CEL-SCI
Empowering Immune Defenses

CEL-SCI Corporation
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Ticker (Exchange)	CVM-NYSE
Recent Price (03/20/2023)	$2.25
52-week Range	$1.88 - $6.51
Shares Outstanding	43.7 million
Market Capitalization	$99 million
Average 10-day volume	228,700
Insider Ownership +>5%	3.9%
Institutional Ownership	13.4%
EPS (Qtr. ended 12/31/22)	($0.18)
Employees	75

CVM (NYSE) One-year Stock Chart

PRODUCT PIPELINE	
MULTIKINE®	
Head and Neck Cancer	Phase 3 Pivotal Study
HPV	Phase 1
LEAPS™ TECHNOLOGY	
Rheumatoid Arthritis	Phase 1 enabling studies

Source: CEL-SCI Corporation.

COMPANY DESCRIPTION

CEL-SCI Corporation ("CEL-SCI" or "the Company") is a clinical-stage biotechnology company developing **immunotherapy†** technologies to treat cancer, autoimmune and infectious diseases. The Company is targeting novel therapy candidates that activate and utilize the body's own immune system against disease. CEL-SCI is developing products based on two technologies: (1) Multikine® (Leukocyte Interleukin, Injection), a novel immunotherapy **first-line** treatment that has completed a 10 year Phase 3 trial for head and neck cancer; and (2) LEAPS™ (Ligand Epitope Antigen Presentation System), an immunotherapy peptide vaccine technology platform. The goal of Multikine® is to modulate the body's immune system to create a two-pronged mechanism of action: eliciting the direct killing of tumor cells and **micrometastasis** while generating a sustainable anti-tumor response to extend survival. Multikine® is being developed for **neoadjuvant (before surgery)** administration and could become an integral first-line component of the **standard of care (SOC)** regimen for locally advanced primary (previously untreated) head and neck cancers. As a neoadjuvant, Multikine® can stimulate the immune system before it is weakened by the toxic cancer therapies, improving its long-term therapeutic effect. The LEAPS™ platform is designed to stimulate the immune system to fight bacterial, viral, and parasitic infections more effectively, as well as autoimmune conditions (e.g., rheumatoid arthritis) and cancer. LEAPS™ can be designed to produce a specific natural immune response required for the desired therapeutic effect, depending on the type of LEAPS™ construct used.

KEY POINTS

- CEL-SCI's initial indication for Multikine® is as the first treatment immediately following diagnosis (given prior to any other treatment) in advanced primary (previously untreated) **squamous cell carcinoma** of the head and neck (SCCHN). CEL-SCI received **Orphan Drug** Status/designation from the U.S. Food and Drug Administration (FDA) for this indication.
- The Company's 10-year Phase 3 trial showed that Multikine® significantly extended the lives of patients with locally advanced primary SCCHN treated with surgery and radiotherapy (noting there has been no FDA approval for new products in first-line therapy for those who get surgery as a first treatment in over 50 years).
- CEL-SCI is completing and submitting a **Biologics License Application (BLA)** to the FDA for approval of Multikine® to treat advanced primary head and neck cancer on patients scheduled to receive surgery and radiotherapy as their primary treatments.
- Roughly 210,000 patients globally and 25,000 in the U.S. would be eligible for Multikine® treatment if approved. CEL-SCI's data is favorable compared to approved SCCHN therapies, with an absolute survival benefit of 14.9% (difference between 62.7% versus 48.6% survival at five years), a good percentage of partial and even complete tumor responders in only three weeks, and a favorable toxicity profile.
- CEL-SCI has completed the commercial scale buildout of its 73,000 sq. ft. Multikine® manufacturing and R&D facility in anticipation of market demand once it receives regulatory approval and is finishing the validation of the manufacturing facility.
- As of December 31, 2022, CEL-SCI's cash position was $18 million.

Table of Contents

Executive Overview

CEL-SCI Corporation ("CEL-SCI" or "the Company") is a clinical-stage biotechnology company focused on developing immunotherapy products and technologies to treat cancer, autoimmune, and infectious diseases that address significant unmet medical needs. The Company aims to develop novel therapies with the potential to activate and utilize the body's own immune system against the disease, while imparting minimal toxicity to normal cells and organ systems (which is rare for any drug, but even more so in oncology). The Company is focused on developing products based on two innovative technologies: (1) Multikine® (Leukocyte Interleukin, Injection), a next-generation, comprehensive immunotherapy in late Phase 3 development as a first-line treatment for newly diagnosed advanced primary head and neck cancer; and (2) LEAPS™ (Ligand Epitope Antigen Presentation System), a **peptide**-based immunotherapy vaccine technology platform. A summary of the Company's product pipeline based on these proprietary technologies is provided in Figure 1, with further details in the accompanying pages.

Figure 1
PRODUCT PIPELINE

MULTIKINE®		
Head and Neck Cancer	Neoadjuvant therapy for squamous cell carcinoma of the head and neck	Phase 3 Pivotal Study
HPV	Cervical dysplasia in HIV/HPV co-infected patients	Phase 1
LEAPS™ TECHNOLOGY		
LEAPS™	Rheumatoid Arthitis CEL-2000	Phase 1 enabling studies (NIH Grant)

Source: CEL-SCI Corporation.

MULTIKINE® IMMUNOTHERAPY

The Company's lead product candidate, Multikine®, is an investigational immunotherapy under development for the neoadjuvant treatment of advanced (Stages 3 and 4) primary (previously untreated) squamous cell carcinoma of the head and neck (SSCHN), as well as Phase 1 for **cervical dysplasia** in human immunodeficiency virus (HIV) and human papillomavirus (HPV) co-infected patients. Head and neck cancer is the fifth largest cancer with almost 900,000 cases per year worldwide. SCCHN represents about 90% of all head and neck cancers. Current standard of care (SOC) for this advanced primary head and neck cancer is surgery, followed by radiation therapy alone or surgery followed by concurrent radio-chemotherapy (as defined by the **National Comprehensive Cancer Network [NCCN]** guidelines), depending on the severity of the disease.

Multikine® is comprised of a patented defined mixture of 14 human natural **cytokines** and cellular products. The pro-inflammatory cytokine mixture includes **interleukins**, **interferons**, **chemokines**, and other elements of the body's natural mix of defenses against cancer. The drug is being used in a unique way compared to other cancer immunotherapies. Unlike conventional immunotherapies, which have traditionally been administered late in the disease progression (often after surgery, chemotherapy, and/or radiation therapy), Multikine® is being developed as a first-line treatment to be given as a neoadjuvant, before any other therapies, as these can weaken the integrity of the immune system. Multikine® is administered locally and stimulates the immune system before it is weakened by both surgery and the toxic therapies that are administered to cancer patients, and by the cancer itself. The goal of Multikine® administration is to modulate the body's healthy immune system to elicit its own anti-tumor response to kill the tumor and the micrometastases that usually cause recurrence. Following approval, Multikine® would be the world's first cancer immunotherapy drug in head and neck cancer to be administered immediately after diagnosis and before surgery.

CEL-SCI has received Orphan Drug Status/designation from the U.S. Food and Drug Administration (FDA) for the neoadjuvant treatment of SCCHN. Advanced primary head and neck cancer is a large unmet medical need that currently has only one recommended standard of care (SOC), which is surgery, followed by either radiation or concurrent radiation/chemotherapy—with the last treatment for this indication approved by the FDA over 50 years ago. CEL-SCI intends to demonstrate that Multikine® can become an integral first-line component of the current SOC regimen due to its effectiveness and safety profile.

The Company conducted a series of Phase 1 and Phase 2 clinical trials in over 200 patients throughout the U.S., Europe, Canada, and Israel, which demonstrated that Multikine® was safe and well tolerated, with significant clinical impact. In its Phase 2 clinical trial in advanced primary head and neck cancer, CEL-SCI reported that approximately 10% of patients administered the Multikine® treatment regimen over a three-week period had no clinical or pathologic evidence of any remaining tumor after treatment. The Company also reported a 33% improvement in overall survival of Multikine®-treated patients over that in the literature for the same indication in that same study. In addition, these clinical studies found that Multikine® treatment resulted in positive effect on quality of life observations, including weight gain and reduction in pain, among others. Investigators did not report severe adverse events directly associated with the use of Multikine® in any of the completed Phase 1 and 2 trials.

Phase 3 Study (IT-MATTERS)

In 2011, CEL-SCI initiated the Multikine® global pivotal randomized Phase 3 trial (IT-MATTERS) for patients with locally advanced primary head and neck cancer. This was the largest and longest study in head and neck cancer ever. The pivotal trial, composed of 928 newly diagnosed not yet treated head and neck cancer patients, was a global, randomized, controlled multi-center Phase 3 study. The study was designed to be event-driven, requiring 298 deaths (events) to occur in the combined comparator arms to achieve an adequate level of statistical power to prove the survival benefit. Key highlights from CEL-SCI's Phase 3 study of the Multikine®-treated study population who receive surgery and radiotherapy as their SOC treatments showed the following advantages over control:

- A median overall survival improvement of 46.5 months (nearly four years);
- 62.7% of Multikine® patients were alive after five years versus 48.6% in the control;
- Nearly one out of every six patients had their tumors shrink by more than 30% in just three weeks and prior to surgery;
- Five patients had their tumors completely disappear in just three weeks and prior to surgery (confirmed by pathology at surgery); and
- Tumor shrinkage/disappearance cut the death rate by a factor of three.

CEL-SCI's data compares favorably to other already approved SCCHN therapies, which are not indicated for the type of patient that Multikine® treated in the Phase 3 study. Specifically, Merck & Company's (MRK-NYSE) product, Keytruda®, was approved for recurrent SCCHN based on a single-arm trial with a 16% tumor response rate (CEL-SCI showed the same response rate in a randomized controlled trial). Keytruda® did not show a survival improvement (while CEL-SCI showed an absolute survival benefit of 14.1% at five years). Bristol Myers Squibb's (BMY-NYSE) drug, Opdivo®, was approved based on only a 2.4-month life extension (CEL-SCI showed a median 46-month improvement in life extension). Multikine® further has demonstrated a much more favorable toxicity profile than these approved products. CEL-SCI's Phase 3 trial results are intended to support a Biologics Licensing Application (BLA) to the FDA (which has not yet been submitted as the validation of the manufacturing facility has been delayed by the Defense Procurement Act favoring any orders for COVID vaccine related materials, some of which CEL-SCI also uses for the manufacture of Multikine®).

The Company recently published and presented data from this clinical trial at two prestigious cancer conferences: 2022 ASCO Annual Meeting in Chicago, Illinois and the 2022 European Society for Medical Oncology (ESMO) annual Congress in Paris, France. Further, results from the Phase 3 clinical trial of Multikine® in advanced primary head and neck cancer were posted to the U.S. government clinical trial website www.clinicaltrials.gov.

CEL-SCI's Multikine® Phase 3 Cancer Study Shows 43% Survival Extension

On March 8, 2023, CEL-SCI reported new data from its pivotal Phase 3 study, the largest study ever conducted in newly diagnosed locally advanced SCCHN. A poster presentation titled "Leukocyte Interleukin Injection (LI) immunotherapy followed by radiotherapy extends overall survival (OS) in treatment naïve locally advanced primary squamous cell carcinoma of the head & neck: the IT-MATTERS Study" was delivered by Eyal Talor, Ph.D., CEL-SCI's Chief Scientific Officer (biography on page 8) at the 10th European Congress on Head & Neck Oncology (ECHNO) in Lisbon, Portugal. Greater details of the key findings from this study are provided on page 41

Current Development Status

It is important to note that Multikine®'s development has taken longer due to its new neoadjuvant approach and lack of precedent in treating SCCHN. Proving safety and efficacy from scratch without the foundation and validation of previous discoveries takes time and requires more discussion and proof. While the Company has more limited resources than larger pharmaceutical companies, such as Merck & Company or Bristol Myers Squibb, CEL-SCI has assembled an extraordinary team of experts who is focused on getting Multikine® approved, including consultants who previously worked at the FDA, world-class biostatisticians, and Key Opinion Leaders (as profiled on pages 8-11).

During 2022, CEL-SCI was focused on completing a BLA to the U.S. FDA aimed at gaining approval of Multikine® to treat SCCHN, noting that existing drug therapies from competitors Merck and Bristol Myers Squibb are approved as a last resort for recurrent tumors after treatments have failed or for patients who are not candidates for surgery. In contrast, Multikine® is given to newly-diagnosed patients following initial diagnosis ahead of surgery and is the first of its kind with significant survival benefit in a randomized Phase 3 trial in locally advanced primary SCCHN.

Competitive Advantage

Multikine® is being developed as a first-line treatment to be given to patients following initial definitive diagnosis and before any other therapy options, administered within the short period that normally occurs between diagnosis and surgery. Any new therapy must be able to accommodate this protocol, as any delay of the intent to cure SOC treatment would be unethical. However, if following approval, Multikine® gets accepted as part of a new SOC (as is the Company's objective), CEL-SCI believes that development of competing treatments might be difficult. Any clinical trial of future first-line candidates would not be able to delay SOC therapies, which would include Multikine® as its initial treatment, to avoid ethical concerns, which would mean that they might not be able to take Multikine®'s place as part of the SOC, making comparisons with Multikine® extremely difficult. In addition, Multikine® is a complex biologic requiring special manufacturing (further described on page 7), and the Company has spent over 10 years developing and validating its manufacturing process held as a trade-secret. This signifies a significant barrier to entry for any future similar or generic competitive technologies.

LEAPS™ (LIGAND EPITOPE ANTIGEN PRESENTATION SYSTEM)

CEL-SCI's second proprietary technology platform, LEAPS™, is an immunotherapeutic/vaccine technology designed to stimulate the immune system to fight bacterial, viral, and parasitic infections more effectively, as well as autoimmune conditions, allergies, transplant rejection, and cancer. Administered as an immunotherapeutic/vaccine, the LEAPS™ compound consists of a small **T or Immune-cell binding ligand (TCBL/ICBL)** linked with a disease-associated peptide **antigen** and is delivered directly to the recipient by injection or mucosal absorption.

Regulation of the immune system is mainly conducted by **T-helper (Th) cells** (differentiated into various cell subsets, including the Th1, Th2, Th17, Th9, and Th22 subsets) as well as **T-regulatory (T-reg) cells**, via the secretion of cytokines. Differentiated Th cell subsets secrete different cytokines. Of particular interest to CEL-SCI are the Th1 and Th17-mediated immune responses. Th1 and Th17 are actively involved in an inflammatory cascade, with Th17 cells known to play an important role in the induction of autoimmune disease and Th1 cells associated with **hypersensitivity immune reactions**, exaggerated or inappropriate immune reactions against an antigen.

The TCBL/ICBL activates the immune system by targeting or binding to an antigen presenting cell, such as a **T-cell** and other immune cells. When a LEAPS™ formulation attaches to a certain T-cell, it causes that cell to activate a particular immune response, altering only select cytokines. Thus, the Company believes that its LEAPS™ technology platform has an advantage over other technologies since LEAPS™ vaccines can be designed to produce a specifically (desired) immune response involving the specific T-cells needed for a therapeutic effect, depending on the type of LEAPS™ construct and TCBL/ICBL used. Two TCBLs of particular interest for CEL-SCI are TCBL peptides J (J-LEAPS™) and G (or the modified and more stable version of G, derG [derG-LEAPS™]). Conjugates of these appear to activate different sub-sets of T-cells, with J conjugates eliciting a **Th1 response**, and G conjugates directing a **Th2 response**, promoting **antibody** production.

The Company has conducted a series of preclinical animal studies in several disease indications. In these studies, the LEAPS™ candidates have demonstrated efficacy as a therapeutic agent in rheumatoid arthritis (RA) as well as H1N1 influenza infection, and breast cancer. In addition, LEAPS™ constructs have also shown some level of efficacy in myocarditis, lethal herpes simplex virus (HSV1), malaria, and Hepatitis B in preclinical animal studies.

Rheumatoid Arthritis (RA)

Two LEAPS™-based product candidates—CEL-2000 and CEL-4000—have shown the potential to block the progression of RA, a disease that may be driven by different types of inflammatory responses for each individual. Although the initiating events of RA are unknown, the disease is maintained by pro-inflammatory mediators, primarily Th1 and Th17 cell-driven autoimmune responses. CEL-2000, a J-LEAPS™ vaccine, blocked the progression of **collagen induced arthritis (CIA)** by immunomodulation of the Th17 response. CEL-4000, A derG-LEAPS™ vaccine, demonstrated therapeutic efficacy for the **PGIA/GIA** RA mouse models by stopping Th1 driven disease progression.

Different Approaches to the Same Goal

The importance of LEAPS™'s ability to modulate the specific pro-inflammatory immune response based on what conjugate is used is demonstrated by the difference in efficacy of the J-TCBL (CEL-2000) and derG-TCBL (CEL-4000) versions of the LEAPS™ vaccines in animal models of disease. The CEL-4000 vaccine was effective in curtailing progression of RA in the Th1-driven PGIA/GIA model, whereas CEL-2000 was effective in blocking the progression of RA in the Th17-driven CIA animal model. It is possible that the failure of some patients to respond to certain therapies may reflect differences in the type of inflammatory response that may be driving their disease. Thus, in the future studies in the development of LEAPS™ vaccines and treatments, the knowledge of the T-cell cytokine profiles that drive a particular patient's disease can facilitate the choice of the use of appropriate LEAPS™ vaccine/treatment. Once the nature of the inflammatory response in a patient has been identified, the patient can be treated with the appropriate LEAPS™ vaccine with either a J-TCBL to counteract a Th17-driven response or a derG-TCBL to counteract a Th1-dominated response.

