Zacks Small-Cap Research

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CEL-SCI Corporation (CVM: NYSE)

CVM: Target Population Comes Into Relief

We use a DCF model and apply a 15% discount rate to CEL-SCI's forecasted cash flows to generate our valuation. Our model applies an 75% probability of ultimate approval and commercialization for Multikine in head and neck cancer in lower severity patients that do not need chemotherapy. The model includes contributions from the EU, UK and Canada.

Current Price (11/7/2023)	$2.20
Valuation	**$7.00**

OUTLOOK

CEL-SCI is developing two platforms: Multikine and LEAPS. Multikine has completed a Phase 3 trial for head and neck cancer while LEAPS is conducting preclinical studies for RA, Pandemic Flu and breast cancer. In June 2021, CEL-SCI reported selected data from its IT-MATTERS trial demonstrating a benefit in the non-chemotherapy population. CEL-SCI plans to submit applications in the EU, UK and Canada.

Multikine is an immuno-oncology biologic that contains human blood-derived cytokines that are thought to enhance the body's natural defenses against cancer. For the lead indication, SCCHN, it is used prior to and in conjunction with SoC, which includes surgery, radiation and chemotherapy. LEAPS is a peptide epitope delivery technology that can direct immune response. It is appropriate for diseases where antigenic epitope sequences have been identified.

Our valuation assumes provisional approvals around the globe over the next several years for Multikine. We anticipate a partnership or buyout of the company by a large competitor that will begin and carry through with the commercialization process.

SUMMARY DATA

52-Week High	**3.62**
52-Week Low	**1.04**
One-Year Return (%)	**-36.2**
Beta	**1.2**
Average Daily Volume (sh)	**1,058,918**
Shares Outstanding (mil)	**47.3**
Market Capitalization ($mil)	**104.1**
Short Interest Ratio (days)	**30.1**
Institutional Ownership (%)	**11.9**
Insider Ownership (%)	**3.6**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2023 Estimate	**N/A**
P/E using 2024 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of USD)

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2022	$0.0 A	$0.0 A	$0.0 A	$0.0 A	$0.0 A
2023	$0.0 A	$0.0 A	$0.0 A	$0.0 E	$0.0 E
2024					$0.0 E
2025					$0.0 E

Earnings per Share

	Q1	Q2	Q3	Q4	Year
2022	-$0.20 A	-$0.23 A	-$0.23 A	-$0.21 A	-$0.87 A
2023	-$0.18 A	-$0.18 A	-$0.19 A	-$0.16 E	-$0.71 E
2024					-$0.48 E
2025					-$0.38 E

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WHAT'S NEW

Multikine Clinical Data

CEL-SCI Corporation (NYSE: CVM) has continued to generate data and analysis related to its IT-MATTERS trial - a Phase III study evaluating Multikine in advanced primary squamous cell carcinoma of the oral cavity and soft palate. Since our previous update a month ago, CEL-SCI has continued to prepare its manufacturing facility for commercial scale production and has released new data, further refining the target population that benefits from the pre-surgery administration of the leukocyte interleukin injection.

In the most recent poster presentation at European Society for Medical Oncology (ESMO), CEL-SCI further identified downstaging of disease after Multikine therapy as a predictor of better survival. Combined with the selection criteria that can be identified upon diagnosis, including no involvement of disease in the lymph nodes, no extracapsular spread of the tumor and low PD-L1 expression, CEL-SCI has identified a population that may support regulatory approval in multiple jurisdictions.

What Is Surgical Downstaging and Upstaging?

Surgical downstaging and upstaging reflect changes in the stage of a cancer, and in the context of this poster, from before surgery to after surgery, based on what is found during the surgery. Cancer stages are a way to measure cancer's spread based on tumor size, invasion of nearby tissue, spread to lymph nodes and metastasis. The stage ranges from I to IV indicating less severe to more severe disease.

Downstaging occurs when the stage is lowered after surgery compared to before. For instance, a cancer that was thought to be stage III before surgery, but re-evaluated at stage II after surgery is an example of downstaging. Some reasons for downstaging include:

- Imaging tests before surgery overestimated the extent of the tumor. The surgeon finds the tumor is not as advanced as thought;
- Neoadjuvant therapy (chemo/radiation or agent such as Multikine given before surgery) was effective and shrank the tumor more than expected.

