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Zacks Small-Cap Research

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CytoSorbents Corporation (NASDAQ: CTSO)

CTSO: CytoSorbents reports preliminary 4th quarter and 2024 financial results which showed impressive growth in the core international business that exceeded our expectations.

Utilizing a DCF valuation process containing conservative estimates combined with other valuation methodologies, we believe CTSO could be worth **$4.00** per share.

Current Price (1/3/25)	$0.88
Valuation	**$4.00**

OUTLOOK

CytoSorbents is commercializing its E.U. approved CytoSorb blood purification technology to treat life-threatening conditions in the intensive care unit and cardiac surgery. The company also seeks U.S. and Canadian approval of a second product, DrugSorb-ATR, to reduce perioperative bleeding risk in patients on blood thinners during cardiac surgery. Based on the results of its pivotal U.S. and Canadian STAR-T trial, the company submitted for FDA De Novo approval on September 27, 2024, and Health Canada on November 1, 2024, with regulatory decisions expected in 2025. CytoSorbents reported preliminary 4th quarter and 2024 results which showed product revenue growth that exceeded our expectations.

SUMMARY DATA

52-Week High	**$2.15**
52-Week Low	**$0.70**
One-Year Return (%)	**-31.2**
Beta	**0.56**
Average Daily Volume (sh)	**125,626**
Shares Outstanding (mil)	**54.7**
Market Capitalization ($mil)	**$48.0**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**36**
Insider Ownership (%)	**7.0**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**24.9**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2024 Estimate	**N/A**
P/E using 2025 Estimate	**N/A**

Risk Level	**High**
Type of Stock	**Small-Growth**
Industry	**Medical Device**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2022	$8.7 A	$8.5 A	$8.1 A	$9.4 A	$34.7 A
2023	$9.4 A	$9.4 A	$8.8 A	$8.7 A	$36.3 A
2024	$9.8 A	$9.9 A	$9.4 A	$9.8 E	$38.8 E
2025					$42.8 E

EPS / Loss Per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2022	-$0.21 A	-$0.25 A	-$0.28 A	-$0.02 A	-$0.75 A
2023	-$0.17 A	-$0.14 A	-$0.21 A	-$0.12 A	-$0.64 A
2024	-$0.12 A	-$0.08 A	-$0.04 A	-$0.06 E	-$0.29 E
2025					-$0.14 E

Quarterly revenues may not equal annual revenues due to rounding. Quarterly EPS may not equal annual EPS due to rounding, dilution, or intangibles.

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WHAT'S NEW



Source: CytoSorbents investor presentation

Preliminary 4th Quarter and Full Year 2024 Results

On January 3, 2025, CytoSorbents reported strong preliminary 4th quarter and full year 2024 financial results which exceeded our expectations. 4th quarter product revenue (excluding grant income) is estimated to be in the range of $9.0-$9.2 million, which is approximately 22% to 25% growth compared to $7.35 million in the 4th quarter of 2023. This quarterly product revenue range also showed sequential improvement from the 3rd quarter of 2024 in which product revenues were $8.6 million. Full year 2024 product revenue (excluding grant income) is estimated to be in the range of $35.4 million to $35.6 million.

The preliminary 4th quarter product revenue estimate exceeded or matched our total revenue estimates, which includes grant income. Assuming grant income is approximately the same as the 3rd quarter of 2024 ($777,593), our 4th quarter total revenue estimate is now approximately $9.8 million.

4th quarter product gross margin is estimated to be approximately 70%, compared to 61% in the 3rd quarter of 2024 and 72% in the 4th quarter of 2023. This sequential improvement indicates the successful resolution of both a planned production slowdown to rebalance inventory and a short-term manufacturing issue which reduced product gross margins to below average levels in the 3rd quarter of 2024.

We expect this strong sales momentum to continue into 2025 and maintain our expectations of double-digit core product revenue growth for the full year. These revenue estimates do not take into account the contribution from the commercialization of DrugSorb-ATR in North American markets which could be meaningful if approved by the FDA and Health Canada in a timely manner.

CEO Dr. Philip Chan stated, *"We are pleased with our topline performance in the quarter. Our strong year-over-year growth represents solid execution in our core international business, and underscores the importance of CytoSorb®, our flagship product, in addressing a diverse range of critical care and cardiac surgery indications. This strong top-line close to 2024, as well as our return to more normalized product gross margins, positions us well to drive improved efficiencies in our core business as we prepare to enter the North American market with DrugSorb-ATR to reduce the severity of perioperative bleeding in CABG surgery due to Brilinta®, pending FDA and Health Canada approvals."*

We adjust our 4th quarter total revenue estimate to $9.8 million and full year 2024 total revenue estimate to $38.8 million. We maintain our price target of **$4.00**.