Rheumatoid Arthritis (RA) Vaccine Grants

Research for the development of the LEAPS™ technology as a treatment for RA has been funded via collaborations with the U.S. National Institutes of Health (NIH), U.S. Army, Navy, and universities. The Company was awarded two **Small Business Innovation Research (SBIR)** grants from the National Institutes of Health: a $225,000 Phase 1 SBIR grant (July 2014) and a $1.5 million Phase 2 SBIR grant (September 2017). The grants provide funding to advance the LEAPS™ product candidates towards an **Investigational New Drug (IND)** application by funding IND enabling and additional mechanism of action studies, among other preclinical development activities.

HEADQUARTERS, FACILITIES, AND EMPLOYEES

CEL-SCI was formed as a Colorado corporation in 1983. It is now headquartered in Vienna, Virginia, in close proximity to the FDA, the National Institutes of Health (NIH), and the National Cancer Institute (NCI). CEL-SCI currently employs 75 individuals and operates its own state-of-the art **current good manufacturing practices (cGMP)** and **Biosafety Level 1 (BSL-1)** manufacturing facility.

Manufacturing Facility

CEL-SCI operates a dedicated state-of-the art facility with over 73,000 square feet of manufacturing and research and development (R&D) space available (with approximately 45,000 square feet of this space fully developed) as shown in Figure 2. The cGMP and BSL-1 facility was built specifically for Multikine® and produced multiple clinical lots of its investigational biological product candidate to supply its global pivotal Phase 3 clinical trial. The facility has a proprietary automated cold fill to ensure no loss of biological activity during fill. Upon commercial approval, CEL-SCI intends to manufacture Multikine® in a proprietary manner in the same commercial scale-ready manufacturing facility. The facility has passed quality systems review by a **European Union Qualified Person (QP)** on several occasions and has been inspected by the QP for the manufacture and release of Sterile Medicinal Products (per **ICH and EU directives**).

CEL-SCI's manufacturing facility is currently being validated following the completion of its commercial scale expansion during the first quarter of 2022 to ensure compliance with all FDA GMP and European regulations. CEL-SCI believes that Multikine®'s manufacturing trade secret is a strategic asset. According to the Company, manufacturing in-house helps protect its intellectual property (IP) and allows for more control when working with the FDA and other regulators to secure approval of Multikine®. Multikine® is a complex **biologic** requiring special manufacturing and the Company has spent over 10 years and over $100 million developing and validating its manufacturing process, acquiring significant "know how" as well as trade secrets. Importantly, this not only produces competitive advantages but provides a significant barrier to entry for any future similar or generic competitive technologies.

Figure 2
MANUFACTURING FACILITY

Source: CEL-SCI Corporation.

Company Leadership

CEL-SCI has added highly experienced individuals to its team, including scientists, biostatisticians, regulatory counsel who worked at the FDA, an oncologist who worked at the FDA as a clinical reviewer, and more than half a dozen independent oncologists to its Scientific Advisory Board, including key opinion leaders (KOLs) from major U.S. medical centers. One of CEL-SCI's team members has helped bring over 80 drugs to market. Biographies of some of these key individuals are provided in the accompanying section.

Management

Geert R. Kersten, Chief Executive Officer (CEO) and Director

Geert Kersten has served in his current leadership role at CEL-SCI since 1995. Mr. Kersten has been with CEL-SCI since the Company's inception in 1987. He has been involved in the pioneering field of cancer immunotherapy for almost two decades and has successfully navigated CEL-SCI through many challenging cycles in the biotechnology industry. Mr. Kersten also provides CEL-SCI with significant expertise in the fields of finance and law and has a unique vision of how the Company's Multikine® product is expected to change the way cancer is treated. Prior to CEL-SCI, Mr. Kersten worked at the law firm of Finley & Kumble and worked at Source Capital, an investment banking firm located in McLean, VA. He is a native of Germany, graduated from Millfield School in England, and completed his studies in the U.S. Mr. Kersten completed his Undergraduate Degree in Accounting, received an M.B.A. from George Washington University, and a law degree (J.D.) from American University in Washington, DC. Mr. Kersten is also the inventor of a patent on the potential use of Multikine® in managing cholesterol.

Eyal Talor, Ph.D., Chief Scientific Officer

Eyal Talor joined CEL-SCI in October 1993. In October 2009, Dr. Talor was promoted to Chief Scientific Officer. Prior to this promotion, he was the Senior Vice President of Research and Manufacturing. Dr. Talor is a clinical immunologist with over 28 years of hands-on management of clinical research and drug development for immunotherapy application; pre-clinical to Phase 3, in the biopharmaceutical industry. His expertise includes; biopharmaceutical R&D and biologics product development, GMP (Good Manufacturing Practices) manufacture, Quality Control testing, and the design and building of GMP manufacturing and testing facilities. He served as Director of Clinical Laboratories (certified by the State of Maryland) and has experience in the design of pre-clinical and clinical trials (Phase 1 to 3) and GCP (Good Clinical Practices) requirements. He also has broad experience in the different aspects of biological assay development, analytical methods validation, raw material specifications, and QC (Quality Control) tests development under FDA/GMP, USP, and ICH guidelines. Dr. Talor has extensive experience in the preparation of documentation for IND and other regulatory submissions. His scientific area of expertise encompasses immune response assessment. He is the author of over 25 publications and has published a number of reviews on immune regulations in relation to clinical immunology. Before joining CEL-SCI, he was Director of R&D and Clinical Development at CBL, Inc., Principal Scientist - Project Director, and Clinical Laboratory Director at SRA Technologies, Inc. Prior to that, he was a full time faculty member at The Johns Hopkins University, Medical Intuitions; School of Public Health. He has invented technologies that are covered by ten issued patents; on Multikine®'s composition of matter and method of use in cancer and two platform peptide technologies, Antigen Directed Apoptosis of T-cells (Adapt) and Ligand Epitope Antigen Presentation System (LEAPS), for the treatment of autoimmune diseases, asthma, allergy, transplantation rejection, and infectious diseases. He also is responsible for numerous product and process inventions as well as a number of pending U.S. and PCT patent applications. He received a Ph.D. in Microbiology and Immunology from the University of Ottawa, Ottawa, Ontario, Canada, and had post-doctoral training in clinical and cellular immunology at The Johns Hopkins University, Baltimore, MD. He holds an Associate teaching position at the Johns Hopkins University Medical Institutions.

Patricia B. Prichep, Senior Vice President, Operations

Patricia Prichep has over 30 years of experience in business operations and administration. She joined CEL-SCI in 1992 and has been the Company's Senior Vice President of Operations since March 1994. Between December 1992 and March 1994, Ms. Prichep was CEL-SCI's Director of Operations. She became CEL-SCI's Corporate Secretary in May 2000. Ms. Prichep is responsible for all day-to-day operations of the Company, including human resources and is the liaison with the auditing firm for financial reporting. From June 1990 to December 1992, Ms. Prichep was the Manager of Quality and Productivity for the NASD's Management, Systems and Support Department. She was responsible for the internal auditing and workflow analysis of operations. Between 1982 and 1990, Ms. Prichep was Vice President and Operations Manager for Source Capital, Ltd. She handled all operations and compliance for the company and was licensed as a securities broker. Ms. Prichep received a B.A. from the University of Bridgeport in Connecticut.

Dan Zimmerman, Ph.D., Senior Vice President of Research, Cellular Immunology

Daniel Zimmerman, Ph.D., is the Senior Vice President of Research, Cellular Immunology for CEL-SCI Corporation and head of the LEAPS™ technology program. Dr. Zimmerman has invented technologies which are covered by over a dozen U.S. patents as well as many foreign equivalent patents. He is the author of over 40 scientific publications in the area of immunology and infectious diseases. Dr. Zimmerman has been awarded numerous grants from NIH and DOD. From 1969-1973, he was a Senior Staff Fellow at NIH. For the following 25 years, he continued on at NIH as a guest worker. Dr. Zimmerman received a Ph.D. in Biochemistry in 1969, a Masters in Zoology in 1966 from the University of Florida, and a B.S. in Biology from Emory and Henry College in 1963.

John Cipriano, Senior Vice President, Regulatory Affairs

John Cipriano is CEL-SCI's Senior Vice President of Regulatory Affairs. Mr. Cipriano brings to CEL-SCI over 30 years of experience in both biotechnology and pharmaceutical companies. In addition, he held positions at the FDA as Deputy Director, Division of Biologics Investigational New Drugs, Office of Biologics Research and Review and was the Deputy Director, IND Branch, Division of Biologics Evaluation, Office of Biologics. Mr. Cipriano completed his B.S. in Pharmacy from the Massachusetts College of Pharmacy in Boston, Massachusetts. He received his M.S. in Pharmaceutical Chemistry from Purdue University in West Lafayette, Indiana.

William "Brooke" Jones, Quality Assurance

William "Brooke" Jones has been with CEL-SCI since 1999 and has overall responsibility for Quality Assurance. Mr. Jones began his career in biotechnology in 1978 at the Fort Detrick, NCI-Frederick Cancer Research Center, where he was responsible for GMP compliance of fermentation-based, clinical trial drug products used by the National Cancer Institute (NCI). With nearly 30 years of management experience in biotechnology at such companies as Biogen and Novartis, Mr. Jones brings significant experience (both American and European) in the areas of quality, regulatory, and validation. In addition to his responsibilities at Novartis in the U.S., Mr. Jones was also the Director of Quality Control and Quality Assurance at the Systemix Facility in Lyon, France, where he was involved in developing cell therapy-based clinical trial products derived from the Hematopoetic Stem Cell. Mr. Jones completed his Undergraduate degree in Biology at George Mason University and his Graduate Degree course work in Environmental Biology at Hood College.

Board of Directors

Geert R. Kersten, CEO and Director

Biograph on page 8.

Peter R. Young, Ph.D., Director

Peter Young has been a Director of CEL-SCI since August 2002. Dr. Young has been a senior executive within the pharmaceutical industry in the U.S. and Canada for most of his career, originally in organizations that are now part of Sanofi S.A. Over the last 20 years, he has primarily held positions of Chief Executive Officer or Chief Financial Officer and has extensive experience with acquisitions and equity financing. Since November 2001, Dr. Young has been the President of Agnus Dei, LLC, which has acted as a partner in an organization managing immune system clinics that treat patients with diseases such as cancer, multiple sclerosis, and hepatitis. Between 1997 and 2006, Dr. Young was also the President and Chief Executive Officer of SRL Technology, Inc., a company involved in the development of pharmaceutical drug delivery systems. Between 1998 and 2001, Dr. Young was the Chief Financial Officer of Adams Laboratories, Inc, the developer of Mucinex®. Dr. Young received a Ph.D. in Organic Chemistry from the University of Bristol, England after obtaining a Bachelor's degree in Honors Chemistry, Mathematics, and Economics. Subsequently, he qualified as a Fellow of the Chartered Institute of Management Accountants.

Bruno Baillavoine, Director

Bruno Baillavoine has been a Director of CEL-SCI since June 2015. Since 2017, Mr. Baillavoine has been the Director, Head of Pericles Group UK the subsidiary of the Paris-based leading French consulting firm, which is an expert in the field of banking, finance, asset management, and insurance with over 350 institutional clients. He has also been an advisor to the Board of CSL Inc, Combatives Sports League a U.S. Mix Martial Arts Company since 2017. Between 2010-2016, Mr. Baillavoine was a partner of Globomass Holdings Limited, a London, England-based developer of renewable energy projects from concept through final operations. From 2012-2016, Mr. Baillavoine was the Executive Chairman of Globomass Holdings. Globomass was acquired by CleanBay Inc. to which Mr. Baillavoine is an advisor to the Board and an investor. Between 1978 and 1982, he was the marketing manager of Ravenhead Ltd., a manufacturer of glass tableware, and part of United Distillers Group (later acquired by Grand Metropolitan). During this time Mr. Baillavoine became the UK Business Manager, where he restored market share and profit for United Distillers. From 1982 to 1986, Mr. Baillavoine was Group Corporate Planning and Group Marketing Director for Prontaprint, where he expanded the number of shops to 500 locations in four years. Mr. Baillavoine joined Grand Metropolitan Plc between 1986-1988 (now Diageo Plc), an FTSE 100 beverage, food, hotel, and leisure company, as director in the Special Operations division. In this capacity, he developed plans for Grand Met's trouble-shooting division for over 20,000 Grand Met retail outlets. From 1988-1991, he was the Managing Director of Nutri Systems (UK) Ltd., a subsidiary of the US based provider of professionally supervised weight loss programs. Between 1991 and 1995, Mr. Baillavoine was Director of BET Group plc, a multinational business support services group, and in 1992, was promoted to the Managing Director for the manufacturing businesses. The £2.3 billion turnaround of BET during his tenure is one of the most successful turnarounds of a top 100 FTSE company. Since 1995, Mr. Baillavoine has held a number of CEO positions across a wide range of industries and geographical locations. Mr. Baillavoine has European and American educations (U.S. high school and University of Wisconsin Eau Claire 1972-1976).

Robert Watson, Director

Robert Watson joined Intermedix, Inc. in July 2017 as President of their Preparedness Technology Division. Prior to joining Intermedix, Mr. Watson was the President and Chief Growth Officer of NantHealth, Inc. (Nasdaq: NH) from January 2015 to May 2017. Prior to NantHealth, he was President and CEO of Streamline Health, Inc. (Nasdaq: STRM) from January 2011 to January 2015. Mr. Watson has over 35 years of experience in the healthcare information technology industry as a CEO, board member, and advisor to multiple HCIT companies. He has participated in over 75 acquisitions, raised nearly $750 million in capital, completed three public offerings, and successfully sold four companies. Mr. Watson holds an MBA from the Wharton School of Business at the University of Pennsylvania and a BA degree from Syracuse University.

Gail K. Naughton, Ph.D., Director

Gail Naughton has been a Director of CEL-SCI since August 2022. Dr. Naughton is a pioneer in the field of regenerative medicine for over 35 years. She was the founder of Advanced Tissue Sciences, where she oversaw the design and development of the world's first up-scaled manufacturing facility for cell-based products, established corporate development and marketing partnerships with companies, including Smith & Nephew, Ltd., Medtronic, and Inamed Corporation, was pivotal in raising over $350 million from the public market and corporate partnerships, and brought four human cell-based products from concept through FDA approval and market launch. Dr. Naughton founded Histogen Inc. in 2007 and holds more than 125 U.S. and foreign patents and has been extensively published in the field. She has served as Dean of the College of Business Administration at San Diego State University from 2002 until 2011, where she helped to make SDSU the first U.S. campus to establish a Ph.D./MBA in life sciences. In 2000, Dr. Naughton received the 27th Annual National Inventor of the Year award by the Intellectual Property Owners Association in honor of her pioneering work in the field of tissue engineering and regenerative medicine. Dr. Naughton received her Ph.D. and M.S. from NYU Medical Center, and an MBA from UCLA. She is the Chair of the Board of the La Jolla Institute for Immunology.

Milestones

Potential Future Milestones

- More presentations and data submissions to top peer reviewed scientific venues/journals
- Completion of CSR
- FDA Biologics License Application (BLA) filing for Multikine®
- Discussions outside of U.S. with regard to Multikine® approval
- Validation of the Company's manufacturing facility
- Global Phase 3 study spanned 20 countries; FDA approval is expected to lead to approval in many countries

Intellectual Property

Patents and other proprietary rights are essential to CEL-SCI's business, however, CEL-SCI considers the protection of the Multikine® manufacturing process to be its most important protection from competitors. CEL-SCI files patent applications to protect its technologies, inventions, and improvements to its inventions that the Company considers important to the development of its business. CEL-SCI'S intellectual property (IP) portfolio covers its proprietary technologies, including Multikine® and LEAPS™, by multiple issued patents and pending patent applications in the U.S. and in key foreign markets.

Multikine® is protected by a U.S. patent, which is a **composition-of-matter** patent issued in May 2005 that, in its current format, expires in 2023. Additional composition-of-matter patents for Multikine® have been issued in Germany, China, Japan, and three in Europe. In addition to the patents that offer certain protections for Multikine®, the method of manufacture for Multikine®, a complex biological product, is held by CEL-SCI as a trade secret. Figure 3 (page 14) lists the Company's IP portfolio as it relates to Multikine®.

LEAPS™ is protected by patents in the U.S. issued in February 2006, April 2007, August 2007, January 2019, and March 2019. The LEAPS™ patents include overlapping claims, with composition of both matter (new chemical entity), process, and methods-of-use to maximize and extend the coverage in their current format. One issued U.S. application is a joint application with Northeast Ohio Medical University (Neoucom), and CEL-SCI will share the ability to use the patent, unless CEL-SCI licenses the rights to the patent from Neoucom. CEL-SCI has four patent applications pending in the U.S. and one in Europe for LEAPS™, which, if issued, would extend protection through 2034, subject to any potential patent term extensions. Figure 4 (page 15) lists the Company's IP portfolio as it relates to LEAPS™.

