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Zacks Small-Cap Research

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CytoSorbents Corporation (NASDAQ: CTSO)

CTSO: CytoSorbents reports 1st quarter 2025 financial and operating results which were largely in line with expectations. The company plans to appeal the FDA denial decision on DrugSorb-ATR.

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 (5/20/25)	$0.84
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 final regulatory decisions expected in 2025. Based on $35.6 million in high margin 2024 product revenue and the near-term potential of DrugSorb-ATR, we believe CTSO stock to be significantly undervalued at this time.

SUMMARY DATA

52-Week High	**$1.61**
52-Week Low	**$0.70**
One-Year Return (%)	**10.1**
Beta	**0.78**
Average Daily Volume (sh)	**245,546**
Shares Outstanding (mil)	**62.5**
Market Capitalization ($mil)	**$52.6**
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)
2023	$7.9 A	$8.1 A	$7.8 A	$7.3 A	$31.1 A
2024	$9.0 A	$8.8 A	$8.6 A	$9.2 A	$35.6 A
2025	$8.7 A	$8.9 E	$9.3 E	$10.1 E	$37.0 E
2026					$41.7 E

EPS / Loss Per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2023	-$0.17 A	-$0.14 A	-$0.21 A	-$0.12 A	-$0.64 A
2024	-$0.11 A	-$0.08 A	-$0.05 A	-$0.14 A	-$0.38 A
2025	-$0.02 A	-$0.07 E	-$0.06 E	-$0.05 E	-$0.21 E
2026					-$0.11 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

1st Quarter 2025 Financial & Operating Results

On May 14, 2025, CytoSorbents reported 1st quarter 2025 financial and operating results. In the 1st quarter, product revenue was $8.7 million, which was flat on a constant currency basis compared to the prior year period. There was a slight disruption in the key Germany market due to the proactive reorganization and strategic realignment of the German commercial team and sales approach. These efforts are intended to reinvigorate sales growth in the country through deeper customer engagement, more effective market development, and improved sales representative productivity.

Gross margin decreased to 71% compared to 77% in the 1st quarter of 2024. The 1st quarter 2024 gross margin was unusually high due to sales mix and improved efficiencies at the new manufacturing facility in New Jersey. We expect gross margins to stabilize in the 71%-73% range throughout 2025. Long-term gross margins could increase to the mid-70% range as product volumes continue to grow over time.

Operating loss improved to ($3.9) million compared to ($4.7) million in the prior year period. Net loss was ($1.5) million or ($0.02) per share, which compares to a net loss of ($6.1) million or ($0.11) per share in the 1st quarter of 2024. Adjusted net loss (which eliminates stock comp and currency translation items) was ($3.7) million or ($0.06) per share, compared to ($3.7) million or ($0.07) per share in the prior year period. Adjusted EBITDA loss improved by 17% to ($2.7) million compared to a loss of ($3.3) million in the 1st quarter of 2024.

Liquidity and Capital Resources

As of March 31, 2025, the company had total cash (including restricted cash) of $13.1 million and total debt of $14.2 million. Subsequent to the end of the quarter, the company sold certain NOLs and R&D tax credits totaling $1.7 million. Current assets were approximately $24.5 million and current liabilities were $9.8 million. Net working capital was positive at $15.7 million.

We believe the company is fully funded to support its business model through the expected regulatory approval of DrugSorb-ATR and the subsequent commercial launch in late 2025 or early 2026.

Valuation and Estimates

Our 2025 revenue estimate is adjusted to $37.0 million, and our 2025 EPS estimate is adjusted to a loss of ($0.21) based on better than expected EPS in the 1st quarter of 2025. We believe 2026 revenues could exceed $41.0 million with the approval and commercialization of DrugSorb-ATR. Our 2026 GAAP EPS estimate is a loss of ($0.11) per share.

With ongoing cost controls and the maintenance of gross margins above 70%, we believe the core business of the company (i.e. the existing CytoSorb business) could reach near cash flow breakeven at some point in late 2025, which will free up cash for investment in the expected DrugSorb-ATR launch later this year and into 2026.

Beginning in 2025, the company began a significant reorganization of the direct sales team and strategy in Germany. This includes the rebalancing of territories and hospital accounts with the goal of restoring sales growth through deeper customer engagement, more effective market development, and improved sales representative productivity. This process caused a short-term disruption in Germany sales that resulted in slightly lower product sales overall in the 1st quarter of 2025 compared to the prior year period. However, these actions should produce improved sales results in the 2nd half of 2025 with the goal of moving the core business toward cash flow breakeven.

Last year, the company 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, with management voluntarily reducing salaries in exchange for stock options in 2024. The benefit of these cost cuts on operating expenses have been apparent in the significant cash burn reduction for the past three quarters.

In addition, the company has worked diligently to optimize manufacturing efficiencies. The company had product gross margins of 71% in the 1st quarter of 2025 and expects product gross margins in 2025 to be in the low 70% range. In the long term, we expect gross margins to expand to the mid-high 70% range after full commercialization of DrugSorb-ATR in North American markets.

Based on these factors, we maintain our price target of $**4.00** per share.