OTHER RECENT NEWS

CytoSorbents Announces Rights Offering

On December 9, 2024, CytoSorbents announced a shareholder friendly anticipated Rights Offering which is expected to substantially increase its liquidity position. Investors who own or have bought CTSO stock by the close of trading on Friday, December 13, 2024 will be considered stockholders of record on

December 16, 2024. These shareholders will receive a dividend at no cost of one non-transferable Subscription Right Warrant for each share of common stock owned. Each Subscription Right, if exercised before the expiration date on January 10, 2025, enables a Unit purchase at a Unit subscription price of $1.00. Each Unit will consist of one share of common stock and two transferable short-term Right Warrants to purchase up to two additional shares of common stock, if available.

All net proceeds from the offering will go to the company and be used for general corporate purposes and to satisfy a debt covenant where raised equity proceeds of $3.0 million to $5.0 million will unlock $3.0 million to $5.0 million in restricted cash currently on our balance sheet on a dollar-for-dollar basis. For example, Aggregate proceeds of $5.0 million would result in increased liquidity to the company of approximately $10.0 million (which includes the $5.0 million in restricted cash). The offering is expected to fund the company's operations through FDA and Health Canada decisions on its DrugSorb-ATR marketing applications in 2025, and if approved or cleared, the initial launch and commercialization of the product.

Each Subscription Right will provide the stockholder the opportunity, but not the obligation, to purchase a Unit at a subscription price of $1.00. Each Unit consists of:

- One share of CTSO common stock.

- One Series A Right Warrant to purchase an additional share of common stock 45 days from the initial Unit subscription closing date, or February 24, 2025, at an exercise price that is 90% of the 5-day volume weighted average price prior to February 24th, but no lower than $1.00 and no higher than $2.00, irrespective of the share price at the time.

- One Series B Right Warrant to purchase an additional share of common stock 90 days from the initial unit subscription closing date, or April 10, 2025, at an exercise price that is 90% of the 5-day volume weighted average price prior to April 10th, but no lower than $2.00 and no higher than $4.00, irrespective of the share price at the time.

The maximum number of Units to be issued is 6.25 million and the maximum number of shares to be issued through the total Offering as a whole is 12.5 million. This implies that if the Offering is successful, it could generate gross proceeds of at least $12.5 million and possibly higher.

We believe this rights offering provides benefits and advantages to the company and its shareholders when compared to a traditional secondary public offering. The financing overhang of available liquidity and cash burn rates has likely created a disconnect between the prevailing market value of the company and the true underlying value of the company's overall business and potential. The current CTSO market value appears to be discounting the existing CytoSorb business that we estimate may generate total revenues of $38.0 million of which roughly $35.0 million would be in high gross margin product sales in 2024. The market also appears to be ignoring the proximity of potential major catalysts to the business such as the expected regulatory decisions on DrugSorb-ATR by the U.S. FDA and Health Canada.

We believe the rights offering is a creative solution to both the financing overhang and the dilution dilemma to existing shareholders that comes with a typical secondary public offering to outside investors.

A summary of potential benefits to shareholders who participate in this offering include:

- All net proceeds of this offering go directly to the company, which typically does not happen with open market purchases in the stock market.

- This is a BOGO (Buy One, Get One) leveraged match with regards to the company's current liquidity situation. A raise of $3.0 million to $5.0 million will unlock, on a dollar-for-dollar basis, $3.0 million to $5.0 million in restricted cash already on the balance sheet that was received from its credit facility.

- The increase in cash position is expected to help protect shareholders' existing investments in the company by financially strengthening the company and reducing and potentially eliminating the financing overhang. Net proceeds are expected to fund the company through Health Canada and FDA decisions, and if approved/cleared, through the initial commercial launch.

- Participation can help to reduce or prevent shareholder dilution, and can even increase ownership, depending on the level of participation.

- The right warrants represent a potential upside kicker, if the stock price or market value rises because of a positive regulatory decision, or a relief of the financing overhang from the rights offering, or another catalyst.

- Management and the Board of Directors of CytoSorbents are also large shareholders and are technically aligned with the interests of existing shareholders.

A detailed presentation of the Rights Offering can be found here. In addition, an updated December 2024 investor presentation can be found on the company's investor website here.

3rd Quarter 2024 Financial Results

CytoSorbents reported 3rd quarter 2024 results on November 7th and the results came in above the company's updated guidance provided on October 1st. Total revenues increased approximately 6.6% to $9.4 million with product sales increasing 11.0% to $8.6 million. Product revenue guidance was in the $8.3-$8.5 million range. Grant income was $777,593 in the 3rd quarter compared to $1.06 million in the prior year period.

Product gross margins decreased to 61.0%, compared to 72.0% in the 3rd quarter of 2023 which reflects the impact of a planned production slowdown to rebalance inventory and a short-term manufacturing issue that has since been resolved. This was above the company updated guidance of gross margins in the 50%-60% range. We expect product gross margins to return to normalized levels in the 4th quarter. After approval and full commercialization of DrugSorb-ATR in North American markets, we expect gross margins to reach the 75%-80% range over the long-term.