Figure 3

INTELLECTUAL PROPERTY - MULTIKINE®

	Filing Date	Application #	Country	Status	Patent #	Issue Date	Expiration
CS-120	Method of Pre-Sensitizing Cancer Prior to Treatment with Radiation/Chemotherapy and a Novel Cytokine Mixture						
CS-120	7/3/2003	10/611,914	USA	Granted	6,896,879	5/24/2005	9/2/2023
CS-120	7/1/2004	PCT/US04/020998	PCT	Nationalized			
CS-120	7/1/2004	200480025403.6	PCT-China	Granted	200480025403.6	5/25/2011	7/1/2024
CS-120/CIP	6/28/2005	PCT/US05/22678	PCT	Nationalized			
CS-120/CIP	6/28/2005	5789138.4	PCT-Europe	Granted	1,773,368	5/4/2016	6/28/2025
CS-120/CIP	6/28/2005	2007-519321	PCT-Japan	Granted	5,122,279	11/2/2012	6/28/2025
CS-120/CIP	6/28/2005	60 2005 049 252.6	PCT-Germany	Granted	1,773,368	5/4/2016	6/28/2025
CS-120/CIP	6/28/2005	5789138.4	PCT-France	Granted	1,773,368	5/4/2016	6/28/2025
CS-120/CIP	6/28/2005	2 581 978	PCT-Spain	Granted	1,773,368	5/4/2016	6/28/2025
CS-122	A Method for Altering the Cd4/Cd8 Ratio and the Mononuclear Cellular Infiltrate into a Tumor						
CS-122	6/3/2005	PCT/US05/019263	PCT	Nationalized			
CS-122	6/3/2005	5756247.2	PCT-Europe	Granted	1,753,452	10/28/2015	6/3/2025
CS-122	6/3/2005	60 2005 047 788.8	PCT-Germany	Granted	1,753,452	10/28/2015	6/3/2025
CS-122	6/3/2005	5756247.2	PCT-France	Granted	1,753,452	10/28/2015	6/3/2025
CS-122	6/3/2005	5756247.2	PCT-Spain	Granted	1,753,452	10/28/2015	6/3/2025
CS-122	6/3/2005	5756247.2	PCT-Italy	Granted	1,753,452	10/28/2015	6/3/2025
CS-122	6/3/2005	5756247.2	PCT-UK	Granted	1,753,452	10/28/2015	6/3/2025
CS-123	Method for Managing Cholesterol with a Serum-Free and Mitogen Free Cytokine Mixture						
CS-123	7/29/2005	PCT/US05/26819	PCT	Nationalized			
CS-123	7/29/2005	5775596.9	PCT-Europe	Granted	1,773,395	6/22/2011	7/29/2025
CS-123	7/29/2005	5775596.9	PCT-Germany	Granted	1,773,395	6/22/2011	7/29/2025
CS-124	Method for Modulating HLA Class II Tumor Cell Surface Expression with a Cytokine Mixture						
CS-124	5/10/2006	PCT/US06/018055	PCT	Nationalized			
CS-124	5/10/2006	6770164.9	PCT-Europe	Granted	1,879,618	10/4/2017	5/10/2026
CS-124	5/10/2006	6770164.9	PCT-France	Granted	1,879,618	10/4/2017	5/10/2026
CS-124	5/10/2006	6770164.9	PCT-Germany	Granted	1,879,618	10/4/2017	5/10/2026
CS-124	5/10/2006	6770164.9	PCT-UK	Granted	1,879,618	10/4/2017	5/10/2026

Source: CEL-SCI Corporation.

Figure 4

INTELLECTUAL PROPERTY - LEAPS™

	Filing Date	Application #	Country	Status	Patent #	Issue Date	Expiration
CS-110	Peptide Constructs for Treating Autoimmune and Related Diseases						
CS-124	10/27/2000	PCT/US00/41647	PCT	Nationalized			
CS-124	4/26/2002	10/111,602	USA	Granted	7,199,216	4/3/2007	7/13/2022
CS-124	1/19/2007	11/625,202	USA-Cont.	Pending			
CS-111	Methods of Preparation and Composition of Peptide Constructs Useful for Treatment						
CS-111	10/27/2000	PCT/US00/41646	PCT	Nationalized			
CS-111	4/26/2002	10/111,645	USA	Granted	6,995,237	2/7/2006	9/17/2021
CS-111	12/12/2005	11/298,718	USA-Cont.	Granted	7,256,254	8/14/2007	9/17/2021
CS-127	Methods of Preparation and Composition of Peptide Constructs Useful for Treatment of Rheumatoid Arthritis						
CS-127	3/14/2008	61/036,566	USA-Prov.	Converted to PCT			
CS-127	9/26/2008	61/100,383	USA-Prov.	Converted to PCT			
CS-127	3/16/2009	PCT/US09/37312	PCT	Nationalized			
CS-127	3/16/2009	12/922,687	USA	Pending			
CS-127	9/14/2010	9718824.7	PCT-Europe	Granted	2,254,588	10/11/2017	3/16/2029
CS-127	9/14/2010	9718824.7	PCT-UK	Granted	2,254,588	10/11/2017	3/16/2029
CS-127	9/14/2010	9718824.7	PCT-France	Granted	2,254,588	10/11/2017	3/16/2029
CS-127	9/14/2010	9718824.7	PCT-Germany	Granted	2,254,588	10/11/2017	3/16/2029
CS-130R	Method for Inducing an Immune Response Against Avian, Swine, Spanish, H1N1, H5N9 Influenza Viruses						
CS-130R	12/13/2010	61/422,474	USA-Prov.	Converted to PCT			
CS-130R	12/13/2011	PCT/US11/64746	PCT	Nationalized			
CS-130R	6/13/2013	13/994,092	USA	Granted	10,238,747	3/26/2019	5/14/2032
CS-1334	Method for Inducing an Immune Response for Treatment of Cancer and Autoimmune Diseases or Conditions						
CS-1334	5/24/2012	PCT/US12/39474	PCT	Nationalized			
CS-1334	11/25/2013	14/122,240	USA	Granted	10,179,164 B2	1/15/2019	5/24/2032
CS-1325	Method for Inducing an Immune Response and Formulations Thereof						
CS-1325	5/24/2012	PCT/US12/39473	PCT	Nationalized	(Ownership-CEL-SCI/NIH)		
CS-1325	11/25/2013	14/122,238	USA	Granted	10,179,174 B2	1/15/2019	5/24/2032
CS-136	Methods of Preparation and Composition of Peptide Cnstructs Useful for Treatment of Rheumatoid Arthritis						
CS-136PROV2.3	4/28/2014	PCT/US2014/035757	PCT	Nationalized			
CS-136PROV2.3	10/23/2015	14787690.8	PCT-Europe	Pending	(Ownership-CEL-SCI/Rush		
CS-136PROV2.3	1/25/2016	14/907,520	PCT-USA	Pending	(Ownership-CEL-SCI/Rush		
CS-138/R	Peptides and Conjugates for Treatment of Arthritis						
CS-138/R	5/11/2019	62/846,609	USA-Prov.	Pending	(Ownership-CEL-SCI/Rush		

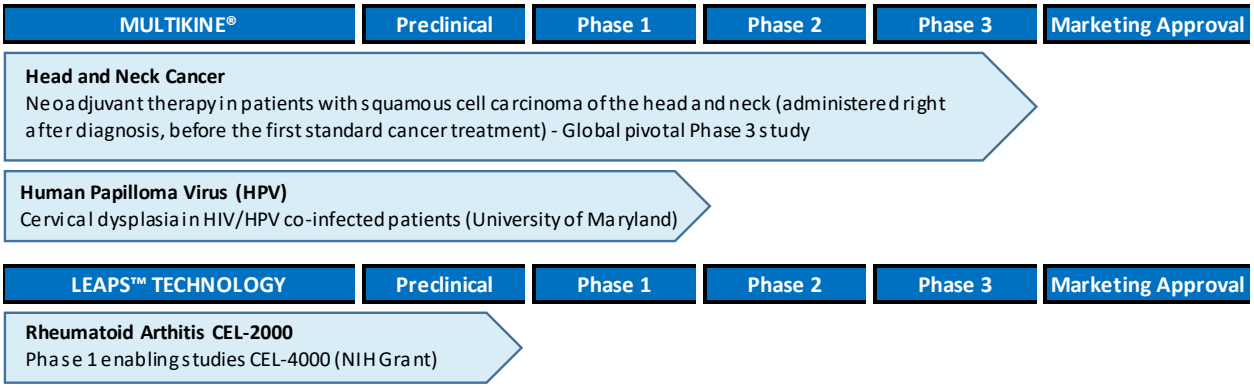
Source: CEL-SCI Corporation.

Core Story

CEL-SCI Corporation ("CEL-SCI" or "the Company") is a Phase 3 clinical-stage biotechnology company involved in the research and development of immunotherapy products and technologies to treat cancer, autoimmune and infectious diseases that address significant unmet medical needs. The Company's vision is to change the way cancer and other diseases are treated as it strives to develop novel therapies with the potential to activate and utilize the body's own immune defense system against the disease while delivering minimal toxicity to normal cells and organ systems. The Company is currently focused on developing product candidates based on two innovative technologies, shown in Figure 5: (1) Multikine® (Leukocyte Interleukin, Injection), a next-generation, comprehensive immunotherapy with a completed Phase 3 study as a first-line treatment for head and neck cancer; and (2) LEAPS™ (Ligand Epitope Antigen Presentation System), a peptide-based immunotherapy vaccine technology platform.

Figure 5

PRODUCT PIPELINE



Source: CEL-SCI Corporation.

The Company's lead product candidate, Multikine®, is an investigational immunotherapy under development to treat certain head and neck cancers, as well as cervical dysplasia in HIV/HPV co-infected patients. Multikine® is a consistent mixture of cytokines and cellular products. Research at the U.S. National Institutes of Health (NIH) has shown that the cytokines play a key role to reject a tumor. Multikine® is injected five days a week for three consecutive weeks prior to any other cancer therapy around the tumor and near adjacent lymph node chain to stimulate the immune system to recognize the cancer cell antigens. Once the immune system is able to "see" the cancer, the immune system does what it is meant to do and destroys the cancer, with a goal of activating an anti-tumor immune response and increasing survival.

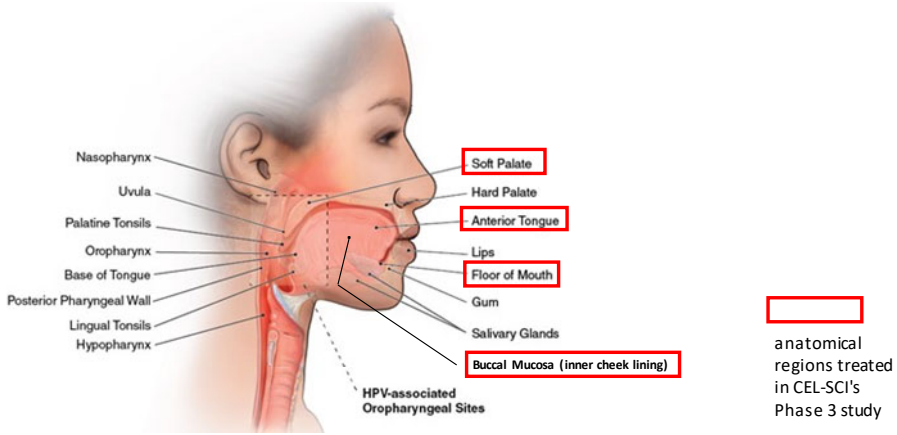
Multikine® completed a global pivotal randomized Phase 3 clinical trial for patients who are newly diagnosed (not yet treated) with advanced cancer of the head and neck, for which the Company has received Orphan Drug Status/designation from the U.S. Food and Drug Administration (FDA). The Phase 3 trial is the largest head and neck cancer study ever conducted and took place in the U.S. and 20 other countries on three continents. CEL-SCI believes that advanced primary head and neck cancer is a large unmet medical need that has only one recommended standard of care (SOC), with the last FDA approval for advanced primary head and neck cancer made over 50 years ago.

HEAD AND NECK CANCER

Head and neck cancer is the fifth most frequently occurring cancer worldwide. Approximately 90% of head and neck cancers originate in the squamous cells—thin, flat cells that line the mucosal surfaces (mouth, nose, and throat) of the head and neck (and other mucosal surfaces)—and are thus called squamous cell carcinomas. As depicted in Figure 6, this group of cancers include cancer of the oral cavities (cheeks, lips, gums, tongue, hard and soft palate, and mouth floor), salivary glands, paranasal sinuses and nasal cavity, pharynx, larynx (voice box), and lymph nodes. In total, there are more than 30 locations in the head and neck for cancer to develop (Sources: American Dental Association). Cancers of the brain, eye, and thyroid are not typically classified as head and neck cancers. Most squamous cell carcinomas are traditionally considered tobacco and alcohol exposure related. However, high risk human papillomaviruses (HPV), mainly HPV type 16 (HPV16), have recently been recognized as causally related to a subset of oropharyngeal squamous cell carcinomas (Source: *PLoS One*, 13(2), 2018).

Figure 6

COMMON HEAD AND NECK CANCER SITES



Source: Centers for Disease Control and Prevention (CDC).

Often cancer begins in one area, such as the tongue, and spreads to other adjacent anatomical areas, including the lymph nodes. This effect is known as tumor **metastasis** and is associated with cancer recurrence and decreased survival. Metastasis and cancer recurrence are significant clinical issues in head and neck cancers. The American Cancer Society estimates that 10% to 40% of patients whose oral cancer was considered "cured" will likely develop cancer of the oral cavity again (a local recurrence) or of a nearby organ, such as the larynx, esophagus (regional recurrence), or lung (distal recurrence).

This number increases for patients diagnosed at a late-stage disease, such as in the CEL-SCI study, where even after successful treatment and remission, 30% to 60% will develop recurrent local cancer or second primary cancers (Source: *Annals of Oncology*, Vol. 30 (5):744–756, 2019). The recurrence rate affects the five-year survival of the disease. In the U.S., the five-year relative survival rate for head and neck cancers in general is 65% (for all the types of head and neck cancer, encompassing all stages at diagnosis). Although this constitutes a 28% increase from the 1975-1977 levels (53% five-year survival rate), this improvement considerably lags the 40% increase in five-year survival rate for overall cancer during the same period (Source: American Cancer Society's *Cancer Facts and Figures 2020*).

There are some head and neck cancer sites that have a worse outcome than others. CEL-SCI's Phase 3 study focuses on patients with Stage 3 and 4 cancer (advanced) in anatomical locations of the head and neck that are known to present a worse prognosis (cancers of the anterior tongue, soft palate, floor of the mouth, and cheek). An analysis conducted by external statistical experts using the **SEER database** found that the combined overall survival of the 'SEER' population having the same characteristics of the specific type of patients enrolled in the Phase 3 study (type of cancer, tumor stage, location, etc.) was found to be 47% at three years and about 37% at five years. This analysis reflects the U.S. (SOC) treatment during the time of the Company's Phase 3 trial. Treatment has not gotten better and the SOC has not changed during this long Phase 3 study.

CEL-SCI believes that the low rate of long-term survival from head and neck cancers is due to inadequacies in the treatment regimen that composes the current SOC. The current SOC for head and neck cancer patients is surgery followed by radiation or concurrent radiochemotherapy. However, if after surgery, patients still exhibit micrometastases around the area of the tumor or in the adjacent or distally located lymph nodes, surgery is followed by concurrent radiation and chemotherapy. Nevertheless, surgeries, radiation, and chemotherapy often miss outlying tumor cells that are located around the **margins** of the tumor (causing local recurrence) or in the lymph nodes (responsible for regional recurrence). Additionally, concurrent radiation and chemotherapy subjects patients to high levels of toxicity, which can cause severe side effects or even death. Another side effect of these SOC treatments is immunosuppression, which negatively impacts the efficacy of utilizing immunotherapy after SOC and chemotherapy.

CEL-SCI's comprehensive cancer immunotherapeutic approach with Multikine® has been shown in early studies to address both local and regional cancer recurrences by eliminating tumor cells from these areas prior to a patient undergoing first-line SOC therapies. If Multikine® treatment is approved for sale, patients who are scheduled to receive radiation after their surgery should have a much better prognosis with Multikine®. Consequently, the Company believes that following approval, Multikine® could become a new routine and vital addition to the SOC regimen, administered before surgery, when the immune system has not yet been suppressed by subsequent treatments.

Incidence, Prevalence, and Market Size

Worldwide, head and neck cancer is believed to be the fifth most common cancer in the world, accounting for approximately 890,000 cases and over 400,000 deaths annually (Source: Global Cancer Observatory, International Agency for Research on Cancer). In the U.S., there are about 68,000 new cases annually and 15,000 deaths. Of those cases, 90% are squamous cell carcinomas and approximately two-thirds of these patients present on their first visit with locally advanced primary (untreated) disease. Of the advanced primary patients, approximately 40% (210,000) are prescribed surgery and radiation therapy as SOC. According to Global Cancer Observatory (GLOBOCAN), the incidence of SCCHN continues to rise and is anticipated to increase by 30% (that is, 1.08 million new cases annually) by 2030.