Upstaging is when evaluation of the stage increases after surgery. If a cancer was thought to be stage II before the surgical procedure, but more extensive disease is later found to support stage III, this represents upstaging. Reasons for upstaging include:

- Imaging tests before surgery underestimated the extent of the tumor. More disease is found during surgery;
- There was undetected regional lymph node spread or microscopic metastatic disease not seen on scans before surgery.

Therefore, downstaging results from a post-surgical assessment that cancer is less extensive than expected. This is in contrast to upstaging which indicates more advanced disease and typically has a worse prognosis.

ESMO Poster Presentation

CEL-SCI presented data from the IT-MATTERS clinical trial at the European Society of Medical Oncology (ESMO) Congress in Spain on October 22, 2023. The presented poster was accompanied by a press release which explained the details presented at the conference and detailed the finalization of the selection criteria for the target population and CEL-SCI next steps. CEL-SCI has identified a population that is particularly responsive to Multikine which can be identified upon diagnosis. This includes patients with no involvement of disease in the lymph nodes, no extracapsular spread of the tumor and low PD-L1 tumor expression.

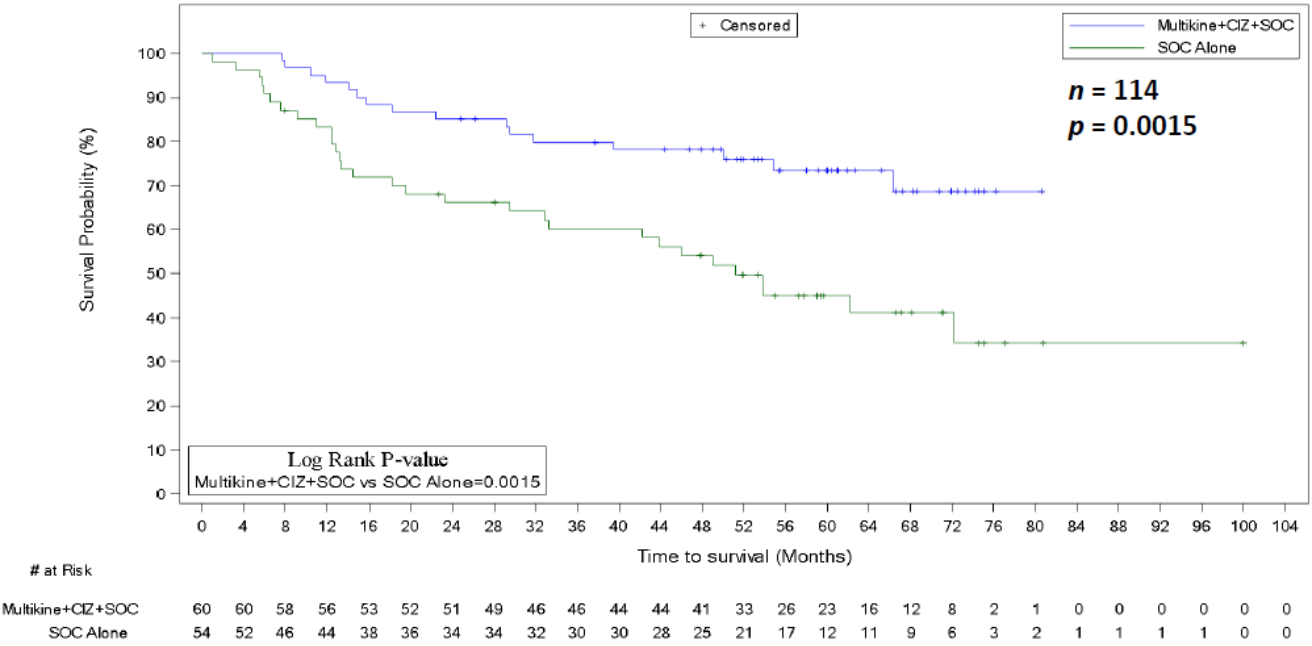
Lack of spread to the lymph nodes indicates less severe disease and that the cancer is more contained. When cancer spreads to lymph nodes, it increases the risk that cancer cells will then spread further through the body through the bloodstream or lymphatic system and metastasize. Extracapsular spread (ECS) is another indicator that cancer has spread outside its origin and occurs when cancer cells expand beyond the capsule of a lymph node. The capsule of a lymph node is a thin layer of tissue that surrounds the node and helps to keep the cancer cells

inside. When cancer cells spread beyond the capsule, it is called ECS. ECS is a serious finding because it indicates that the cancer is more likely to spread to other parts of the body.