During the quarter, research and development expenses were approximately $1.8 million compared to approximately $3.7 million for the 3rd quarter of 2023. This decrease was primarily due to a decrease in clinical trial costs related to the completion of the STAR-T trial in 2023.

GAAP net loss for the 3rd quarter was ($2.3) million, which was an improvement from a net loss of ($9.2) million in the prior year period. Operating cash flow for the first nine months of 2044 was a use of cash of ($12.1) million. The company's burn rate is expected to improve throughout 2024 and 2025 as cost saving measures take effect and the company's product sales continue to increase. Cash burn rate is expected to be in the $3.0 million range over the next several quarters. However, it's possible the company could reach breakeven status in terms of cash flow at some point in the 2nd half of 2025 due to ongoing cost savings initiatives.

Adjusted EBITDA loss improved to ($3.6) million compared to a loss of ($5.6) million in the 3rd quarter of 2023. Adjusted EBITDA eliminates the effects of stock compensation and foreign currency translation.

Liquidity and Capital Resources

As of September 30, 2024, the company had current assets of approximately $16.6 million and current liabilities of approximately $8.4 million. Cash balances at quarter end were $5.7 million in unrestricted cash and restricted cash of $6.5 million. The restricted cash primarily consists of $5.0 million in loan

proceeds that can be released upon 1) submission of the DrugSorb-ATR De Novo application to the FDA and 2) equity raises of up to $5.0 million.

With the successful completion of a $5.0 million equity raise, which would unlock $5.0 million in restricted cash on its balance sheet, the company believes it will be sufficiently funded through the approval and launch of DrugSorb-ATR in 2025. An additional $5.0 million in loan proceeds is available upon FDA marketing clearance of DrugSorb-ATR in the U.S.

DrugSorb-ATR FDA Submission & Acceptance

On October 1, 2024, CytoSorb announced the submission of its DrugSorb-ATR medical device De Novo marketing application to the U.S. Food and Drug Administration (FDA) on September 27, 2024. The goal of this product is to reduce the severity of perioperative bleeding in patients on ticagrelor (Brilinta®, AstraZeneca) who are undergoing coronary artery bypass graft (CABG) surgery. The FDA has previously granted Breakthrough Device Designation to DrugSorb-ATR to address this major unmet medical need which makes it eligible for priority review.

Dr. Phillip Chan, Chief Executive Officer of CytoSorbents, stated, *"The DrugSorb-ATR De Novo submission to FDA is the culmination of multiple years of significant clinical, regulatory, and manufacturing accomplishments company-wide, centered on the execution and data analysis from the U.S. and Canadian pivotal STAR-T randomized controlled trial and the product development of DrugSorb-ATR. "We are very proud of our dedicated CytoSorbents team and external clinicians, collaborators, and consultants who helped to achieve this major milestone. Meanwhile, we have also completed our DrugSorb-ATR Health Canada Medical Device License (MDL) application, which will be submitted with the expected near-term receipt of MDSAP certification."*

Ticagrelor is a blood thinning drug frequently administered in the hospital to patients suffering from a heart attack. If patients are not eligible for a coronary stent, they will often require CABG surgery to restore blood flow to heart muscle. Current guidelines recommend the delay of surgery by three to five days to allow "washout" or natural elimination of the drug to reduce the high risk of serious and potentially fatal perioperative bleeding from the use of the blood thinner.

The recent 140-patient North American STAR-T randomized, double-blind, sham-controlled trial evaluated the safety and efficacy of DrugSorb-ATR in patients undergoing urgent CABG surgery on ticagrelor to remove the drug and reduce the severity of perioperative bleeding complications compared with patients operated without the device. These safety and efficacy data from STAR-T form the basis of the marketing approval submissions (see more details below).

On October 24, 2024, the company announced that the FDA has accepted the application and has initiated the substantive review process.

DrugSorb-ATR Submission to Health Canada

On November 4, 2024, the company announced the submission of its DrugSorb-ATR Medical Device License (MDL) application to Health Canada on November 1, 2024, which was concurrent with the receipt of its Medical Device Single Audit Program (MDSAP) certification.

CEO Dr. Phillip Chan stated, *"National treatment guidelines in Canada preferentially recommend ticagrelor over other antiplatelet agents, resulting in its near universal adoption in acute coronary syndrome (ACS) treatment protocols. Because of this, a future Health Canada approval of DrugSorb-ATR has the potential to improve the standard of care in heart attack patients requiring CABG surgery by enabling safe and timely surgery while eliminating treatment delays that expose patients to additional risk and consume valuable hospital resources. We believe the high rates of enrollment from Canadian sites in the STAR-T trial have helped to validate the unmet medical need and strong interest in DrugSorb-ATR*

among cardiac surgeons for this application. Meanwhile, the market for DrugSorb-ATR, if approved, is concentrated in approximately 20 cardiac surgery centers in Canada where we believe our team can quickly launch and support our therapy in this important market. We expect regulatory decisions in 2025, with Health Canada likely preceding FDA."