OTHER RECENT NEWS

Regulatory Update on DrugSorb-ATR

On April 25, 2025, the FDA issued a denial letter regarding the company's De Novo Request for DrugSorb-ATR authorization. The agency identified remaining deficiencies that must be addressed before the De Novo Request can be granted, and the device can be authorized for commercialization in the U.S. CytoSorbents has already met with the FDA subsequent to receiving the letter. The company believes these items can be most effectively and expeditiously resolved through the formal appeal process that enables direct interaction and engagement with FDA senior leadership and external experts. The company has 60 days from the notice (approximately June 25, 2025) to file the formal appeal with the FDA. After the appeal is filed, the FDA has 30 days to establish a hearing and 30 days after to make a decision. The company still anticipates a final regulatory decision from the FDA in 2025, which remains consistent with its prior guidance.

There are three potential outcomes from the final FDA regulatory decision:

1) The original decision is reversed, and the De Novo authorization is granted and the company can proceed with commercialization efforts.

2) The original decision is reversed, and the De Novo authorization is granted, but under certain conditions that will need to be satisfied, sometimes on a post market basis.

3) The original decision is upheld, and the De Novo authorization is denied.

The company states that it remains extremely committed to bringing DrugSorb-ATR to market as an important solution to address the serious, unmet medical need of preventing life-threatening bleeding in CABG patients treated with Brilinta. There are no effective therapies currently available in the U.S., resulting in tens of thousands of patients facing this risk every year. FDA granted DrugSorb-ATR two separate Breakthrough Device designations, one for Brilinta and one for the direct oral anticoagulants such as Eliquis and Xarelto because of its potential to solve this major problem.

Additional Commentary on the FDA Letter and Appeals Process

CytoSorbents has not disclosed the specific remaining issues cited in the FDA's denial letter. However, the company stated that, following a subsequent meeting with the FDA to clarify these issues, it believes they can be resolved promptly—through the appeals process—which could lead to a final FDA decision later this year. This confidence in a short timeline suggests that the data from the STAR-T trial may be deemed sufficient, and that a new pre-approval study may not be required, which is a significant positive outcome if accurate.

The appeals process is the most common and established pathway companies pursue following a denial of a De Novo request. It allows for a higher-level review within the FDA, during which the original decision can be upheld, reversed, or modified. The process includes a supervisory review of the appeal summary submitted by the sponsor, as well as a meeting involving FDA officials, the company, and relevant external experts. The typical timeline from submission to final decision is approximately 60 days.

The question arises why the outstanding issues were not resolved prior to the issuance of the denial letter. Under the Medical Device User Fee Amendments of 2022 (MDUFA V), the FDA is expected to reach a decision on 70% of De Novo applications within 150 days, excluding any time the application is placed on hold for additional data requests. The agency's performance is closely tracked against these metrics. We believe these metrics may be under even greater scrutiny under the current administration, and more important for the FDA to achieve.

Based on our analysis, we continue to believe that DrugSorb-ATR, as an FDA Breakthrough Device with the potential to safely mitigate the risk of serious perioperative bleeding caused by Brilinta in CABG patients, merits marketing approval. Its effectiveness has been demonstrated both in a randomized controlled trial and real-world data. The safety profile appears benign. Most importantly, the alternative—either doing nothing and accepting high rates of serious or life-threatening bleeding, or delaying surgery to allow drug washout while the patient remains at risk from an ongoing heart attack—is unacceptable when a viable therapeutic option exists.

Health Canada

According to prior statements, DrugSorb-ATR is under advanced review by Health Canada. We note that seven of the 32 adult cardiac surgery centers throughout Canada participated in the pivotal U.S. and Canadian STAR-T randomized controlled trial, representing nearly a quarter of the participating surgical institutions in the trial and contributing approximately a third of all patients into the trial. We believe these factors will be viewed favorably by Health Canada.

Recently, Health Canada has indicated that application reviews are currently delayed beyond their target Market Authorization Times (MAT) due to a growing backlog. Health Canada has confirmed its commitment to issuing a decision at the earliest opportunity. The company remains confident in receiving a final regulatory decision in 2025.

Dubai Expansion

The company recently expanded its international footprint with the opening of a new regional sales subsidiary in Dubai, United Arab Emirates. Dubai is a dynamic epicenter of healthcare business in the Middle East. Establishing this hub is expected to accelerate access to high growth markets in the Middle East and Africa which will enable faster market entry, stronger partnerships, and regional revenue diversification.

Update on the DrugSorb-ATR Regulatory Process in the Q4 and Full Year 2024 Press Release

Management reiterated that their De Novo DrugSorb-ATR submission continued to be in interactive review with FDA, that their Medical Device License application to Health Canada was in advanced review, and that they continue to expect regulatory decisions in 2025. Meanwhile, the company has begun some premarket launch planning, including engaging with leading U.S. and Canadian key opinion leaders, recruiting key talent, and proceeding with market access activities, including developing a clear value proposition for patients, surgeons, and hospitals. The company also disclosed that if DrugSorb-ATR is approved, it plans a controlled market release to key clinical trial centers for several months prior to a broader national launch.