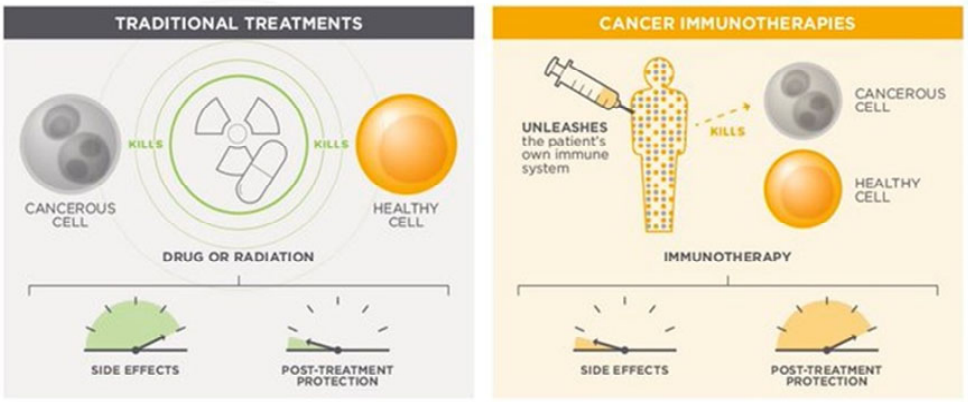
The oncology market is one of the largest pharmaceutical markets and, with the introduction of improved treatments, it is expected to continue to expand. The global oncology market was valued at $283.5 billion in 2021 and is projected to reach a value of $447.3 billion by 2028, growing at a CAGR of 7.9% over the forecast period. (Source: Vantage Market Research). Specifically, the global market for head and neck cancer is anticipated to reach $6.2 billion by 2029, expanding at a double-digit CAGR of 18.5% over the forecast period, driven by rising epidemic of oropharyngeal cancer associated with HPV, and anticipated approval of checkpoint inhibitors in the near future (Source: iHealthcareAnalyst, January 2023).

IMMUNOTHERAPY

Healthcare companies are focused on developing new cancer therapies with improved efficacies and more favorable safety profiles, in part due to the severe toxicities and stagnant survival rates associated with many current cancer treatments. Specifically, companies are attempting to create treatments that selectively address only the cancer cells without damaging surrounding healthy cells. One prominent method, called immunotherapy, utilizes the body's own immune system to fight the disease. Immunotherapy, or biological therapy, is a type of cancer treatment that boosts the body's natural defenses to fight cancer. It uses substances made by the body or in a laboratory to improve immune system function, helping the body fight cancer by eliciting the following effects: (1) stop or slow the growth of cancer cells; (2) stop cancer from spreading to other parts of the body; and (3) help the immune system to be better at destroying cancer cells.

Immunotherapies also provide significant advantages over conventional cancer treatments, such as chemotherapy or radiation. Since immunotherapy can train the immune system to recognize and remember cancer cells, this "immune memory" may result in longer-lasting remissions. Clinical studies on long-term overall survival have shown that the beneficial responses to cancer immunotherapy treatment are maintained even after treatment is completed. Furthermore, since cancer immunotherapy is focused on the immune system and may be more targeted than conventional cancer treatments, it normally presents a better safety profile when it comes to side effects. Conventional chemical or radiological cancer therapy normally affects both the cancerous cells as well as healthy tissues, which results in common side effects, such as hair loss and nausea, but also can cause immunosuppression, weakening the body's immune system and affecting the body's post-treatment protection against infections and recurrent cancers, as illustrated in Figure 7 (Source: Cancer Research Institute).

Figure 7
IMMUNOTHERAPY VS. CHEMOTHERAPY



Source: Adaptive Biotechnologies.

As part of its normal function, the immune system detects and destroys abnormal cells and most likely prevents or curbs the growth of many cancers. However, on its own, the body's immune system cannot typically eliminate all cancers. This is due to several causes: (1) development of **tumor tolerance**; (2) inadequate immune responses; and (3) the cancer cell's ability to ward off an attack. Since cancer cells are not physically introduced to the body as foreign substances, but rather are derived from the body's own cells, the immune system does not always recognize cancer cells as foreign. When the immune system views cancer cells as part of the "self," the effect is called tumor tolerance. Moreover, even if the immune system distinguishes tumor cells from the "self" and attempts to attack them, the response is often inadequate because it is too weak to destroy cancer cells, is not targeted to the correct body region, or is not utilizing the most effective "killer" cells. In addition, tumors protect themselves against discovery by secreting substances that suppress the activation of the body's anti-tumor killer cells, eliminating cellular components that the immune system uses to recognize diseased or cancerous cells, and not expressing cell-surface molecules that are typically needed for an immune cell to induce **apoptosis** of the cancer cell. These tumor defense mechanisms allow cancer cells to grow into a large tumor mass.

Outside stimulation with immunotherapies designed to overcome the immune system's natural limitations can both enable recognition of a tumor as a foreign diseased entity and increase the efficacy of killer cells at combating the cancer. Immunotherapies and biological agents encompass passive and active therapies. These therapies differ based on mechanisms of action and effect on the immune system but have many of the same limitations.

- ***Passive Agents***. Passive immunotherapies do not stimulate the immune system to eradicate diseased cells. Rather, components of the immune system are formulated *ex vivo* and then administered to patients.

- ***Active Agents***. An active immunotherapy triggers the immune system to attack cancer cells. Primary examples of active immunotherapies include cancer vaccines, which aim to cause the immune system to react against a select antigen; cellular therapies, a technique designed to improve upon distinct parts of the immune system; and **adjuvants**, which are given in conjunction with another treatment.

Types of Cancer Immunotherapies

The most conventional immunotherapy approaches are described in the accompanying section, followed by an in-depth description of CEL-SCI's novel immune simulator and comprehensive immunotherapy, Multikine®.

Monoclonal Antibodies (mAbs)

Monoclonal antibodies (mAbs) are one of the more widely used passive immunotherapies. Antibodies are produced naturally by a person's body to help the immune system recognize germs that cause disease, such as bacteria and viruses, and mark them for destruction. Monoclonal antibodies consist of a single antibody type that has been engineered to recognize and bind to one particular antigen. Antigens are the substances on diseased cells, viruses, fungi, bacteria, and toxins that signal a foreign entity. mAbs are highly specific in that they target and attach only to defined antigenic sites on a select cell. After binding to the predetermined antigen on the surface of a diseased cell, the mAbs induces apoptosis of that cell.

Some mAbs mark cancer cells so that the immune system will better recognize and destroy them. An example is rituximab, which binds to a protein present on some types of cancer cells, causing the immune system to kill them. Other mAbs bring T-cells close to cancer cells, helping the immune cells kill the cancer cells. In addition, some mAb technologies, called **immunomodulatory** mAbs, are considered active therapy as they operate by interacting with components of the immune system in order to elicit a novel response or reinstate an existing anticancer immune response (Source: *Oncotarget*. Vol. 5(24): 12472–12508, 2014). Yet, mAbs do not always function as anticipated and are associated with several limitations, including usage, antigen expression, mutated tumor cells, and toxicity, as briefly described below.

- *Usage.* After chemotherapy and radiation, the immune system is weakened and the effectiveness of mAbs therapy is limited. Yet, many mAbs are not administered as a first-line therapy, or if they are, are given in conjunction with a SOC and not before the SOC is employed.

- *Antigen Expression.* The same antigen is not always expressed on every patient's cancer. For instance, Genentech, Inc.'s (DNA-NYSE) Herceptin® treats metastatic breast cancer that possesses **human epidermal growth factor receptor 2 (HER2+)**; however, only approximately 25% of breast cancer patients have HER2+ on their tumors (Source: Genentech, Inc.). CEL-SCI believes that developing an antigen-targeted therapy for each subgroup of patients within a cancer indication could likely be a costly endeavor.

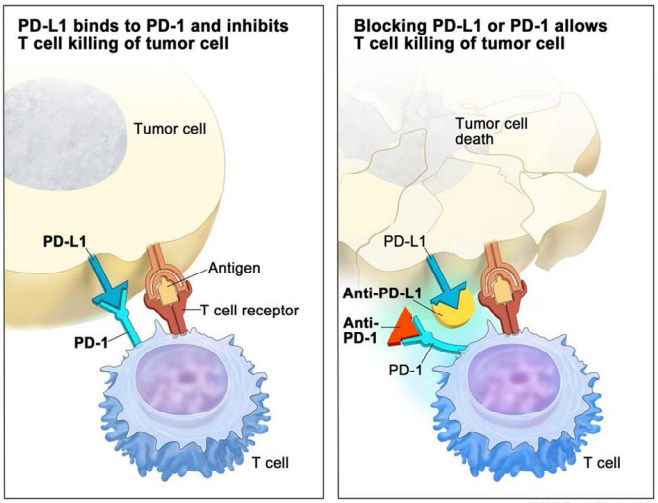
- *Mutations and Toxicity.* As a result of chemotherapy and radiation, tumor cells can mutate. The target antigens on the tumor's surface can change, limiting the effectiveness of the targeted mAbs therapy. In addition, mAbs have not always been as pure, specific, or as safe in practice as originally thought. When administered systemically in high doses, some mAb therapies are more toxic than expected. In contrast, Multikine® appears to have a favorable safety profile and has not been found to add toxicity to the overall treatment.

Checkpoint Inhibitors

Checkpoint inhibitors are immunomodulatory therapies that work by exposing cancer cells to the immune system for attack. Adaptive immune cells, like T-cells, are selective components of the immune system attacking specific antigens. T-cells roam the body looking for foreign cells by using protein receptors located on their surface to exchange signals with other cells and help them differentiate healthy cells from cancer cells. During this exchange of signals, called a checkpoint, cell surface proteins bind together with the T-cell, telling the immune system they are normal cells and sending an "off" signal to the T-cell. However, because cancer cells are the body's own mutated cells, the immune system does not always recognize them as foreign. Many types of cancer cells can send deceptive signals at checkpoints that bind to the protein receptors of the T-cells, making them appear as normal cells.

Checkpoint inhibitors work by blocking the receptors that cancer cells use to send signals to T-cells. This prevents the "off" signal from being sent, allowing the T-cells to kill cancer cells, as seen in Figure 8. When the signal is blocked, T-cells may be better able to differentiate a cancer cell from a healthy cell and launch an attack. However, because checkpoint inhibitors stimulate the immune system, they may cause immune cells to attack healthy cells, triggering a variety of side effects. Although relatively well tolerated, given the mechanism of action for these agents, most side effects are immune-related and result from an overactive immune system (Source: Cancer Research Institute).

Figure 8
CHECKPOINT INHIBITORS



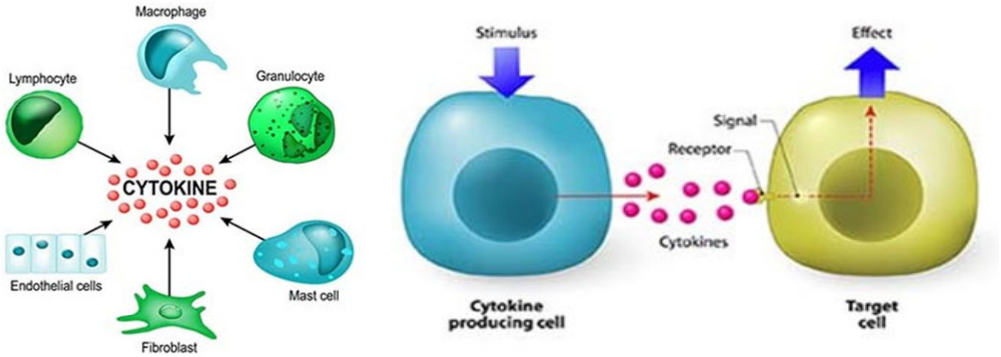
Source: NIH's National Cancer Institute.

In 2011, the FDA approved the first checkpoint inhibitor immunotherapy for the treatment of cancer—ipilimumab (Yervoy®) from Bristol-Myers Squibb for melanoma. Today, the FDA has approved 16 different immunomodulators—nine checkpoint inhibitors, four cytokines, two adjuvants, and a small molecule with immunomodulatory properties—for the treatment of more than a dozen major cancer types. In particular, two check point inhibitors have received FDA approval for the treatment of head and neck cancer: Pembrolizumab (Keytruda®) by Merck & Company for the treatment of head and neck squamous cell cancer; and Nivolumab (Opdivo®) by Bristol-Myers Squibb for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck. Due to their potential to enhance the effectiveness of immune responses, many different checkpoint inhibitors are currently being evaluated, both alone and in combination with other treatments, in a variety of cancer types in clinical trials.

Cytokine Immunomodulatory Therapy

Cytokines are protein molecules that help regulate and direct the immune system. Cells release cytokines, which act as messengers to other cells and are crucial in controlling the growth and activity of other immune system cells and blood cells, as depicted in Figure 9. Cytokines play a key role in controlling the body's immune and inflammation responses. They also help to boost anti-cancer activity by sending signals that can help make abnormal cells die and normal cells live longer (Source: American Cancer Society).

Figure 9
CYTOKINES



Source: microbenotes.com.

Taken as a family, cytokines regulate virtually all biological functions. Thus, these messenger molecules can be used as cancer therapeutic agents by trying to harness the biological potency of specific cytokines to elicit novel or strengthen pre-existent tumor-targeting immune responses and to prevent or manage chemotherapy side effects. To accomplish this, specific cytokines are synthesized in the lab and injected in larger doses than the body would normally produce. The two most common cytokines used in cancer therapy are interleukins (IL) and interferons (IFN).

Interleukins (IL) are a group of cytokines that act as chemical signals between white blood cells. There are more than a dozen interleukins, including Interleukin 2 (IL-2), which is also called T-cell growth factor. IL-2 is naturally produced by the body to help fight infection and prevent autoimmune diseases. IL-2 boosts the number of white blood cells in the body, including **natural killer (NK) cells**. Increasing these cells can cause an immune response against cancer. IL-2 also helps B cells (another type of white blood cell) produce certain substances that can target cancer cells. IL-2 can be used as a single drug treatment or can be combined with chemotherapy or with other cytokines. A man-made version of IL-2, Aldesleukin (Proleukin® marketed by Clinigen Group), is approved to treat advanced kidney cancer and metastatic melanoma. Other interleukins, such as IL-7, IL-12, and IL-21, continue to be studied for use against cancer as well as both as adjuvants and as stand-alone agents.

Interferons (IFN) are immune proteins that help the body resist virus infections and cancers. The types of interferon are named after the first 3 letters of the Greek alphabet: IFN-alfa, IFN-beta, and IFN-gamma. Only IFN-alfa is used to treat cancer as it boosts the ability of certain immune cells to attack cancer cells. It may also slow the growth of cancer cells directly, as well as the blood vessels that tumors need to grow (Source: American Cancer Society).

Cancer Vaccines

Unlike traditional vaccines intended to directly prevent diseases such as polio, smallpox, or measles, cancer vaccines do not prevent cancer but are used to treat specific cancers and prevent conditions that may cause cancer. Vaccines for cancer come in two categories: prophylactic and therapeutic. There are currently four vaccines that are approved by the FDA that can help prevent cancer (prophylactic), in addition to three FDA-approved vaccines for the treatment of cancer (therapeutic).

Prophylactic or preventative vaccines attack viruses that may cause cancer. The human papillomavirus (HPV) vaccine, for example, targets the high-risk strains of HPV responsible for most cases of cervical cancer and linked to some throat, anal, vaginal, vulvar, and penile cancers. The hepatitis B virus (HBV) vaccine targets the disease that has been linked to an increased risk for liver cancer in people who have chronic (long-term) infections with the virus. Thus, vaccinating certain people against HPV and HBV could have a positive effect in protecting against the types of cancers linked to each condition.

Therapeutic cancer vaccines are a type of immunotherapy that treats cancer by stimulating the immune system to attack cancer in a specific location of the body. Unlike cancer prevention vaccines, cancer treatment vaccines are designed to get the immune system to attack a disease that already exists. Therapeutic cancer vaccines either delay or stop cancer cell growth, shrink the tumor, and prevent tumor growth. They work by presenting the immune system with antigens it will recognize as foreign or dangerous.

Some cancer treatment vaccines are made up of cancer cells, parts of cells, pure antigens (certain proteins on the cancer cells), or even modified bacteria or viruses. Sometimes a patient's own immune cells are removed and exposed to these substances in the lab to create the vaccine. Once the vaccine is ready, it is injected into the body to increase the immune response against cancer cells.

Cellular Therapies

Cellular therapy is the use of cells to repair or replace tissue. For cancer patients, cellular therapy involves the removal of certain immune cells from the patient, which are then modified in a laboratory to better attack the specific cancer cells, replicated in cell culture, and then administered back to the patient. Cellular therapies can be customized to the patient so that the engineered cells are trained specifically for the type of tumor present in the patient's body. In this way, this technique aims to improve upon the patient's current immune abilities to make the immune system more likely to kill cancer cells.

The most common cellular therapy used for cancer is **T-cell transfer therapy**, which is a treatment that boosts the natural ability of T-cells to fight cancer. There are two main types of T-cell transfer therapy: tumor-infiltrating **lymphocytes** (or TIL) therapy and CAR T-cell therapy.

- TIL therapy uses T-cells, called tumor-infiltrating lymphocytes, that are found in the tumor. Doctors test these lymphocytes in the lab to find out which ones best recognize a patient's tumor cells and then these selected lymphocytes are treated with substances that make them grow to large numbers quickly before injecting them back into the patient. The idea behind this approach is that the lymphocytes that are in or near the tumor have already shown the ability to recognize a patient's tumor cells.

- CAR T-cell therapy is similar to TIL therapy, but the T-cells are changed so that they make a type of protein known as CAR before they are grown and administered. CAR stands for chimeric antigen receptor. CARs are designed to allow the T-cells to attach to specific proteins on the surface of the cancer cells, improving their ability to attack the cancer cells (source: NIH's National Cancer Institute).

The process of growing a patient's T-cells in a lab can take two to eight weeks. During this time, a patient may be treated with chemotherapy and/or radiation therapy to get rid of other immune cells. Reducing a cancer patient's immune cells helps the transferred T-cells be more effective. However, in the same way that **autologous** vaccines may be costly and difficult to mass produce, CEL-SCI believes that cellular therapies, since they require cells from the patient, could also have high costs and limited abilities for commercial scale manufacturing. Furthermore, the infusion of billions of cells into the patient could cause adverse reactions. The Company also believes that certain tumor-infiltrating agents may not always grow well in cell culture, thereby not reaching the quantity or engineered quality that is needed for efficacy against tumors.