Source: CytoSorbents investor presentation

CytoSorbents Secures $20 Million Credit Facility

On July 2nd, the company announced that they had secured a $20 million non-dilutive credit facility. The credit agreement, which has an initial term of three years, provides up to $20 million in total term loan proceeds including an initial tranche of $15 million. $10 million will be immediately available and an additional $5 million will be held in restricted cash and will be released with the acceptance by the FDA of the company's planned De Novo application for DrugSorb-ATR and an equity capital raise of up to $5.0 million. A second tranche of $5 million would be available in the 2nd half of 2025 with FDA marketing clearance for DrugSorb-ATM to help support an anticipated launch of the therapy in the U.S..

CytoSorbents Announces the Launch and Availability of the PuriFi Blood Pump in the EU

On June 13th, the company announced the launch and immediate availability of its PuriFi™ hemoperfusion machine in the EU, following approval and certification under the EU Medical Device Regulation (MDR).

The PuriFi peristaltic blood pump features a number of innovations that separate it from other hemoperfusion pumps including a pre-assembled adult and pediatric blood line kit, auto-priming, an auto-leveling bubble catcher, an intuitive touchscreen graphical user interface with a step-by-step user-friendly set-up guide, optional blood warming, and a rapid 10-minute set-up time. These unique features enable an easy and fast method to administer the CytoSorb® blood purification cartridge for critically ill and cardiac surgery patients.

More information can be found here.

CytoSorbents Announces Regulatory Approval of CytoSorb in Taiwan

On June 24th, the company announced the regulatory approval of CytoSorb in Taiwan by the Taiwan Food and Drug Administration (TFDA). The approved indications include the extracorporeal removal of cytokines (cytokine storm, sepsis), bilirubin (liver disease), and myoglobin (trauma) from a patient's circulating blood. The removal of the antithrombotic drugs Brilinta® (ticagrelor, AstraZeneca) and Xarelto® (rivaroxaban, Janssen/Bayer) during cardiothoracic surgery is also approved, with the goal of reducing perioperative bleeding. CytoSorb will be distributed throughout Taiwan by Hemoscien Corporation.

Valuation and Estimates

Our 2024 revenue estimate is adjusted to $38.8 million and our 2024 EPS estimate is adjusted to a loss of ($0.29) per share based on improved cost controls at the company. We believe 2025 revenues could exceed $43.0 million. Our 2025 GAAP EPS estimate is a loss of ($0.14) per share.

The company has implemented significant cost-cutting measures to reduce the cash burn, including major reductions in headcount, termination of non-core R&D programs, termination of the STAR-D trial to focus on STAR-T, and a third consecutive year of salary freezes for executive management. The benefit of these cost cuts on operating expenses, particularly the headcount reductions, will become more apparent going forward as notice periods and severance payments are completed.

In addition, the company has worked diligently to optimize manufacturing efficiencies. The company expects product gross margins to be more consistently in the 75-80% range after full commercialization of DrugSorb-ATR in North American markets.

We are still confident the company can generate substantial levels of free cash flow over time, particularly if the approval and commercialization of DrugSorb-ATR is successful in 2025. We maintain our price target of **$4.00** per share.

Source: CytoSorbents investor presentation

Review of STAR-T Trial

Brilinta® (ticagrelor, AstraZeneca) is one of the leading anti-thrombotic drugs used as part of dual-antiplatelet therapy in patients with acute coronary syndrome. However, up to 10% of these patients will need to undergo CABG surgery and risk serious bleeding complications if the surgery is performed within the first few days from the last ticagrelor dose. Waiting in the hospital to washout the drug over the span of 3-5 days is the only acceptable alternative but comes with potential clinical risk for complications while waiting, and higher added hospital costs. The goal of DrugSorb-ATR is to allow patients to safely get the critical CABG surgery they need without requiring extensive drug washout. This was investigated in the U.S. and Canadian pivotal STAR-T (Safe and Timely Antithrombotic Removal of Ticagrelor) randomized controlled trial.

April 2024 Cardiothoracic Surgery Conference STAR-T Presentation

On April 28, 2024, the company announced that data from the pivotal STAR-T randomized controlled trial were presented for the first time publicly by Principal Investigator Dr. Michael Mack during a Breakout Presentation at the American Association for Thoracic Surgery (AATS) Annual Meeting. This event, held in collaboration with the Society of Cardiovascular Anesthesiologists (SCA), took place in Toronto, Canada. Previously, the data were under embargo, as required by AATS to be eligible for presentation at the conference, one of the world's most prestigious cardiothoracic surgery events.

