iPSC-derived Cell Pouch partnership with Evotec making significant strides; on track for regulatory filings in 2024. Sernova previously announced that its partnership with Evotec (EVO; Buy; Tsao) for the development of an induced Pluripotent Stem Cell (iPSC)-based human beta cells for use with its Cell Pouch system has made significant headway. This progress includes advancement of Evotec's iPSC derived islet-like clusters in combination with Sernova's implantable Cell Pouch device toward a first-in-human Phase 1/2 clinical trial for the treatment of patients with T1D and severe hypoglycemia. We remind investors, the objective of the collaboration is to produce an off-the-shelf, commercially viable, cell therapy treatment for T1D patients. Importantly, such an approach would have the potential to provide a functional cure for T1D patients by eliminating the need for daily insulin injections. The current progress is supported by T1D preclinical models using the iPSC technology in combination with Sernova's Cell Pouch demonstrating consistent long-term insulin independence. For the year ahead, the company plans to continue performing standard formal safety/toxicology studies and other required preclinical studies to further de-risk the combined technologies, along with potential clinical study site identification, in preparation for regulatory filings in 2024.

Next generation iPSC technology looks to expand the Cell Pouch's reach. While the initial T1D Cell Pouch clinical program utilizing donor islet cells is a key focus, investors should also focus on the long-term promise of the system with next generation technologies, led by the recently announced partnership with Evotec. More specifically, the company has recently acquired an option for an exclusive license to Evotec's autologous, iPSC-based human beta cells for use with its Cell Pouch system. This agreement, in our opinion, removes current supply chain constraints from solely using donor human islets and now provides an otherwise unlimited supply of iPSC-based islet cells with potential to treat a significantly larger patient population with an "off the shelf" approach.

Following 8-channel cell pouch cohort; 10-channel devices take the lead in ongoing Phase 1/2. Recently, Sernova announced that the first two patients have been implanted with the company's 10-channel Cell Pouch, as part of the second cohort (enrolling up to seven participants) of the ongoing U.S. Phase 1/2 clinical trial in patients with type 1 diabetes (T1D), who suffer from both hypoglycemic unawareness and severe hypoglycemic episodes. As a reminder, this is an open-label, single-arm trial evaluating the safety, tolerability, and efficacy of Sernova's Cell Pouch System for clinical transplantation of human donor islets in patients with T1D (NCT03513939). The first cohort of six patients was transplanted with the 8-channel Cell Pouch, and initial data showed favorable safety and functional activity of the device (additional details below). Following the recent approval of the protocol amendment and the authorization to begin enrollment of the second cohort, now the 10-channel Cell Pouches, which expect to provide >50% more islet capacity and shorter time to efficacy evaluation relative to the 8-channel Pouches used in the first cohort, are being implanted. Recall, donor islets are transplanted into the Cell Pouch approximately six weeks after implantation and safety and efficacy are assessed at 90 days post-islet transplant. After a second transplant of islet, safety and efficacy endpoints are again evaluated. Sernova anticipates interim data from the second cohort in 2023, and believes that results from the combined cohorts will provide guidance for the future Phase 3 pivotal study.

T1D is first on the menu for Cell Pouch; reaching insulin independence is a big win for the platform. Sernova's most advanced clinical progress is in patients diagnosed with T1D. A Phase 1/2 trial is ongoing, assessing a donor islet cell containing Cell Pouch in T1D patients. We remind investors, T1D is estimated to affect 50 million individuals globally. Due to the significant market size, as well as the Cell Pouch's MoA, we believe the T1D addressable population represents low-hanging fruit on the way to even broader potential market opportunities. In the meantime, the company's diabetes trial intends to enroll seven insulin dependent T1D patients with hypoglycemia unawareness. To date, six patients have been successfully administered the Cell Pouch and subsequently, islet cells. In recent data disclosures, Sernova has detailed that the device is well-tolerated, effective, and has demonstrated impressive durability (functional activity of the pouch has been recorded for up to 32 months). Moreover, we believe the implant's preliminary efficacy is particularly encouraging. Clinical benefits in T1D patients worth highlighting, in our opinion, include: 1) sustained blood levels of C-peptide; 2) a reduction of HbA1c; 3) overall improvement in glucose control, including reduction/elimination in hypoglycemia unaware events; and 4) reduction or an elimination of the need for daily insulin injections. Critically, the first three patients are now considered to have reached complete and sustained insulin independence for over 2 years, 6 months, and 3 months, respectively. While insulin independence is not yet a primary objective of current or future studies, reliably achieving this result would represent a significant improvement to patient quality of life, and could make Cell Pouch the preferred method of treatment for T1D patients upon approval. Subsequent any positive results, Sernova intends to meet with the FDA to discuss next steps, including the design, initiation, and timeline of a Phase 3 study.