In addition, the company detailed a April and May 2025 scientific conference schedule and data presentations on the use of its technology to reduce perioperative bleeding in CABG patients due to Brilinta. These included American College of Cardiology, Society of Cardiovascular Anesthesiologists, EuroPCR, Canadian Society of Cardiac Surgery, and the European Society of Cardiology Heart Failure.

CytoSorbents Successfully Completes Rights Offering

On December 9, 2024, CytoSorbents announced a shareholder friendly anticipated Rights Offering which was expected to substantially increase its liquidity position. Shareholders of record on December 16, 2024 received a dividend at no cost of one non-transferable Subscription Right Warrant for each share of common stock owned. Each Subscription Right, when exercised before the expiration date on January 10, 2025, enabled a Unit purchase at a Unit subscription price of $1.00. Each Unit consisted 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.

Each Subscription Right provided the shareholder the opportunity, but not the obligation, to purchase a Unit at a subscription price of $1.00. Each Unit consisted 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 (which was subsequently extended to June 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 was 6.25 million and the maximum number of shares to be issued through the total Offering was 12.5 million.

On January 10, 2025, the company successfully completed the Rights Offering, raising aggregate gross proceeds of $6.25 million from the sale of all 6.25 million Units reserved for the Rights Offering and was oversubscribed by 68% with total demand of approximately 10.5 million Units, including the exercise of both basic subscription rights and oversubscriptions. The leadership team and the Board of Directors of the company are estimated to have subscribed for approximately 450,000 of the total Units prior to any pro rata adjustment. Proceeds from the closing of the subscription period satisfied a debt covenant which unrestricted $5.0 million of restricted cash on CytoSorbents' balance sheet, further increasing liquidity.

On February 25, 2025, the company announced the receipt of $1.6 million in gross proceeds from the exercise of 1.4 million Series A Right Warrants, at an exercise price of $1.13 per warrant. The Series B Right Warrant initially was set to expire on April 10, 2025, however, the company extended the expiration by 60 days to June 10, 2025. To date, the company has raised $7.85 million in gross proceeds from the rights offering and Series A Right Warrant exercise, increasing net liquidity by $12.3 million.

On February 25, 2025, the company announced the receipt of $1.6 million in gross proceeds from the exercise of 1.4 million Series A Right Warrants, at an exercise price of $1.13 per warrant. The Series B Right Warrant expires on April 10, 2025, however during the Q4 and Full Year 2024 earnings call, management stated that they were considering extending this expiration date. To date, the company has raised $7.85 million in gross proceeds from the rights offering and Series A Right Warrant exercise, increasing net liquidity by $12.3 million.

We believe this rights offering provides benefits and advantages to the company and its shareholders when compared to a traditional secondary public offering. The prior financing overhang of available liquidity and cash burn rates have 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 generated $35.6 million 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 was 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 detailed presentation of the Rights Offering can be found here.

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."*

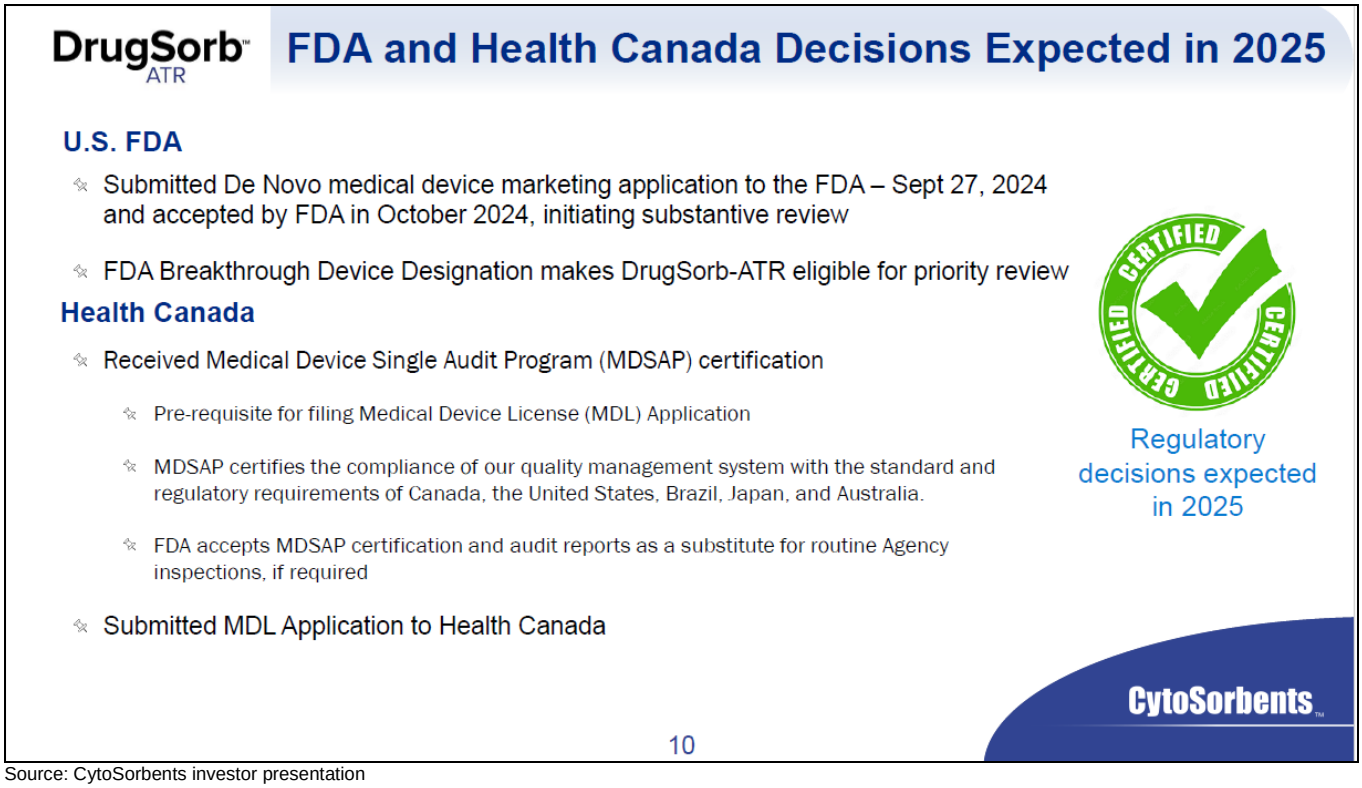
Ticagrelor is a blood thinning drug frequently administered in the hospital to patients suffering from a heart attack. If patients are not eligible for a coronary stent, they will often require CABG surgery to restore blood flow to heart muscle. Current guidelines recommend the delay of surgery by three 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).