Following the event, Principal Investigators Drs. Mack and C. Michael Gibson discussed the results of the study, stating that the results demonstrated a reduction in fatal and severe surgical bleeds and chest tube drainage in a WIN ratio analysis.

The link to the interview can be found here.

This follows the initial disclosure on December 28, 2023, when the company announced an update on the primary safety and effectiveness endpoints and the final independent Data and Safety Monitoring Board (DSMB) analysis of the study. The DSMB performed the final review of the full unblinded data on all 140 patients in the STAR-T trial and concluded there were no issues with device safety, thus meeting the primary safety endpoint of the study. The company also performed the initial data analysis on the primary efficacy endpoint of STAR-T, which was a hierarchical composite endpoint covering the full spectrum of perioperative bleeding including:

- Fatal bleeding within 48 hours
- Universal Definition of Perioperative Bleeding (UDPB ≥ 2)
- Chest tube drainage in 24 hours

Based on this analysis, the study did not meet the primary effectiveness endpoint in the overall patient population that underwent different types of cardiac surgeries. However, the study demonstrated reduced bleeding complications in patients in the prespecified isolated coronary artery bypass graft (CABG) surgery population, which represented more than 90% of the overall study population. Due to the conference data embargo, no data were presented at that time.

New Data Presented for the First Time

In the AATS presentation, the use of DrugSorb-ATR resulted in a statistically significant reduction (as calculated by the WIN ratio) in the severity of perioperative bleeding. This was measured by a prespecified alternative composite primary efficacy endpoint consisting of fatal bleeding, UDPB ≥ 3 (severe bleeding), and 24-hour chest tube drainage in the isolated CABG per protocol population.

For CABG patients with moderate bleeding events (UDPB = 2), investigators noted that moderate bleeders in the DrugSorb arm were less serious than moderate bleeders in the control arm. Patients in the DrugSorb-ATR arm required 50% fewer units of blood transfusion products, with a total mean transfusion volume of 537 mL in the DrugSorb-ATR arm versus 1,066 mL in the control arm (p=0.025). In a post-hoc sensitivity analysis, Principal Investigators conducted a blinded re-adjudication of all CABG patients with at least moderate bleeding events, aiming to identify patients with real clinical evidence of bleeding versus those receiving prophylactic transfusions (reclassified to mild bleeding). When this analysis was performed, the data achieved statistical significance in the original composite endpoint including moderate to severe bleeding (UDPB ≥ 2) as well as the alternative composite endpoint including only severe bleeding (UDPB ≥ 3).

Additionally, in an exploratory “major bleeding” analysis in patients with either severe UDPB events (UDPB ≥ 3) or 24-hour chest tube drainage > 1L, there was a 73% relative reduction, or 16% absolute reduction, in major bleeding in the DrugSorb-ATR arm (6%) versus control (22%). This indicates a Number Needed to Treat (NNT) of six patients, meaning that for every six patients treated, one severe bleed was prevented. This was noted to be a compelling number.

The reason for the original missed primary endpoint was clarified with the definition of the “per protocol” population, which excluded patients undergoing “other surgeries” or with major protocol deviations. Despite being a randomized trial, there was an imbalance in the number of non-CABG “other surgeries” in the DrugSorb-ATR arm (10.6%) versus control (4.5%). Patients undergoing “other surgeries” had worse pre-operative risk scores, longer surgeries, longer cardiopulmonary bypass times, more chest tube drainage, more moderate to severe perioperative bleeding, and longer ICU and hospital stays. Additionally, there were more patients with major protocol deviations in the treatment arm (12.1%) versus control (4.5%), with the most common major protocol deviation being acute normovolemic hemodilution (ANH) in 8 of the 11 cases. According to Dr. Mack, ANH is an excluded practice in the study as it removes up to a liter of blood containing ticagrelor at the beginning of the procedure, then transfuses it back into the patient after surgery, circumventing DrugSorb-ATR's removal of the drug and increasing the risk of perioperative bleeding.

The investigators concluded:

- Primary safety endpoint was met
- Primary efficacy endpoint was not met in the all-comer surgery population
- Severe bleeding efficacy endpoint was met in the I-CABG per protocol population
- In isolated CABG patients, the intraoperative use of DrugSorb-ATR was associated with:
    - Reduced bleeding severity by either UDPB grade or chest tube drainage volume
    - NNT of 6 to prevent a major bleed (UDPB 3 event or >1 L chest tube drainage
    - Overall favorable benefit-to-risk profile

Source: CytoSorbents investor presentation

Additional Commentary on FDA Approvals

The U.S. Food and Drug Administration (FDA) has typically shown regulatory flexibility in approving novel therapies, encompassing medical devices, drugs, and biologics, particularly those that address significant unmet medical needs. This flexibility is evident in cases where pivotal trials have either missed primary endpoints or demonstrated marginal efficacy.