Adjuvants

An adjuvant is any agent that may increase the efficacy or potency of a treatment. As it relates to biologic products, adjuvants are substances usually injected with antigens to enhance or modify the body's immune response. When administered in conjunction with a cancer vaccine or mAb treatment, adjuvants are intended to increase the effectiveness of the treatment by augmenting the body's immune response. When chemotherapy is administered to a patient prior to or following surgery to remove the patient's cancer, it is considered either a neoadjuvant or adjuvant therapy depending upon when it is given.

The toxicity of adjuvants may vary depending on what substance is being used and its route of administration. Some adjuvants cannot be administered more than a few times sequentially to humans and others can only be administered as a percutaneous injection through the skin. Some commonly used adjuvants for use in cancer treatments include aluminum sulfate (Alum), keyhole limpet hemocyanin (KLH), incomplete Freund's adjuvant (IFA), QS21, Detox-B, dinitrophenyl (DNP), and granulocyte-**macrophage** colony-stimulating factor (GM-CSF).

Multikine® Comprehensive Immunotherapy

CEL-SCI has designed a novel type of biological immunotherapy—an immune stimulator called Multikine®—that acts as a comprehensive immunotherapeutic agent. The Company believes that Multikine® more closely mimics natural immune functions as it leverages the roles of both passive and active immunotherapies to accomplish the following two goals:

- Activating the immune system to produce a more robust and sustainable anti-tumor response; and
- Causing a direct, multi-targeted elimination of tumor cells.

Multikine® is comprised of a patented defined mixture of 14 human natural cytokines and cellular products, listed in Figure 10. The pro-inflammatory cytokine mixture includes interleukins, interferons, chemokines, and colony-stimulating factors, which contain elements of the body's natural mix of defenses against cancer. Research at the U.S. National Institutes of Health (NIH) has shown the vast majority of Multikine®'s cytokine components to be biologically/immunologically active, potentially simulating the natural immune system to mount an immune rejection episode, including tumor rejection.

Figure 10
MULTIKINE® COMPONENTS

▪ Interleukin 1 α (IL-1 α)	▪ Tumor Necrosis factor α (TNF-α)	▪ Granulocyte-colony stimulating factor (G-CSF)
▪ Interleukin 1 β (IL-1β)	▪ Tumor Necrosis factor β (TNF-β)	▪ Granulocyte-macrophage colony-stimulating factor (GM-CSF)
▪ Interleukin 2 (IL-2)	▪ Interleukin 6 (IL-6)	▪ Macrophage Inflammatory Protein 1α (MIP-1α)
▪ Interleukin 3 (IL-3)	▪ Interleukin 8 (IL-8)	▪ Macrophage Inflammatory Protein 1β (MIP-1β)
▪ RANTES (CCL5)	▪ Interferon Gamma (IFN-γ)	

Source: CEL-SCI Corporation.

CEL-SCI believes that available immunotherapies, as well as those currently being developed, are limited by their abilities to target only one or two specific tumor-associated antigens. Conversely, Multikine®'s multitargeted therapy effect is directed at several targets on the cancer cell and activates multiple cellular components of the immune system in order to fight cancer more effectively. Multikine® kills tumor cells and, at the same time, activates a robust anti-tumor immune response.

The first indication CEL-SCI is pursuing for Multikine® is for the neoadjuvant therapy in patients with squamous cell carcinoma of the head and neck (SCCHN), (locally advanced primary head and neck cancer). CEL-SCI has completed Phase 1, Phase 2, and a global pivotal randomized controlled Phase 3 clinical trial. Data from Phase 1 and Phase 2 clinical trials indicates that Multikine® may help the immune system "see" the tumor and then attack it, enabling the body's own anti-tumor immune response to fight the tumor. Furthermore, no severe toxicity was reported as being associated with Multikine® during the clinical trials. The Company plans to capitalize on the full potential of Multikine®'s multi-target capabilities to assess the immunotherapy for treating cervical dysplasia in HIV/HPV co-infected patients (completed a Phase 1), as well as other solid cancer targets, including breast, skin, bladder, cervical cancers, and melanoma.

In June 2007, the FDA granted Multikine® Orphan Drug status as a neoadjuvant therapy in head and neck cancer which is expected to be helpful for approval. Results of the Phase 1 and Phase 2 trials are presented on pages 31-34 as well as a description of the pivotal Phase 3 trial. The Company recently published and presented data from its Phase 3 IT MATTERS clinical trial at two prestigious cancer conferences: 2022 ASCO Annual Meeting in Chicago, Illinois and the 2022 European Society for Medical Oncology (ESMO) annual Congress in Paris, France. Further, results from the Phase 3 clinical trial of Multikine® in advanced primary head and neck cancer were posted to the U.S. government clinical trial website www.clinicaltrials.gov (described on pages 38-39).

A Novel First-Line Treatment

Multikine®'s first indication is for locally advanced (Stages 3 and 4) primary (not yet treated) head and neck cancer. This was selected as CEL-SCI believes there is a large, unmet medical need among head and neck cancer patients as a whole, and for this very prevalent cancer in particular. According to the Company, the last FDA approval of a therapy for the treatment of locally advanced resectable primary head and neck cancer was many decades ago. In addition, there is only one standard of care (SOC) for this type of cancer based on the recommendations of the NCCN Guidelines.

Multikine® is being used differently from other cancer immunotherapy options. Unlike conventional immunotherapies, which have traditionally been administered late in the disease process (often after chemotherapy and radiation therapy), Multikine® is being developed as a first-line treatment to be given to patients before any other therapy options, including surgery, radiation, or chemotherapy are initiated. (i.e., as a neoadjuvant). CEL-SCI designed Multikine® for use in this manner because the Company believes that one of the primary impediments to immunotherapy efficacy has been that these products are traditionally administered after the immune system has already been ravaged by the disease and destroyed by current first-line treatments (e.g., chemotherapy, radiation, or surgery). In later cancer stages, the immune system is less likely to wage an effective anti-tumor response because it has been weakened by both the toxic therapies and the cancer itself. On the contrary, Multikine® is able to stimulate the immune system before it is weakened by surgery, chemotherapy, or radiation, resulting in an effective anti-tumor response.

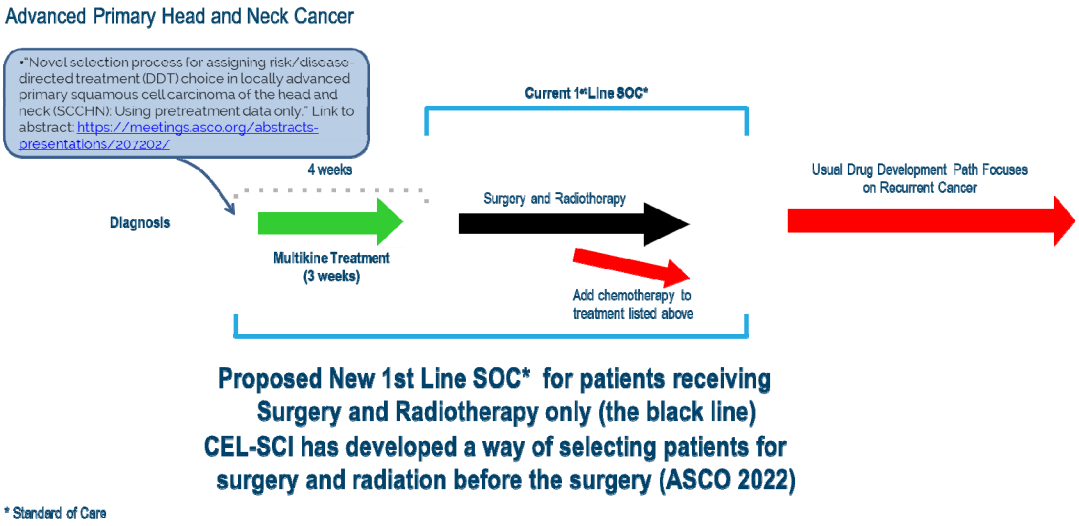
There is one recommended SOC for advanced primary head and neck cancer, which did not change during the Company's 10-year Phase 3 trial: surgery followed by either radiation or concurrent radiation and chemotherapy. The determination as to which treatment the patient is supposed to receive after surgery is based on the pathology of the patient's tumor. If certain risk factors that are likely to increase the chance for recurrence are present, chemotherapy is supposed to be added to the radiotherapy (per the recommendation of the NCCN Guidelines).

Following diagnosis, many patients have an average of four weeks of preparation before surgery. Multikine® is administered to previously untreated, newly diagnosed resectable head and neck cancer patients in the period between diagnosis and surgery. Delay of surgery is not recommended because it is an "intent to cure" treatment. Therefore, Multikine® can only be given for three weeks. During the three-week period, the Multikine® investigational treatment regime is administered locally around the tumor and near the draining lymph nodes chain five times per week for three consecutive weeks.

CEL-SCI believes that Multikine® can establish itself as a new first line as part of the existing SOC for patients receiving surgery and radiotherapy only, if approved, as illustrated in Figure 11 (page 25). The Company has developed a way of selecting patients for surgery and radiation before the surgery (ASCO 2022).

Figure 11

PHASE 3 STUDY DESIGN: TIMING OF MULTIKINE® TREATMENT REGIMEN



Source: CEL-SCI Corporation.

Mechanism Of Action

Micrometastases around the tumor and in the lymph nodes are believed to be a major cause of cancer recurrence. The American Cancer Society estimates that up to 40% of patients whose oral cancer was considered "cured" will likely develop recurrent local cancer or second primary cancers, with this number going up to 60% for patients diagnosed at a late-stage disease (Source: *Annals of Oncology*, Vol. 30 (5):744–756, 2019). Cancer treatment today involves aggressive surgery, including the removal of the affected organ or area, as well as radiation or radio-chemotherapy due to fear that tumor micrometastases will survive the first round of cancer treatments and cause tumor recurrence.

Multikine®'s primary function in cancer treatment is to eliminate cancer cells from around the margin of the tumor as well as from the regional lymph nodes. The effect is intended to render the margins of the tumor free of cancerous cells and thus decrease the likelihood that the surgeons will miss cancer that has begun to spread outside of the main tumor mass and therefore lead to improved survival.

Clinical and pathology data from Phase 1 and Phase 2 clinical trials suggest that Multikine® has the potential to elicit both active and passive immunity, producing both a direct effect on the tumor, as well as activating the immune system to produce an effective and sustainable anti-tumor immune response. A description Multikine®'s functions are summarized in Figure 12.

Figure 12

FUNCTIONS OF MULTIKINE®

- Causes a direct, targeted killing of tumors
- Acts on multiple targets on the cancer cell
- Activates the immune system to produce a more robust and sustainable anti-tumor response
- Works to impede cancer recurrence

Source: CEL-SCI Corporation.

Direct Killing of Tumor Cells

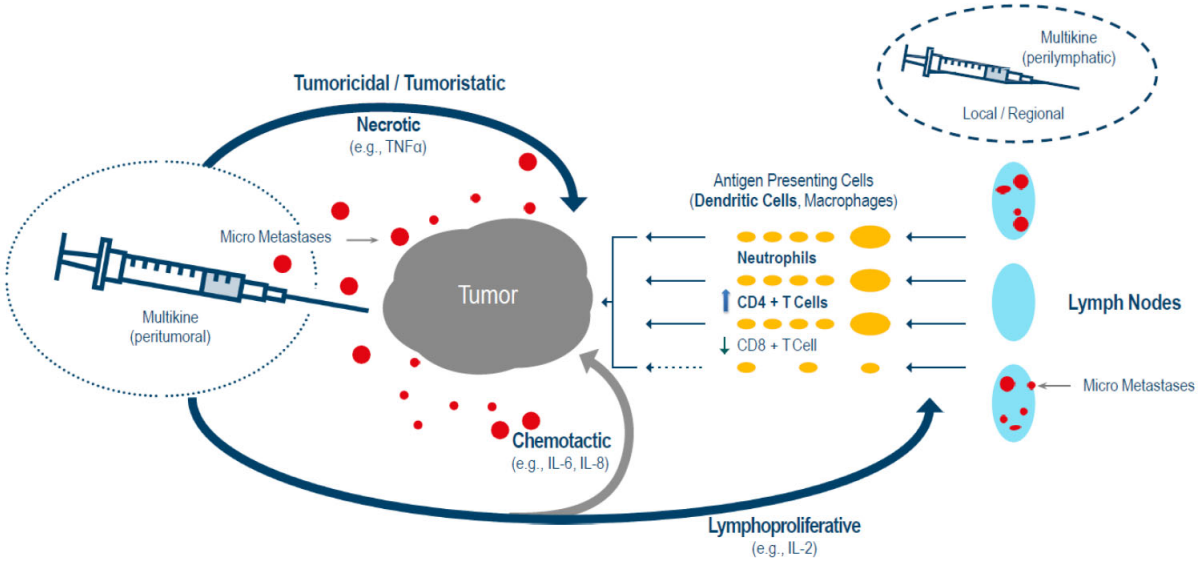
While mAbs and other immunotherapies are targeted at a specific tumor antigen or are formulated from a single cell type, CEL-SCI's Multikine® is composed of a mixture of cytokines. Cytokines are proteins produced by the immune system cells that affect cell behavior and communication, with an important role in regulating the immune response. Traditionally, single cytokine therapies, such as commercial **erythropoietin (EPO)**, have been highly effective for indications with a clear cause and effect relationship. For example, EPO injections stimulate production of red blood cells in patients who have a deficiency of EPO and therefore cannot produce enough of their own red blood cells. However, for complex diseases like cancer, CEL-SCI believes that a single-cytokine approach is less effective than a combination of multiple cytokines with varied functions that can address cancer's numerous causes, and effectively marshal an anti-tumor immune response.

Multikine®'s patented and reproducible cytokine mixture (a complex biologic) contains natural pro-inflammatory interleukins, interferons, chemokines, colony-stimulating factors, and other cytokines, which are biologically active and simulate a healthy immune response. Since Multikine® is produced in a proprietary culture of healthy primary normal donor cells, the natural cytokine mixture produced and presented in Multikine® is thought to have a similar proportion to that, which is found in a natural, healthy immune system. By incorporating all of these active molecules rather than just one cytokine, CEL-SCI is able to mimic the natural immune system more closely. Moreover, the activity of each of these cytokines contributes to Multikine®'s ability to kill cancer cells (Source: *The Journal of Clinical Oncology* May 2005).

Figure 13 summarizes Multikine®'s novel mode of action, which enables this complex biologic to comprehensively assemble an effective anti-tumor attack.

Figure 13

MULTIKINE® MECHANISM OF ACTION: CLEAN TUMOR MARGINS; IMPROVE PATIENT OUTCOME



Source: CEL-SCI Corporation.

(1) **Tumor necrosis factor** alpha (TNFα), a cytokine produced by activated **monocytes** and macrophages that can destroy tumors, aids Multikine®'s ability to cause **necrosis** of cancer cells by attacking the tumor, causing it to release tumor antigens.

(2) The antigen-presenting cells, such as **dendritic cells** (of the treated individual), transport the tumor antigens to the lymph nodes, where Multikine®'s **lymphoproliferative** cytokines induce replication of tumor-specific T-cells to target cancer in the lymph nodes, and have them ready for recruitment to the tumor site.

(3) Subsequently, Multikine®'s **chemotactic** factors recruit anti-tumor specific **CD-4+** T-cells (T-helper cells or Th) from the local lymph nodes, changing the balance of CD-4+ to **CD-8+** T-cells in the tumor microenvironment. The tumor-infiltrating CD-4+ T-cells further instigate a local anti-tumor response, culminating in tumor cell death and necrosis.

(4) Lastly, Multikine® recruits neutrophils from circulation to destroy tumor cell nests. Other cytokines in Multikine®, or those secreted on-site in the tumor microenvironment by the tumor-infiltrating lymphocytes, induce local fibrosis.

Acts on Multiple Targets

Having multiple elements in its composition enables Multikine® to correct a range of immune deficits and target multiple aspects of the tumor that are required for its destruction. This is unlike mAb therapies or some active immunotherapies, which are directed against and react with one specific target. In addition, because Multikine® is not tumor specific, it may potentially be used to address a wide range of solid tumors beyond head and neck cancer.