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.

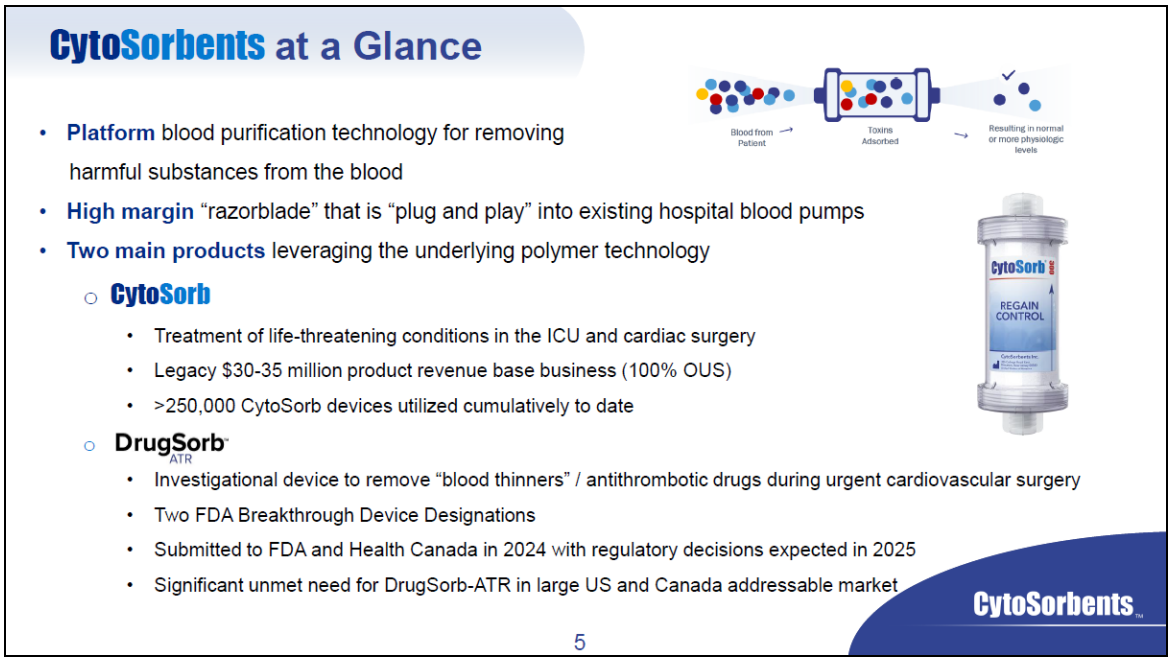
CEO Dr. Phillip Chan stated, *"National treatment guidelines in Canada preferentially recommend ticagrelor over other antiplatelet agents, resulting in its near universal adoption in acute coronary syndrome (ACS) treatment protocols. Because of this, a future Health Canada approval of DrugSorb-ATR has 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..



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).