PD-L1 is programmed death-ligand 1 and appears on the surface of some cancer cells to erroneously communicate to immune cells that the cancer cell is harmless. In circumstances where there is high PD-L1 expression, a checkpoint inhibitor such as Keytruda may improve tumor response and contribute to a higher probability of survival as it can block the receptor which allows the cancer cell to hide. Low PD-L1 expressing cancers do not respond well to checkpoint inhibitors, leaving an unmet need. CEL-SCI's data show that Multikine works well in this population of low PD-L1 expressers and could potentially address this void.

CEL-SCI identifies multiple factors that support its efforts to seek marketing authorization. This includes data supporting Multikine's use in patients with low PD-L1 expression, which was approximately 70% of the IT-MATTERS study population, the ability to identify patients that can respond to the therapy upon diagnosis and a significant increase in 5-year overall survival in the target group from 45% for control patients who did not receive Multikine to 73% for Multikine-treated patients.

Exhibit I – Kaplan-Meier Overall Survival for Multikine Target Population[1]



Under a previous heading earlier in this report we discussed upstaging and downstaging following surgery and some of the reasons behind a change in estimating cancer stage. The ESMO poster refers to pre-surgery changes in stage as it relates to Multikine-treated patients who were downstaged following surgery. These patients had much better survival in the IT-MATTERS study measured with a high degree of statistical significance ($p < 0.0002$). The study showed that patients with disease downstaging survived longer than those who were not downstaged and that there was a 35% rate of pre-surgical downstaging in study subjects who met the above mentioned selection criteria when treated with Multikine. Additional detail related to the overall population in the trial and changes in staging are provided in the following exhibit. Note that upstaging is about the same for Combined LI and SOC, whereas there is an almost 9 percentage point difference in favor of Multikine for downstaging (21.5% vs. 13.0%).

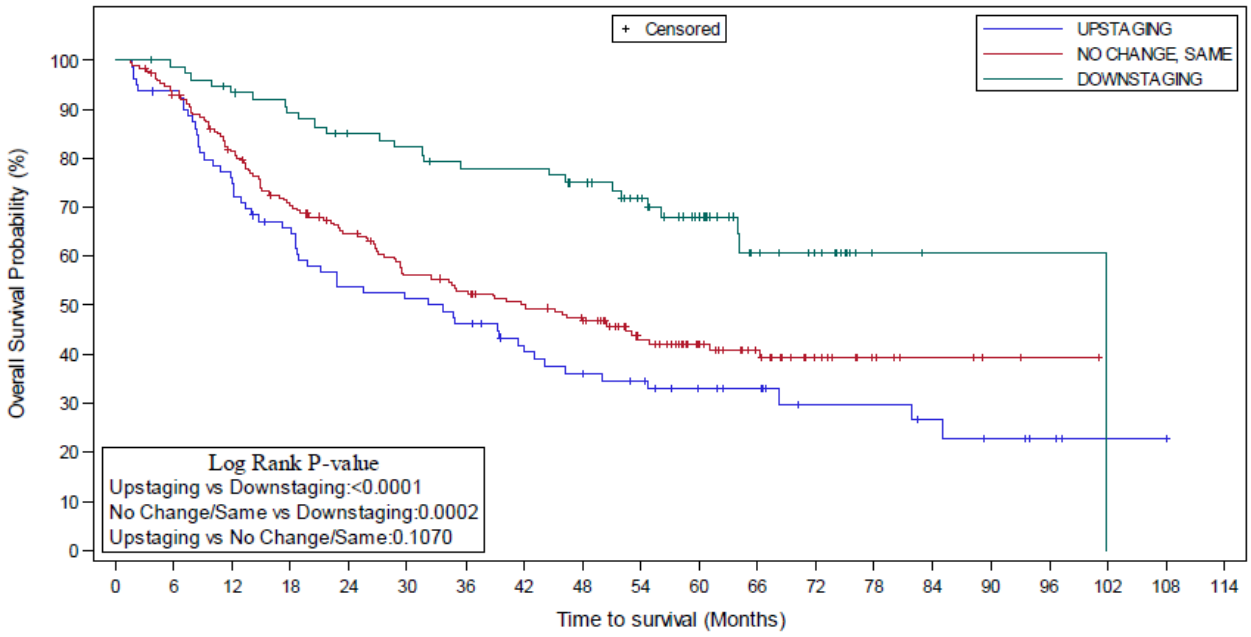
Exhibit II – Surgery Outcome Relative to Screening/Entry[2]