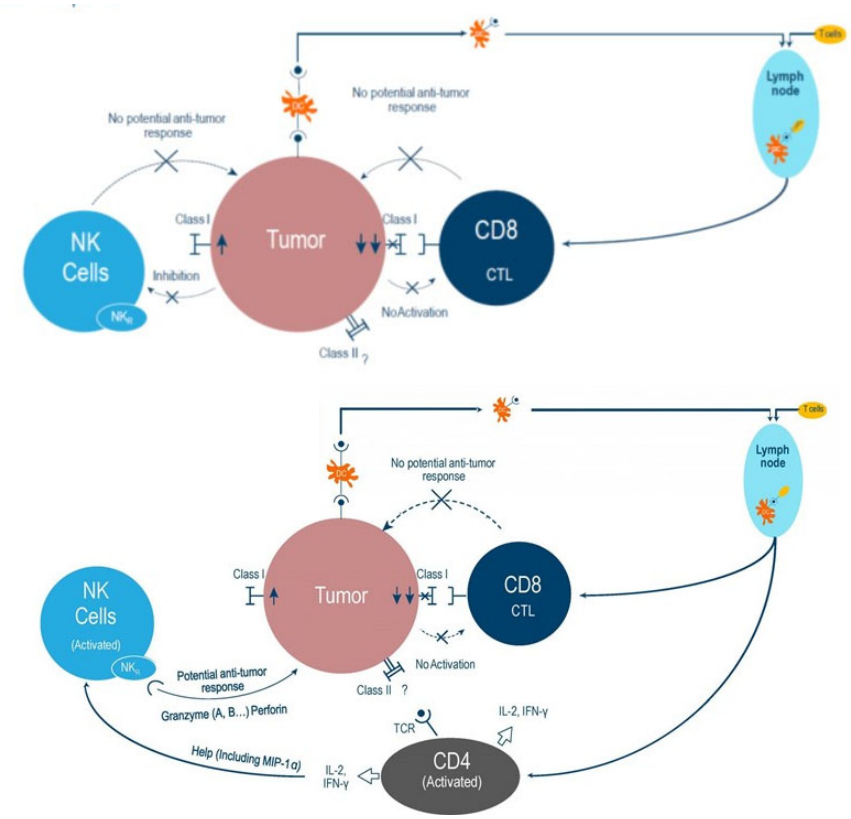
Produces a Robust and Sustainable Anti-Tumor Response

Typically, the immune system sends its CD-8+ T-cells and NK cells to defend against cancer cells. However, due to the tumor tolerance mechanisms, the tumor is able to block these immune cells, making them unable to trigger an effective anti-tumor immune response (illustrated in the top part of Figure 14, page 29). Multikine® leverages CD-4+ cells (Th-cells) instead. Th-cells are believed to enable a more robust anti-tumor response through tumor infiltrating CD4+, CD8+, and NK cells, while also facilitating the immune system's recognition of cancerous cells, thereby functionally "breaking" tumor tolerance.

Involving Th cells in the anti-tumor response is of clinical significance as the tumor is able to shut down the infiltrating CD-8+ cells, but preliminary evidence seems to suggest an inability to shut down the Th-cell. In addition, CD-4+ cells appear to help break "tumor tolerance," thereby potentially allowing the immune system to recognize and destroy tumor cells. The effect of Th-cells in one aspect is similar to that of checkpoint inhibitors, where Th-cells circumvent the inhibitory signal the tumor sends to NK cells, activating the tumor-residing NK cells and allowing them to mount an effective anti-tumor response (bottom part of Figure 14).

Figure 14

MULTIKINE® ANTI-TUMOR EFFECT

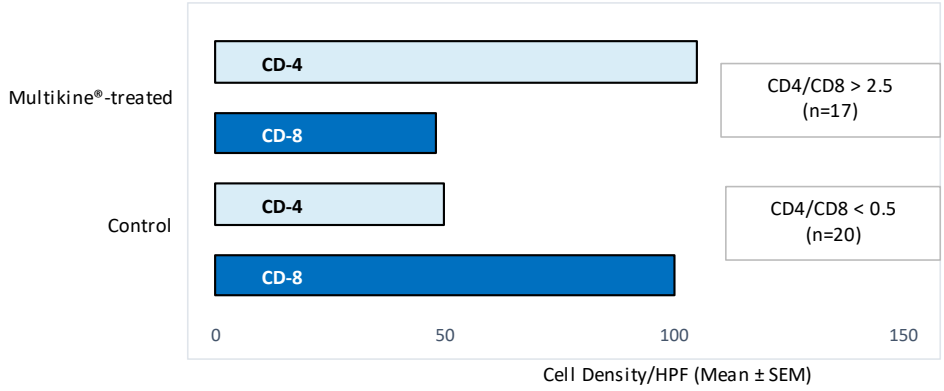


Source: CEL-SCI Corporation.

Figure 15 depicts Multikine®'s effect at decreasing relative quantities of CD-8+ T-cells and increasing CD-4+ T-cells in patients with oral squamous cell carcinoma in a Phase 2 study versus a control group. The matched control group was drawn from matched pathology repository samples of patients who did not receive Multikine®. In addition to improving the CD-4/CD-8 ratio, a three-week regimen of Multikine® treatment resulted in two **complete response**s, indicating the effective elimination of all cancer cells in these two patients as determined by **histopathology**. CEL-SCI's Phase 2 trial also reported that Multikine® stimulates a sustained anti-tumor immunological response that continues for up to 54 days after cessation of Multikine® administration.

Figure 15

MULTIKINE® EFFECT ON HOST CD-4/CD-8 CELL DENSITY



Sources: CEL-SCI Corporation and the Journal of Clinical Oncology (2005).

Works to Impede Cancer Recurrence

CEL-SCI believes that Multikine® harnesses the immune system to prevent the recurrence of cancer in particular areas. Multikine® is injected ½ daily dose **peritumorally** (around the tumor) and ½ daily dose **perilymphatically** (in the vicinity of the nearby draining lymph nodes). These areas are most likely to be the site of future cancer recurrences (noting that Multikine® is not injected into the tumor). Multikine® seeks to primarily eliminate those tumor cells that are likely to be missed in surgery because those cancer cells are thought to be the cause of death for many patients. One key goal is to create "clean margins" before they cause recurrence. A clean margin is essentially an area around the edge of a tumor excised by surgery that has been deemed free of any remaining cancer cells by a pathologist.

As Multikine® is believed to activate the patient's own immune system while it is still strong (before surgery, radiation, and chemotherapy), the body has the capacity to find and kill tumor micrometastases thought to be responsible for recurrence. Therefore, the Company believes that the combination of its immunotherapy drug Multikine® with surgery plus radiation/chemotherapy should be more successful in eliminating all of the tumor cells than the current standard therapies of surgery plus radiation/chemotherapy, alone.

Clinical Trial Results

CEL-SCI has conducted a series of clinical trials throughout the U.S., Europe, Canada, and Israel, which have shown that Multikine® was safe and well tolerated, with significant clinical impact. A summary of these trials is provided in Figure 16.

Figure 16
MULTIKINE® CLINICAL STUDIES

Phase	Indication	No. of subjects	Countries	Published paper
Phase 3	Head & Neck Cancer Recurrent	928	23 countries	5 Abstracts ASCO'22, ESMO'22, ECHNO'23/and 4 Posters 1-ASCO'22; 2-ESMO'22; 1-ECHNO'23 to date
Phase 1/2	Head & Neck Cancer Recurrent	16	U.S. & Canada	N/A
Pilot Study	Head & Neck Cancer Recurrent	4	U.S.	Arch Otolaryngol Head and Neck Surgery
Phase 1/2	Head & Neck Cancer Pre-surgery	12	Israel	Arch Otolaryngol Head and Neck Surgery
Phase 2	Head & Neck Cancer Pre-surgery	28	Canada	N/A
Phase 2	Head & Neck Cancer Pre-surgery	31	Hungary	Laryngoscope, ASCO Annual Meeting
Phase 2	Head & Neck Cancer Pre-surgery	21	Hungary	ASCO, Journal of Clinical Oncology and Oral Oncology
Phase 2	Head & Neck Cancer Pre-surgery	30	Poland & CzechRepublic	N/A
Pilot Study	Prostate Cancer Pre-Surgery Treatment	5	U.S.	Seminars in Oncology
Pilot Studies	Different cancer tumors	54	U.K. & others	Lymphokine
Phase 1	Cervical Dysplasia in HPV Induced Cervical Cancer	8	U.S.	Annals of the 33rd International Congress of the Society of Gynecological Oncologists
Phase 1/2	HIV	15	U.S.	Antiviral Therapy

Source: CEL-SCI Corporation.

Based on its most recent Phase 2 clinical trial for Multikine® in advanced head and neck cancer, CEL-SCI reported that approximately 10% of patients administered the Multikine® treatment regimen over a three-week period had no clinical or pathology evidence of any remaining cancer after treatment. The Company also reported a 33% improvement in overall survival of Multikine®-treated head and neck cancer patients in the same study. CEL-SCI views these findings as significant because its Phase 3 trial designed to replicate the Multikine® treatment regimen utilized in this Phase 2 trial.

In addition, these earlier clinical studies also found Multikine® to result in positive quality of life anecdotal observations, including weight gain and reduction in pain, ability for patients to open their mouths more easily, and ability of patients with tongue cancer to move their tongues again within a few days of treatment initiation. Furthermore, in addition to the clinical trial results of Multikine® for the treatment of advanced head and neck cancer, Multikine® has preliminarily shown the potential for biological activity (in early clinical trials) in cervical dysplasia/neoplasia (pre-cancer and cancer of the cervix) and prostate cancer.

Most importantly, there has not been severe adverse event directly associated with the use of Multikine® reported in any of the Company's early trials. Conversely, traditional cancer therapies (e.g., chemotherapy and radiation) as well as some newer mAb treatments are associated with many toxicities and potentially severe side effects. Further summations of the results of CEL-SCI's largest and most significant trials are presented on the accompanying pages. This is followed by details of CEL-SCI's global pivotal randomized controlled Phase 3 trial.

Phase 1/2 Trial
Source: The Laryngoscope, Vol. 113 (12):2,206-2,217, 2003.

A multicenter Phase 1/2 trial of 54 patients (27 treated with Multikine® and 27 in the control group) with advanced primary oral squamous cell carcinoma studied the effects of escalating doses of Multikine® over a two-week period. Trial participants were assigned to one of several groups: (1) eight patients who received the lowest Multikine® dose—400 international units (IU), three times a week; (2) 12 patients who received 800 IU of Multikine® three times a week; and (3) seven patients who received 800 IU of Multikine® five times a week. Multikine® was injected into the tumor margin.

In conjunction with Multikine® administration, the treatment regimen included a single intravenous infusion of low-dose **cyclophosphamide** (a sub-chemotherapeutic dose) three days before the first Multikine® injections, and oral **indomethacin** three times a day until 24 hours before surgery. These products help to increase Multikine®'s effectiveness. Patients also consumed multivitamins containing zinc daily throughout the treatment regimen until 24 hours before surgery. Between days 21 and 28 after the initial injection of Multikine®, patients had their tumors surgically removed. Two to four weeks after surgery (dependent on surgical wound healing), patients were given standard radiation therapy.

This trial confirmed that Multikine® can stimulate T-cells to migrate into **cancer cell nests** and that oral squamous cell carcinoma is an immunogenic tumor. As published in the *Laryngoscope* in December 2003, the authors/investigators concluded that Multikine®'s novel ability to propel tumor cells into the **cell cycle** could be a result of the drug's synergistic cytokine mixture, which functions in different manners on the immune system and tumor.

Moreover, it was discovered that Multikine®-treated patients did not have an increase in recurrence at 24 months versus the control group (selected from the same institution—for comparison to the Study patients). In fact, one group of eight patients from one of the recruiting centers who were administered the Multikine® treatment regimen did not have a single incidence of recurrence by 24 months.

Phase 2 Trial

Journal of Clinical Oncology, Vol. 23 (15):3421-3432, 2005.

Expanding on its Phase 1/2 trials, CEL-SCI completed a Phase 2 multicenter study in 39 patients with oral squamous cell carcinoma. Nineteen of these patients had previously untreated head and neck cancer and were treated with the Multikine® treatment regimen that closely resembled the protocol used in the Phase 1/2 trial. However, rather than injecting Multikine® only around the tumor, in this trial, investigators/physicians injected Multikine® both peritumorally and in the vicinity of the local draining lymph node chain.

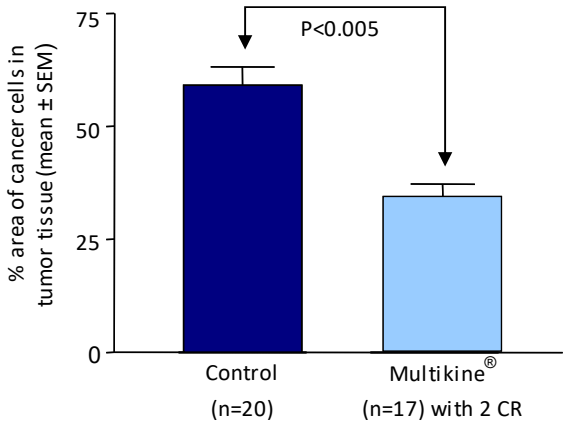
The remaining 20 patients in this study consisted of a historical control group. The investigators and study pathologists selected patients for pathologic evaluation from the pathology specimen repository of the National Institute of Oncology (Budapest, Hungary). The control group was matched to the active treatment arm based on tumor size, location, and disease stage, as well as patient gender and age. Of note, no systemic or local toxicity or severe adverse events related to Multikine® were reported by investigators in this trial.

Tumor Response

As determined by histopathology, Multikine® eliminated tumors in 2 of 19 individuals administered three weeks of Multikine® therapy. In these two patients, it was not possible to detect any cancer tissue in the surgically resected tumor mass, and thus, were considered to be complete responders (i.e., exhibiting 100% tumor reduction). Two other patients had major responses, with a greater than 50% reduction in tumor volume, with four more patients having a minor response, which is characterized by a greater than 30% (but less than 50%) reduction in tumor volume. Only one patient experienced a progression of their disease; the remaining 10 individuals exhibited stable disease. As a result, the study's **objective response rate** (4 of 19 treated patients) was 21%, and the overall response (8 of 19 patients) was 42%.

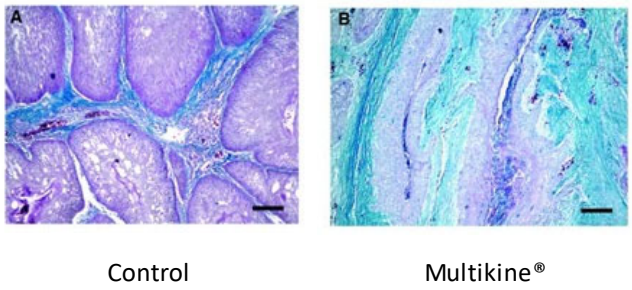
The investigators determined the efficacy of these tumor responses through histopathology, a science that studies microscopic changes in diseased tissues. The study pathologists also found that the Multikine® treatment regimen was associated with a lower percentage of cancer cells, by area, in the tumor tissue than was the control (as seen in Figure 17). Data indicate that in the Multikine®-treated group, the proportion of the connective tissue (versus cancer cells) in tumor tissue was significantly increased compared to those of the control patients, indicating a reduction of cancer cell nest area. The pathology investigation of the study derived tumor samples was performed in a blinded manner such that the reading pathologists were not aware of the sample type (treated or control) they were viewing and scoring . This can be seen in Figure 18, where the left Figure (control group) shows peritumoral (around the tumor) fibrous collagen rim while the right Figure (Multikine® group) shows an accumulation of interstitial collagen fibers between cancer cell nests.

Figure 17
MULTIKINE®'S ANTI-TUMOR EFFECT



Sources: CEL-SCI Corporation and the Journal of Clinical Oncology.

Figure 18
MULTIKINE®'S ANTI-TUMOR EFFECT



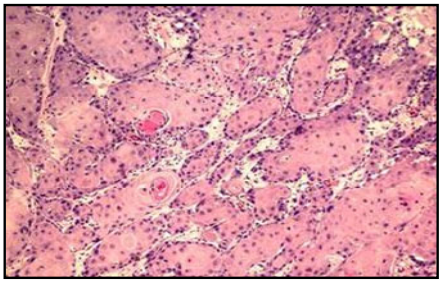
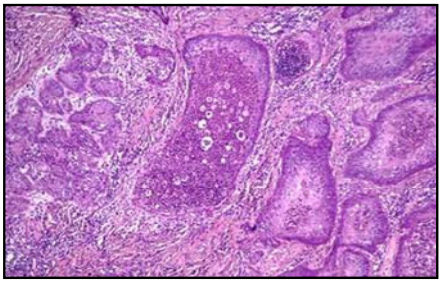
Source: Journal of Clinical Oncology (May 2005).

In addition, CEL-SCI was able to demonstrate that Multikine® stimulated a significant increase in tumor-infiltrating CD-4+ T-cells, while also decreasing the prevalence of CD-8+ T-cells. Involving CD-4+ cells in the anti-tumor response is of clinical significance as these immune cells can help counter the induction of tumor tolerance, allowing the body to recognize tumor cells and mount an effective anti-tumor response. Histopathology showed that the intratumoral CD4:CD8 ratio was low (< 1) in patients not treated with Multikine® (control). An increase in tumor-infiltrating CD4+ and a decrease of CD8+ T-cells was observed in the Multikine®-treated patients, leading to a significantly higher intratumoral CD4:CD8 ratio (> 2.5).

Recruiting CD-4+ T-cells to the tumor site with the use of Multikine® resulted in breaking tumor tolerance and inducing an anti-tumor response culminating in tumor necrosis. This effect is shown in Figure 19, which compares a matched control patient with a tumor (Panel A) to a patient whose tumor was treated with Multikine® (Panel B) samples derived at surgery. Microscopic necrosis was markedly more frequent in the Multikine®-treated group compared with the control group. These changes may reflect the aftermath of an effective anti-tumor immune response raised against the cancer induced by Multikine® treatment regimen neoadjuvant administration.

Figure 19

HISTOLOGICAL APPEARANCE OF NECROSIS WITH MULTIKINE®

Panel A: Control	Panel B: Multikine® Treated
The epithelial nests of oral squamous cell carcinoma lack necrosis.	The entire cancer nest is necrotic, containing debris and leukocytes.
	

Sources: CEL-SCI Corporation and the Journal of Clinical Oncology (May 2005).

The authors/investigators also noted that immunohistopathologic changes could be observed in the tumor 14 to 54 days after Multikine® treatment was discontinued. This finding supports the belief that Multikine® stimulates immune-mediated processes that continue after treatment with Multikine® has ended.