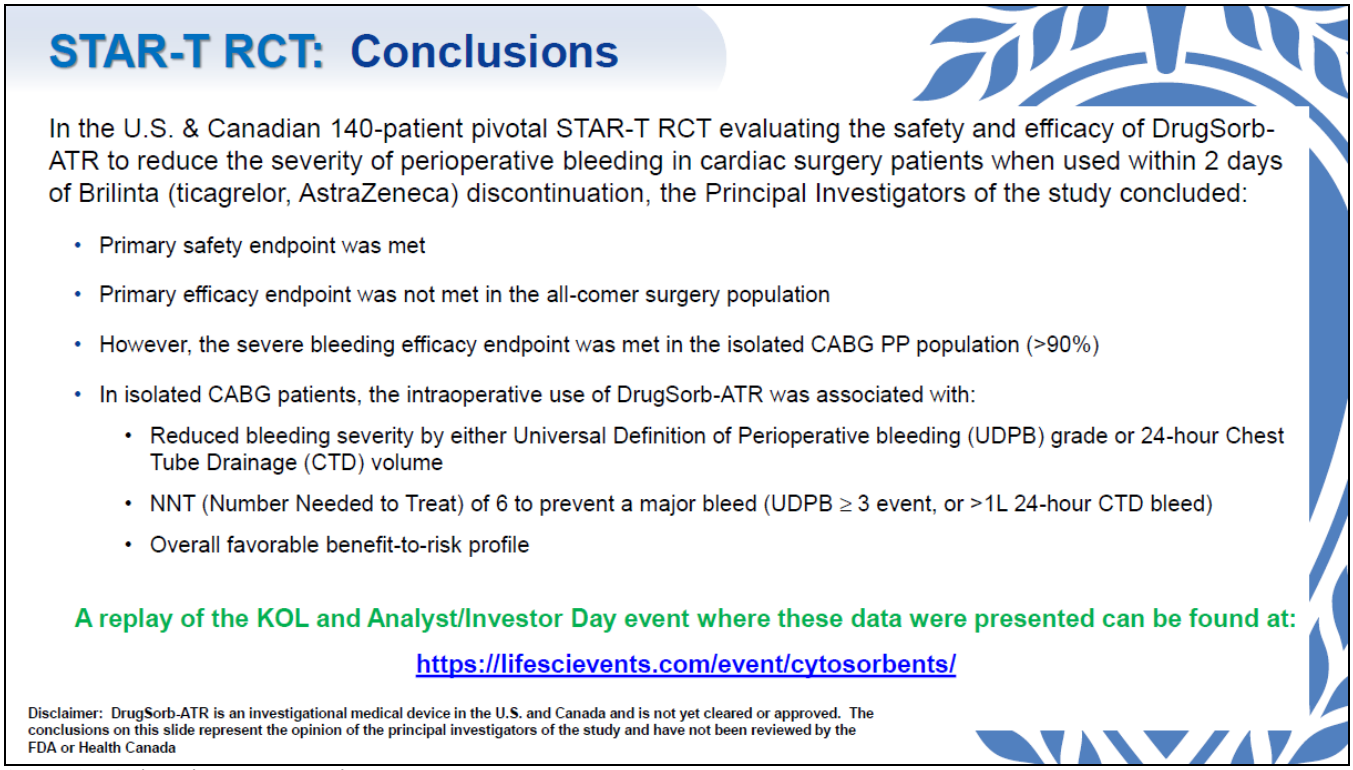
Additionally, in an exploratory "major bleeding" analysis in patients with either severe UDPB events (UDPB ≥ 3) or 24-hour chest tube drainage > 1L, there was a 73% relative reduction, or 16% absolute reduction, in major bleeding in the DrugSorb-ATR arm (6%) versus control (22%). This indicates a Number 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 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

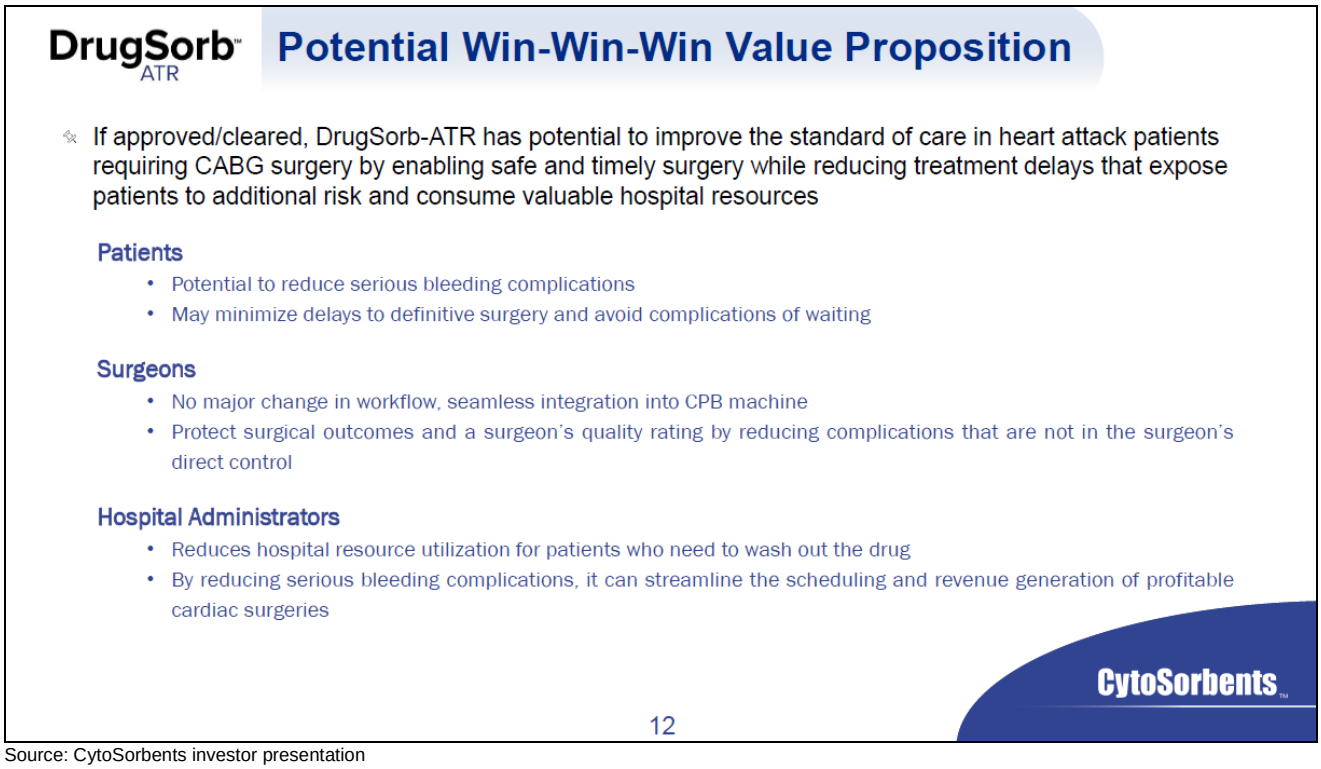
[2] Johnston JL, Ross JS, Ramachandran R. US Food and Drug Administration Approval of Drugs Not Meeting Pivotal Trial Primary End Points, 2018-2021. *JAMA Intern Med.* 2023;183(4):376–380. doi:10.1001/jamainternmed.2022.6444