In a retrospective cross-sectional analysis published in JAMA Internal Medicine in 2021, Johnston et al. scrutinized FDA approvals from 2016 to 2020 for high-risk therapeutic medical devices that did not meet the primary endpoints of pivotal studies. These devices underwent evaluation through the FDA's premarket approval (PMA) regulatory pathway, known for its stringent requirements in assessing device safety and efficacy. The analysis revealed that, during this period, 13.1% of the 107 approved high-risk therapeutic devices did not meet at least one pivotal study primary endpoint. More than half of these cases were related to cardiovascular or cardiothoracic surgery applications. It is important to note the FDA's tendency to justify approvals based on post hoc analyses, success in alternative primary endpoints, and positive trends in secondary outcome measures. In addition, the FDA mandated a post-approval clinical study for 11 of these device approvals. Recently, the FDA granted approval for Medtronic's radiofrequency renal denervation system, Symplicity®, for the treatment of uncontrolled adult hypertension, despite a slim 7-6 majority vote against its risks and benefits by an FDA advisory panel.

This pattern extends to drugs and biologics as well. In another publication in JAMA Internal Medicine in 2023, Johnston et al. reported that between 2018 and 2021, 10% of the 210 new FDA drug approvals missed one or more primary efficacy endpoints in pivotal trials. All these therapies were either first-in-class or designated orphan drugs (affecting < 200,000 patients per year in the U.S.). The FDA's rationale for approval often included success in other pivotal studies, positive findings from secondary or exploratory endpoints, and favorable post hoc analyses. Similar to the medical device space, many approvals necessitated post-market studies to address lingering clinical uncertainties.

Based on information released by CytoSorbents, the DrugSorb-ATR device appears to be safe and relatively low risk, showing clinical benefit in the majority of patients in the study (isolated CABG population), representing the typical expected use-case for DrugSorb-ATR. Considering its designation as an FDA Breakthrough Device for this application, its "first-in-class" status, its apparent favorable benefit-to-risk ratio, and its potential to address a major unmet medical need, we believe it aligns well with the profile of other FDA-approved therapies that have encountered challenges with pivotal trial primary endpoints.

If CytoSorbents chooses to submit a regulatory application, and provided further data analyses from the study are corroborative of device efficacy, we anticipate a receptive FDA audience and the potential for approval, albeit with the requirement for a post-market confirmatory study. If approved, we believe the narrower label for use only in isolated CABG will not materially impact DrugSorb-ATR's total addressable U.S. and Canadian market and will likely increase adoption of CytoSorb internationally for this E.U. approved indication.

References:

[1] Johnston JL, Dhruva SS, Ross JS, Rathi VK. Assessment of FDA Approval for New High-risk Therapeutic Devices Not Meeting Pivotal Study Primary End Points, 2016-2020. *JAMA Intern Med.* 2021;181(10):1409–1412. doi:10.1001/jamainternmed.2021.3042

[2] Johnston JL, Ross JS, Ramachandran R. US Food and Drug Administration Approval of Drugs Not Meeting Pivotal Trial Primary End Points, 2018-2021. *JAMA Intern Med.* 2023;183(4):376–380. doi:10.1001/jamainternmed.2022.6444

Review of DrugSorb-ATR Need

Coronary artery bypass graft (CABG) surgery to bypass blocked heart arteries is the most common type of open heart surgery performed in the U.S. and worldwide. Approximately 300,000 CABG surgeries are performed each year. An estimated 100,000 of these patients are at risk of excessive bleeding due to blood thinners with approximately half of them on Brilinta®. The current CytoSorb product, which uses an equivalent polymer technology to DrugSorb®-ATR, is already approved and is increasingly used in the E.U. to remove Brilinta®/Brilique® and reduce bleeding risk in this indication. The initial results from the International STAR Registry reporting on this real-world experience have shown favorably low rates of serious perioperative bleeding.

Cardiothoracic surgeons in the U.S., Canada, and abroad continue to confirm the difficult and serious clinical and economic problem that blood thinners cause patients, surgeons, and hospitals. For patients, delaying surgery to wash out the drug puts those with active ischemic heart disease at risk, while going to CABG surgery without waiting risks serious perioperative bleeding associated with longer hospital stays and increased risk of worsened clinical outcomes and even death.

For surgeons, excessive intraoperative bleeding due to blood thinners is difficult and unpredictable to manage, often complicating the surgery and requiring significant additional operative time to achieve hemostasis. Postoperatively, bleeding complicates and delays recovery and disposition, and if rapid or persistent, may require expensive and time-consuming re-exploratory surgery.