Valuation and risks to price target achievement. We reiterate our Buy rating and C$6 price target; we also believe visibility for the company should increase around its opportunities around its Cell Pouch system across multiple indications starting with T1D in driving insulin independence in patients. To this end, we currently value Sernova on the proverbial low-hanging fruit addressing hypoglycemic unawareness patients being monitored by their physicians. We currently project that the Cell Pouch system could reach the market in the U.S. in 2027, and currently assign a 25% chance of success on sales of $2.3 billion; importantly these peak sales are based on a very low approximate 2.1% market penetration in the hypoglycemic unawares population. We believe the market could be significantly larger with the broader T1D population and the continuing dramas surrounding insulin supply and its costs. Currently, the data support, at the minimum, a two-year, cell implant impact on insulin independence, which we believe has a significant impact on the broader healthcare costs of T1D patients. Our price target is based on our clinical net present value (NPV) model, which allows us to flex multiple assumptions affecting a drug's potential commercial profile. Factors that could impede reaching our PT include failed or inconclusive clinical trials, the inability of the company

to secure adequate funding to progress its drugs through the development pathway or the occurrence of dilutive capital raises.

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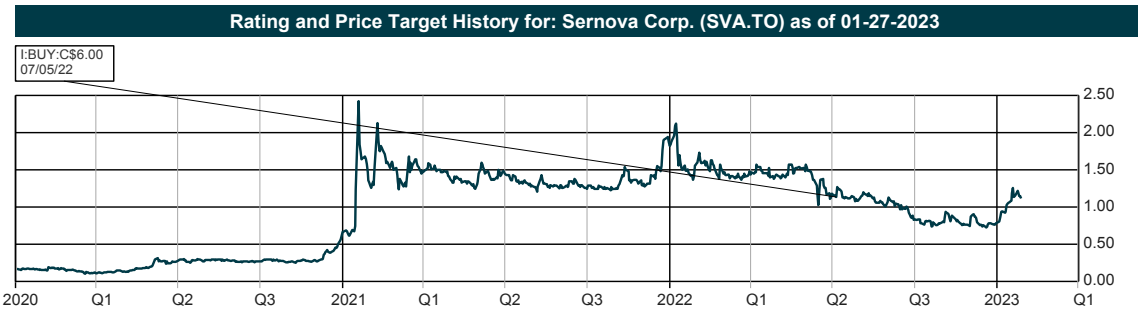

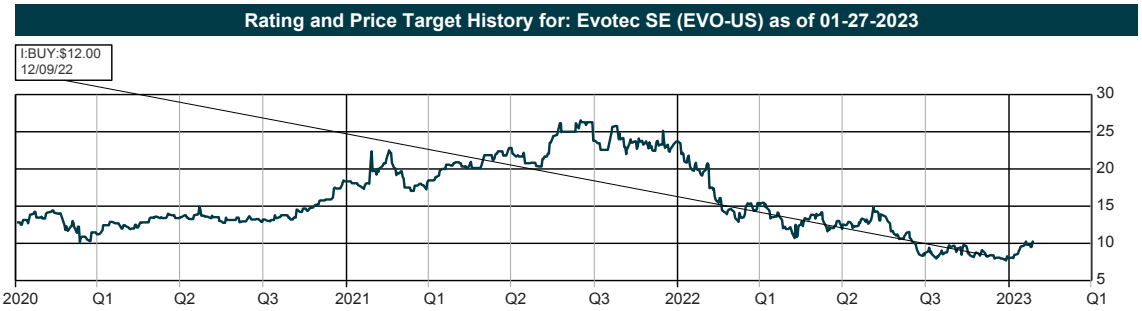

Related Companies Mentioned in this Report as of Jan/27/2023

Company	Ticker	H.C. Wainwright Rating	12 Month Price Target	Price	Market Cap
Evotec SE	EVO	Buy	$12.00	$10.16	$3596

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			IB Service/Past 12 Months	
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Neutral	71	10.61%	12	16.90%
Sell	0	0.00%	0	0.00%
Under Review	18	2.69%	4	22.22%

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