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.



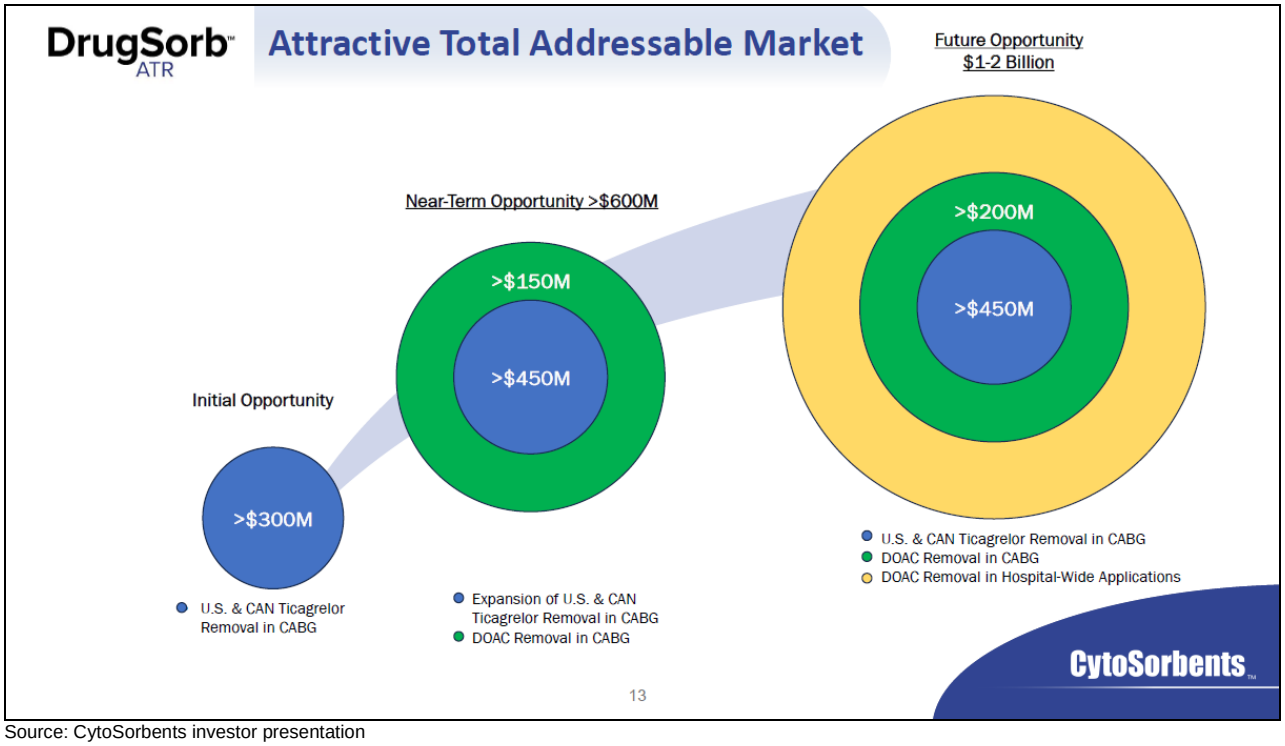
Source: CytoSorbents investor presentation

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.

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 $35.6 million in product sales in 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 final decision from FDA in 2025.

- 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.

- The company currently has approximately $13.1 million in cash on the balance sheet (including restricted cash). We believe the company has the 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 $54.0 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.

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.