Source: CytoSorbents investor presentation

For hospitals, patients on blood thinners consume scarce resources and complicate patient logistics. Preoperatively, patients in the U.S. occupy hospital beds for 3 to 5 days to washout the drug, costing $6,000 to $30,000 to wait, depending on the severity of their condition, based upon an approximate daily cost of $6,000 in the ICU, $4,000 in the ICU step-down, and $2,000-$3,000 for a cardiac monitored ward bed.

Intraoperatively, the inability to stop bleeding delays completion of the case and is very expensive. Shorter overall operative times have been cited in a previous study when CytoSorb was used intraoperatively in patients undergoing cardiac surgery while on Brilinta. Based on average published operating room charges from the Cleveland Clinic hospital system, each additional 30 minute increment adds more than $4,000 in cost to the operation.

Perioperatively, bleeding complications are very expensive as well, due to the need for blood transfusions, reoperations, and longer ICU and hospital stays. Recently, in a study published in the American Journal of Cardiovascular Drugs, Cohen et al. modeled the projected cost savings of less perioperative bleeding that DrugSorb-ATR could provide in the U.S. in patients undergoing surgery before completing washout of Brilinta® – a similar cohort being evaluated in the STAR-T trial.

Using assumptions based on published studies, they found the use of DrugSorb-ATR in these cases had a cost-dominant value proposition based on delivering improved clinical outcomes for patients and substantial cost savings (inclusive of the cost of the device) to the hospital. Finally, outcomes in CABG surgery such as death rates, readmissions, and postoperative hemorrhage reflect heavily in the Hospital's Quality Star Rating patient safety rating, as defined by the U.S. Centers of Medicare & Medicaid Services (CMS). The hospital's overall Star rating is critical as it helps to differentiate the hospital on objective quality measures from others in the area, important in driving patient traffic and procedure revenue to the hospital, and with direct implications on overall profitability.

Source: CytoSorbents investor presentation

Because of this, DrugSorb-ATR could represent a “win-win-win” for patients, surgeons and hospital administrators by potentially allowing safe and timely surgery by actively removing the drug from the bloodstream, while reducing the serious bleeding risk and unnecessary costs in such patients. With the appropriate approvals, the company intends to commercialize CytoSorb in the U.S. and Canada primarily with a direct sales force focused regionally at high volume cardiac surgery centers, including clinical trial centers, and supplemented with cardiac surgery-focused distributors or strategic partners.

Product level gross margins of DrugSorb-ATR could exceed 80% and based on revenue and operating expense projections, U.S. operations could achieve breakeven financial results in the first full year of commercialization.

KEY INVESTMENT POINTS

Source: CytoSorbents investor presentation

- CytoSorbents Corporation (NASDAQ: CTSO) is vertically integrated U.S. based international medical device company that manufactures and markets the European Union approved CytoSorb® blood purification cartridge in 75 countries worldwide, generating $31.1 million in product sales in 2023 and $26.4 million in products sales for the first nine months of 2024.

- The CytoSorb cartridge treats cytokine storms and massive uncontrolled inflammation in life-threatening conditions such as sepsis, COVID-19, shock, lung failure, pancreatitis, and many other applications.

- The company is seeking U.S. FDA and Health Canada approvals for DrugSorb-ATR, an equivalent polymer technology to CytoSorb, to reduce perioperative bleeding during cardiac surgery in patients on the blood thinner, Brilinta®. The pivotal U.S. and Canadian STAR-T trial commenced in October 2021 and was completed in the summer of 2023. Despite missing the primary efficacy endpoint of its pivotal STAR-T trial in an all-comer population, data from the important prespecified isolated CABG subpopulation was presented for the first time in April 2024 at the American Association for Thoracic Surgery (AATS) annual meeting and again at the company-sponsored "KOL and Analyst/Investor Day" in May 2024, demonstrate a statistically significant decrease in severe bleeding complications in an alternate primary efficacy endpoint and support a favorable benefit-to-risk profile of the therapy.

- On September 27, 2024, the company filed for DrugSorb-ATR marketing approval to U.S FDA under the De Novo pathway. DrugSorb-ATR was awarded one of two FDA Breakthrough Device Designations for DrugSorb-ATR which will facilitate a priority review of the application in the U.S. Pending FDA agreement with the De Novo pathway, the company expects a potential decision from FDA between 6-12 months.

- On November 1, 2024, the company announced the submission of its DrugSorb-ATR Medical Device License (MDL) application to Health Canada, which was concurrent with the receipt of its Medical Device Single Audit Program (MDSAP) certification.

- The company's business model incorporates a "razor blade" business model in which the CytoSorb device can be utilized across an installed base of blood pumps such as dialysis, CRRT, ECMO, and heart-lung machines.

- CytoSorbents is led by an experience management team including CEO Phillip Chan and COO and President Vincent Capponi who led the company through the E.U. approval and commercialization of the CytoSorb device.