Treatment Group	Upstage (U)	No Change	Downstage (D) (PSD)	p-value (U *vs* D)*	p-value vs SOC**
LI+CIZ+SOC	80 (23.1%)	191 (55.0%)	76 (21.9%)	0.8103	0.002
LI+SOC	19 (16.59%)	72 (62.6%)	24 (20.9%)	0.5424	0.0499
Combined LI	99 (21.4%)	263 (56.9%)	100 (21.6%)	1.0000	0.0017
SOC alone (Control)	78 (22.1%)	229 (64.9%)	46 (13.0%)	0.0052***	N/A

[1] Cel-Sci's 2023 ESMO Poster Graphic.
[2] Cel-Sci's 2023 ESMO Poster Graphic.

When we examine the Kaplan-Meier curve for intent to treat Multikine patients comparing those who were downstaged, upstaged and remained at the same stage, we can see the wide separation in the curves.

Exhibit III – Overall Intent To Treat Comparing Staging Groups[3]

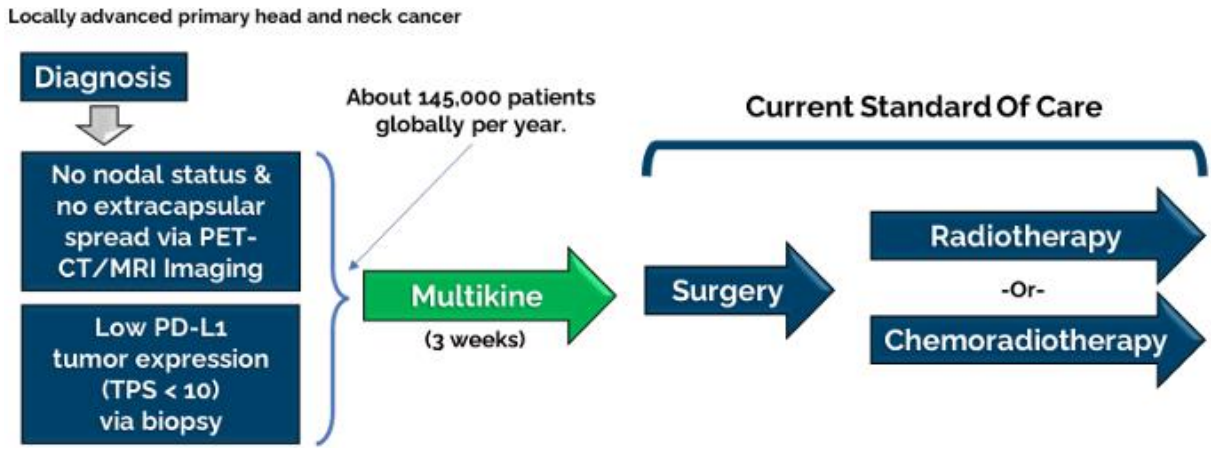


CEO Shareholder Letter

Several CEL-SCI posters have been presented at conferences sponsored by the European Society for Medical Oncology (ESMO) and the American Head and Neck Cancer Society (AHNS) among other scientific conferences. In parallel with their release, CEL-SCI CEO Geert Kersten has published a shareholder letter emphasizing some of the differentiating characteristics of Multikine that have emerged after further analysis of the IT-MATTERS clinical data. He lists several factors that enable physicians to identify patients that respond to Multikine 28.4 percentage points better than the control group, which is a greater than 60% improvement. Survival is improved in cases where there is:

- Low PD-L1 protein receptor expression
- Low risk assessment
- No extracapsular spread
- No lymph node invasion (N0)

Exhibit IV – Multikine Selection Criteria[4]