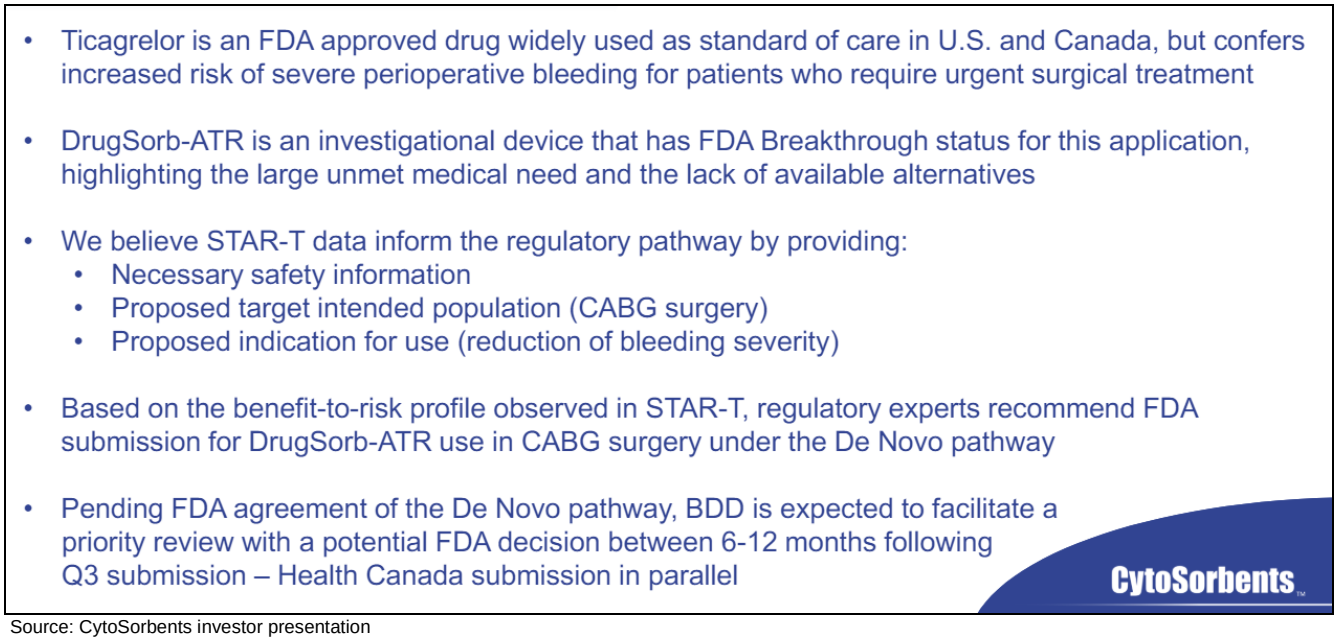
SUMMARY

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. We believe CTSO stock to be significantly undervalued at this time.



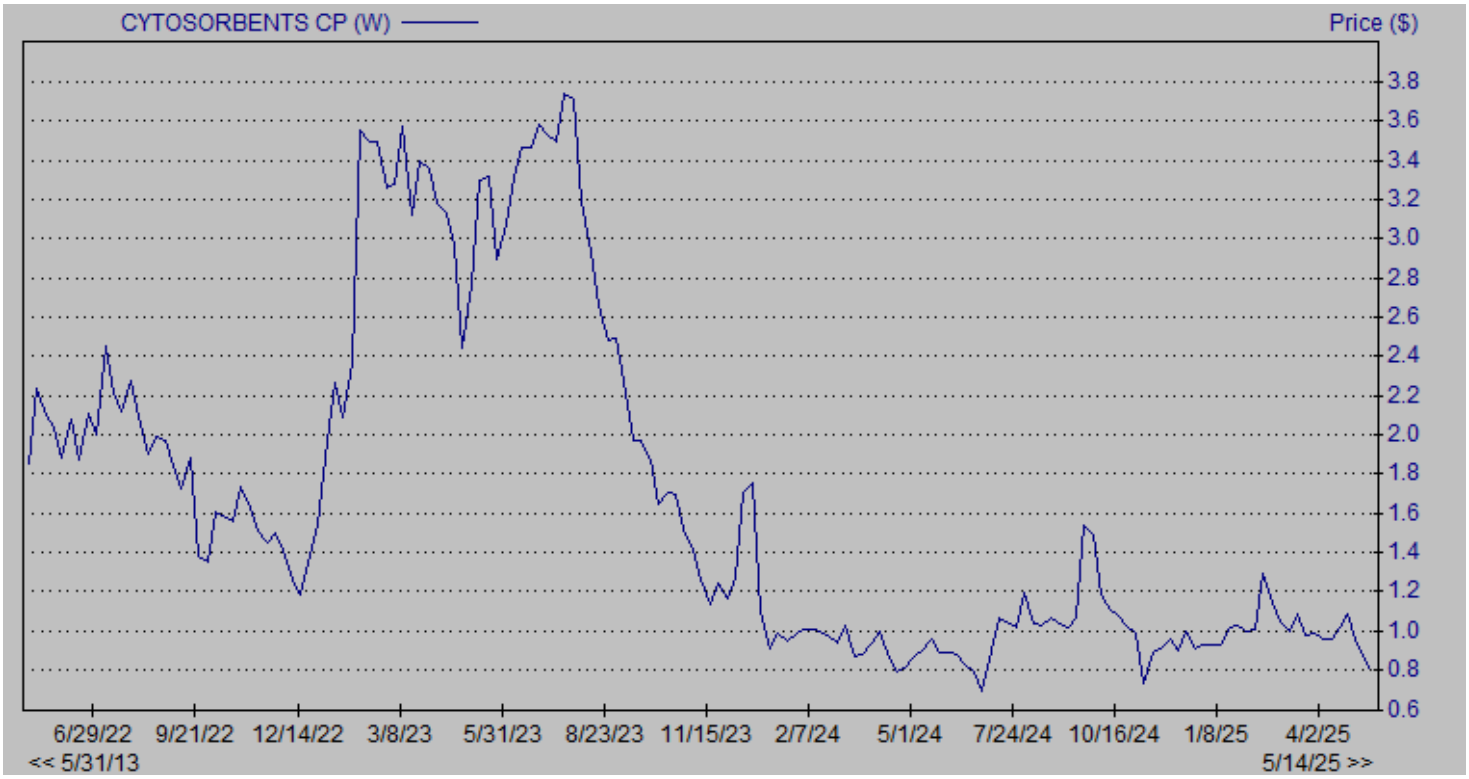
Source: CytoSorbents investor presentation