- The company has approximately $12.2 million in total cash on the balance sheet and $13.8 million in debt as of 9/30/24. We believe the company has liquidity to support planned operations through approval and commercialization of DrugSorb-ATR in North American markets in 2025.

- The company uplisted to the NASDAQ in December 2013 and currently has a market capitalization of approximately $47.8 million.

- We believe CTSO stock is worth **$4.00** based on a conservative discounted cash flow (DCF) calculation and a peer multiple comparison.

RISKS

- The company has experienced substantial operating losses since inception. As of December 31, 2022, the accumulated deficit was $253,997,878. The losses have resulted principally from costs incurred in the research and development of the company's polymer technology, clinical studies and general and administrative expenses.

- The company is currently well capitalized but may require additional financing in the future to complete additional clinical studies and to support the commercialization of proposed products.

- If users of the company's products are unable to obtain adequate reimbursement from third-party payers, or if reimbursement is not available in specific countries, or if new restrictive legislation is adopted, then market acceptance of products may be limited, and the company may not achieve anticipated revenues and profits.

- Clinical study results for the CytoSorb and/or DrugSorb-ATR device may not be indicative of future clinical study results, and no assurance can be made that any clinical study results will lead to results sufficient for necessary regulatory clearances or product sales.

LONG-TERM GROWTH DRIVERS

Stand-alone blood pump strategy:

There are many applications where a simple, low-cost hemoperfusion pump is adequate to implement the CytoSorb blood purification technology, without the complexity of a large dialysis or continuous renal replacement therapy (CRRT) machine, without the need for a dialysis technician, and where patients do not need to have failed kidneys. This would greatly simplify treatment with CytoSorb in the ICU and potentially enable its more ubiquitous and earlier use on more patients while opening the door for more new applications in the emergency room, surgery suites, and elsewhere.

Expansion of direct sales territories

Although opening new countries with a direct sales force requires time, cost, and effort, it also allows the company to directly lead the effort, drive results, and benefit from more profitable sales. With the announcement of expansion of direct sales into the U.K., Ireland and France, CytoSorbents now sell direct in three of the E.U.'s Big 5 Economies (Germany, France and the U.K.) and a total of 15 countries direct overall. The company also works with distributors or partners in Italy and Spain.

Investment in important clinical studies in shock, liver failure, cardiac surgery, ATR, etc

The company is committed to funding company-sponsored studies in key areas that will potentially drive international adoption and usage, with the goal of becoming a standard of care for those applications.

New Products

Over the past couple of years, there has been increasing momentum around two additional marketed products, ECOS-300CY for ex vivo organ perfusion (EVOP) in solid organ transplant under the EU CE mark, and VetResQ in the U.S. for the treatment of companion animals. In particular, prominent research in the field of heart, lung and liver organ transplant highlights the benefits of this technology in controlling inflammation and improving organ function during EVOP.

SUMMARY

We believe CytoSorbents disruptive blood purification technology will provide ample opportunities for high margin, double digit revenue growth going forward. The global addressable market for all of the company's products could exceed $20 billion. This growth will also be driven by the company aggressively investing in therapeutic applications such as sepsis and septic shock, circulatory failure, respiratory failure, liver dysfunction, kidney protection, and organ transplant perfusion and protection.

The company is also seeing positive signs of restored growth of its core CytoSorb device in European markets. There is a strong pipeline of positive data on the device from both critical care and cardiac surgery events. The company is also improving cross-functional synergy internally based on new therapy area vertical strategy and leadership. The company is also seeing increased opportunities outside of Germany such as the U.K., Israel, Turkey and Taiwan. Another important component in bottom line growth is the full transition to the new manufacturing facility which will increase total capacity and improve gross margins.

Based upon the recently presented positive data from STAR-T supporting a favorable benefit-to-risk profile of the DrugSorb-ATR therapy, its designation as an FDA Breakthrough Device, the major unmet medical need to prevent perioperative bleeding due to ticagrelor in cardiac surgery patients, and the established FDA precedent (see above), we believe CytoSorbents will find a receptive FDA and Health Canada despite missing the original STAR-T pivotal trial primary efficacy endpoint. We believe the data release has increased the visibility and probability of FDA and Health Canada marketing approval of DrugSorb-ATR to reduce the severity of bleeding in isolated CABG patients on Brilinta®.

The company's current stock price likely does not reflect the potential for strong profitable growth going forward or the potential for a favorable FDA review of DrugSorb-ATR. Insiders have been accumulating large amounts of stock in the open market in the December 2023 financing, as well as through voluntary reductions in salary in exchange for stock options. Because of this, we believe the stock to be significantly undervalued at this time.

Source: CytoSorbents investor presentation

FINANCIAL PROJECTIONS

Source: Zacks analyst

HISTORICAL STOCK PRICE

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