[3] Cel-Sci's 2023 ESMO Poster Graphic.
[4] CEL-SCI Shareholder Letter, October 25, 2023

For patients with these characteristics at diagnosis, risk of death fell from 55% to 27% at the five year mark in the IT-MATTERS trial. Other metrics related to this population are the hazard ratio, presurgical response (PSR) and presurgical downstaging (PSD). The hazard ratio of 0.35 indicates that deaths occurred at 35% of the rate in the Multikine arm as in the control arm. 13% of Multikine patients compared to 0% control patients exhibited a PSR while 35% of Multikine patients and 13% of control patients showed a PSD. Mr. Kersten puts these elements together and intends to seek immediate approval based on the efficacy and safety of Multikine and the unmet need for squamous cell carcinoma of the head and neck (SCCHN).

CEL-SCI intends to present this new data to regulatory agencies including Health Canada, the FDA, the MHRA and the EMA. It believes that the strongly supportive data will merit submission using a conditional approval pathway, which would not require a new trial before approval. Management thinks that it will be clear whether or not this is an option as soon as January 2024.

Manufacturing Facility

Commissioning of the Multikine manufacturing facility is substantially complete as reported in an October 19th press release. CEL-SCI is commissioning and qualifying the facility's utilities, systems, and equipment in alignment with guidelines for the International Society for Pharmaceutical Engineering (ISPE) and the International Conference for Harmonization (ICH). The facility will be subject to regulatory review prior to the granting of a commercial manufacturing license and marketing clearance for Multikine. Details related to the commissioning of the facility will be included in the company's biologic licensing application (BLA).

MHRA Request Filing

An October 5th announcement outlined CEL-SCI's request with the United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA) to discuss a pathway for approval of Multikine for the treatment of head and neck cancer. The MHRA is an executive agency of the Department of Health and Social Care in the United Kingdom and responsible for ensuring that medicines and medical devices work and are acceptably safe.

CEL-SCI disclosed that it has gathered new results that demonstrate pre-surgical response rates and overall survival advantages that are superior to those previously published. A refined selection algorithm was developed with assistance from regulators and consultants to generate them. The new algorithm can more accurately predict which patients will benefit most from the therapy.

CEL-SCI is planning to present a statistical validation of the outcomes in the new target population. This will consist of a poster to be presented at the Conference of the European Society for Medical Oncology (ESMO) which takes place October 20-24, 2023 in Madrid, Spain.

EMA Scientific Advice Filing

Europe is an important market for Multikine as it has a population one-third greater than the United States and a higher incidence of head and neck cancer.[5] Based on the guidelines published by the regulatory authorities, CEL-SCI believes it can obtain conditional approval in the EU. The European Medicines Agency's (EMA's) Conditional Marketing Authorization is typically granted for one year initially, with annual reassessment for renewal.

CEL-SCI disclosed that it had submitted a Scientific Advice Filing with the European Medicines Agency (EMA) for Multikine in the treatment of head and neck cancer in a September 26th press release. The data package will be reviewed by the EMA's Scientific Advice Working Group. The goal of the submission is to obtain the agency's opinion regarding the available data for Multikine and come to an agreement on a plan to file for marketing authorization in the European Union (EU). CEL-SCI has identified twice as many annual cases of head and neck cancer in the EU as compared to the United States.

A scientific advice filing with the EMA is a process to obtain guidance from the EMA on a development plan for a new medicine. It allows companies to get EMA feedback on development plans so that the sponsor can collect the correct data for regulatory approval. It includes guidance on quality, safety and efficacy testing requirements, interpretation of data and other development considerations. The EMA will respond with written feedback and recommendations.

[5] Gormley, M. *et al*. Reviewing the epidemiology of head and neck cancer: definitions, trends and risk factors. British Dental Journal. November 11, 2022.

Anticipated Milestones:

- Conduct meetings with European Medicines Agency (EMA) – 2H:23
- Request scientific advice from the EMA – 2H:23
- Review feedback from EMA scientific advice meeting

FDA Meeting

CEL-SCI updated investors on its interactions with the FDA in a July 14th, 2023 press release. While the FDA suggested that the company submit a biologic license application (BLA) based on available data, it also requested additional information which will be provided in a subsequent meeting with the agency. Few details were provided regarding the next steps; however, we anticipate another study will be required before the company may successfully file a BLA with the FDA.