Phase 2 Trial Results Overview

An overview of key results from the Multikine® Phase 2 trial is provided on Figure 20.

Figure 20

MULTIKINE® PHASE 2 TRIAL RESULTS

After 3 weeks of Multikine® Administration		
Of the evaluable patients - 10.5% of patients had no remaining cancer cells	The remaining treated patients had about a 50% average reduction in the number of cancer cells	42.1% Overall Response Rate (RECIST) in Phase 2 study

Sources: CEL-SCI Corporation and the Journal of Clinical Oncology (May 2005).

Phase 2 Follow-up Analysis

Approximately three years after the Phase 2 study was completed, CEL-SCI applied for and received permission to request the investigators obtained the patients' and their families' consents for a follow-on survival follow-up study. Survival results in this final "Proof of Concept" Phase 2 study were compared to results from 55 clinical trials in the same patient population (Advanced Primary SCCHN) who were treated only with standard of care and any other follow-on treatment.

In the follow-up analysis, patients who received Multikine® treatment regimen as first-line investigational therapy, followed by surgery and radiotherapy, were reported by the clinical investigators to have had a 63.2% overall survival rate at a median of 3.33 years from surgery. This number was compared to the overall survival rate that was calculated based upon a review of 55 clinical trials conducted in the same cancer population (with a total of 7,294 patients studied) and reported in the peer reviewed scientific literature between 1987 and 2007. Review of this literature showed an approximate survival rate of 47.5% at 3.5 years from treatment. Therefore, the results of CEL-SCI's final Phase 2 study were considered to be favorable, resulting in a 33.1% improvement in the overall survival rate versus patients administered only the SOC. Figure 21 summarizes the results.

Figure 21
MULTIKINE® TREATMENT EFFECT: PHASE 2 CLINICAL RESULTS

	Standard of Care +/- All Other Treatment Modalities	Multikine® + Standard of Care	% Improvement over the Standard of Care
Overall Survival (at 3.3 Years from treatment)	47.5%[1]	63.2%[2]	33.1%[3]

[1] Survey of 55 clinical trials; advanced primary H&N cancer (published 1987 – 2007)
[2] Multikine® Treatment: Phase 2 Clinical Trial (Timar et al, JCO, 23(15): May 2005)
[3] Talor et al, Oral Oncology Supplement (2) No. 1, May 2007

Source: CEL-SCI Corporation.

Clinical and histopathology data collected during Phase 2 clinical trials of Multikine® indicate that Multikine® appears to have reduced the number of recurrences of tumors in the treated head and neck cancer patients beyond that which would otherwise normally be expected in this same patient population based on literature reports. First-line neoadjuvant Multikine® treatment improved the two-year local-regional control rates (recurrence around the tumor [local] and in the lymph nodes [regional]) over previously published local-regional control rates. The median local-regional control at two years (based on the Company's analysis of scientific literature) was approximately 73%. Conversely, Multikine® with the SOC increased this value to roughly 79%.

The results of the various histopathology analyses from multiple Phase 1 and 2 studies with Multikine® suggest a clear benefit to the patients. The overall survival data from the last Phase 2 study, even though the number of patients is not large, confirms that Multikine® appears to confer a clinical benefit to patients with no added toxicity and raising no safety issues. Following these Phase 2 results, CEL-SCI had discussions with a group of U.S. KOLs (experts in head and neck cancer) who reviewed the Phase 1 and 2 data and concurred with CEL-SCI's viewpoint that Multikine® should move into Phase 3 development.

The FDA recommended that CEL-SCI consider having its own dedicated manufacturing facility for Multikine®, a complex biologic, because it was made clear that the same manufacturing facility ought to be supplying both the Phase 3 study and the commercial product. Supplying the Phase 3 study product from a contract manufacturing facility and supplying commercial product from a different facility was deemed to introduce too large of a regulatory and other risks. Based upon the above, CEL-SCI management determined that the risk/benefit weighed heavily in favor of building the Multikine® manufacturing facility before the Phase 3 study was launched. Details of the Company's manufacturing facility are provided on page 7.

Phase 3 IT-MATTERS: Multikine®'s Global Head and Neck Cancer Study

CEL-SCI's 10-year global pivotal randomized controlled Phase 3 trial showed that Multikine® immunotherapy significantly extended the lives of patients with locally advanced primary squamous cell carcinoma of the head and neck (SCCHN) who are scheduled to receive radiotherapy after Multikine® and surgery. This form of cancer is especially difficult to treat and despite major efforts, including by large pharmaceutical companies, there has been no improvement in first-line therapies for those who would get surgery as a first treatment in over 50 years.

Existing drug therapies for SCCHN from Merck & Company and Bristol Myers Squibb are approved as a last resort for recurrent tumors after treatments have failed or for patients who are not candidates for surgery. In contrast, Multikine® is administered to newly-diagnosed patients following initial diagnosis—and is the first of its kind with substantial survival benefit in a randomized Phase 3 trial in locally advanced primary SCCHN.

The Multikine®-treated study population showed the following advantages over control, as summarized below and further detailed in the accompanying section:

- A median overall survival improvement of 46.5 months (nearly four years);
- 62.7% of Multikine® patients were alive after five years versus 48.6% in the control;
- Almost one out of every six patients had their tumors shrink by more than 30% in just three weeks;
- Five patients had their tumors completely disappear in just three weeks (confirmed at surgery by pathology); and
- Tumor shrinkage/disappearance cut the death rate by a factor of three.

There are approximately 210,000 patients diagnosed globally each year who would be eligible for Multikine® treatment following approval, including about 25,000 annually in the U.S. This group reflects patients who are deemed at "lower-risk-of-recurrence" per the Guidelines of the National Comprehensive Cancer Network (NCCN). Despite the lower-risk label, the disease survival rate is only about a 48% chance of living past five years. Multikine® increased the survival rate to more than 62% at five years. For patients deemed at "higher-risk-of-recurrence," Multikine® is not suitable because those patients receive chemotherapy following surgery, which could negate Multikine®'s biological mechanism of action. The lower-risk-for-recurrence patients, by contrast, do not receive chemotherapy.

CEL-SCI's data compares favorably to other already approved SCCHN therapies. Merck's product, Keytruda®, was approved for recurrent SCCHN based on a single-arm trial with a 16% tumor response rate (CEL-SCI showed the same response rate in a randomized controlled trial). Keytruda® did not show a survival improvement (CEL-SCI showed a survival improvement that took five-year survival from about 48% to 62% at five years). Bristol Myers' drug, Opdivo®, was approved based on only a 2.4-month life extension (CEL-SCI showed a median 46-month improvement in life extension). In addition, Multikine® has demonstrated a much more favorable toxicity profile than these approved products.

Creating a New Standard of Care Therapy

The current SOC for locally advanced primary SCCHN is surgery first, with an intent to cure for the removal of the tumor and any involved lymph nodes. Following surgery, the patient gets categorized for risk. If the patient has adverse features, such as positive margins, multiple lymph nodes that are affected, etc. (as listed in the NCCN guidelines), the patient is then scheduled for a prescribed concurrent chemotherapy plus radiotherapy. The patient is administered three doses of chemotherapy, cisplatin, etc. along with a radiotherapy regimen over roughly a two month period and then is followed up. The following (Figure 22, page 36) is the determination of who gets radiation versus who gets chemoradiation following surgery per the NCCN guidelines:

Figure 22

DETERMINATION OF WHO GETS RADIATION VERSUS WHO GETS CHEMORADIATION FOLLOWING SURGERY PER THE NCCN GUIDELINES

TNM Classification	Primary Surgical Treatment	Radiotherapy	Concurrent Chemotherapy*
Resectable, T3-4, N0	Excision of primary and reconstruction as indicated and unilateral or bilateral selective neck at risk dissection.	External RT 60 - 70 Gy in 30-35 fractions for 6-7 weeks	**High-Risk Subject Category** 1. Positive margins or 2. Nodal involvement (≥ 2 positive nodes) or 3. Extracapsular nodal spread
Resectable, T 1-4, N1-2	N1: excision of primary, ipsilateral comprehensive neck dissection (levels 1-5) ± contralateral selective neck dissection. Reconstruction as indicated.	External RT 60- 70 Gy in 30-35 fractions for 6–7 weeks	
	N2: excision of primary, ipsilateral or bilateral comprehensive neck dissection (levels 1-5). Reconstruction as indicated.	External RT 60 - 70Gy in 30-35 fractions for 6-7 weeks	

Source: CEL-SCI Corporation.

In its Phase 3 trial, CEL-SCI intended to demonstrate that Multikine® can be a successful first-line component of the current SOC regimen administered before a patient undergoes surgery. Based on discussions with the FDA, CEL-SCI designed its pivotal Phase 3 trial to evaluate the performance of Multikine® treatment regimen+SOC against the SOC alone. Commercializing Multikine® as the first SOC therapy for newly diagnosed patients could provide the Company with opportunities to receive reimbursement coverage for its product candidate. In addition, CEL-SCI believes that the market for first-line therapies in cancer patients following initial diagnosis is significantly larger than the market for medications aimed at the treatment of recurring cancer.

The Company views the initial market for cancer treatment first, immediately after diagnosis (in the neoadjuvant setting) as can be done with Multikine®, to have limited to no competition, especially should Multikine® become part of the SOC treatment regimen and shown to extend life. A successful Phase 3 trial could result in Multikine® becoming an integral part of a new SOC, which could positively influence its adoption and usage.

Importance of Multikine®'s IT-MATTERS Trial Results

Head and neck carcinomas constitute about 900,000 cases annually worldwide. In the U.S., there are about 68,000 new cases annually. Of those, 90% are squamous cell carcinomas, and approximately two-thirds of these patients present on their first visit with locally advanced primary (untreated) disease. Currently, the median three-year overall survival with the existing SOC is estimated at 55%. The five-year overall survival is approximately 43%. There are many locally advanced primary SCCHN patients who are not well served by the currently available treatment modalities.

The IT-MATTERS trial confirms that a three-week treatment with Multikine® provides objective tumor responses before surgery with statistically significant five-year overall survival benefit for the Proposed Indication (patients deemed by the NCCN Guidelines as lower risk of recurrence and who should receive only radiotherapy following surgery). Multikine® administration as the first therapy after diagnosis, demonstrated improved five-year survival and objective complete and partial tumor responses before surgery in 8.5% of the overall intent to treat (ITT) population and in 16.0% of all Multikine®-treated patients in the lower-risk-for-recurrence treatment arm. A partial response means that the tumor has been reduced by at least 30%, and a complete response means that the tumor has completely disappeared. These objective tumor responses were noted within three-weeks of the beginning of Multikine® treatment up to surgery and provided direct evidence of Multikine®'s anticancer activity, as no other study-directed therapy was given to these patients during that time.

Although objective tumor responses to cancer drugs do not always lead to improved survival, in the case of Multikine®, objective responses resulted in a significantly reduced death rate. For Multikine® patients in the Proposed Indication, the death rate fell from 41% for non-responders to 12.5% for objective responders. A similar effect was similarly seen for objective responders in the overall ITT as well.

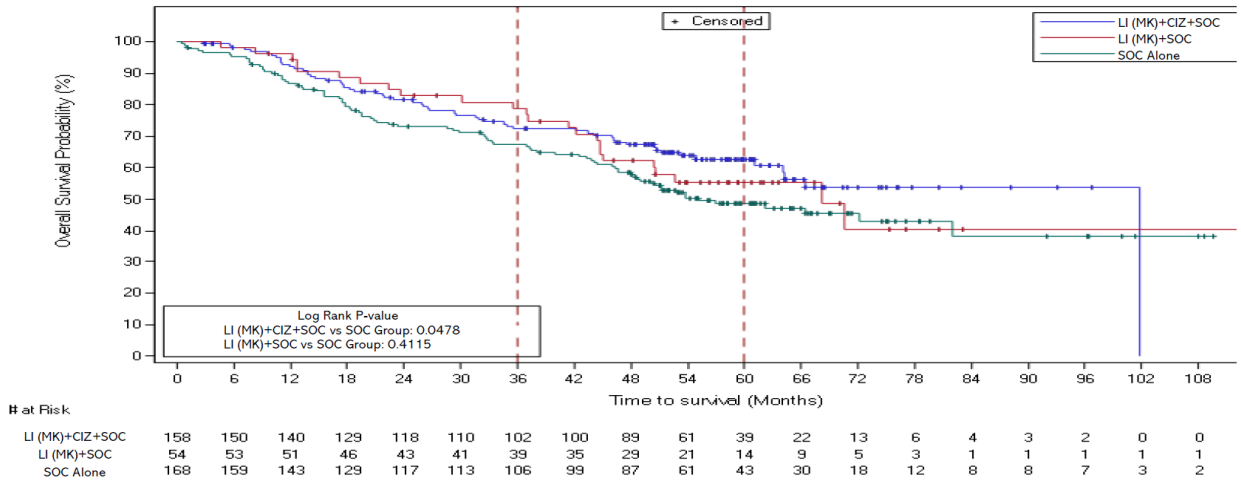
These reduced death rates yielded an absolute overall survival advantage of 14.1% at five-years versus the SOC alone in the lower-risk-for-recurrence treatment arm, with a proportional hazard p-value of 0.0236, a hazard ratio of 0.68 (representing 47% prolongation of survival), a median overall survival that is nearly four-years longer than from the SOC alone, confirmatory progression-free survival (PFS) benefit, and histopathological data showing the direct effect of the Multikine® treatment on the tumor and the tumor microenvironment.

These statistics mean that for every 100 patients who would receive Multikine® (if approved) followed by surgery and radiotherapy only, the likelihood is that about 14 more people would be alive at five-years compared to the existing SOC. Since about 210,000 advanced primary SCCHN patients globally would be eligible for this treatment, the overall survival advantage seen in this study could mean that about 29,000 more people would be alive at five-years post-therapy versus the SOC if all these patients received the Multikine+CIZ treatment regimen followed by surgery and radiotherapy. By contrast, the SOC control group did not see any objective tumor responses before surgery.

The survival curve below (Figure 23) shows that the blue line (the main Multikine® treatment arm) is always better than the green line which is the SOC control group. The red line is a much smaller group that FDA had requested for data related to the toxicity of drugs given with Multikine®.

Figure 23

OS KAPLAN-MEIER CURVE FOR THE LR GROUP (N=380)



Source: CEL-SCI Corporation.

Importantly, Multikine® is unique from existing therapies as it is designed to be administered locally first, immediately following diagnosis, to previously untreated patients whose tumors and any involved lymph nodes are slated for surgical resection with "intent-to-cure" SOC. To CEL-SCI's knowledge, there has been no such therapy or neoadjuvant approved by FDA in at least several decades for resectable locally advanced primary SCCHN. While existing checkpoint inhibitor drug therapies (such as Keytruda®) have been approved and marketed as "first-line" treatments for head and neck cancer, their indications are limited to the first-line treatment of recurrent or non-resectable tumors. In contrast, Multikine®'s proposed indication would be for previously untreated, locally advanced primary SCCHN patients scheduled for surgery and radiation without chemotherapy, encompassing about 40% of the entire advanced primary SCCHN population.

CEL-SCI's Phase 3 study represents the first reported survival benefit in a randomized controlled study for patients with previously-untreated advanced primary SCCHN in many decades. Others have attempted and failed in head and neck cancer, including two recent failures by Merck and AstraZeneca PLC (AZN-ADR) in 2022, as well as others, as shown in Figure 24.

Figure 24
HEAD AND NECK CANCER UNSUCCESSFUL DEVELOPMENT EFFORTS

Manufacturer	Drug	Study	Outcome
Boehringer Ingelheim	Afatinib	LUX-Head&Neck 2	Failed June 2019
Pfizer & Merck	Bavencio	JAVELIN 100	Terminated March 2020
AstraZeneca	Durvalumab	KESTREL	Failed February 2021
Glaxo	Feladilimab	INDUCE-3/ INDUCE-4	Terminated April 2021
Bristol Meyers	Opdivo + Yervoy	CHECKMATE-651	Failed September 2021
Pfizer & Merck	Bavencio	GORTEX-REACH	Failed September 2021
Merck	Keytruda	KEYNOTE-412	Failed July 2022
AstraZeneca & Innate	Monalizumab + Erbitux	INTERLINK-1	Terminated August 2022

Source: CEL-SCI Corporation.

Phase 3 Multikine® Head and Neck Cancer Results Posted on Clinicaltrials.gov

In August 2022, CEL-SCI announced that the results of its 10-year IT-MATTERS pivotal Phase 3 clinical trial in head and neck cancer with its investigational immunotherapy Multikine® had been posted on clinicaltrials.gov, per U.S. government requirements.

(https://clinicaltrials.gov/ct2/show/results/NCT01265849?term=multikine&draw=2&rank=2)

Clinicaltrials.gov is the largest clinical trial database in the world. It is run by the U.S. National Library of Medicine at the National Institutes of Health (NIH). Some of the trial's results were published in two peer-reviewed abstracts and a poster at the ASCO conference in June 2022.

(https://www.businesswire.com/news/home/20220527005092/en/)

The 928-patient IT-MATTERS study was designed to determine if Multikine® provided survival and other clinical benefits to patients suffering from locally advanced primary squamous cell carcinoma of the head and neck (SCCHN), oral, cavity and soft-palate. Multikine® is the first investigational cancer immunotherapy being developed as a first-line neo-adjuvant treatment to be provided to previously untreated locally advanced primary disease SCCHN patients before they receive the SOC. The global IT-MATTERS trial was conducted in 23 countries on three continents together with a total of approximately 100 sites in accordance with Good Clinical Practices, International Counsel for Harmonization standards, and all other country-specific regulatory requirements.