FINANCIAL PROJECTIONS

Income Statement	Dec-22	Dec-23	Dec-24	Dec-25	Dec-26
Product Sales	**29,359,910**	**31,084,953**	**35,594,520**	**37,024,076**	**41,652,085**
Growth	*-26.8%*	*5.9%*	*14.5%*	*4.0%*	*12.5%*
Cost of Goods Sold	**0**	**7,672,650**	**8,898,425**	**9,110,922**	**9,000,225**
%	*0.0%*	*24.7%*	*25.0%*	*24.6%*	*21.6%*
Depreciation & Amort	**0**	**1,459,066**	**1,570,104**	**1,559,873**	**1,559,873**
Gross Profit	**0**	**21,953,237**	**25,125,991**	**26,353,281**	**31,091,987**
Margin	*0.0%*	*70.6%*	*70.6%*	*71.2%*	*74.6%*
SG&A Expenses	**0**	**38,307,415**	**34,995,749**	**33,224,960**	**29,902,464**
% of sales	*0.0%*	*123.2%*	*98.3%*	*89.7%*	*71.8%*
Other	**0**	**0**	**0**	**0**	**0**
% of sales	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Research & Development	**0**	**15,594,442**	**6,916,181**	**6,718,215**	**6,046,394**
% of sales	*0.0%*	*50.2%*	*19.4%*	*18.1%*	*14.5%*
Amortization	**0**	**0**	**0**	**0**	**0**
% of sales	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Operating Income	**0**	**(31,948,620)**	**(16,785,939)**	**(13,589,894)**	**(4,856,870)**
Margin	*0.0%*	*-102.8%*	*-47.2%*	*-36.7%*	*-11.7%*
EBITDA	**0**	**(30,489,554)**	**(15,215,835)**	**(12,030,021)**	**(3,296,997)**
Margin	*0.0%*	*-98.1%*	*-42.7%*	*-32.5%*	*-7.9%*
Other Expenses/(Income)	**0**	**(2,046,012)**	**4,224,751**	**(3,013,984)**	**0**
%	*0.0%*	*-6.6%*	*11.9%*	*-8.1%*	*0.0%*
EBIT	**0**	**(29,902,608)**	**(21,010,690)**	**(10,575,910)**	**(4,856,870)**
%	*0.0%*	*-96.2%*	*-59.0%*	*-28.6%*	*-11.7%*
Total Interest Exp (net)	**0**	**157,981**	**1,399,092**	**2,420,536**	**2,178,482**
%	*0.0%*	*0.5%*	*3.9%*	*6.5%*	*5.2%*
Net Profit Before Tax	**0**	**(30,060,589)**	**(22,409,782)**	**(12,996,446)**	**(7,035,353)**
%	*0.0%*	*-96.7%*	*-63.0%*	*-35.1%*	*-16.9%*
Income Tax	**0**	**(813,739)**	**(1,690,825)**	**0**	**0**
% Effective Rate	*0.0%*	*2.7%*	*7.5%*	*0.0%*	*0.0%*
% Cash Tax Rate	*0.0%*	*2.7%*	*7.5%*	*0.0%*	*0.0%*
Minority Interests or Preferred Stock	**0**				
Net Profit	**0**	**(29,246,850)**	**(20,718,957)**	**(12,996,446)**	**(7,035,353)**
%	*0.0%*	*-94.1%*	*-58.2%*	*-35.1%*	*-16.9%*
	0.0%				
Non-recurring income (expense)	-				
	0				
Average Diluted Shares Outstanding	-	44,656,391	54,441,811	62,057,982	62,500,000
Reported FD EPS					
Zacks Cash EPS	**0.00**	**(0.65)**	**(0.38)**	**(0.21)**	**(0.11)**
Zacks EPS	**0.00**	**(0.65)**	**(0.38)**	**(0.21)**	**(0.11)**

Source: Zacks analyst

HISTORICAL STOCK PRICE



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