Anticipated Milestones:

- Conduct further meetings with the FDA
- Compile additional information requested
- Collaborate with agency to identify approval pathway and clinical trial protocol
- Conduct confirmatory trial

Pursuing Conditional Approval from Health Canada

In an April 19th press release CEL-SCI announced its intent to pursue a conditional approval pathway for Multikine in advanced primary head and neck cancer. Conditional pathways are justified by limiting eligibility to drugs intended for serious and life-threatening diseases or where there is unmet need. It is an appropriate pathway for an indication that is considered a rare disease that lacks effective treatment.

Conditional approval is a regulatory mechanism used by Health Canada to provide approval for marketing in Canada and is based on less rigorous submission requirements as compared to full approval. It is intended for serious conditions that have few if any other treatments available and allows patients earlier access. To be eligible, the condition being treated must be serious, life-threatening or severely debilitating. The drug must show promising clinical benefit and acceptable safety risks given the condition being treated. If Health Canada grants conditional approval it is usually for a limited period while additional studies are conducted to support the product's safety and effectiveness.

CEL-SCI reported that it held a productive pre-submission meeting with Health Canada. The conversation with the agency explored how patients at lower risk for recurrence could be targeted for treatment and which post-market commitments could help ensure that only the most suitable patients would be treated with Multikine.

Anticipated Milestones:

- Prepare Notice of Compliance with Conditions (NOCC)
- Request advance consideration for approval under NOCC – 1H:24
- Assuming NOCC granted, begin commercialization – 2H:24
- Conduct post-marketing studies or additional clinical trials

CEL-SCI Milestones

- Presentation of poster at ECHNO – March 2023
- Pre-submission meeting with Health Canada – April 2023
- Presentation of poster at ESTRO – May 2023
- Presentation at AHNS – June 2022
- Public offering of common stock – July 2023
- Presentation at ESMO – October 2023
- Development of clinical study report – 2023
- Development of paper(s) for publication in peer reviewed journal – 2023
- Feedback from various regulatory agencies - 2024
- Submission of license application to various agencies – 2024+

Summary

CEL-SCI continues to refine the factors that identify which patients best respond to Multikine. With the latest poster that was presented at ESMO, the research finds that patients with disease that has not spread and with low PD-L1 expression perform best. Further, the research shows that those whose cancer severity is downgraded following Multikine treatment and prior to surgery relative to baseline have materially better survival. Along with the presentation of new scientific data, CEL-SCI continues to prepare its manufacturing facility for production and regulatory approval. In parallel with these efforts the regulatory team is consulting with leading regulatory agencies in preparation for an application for conditional approval. We maintain our price target of $7.00 per share.

PROJECTED FINANCIALS

CEL-SCI Corporation - Income Statement

CEL SCI Corporation	2022 A	Q1 A	Q2 A	Q3 A	Q4 E	2023 E	2024 E	2025 E
Total Revenues	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**
Research & Development	$25.4	$5.4	$6.1	$5.7	$5.0	$22.2	$18.0	$12.0
General & Administrative	$10.7	$2.3	$2.1	$2.5	$2.5	$9.3	$10.0	$10.0
Income from operations	($36.1)	($7.7)	($8.2)	($8.2)	($7.5)	($31.5)	($28.0)	($22.0)
Other Income	($0.5)	($0.2)	($0.0)	($0.0)	$0.0	($0.2)	$0.0	$0.0
Interest Expense	($1.1)	($0.2)	($0.2)	($0.2)	($0.2)	($0.7)	($0.8)	($0.8)
Pre-Tax Income	($37.6)	($8.0)	($8.3)	($8.4)	($7.7)	($32.4)	($28.8)	($22.8)
Provision for Income Tax	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	0.0%	0.0%	0.0%	0.0%	0.0%	29.0%	29.0%	29.0%
Net Income	**($37.6)**	**($8.0)**	**($8.3)**	**($8.4)**	**($7.7)**	**($32.4)**	**($28.8)**	**($22.8)**
Reported EPS	**($0.87)**	**($0.18)**	**($0.18)**	**($0.19)**	**($0.16)**	**($0.71)**	**($0.48)**	**($0.38)**
Basic Shares Outstanding	43.15	44.44	45.59	44.25	49.00	45.82	60.00	60.00

Source: Company Filing // Zacks Investment Research, Inc. Estimates

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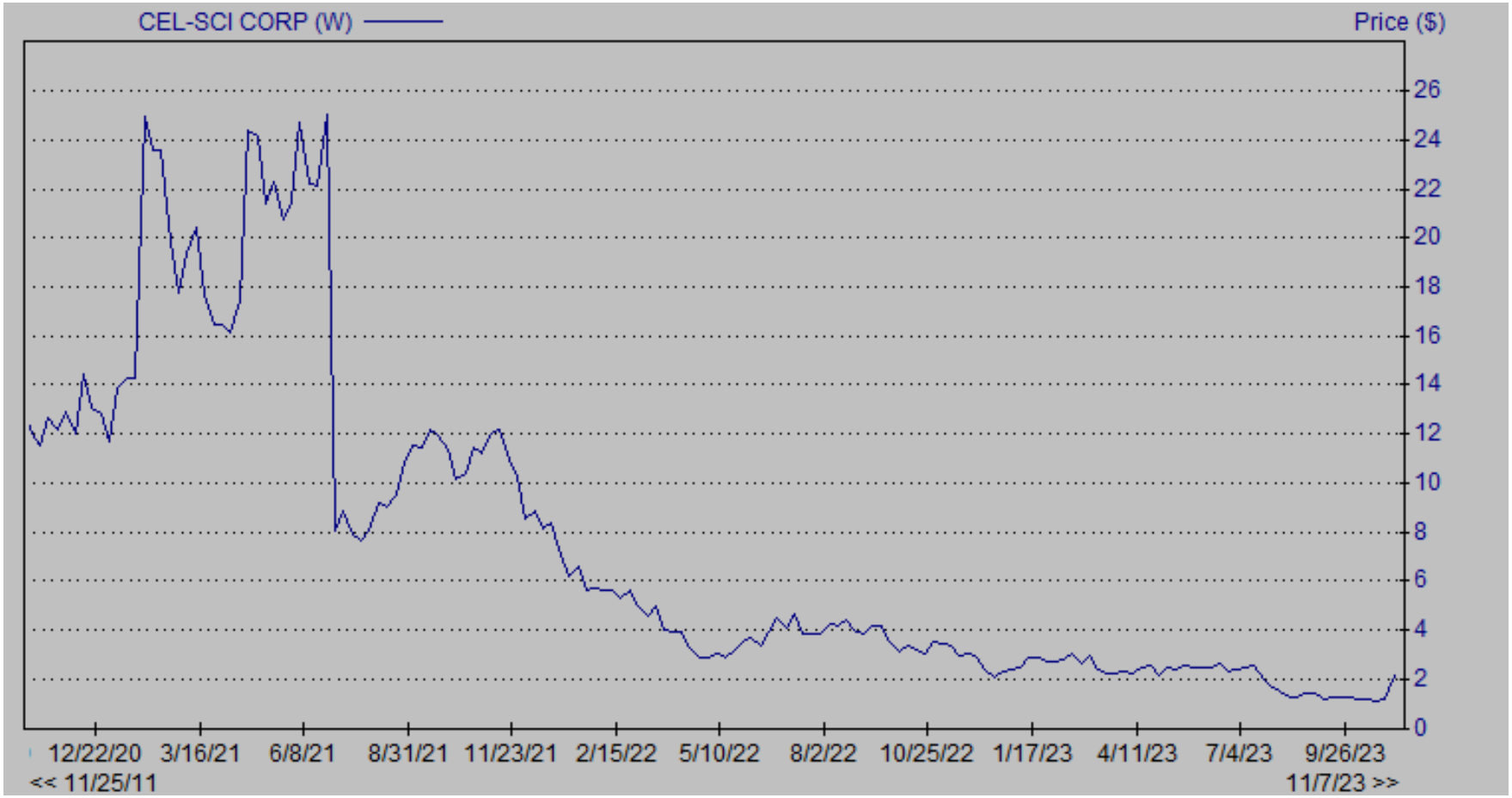
HISTORICAL STOCK PRICE

CEL-SCI Corporation – Share Price Chart



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