Following diagnosis, subjects were randomized into one of three treatment arms. In the primary treatment arm (3/7) subjects received three consecutive weeks of treatment with Multikine® injected 5x/week peritumorally and perilymphatically plus "CIZ" prior to receiving the SOC. CIZ comprised a non-chemotherapeutic dose of cyclophosphamide administered one-time only IV-bolus, three days prior to the first dose of Multikine®, and indomethacin and zinc-multivitamins daily from day one of Multikine® administration to one day before surgery to enhance Multikine® activity. In the second arm (1/7), subjects received the three-week Multikine® regimen without CIZ prior to receiving the SOC. In the third arm (3/7), which was study control arm, subjects received only the SOC (with no Multikine® or CIZ). All subjects in the study received the SOC, but some subjects received Multikine® prior to the SOC (the two study treatment arms) and some did not (study control arm). The two main comparator groups in the study were the primary arm (Multikine+CIZ+SOC) and the study control arm (SOC alone).

The SOC for all research subjects was identical and involved a bifurcated treatment path following surgery (i.e., a radiotherapy-only arm and a concurrent chemoradiotherapy arm). To determine the path a patient should take, the treating physicians decided after surgery based on pathology and medical judgment, as guided by the National Comprehensive Cancer Network (NCCN) Guidelines, whether the patient was at a higher risk for tumor recurrence. These patients would receive concurrent chemoradiotherapy. All other patients were classified as lower risk for recurrence and would receive only radiotherapy after surgery.

The "Proposed Indication" for Multikine® will be limited by certain eligibility criteria to select patients for Multikine® neoadjuvant treatment who are deemed as lower-risk-for-recurrence by physicians based on NCCN Guidelines. Patients would not meet the eligibility criteria for Multikine® neoadjuvant treatment if they present at screening/entry with adverse features that would place them in the higher-risk-for-recurrence category (per NCCN Guidelines). (Note that the term "lower risk for recurrence" should not be confused with a low risk of death, because the five-year survival for such patients is still less than 50%, even after receiving the current SOC treatment).

Importantly, the bifurcated treatment path described above was not created by CEL-SCI for its study but was, and still is, the SOC per NCCN Guidelines for locally advanced primary SCCHN patients. Because it would have been unethical to deprive any subjects of the SOC, the only ethical way to have conducted the study was to use the bifurcated SOC following surgery—it would not have been ethically permissible to study Multikine® in only one treatment arm at a time (lower-risk or higher-risk only).

Additionally, because it was obvious when the study was designed that Multikine® might provide a benefit in only one of the two SOC risk groups, CEL-SCI pre-specified in its original study protocol that analyses of the trial results should take place for all, as well as for each of these risk groups. Separate analyses of the lower-risk-for-recurrence and higher-risk-for-recurrence treatment arms were also pre-specified in the study's statistical analysis plan, which was completed before data lock and the study result were analyzed.

Approximately 40% of study subjects (n=380) were classified by the study physicians as having a lower risk of tumor recurrence, and it was in this arm of the study that the vast majority of the objective tumor responders discussed above were observed. It was also observed in this arm that Multikine+CIZ-treated non-responders still saw overall survival benefit. Thus, when the lower-risk-for-recurrence arm was viewed as a whole (responders plus non-responders together), a statistically significant overall survival benefit from Multikine® was observed, which provided a nearly four-year extension of median overall survival time versus the lower risk for recurrence control group, which did not receive Multikine®.

Using data from the study, CEL-SCI developed eligibility criteria (https://meetings.asco.org/abstracts-presentations/207202/) to select, prior to surgery, the patients who would be slated for classification by the NCCN Guidelines as lower-risk-for-recurrence. This distinction currently can be determined only after surgery. Based on the ability to select subjects who should receive Multikine® prior to surgery, CEL-SCI plans to seek FDA approval for the treatment of locally advanced primary disease SCCHN subjects who would receive Multikine® first, then receive surgery, and then receive only radiotherapy, per NCCN Guidelines.

The proposed indication represents about 210,000 patients worldwide per year. To CEL-SCI's knowledge, the last medical advance for such patients impacting their overall survival occurred when Methotrexate was approved over 60 years ago. Multikine® has received FDA Orphan Drug Designation for the neoadjuvant therapy in patients with SCCHN.

Reduced and Eliminated Tumors Within Three Weeks and Prior to Surgery

The most important result of CEL-SCI's study, other than the overall survival benefit, was that 16% (34 patients) of Multikine® patients in the radiation-only group (212 patients) in the Company's Phase 3 study had at least a 30% tumor reduction within just a few weeks of treatment before surgery. Five of these responders had their tumors completely disappear before surgery. These patients presented with locally advanced primary disease and within three weeks of Multikine® treatment, prior to surgery, the tumors were completely gone.

In contrast, there was not one tumor response in the study control group, which did not receive Multikine®. This means that the responses to Multikine® could not have been by chance ($p<0.00000001$). The Company already realized the same type of responders in its Phase 2 studies, with the corroboration of these studies providing additional evidence of Multikine®'s direct anti-tumor effect. In reality, oral cavity/soft-palate locally advanced treatment naïve head and neck cancer tumors have not been reported to regress on their own before any treatment is given (as far as the Company is aware).

Regarding the "radiation-only" group, every patient in CEL-SCI's Phase 3 study was slated to undergo surgery. Patients were then assigned by their doctors to one of two risk groups, which determined whether the patient went on to receive only radiation or radiation plus chemotherapy (concurrent chemoradiation) following surgery. This was the SOC treatment for these patients when CEL-SCI began its study and is still the SOC today.

Responses prior to surgery were seen across all groups of Multikine®-treated patients (not just in those who would receive radiation-only after surgery). While most tumor responses occurred in the patients who were treated with Multikine® and would receive radiation-only following surgery, some also occurred in the Multikine®-treated patients who would receive chemoradiation. There were zero tumor responses in the control group (394) who did not get any Multikine® treatment prior to surgery, so the statistical significance of tumor responses in the total Multikine® population is exceptionally strong ($p<0.00000000001$), demonstrating that these responses to Multikine® could not have been seen by chance and evidence of the direct anti-cancer effect the drug has on the tumor.

Nearly Four-Year Median Overall Survival Benefit in the Radiation-Only Group

Seventy eight percent of responders in the Multikine® radiation-only group were still alive at the five-year follow up versus approximately 48% in the control group who never received Multikine® and were given SOC only (surgery + radiotherapy as they were categorized as lower risk for recurrence). Radiation-only patients who received Multikine® but who did not have at least a 30% reduction of tumor burden from baseline (classified as tumor response by RECIST) still benefited from Multikine®.

When all radiation-only Multikine+CIZ patients (CIZ contains supplements to enhance Multikine®'s activity) were considered together, the five-year overall survival was significantly improved—62.7% versus 48.6% for the control. This is an absolute benefit of 14.1 percentage points, where on average, 14 more people out of 100 Multikine® patients would be alive after five years.

Even as today's best immunotherapies provide just a few months of survival benefit for recurrent or metastatic tumors, Multikine® provided 46 months of survival benefit for newly-diagnosed locally advanced disease in the radiation-only group—providing nearly four more years of median survival. Patients in the chemoradiation group did not benefit from Multikine®. This is likely due to the fact that their disease is much more advanced and therefore requires an immediate removal of their tumors as opposed to delaying surgery for an extra three weeks required to receive Multikine® plus that subsequent chemotherapy interferes with the Multikine® induced anti-tumor immune response. If the FDA approves Multikine®, the product labeling is expected to be contraindicated for use in patients who would require chemoradiation after surgery.

CEL-SCI has developed eligibility criteria to identify, with high accuracy, patients who are slated to receive only radiotherapy (not chemoradiotherapy) after surgery. These patients should be the individuals to receive Multikine®. This method was published at the peer-reviewed ASCO cancer conference in June 2022, and was very well received by the oncologists in attendance.

Phase 3 Results Published at European Society for Medical Oncology (ESMO)

In October 2022, CEL-SCI announced the availability of an oral presentation delivered by Dr. Philip Lavin of revolutionary tumor response and increased overall survival in head and neck cancer. This presentation included data presented at the European Society for Medical Oncology (ESMO) Annual Congress on September 10, 2022 in Paris, France. The ESMO poster presentation was titled "Early response to Neoadjuvant Leukocyte Interleukin Injection (LI) immunotherapy extends overall survival in locally advanced primary squamous cell carcinoma (SCC) of the head & neck (HN): the IT-MATTERS Study." The presentation can be viewed through the following link: https://youtu.be/zMoFtweVGzs.

Dr. Lavin is a well-known biostatistician with a long history of supporting clinical trials for product registrations, reimbursements, and public health advancement. He has served on the faculty of Harvard Medical School at the Harvard School of Public Health for over 25 years and has been in the oncology field since 1974. He also advised the FDA from 1983 through 2015 on product approvals and public policy matters as a Special Government Employee.

A summary of the most recent data presented from this Phase 3 clinical trial is that a three-week administration of Multikine® treatment achieved groundbreaking tumor response and increased overall survival in treatment naïve locally advanced primary head and neck cancer patients who are scheduled to receive surgery and radiotherapy as their indicated treatment. The study had 45 early tumor responses, including five complete (with surgical confirmation of clearing all signs of cancer in the oral cavity) and 40 partial responses to Multikine® after three weeks of treatment, prior to any SOC treatment; all were early tumor responses in that they followed a three-week Multikine® treatment, were observed at surgery, and occurred before radiotherapy. Early tumor response to Multikine® treatment was associated with (and may be considered as both prognostic and predictive of) overall survival. The Multikine® tumor response was differentiating in that it was observed within a week after completing the fixed three-week Multikine® treatment. The degree of response had a significant impact on subsequent survival, which should qualify Multikine® early tumor response as a surrogate marker.

Phase 3 Results Published at ASCO

In June 2022, CEL-SCI announced that its abstract and poster titled "Leukocyte interleukin injection (LI) immunotherapy extends overall survival (OS) in treatment-naive low-risk (LR) locally advanced primary squamous cell carcinoma of the head and neck: The IT-MATTERS study" was presented on June 6, 2022 at the American Society of Clinical Oncology (ASCO)'s 2022 ASCO Annual Meeting in Chicago, Illinois.

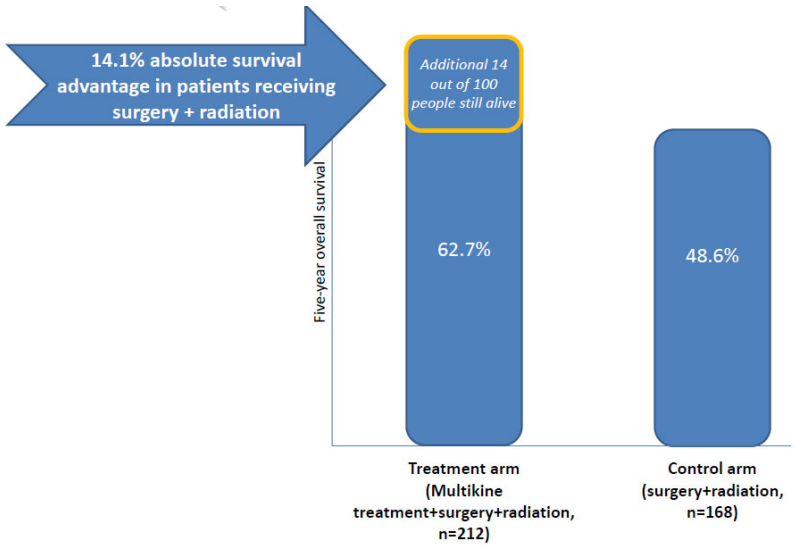
With regard to overall survival advantage for patients with surgery and radiation, there was a 14.1 percentage point absolute advantage (62.7% versus 48.6%, Figure 25, page 42) in overall survival in surgery followed by radiotherapy treatment arm (lower risk for recurrence) at five years in patients with locally advanced primary SCCHN. This group is called the lower risk for recurrence group (however, "lower risk" does not mean low risk). The control group without Multikine® still faced a high risk of death of over 50% at year five post-therapy. Regarding overall survival prolongation for Multikine-treated patients with surgery and radiation, there was nearly a four-year increase in median survival in the Multikine® treatment arm, with 101.7 months versus 55.2 months for control.

As summarized in Figure 26 (page 42), partial and complete tumor responses before surgery (early responses) were as follows:

- 8.5% of Multikine®-treated patients (45 of 529) in the overall intent-to-treat (ITT) population (N=923)
- 16.0% of Multikine®-treated patients (34 of 212) in the surgery plus radiation treatment arm
- Five of these early responders in the Multikine®+CIZ treatment arm were confirmed to have complete tumor response at surgery
- Zero early response were seen in the SOC (control) alone (consistent with literature).

Figure 25

PHASE 3 TRIAL RESULTS: SUMMARY OF SIGNIFICANT SURVIVAL BENEFIT



Source: CEL-SCI Corporation.

Figure 26

EARLY TUMOR RESPONSE RESULTS IN DECREASED DEATH RATE (PROGNOSTIC AND PREDICTIVE OF SURVIVAL)

In Randomized ITT Population - LI (MK) Early Response (CR/PR) prior to surgery

	Early Responders ([CR+PR]/n), (%)	Deaths % LI (MK) Early Responders / Remaining LI (MK)-Treated (n)	Hazard Ratio (HR) [95% CI]
All LI (MK) treated (Lower, Higher, and Missing Risk) (n=529)	45/529 (**8.5%**)	22.2% (10/45) Early Responders vs 54.1% (262/484) Early non-Responders 2-Sided Fisher Exact p-Value [**p<0.0001**]	**HR=0.301** [0.16, 0.566]
Combined Lower Risk LI (MK) treated (n=212)	34/212 (**16.0%**)	17.6% (6/34) Early Responders vs 42.7% (76/178) Early non-Responders 2-Sided Fisher Exact p-Value [**p=0.0067**]	**HR=0.348** [0.152, 0.801]
Lower Risk Group 1 LI (MK)+CIZ+SOC (n=158)	24/158 (**15.2%**)	12.5% (3/24) group 1 Early Responders vs 41.0% (55/134) Early non-Responders 2-Sided Fisher Exact p-Value [**p=0.0101**]	**HR=0.246** [0.077, 0.787]

NOTES: (1) Early response is highly prognostic for future survival. (2) No early responses in the control group.

Source: CEL-SCI Corporation.

Early tumor responders had very significant reductions in death rates:

- In the overall intent to treat (ITT) population, 22.2% death rate (n=45) among Multikine® responders versus 54.1% death rate for the Multikine® non-responders (n=484) (two-sided Fisher Exact test p<0.0001; HR=0.301)

- In the surgery plus radiation treatment arm, 17.6% death rate (n=34) among Multikine® responders versus 42.7% death rate for the Multikine® non-responders (n=178) (two-sided Fisher Exact test p=0.0067; HR=0.348)

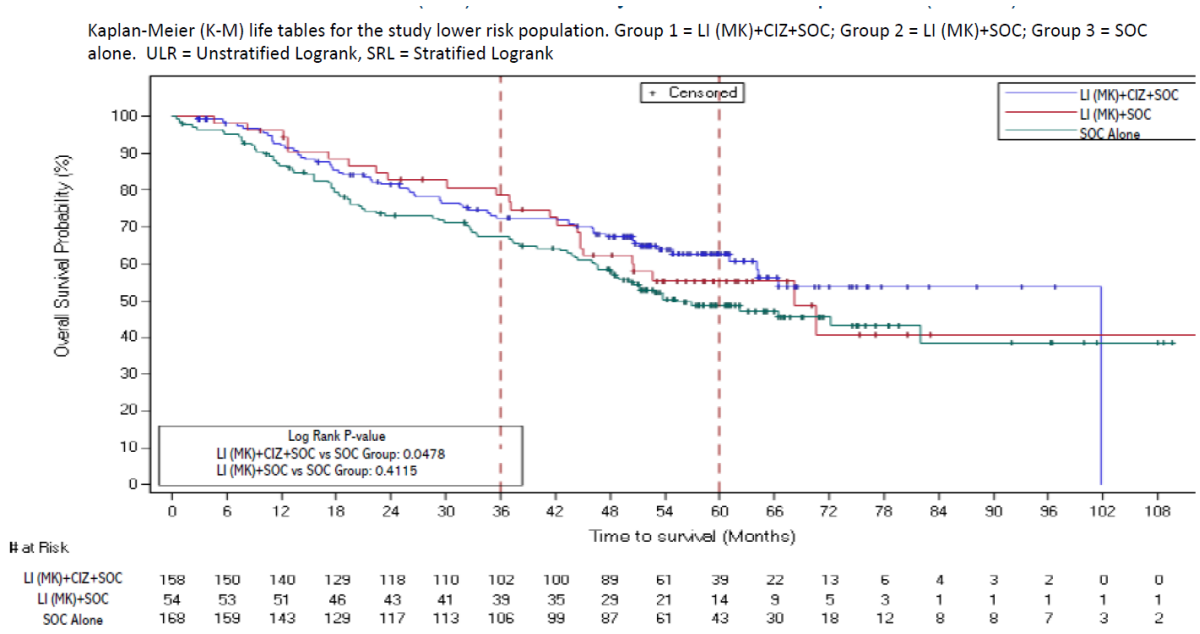
Histopathological analysis confirmed the effect of Multikine®, with 61 markers, ratios, and combinations showing a statistically significant effect (two-sided p<0.05) favoring the Multikine®+CIZ cohort versus the SOC alone (control). There was additional (confirmatory) progression-free survival (PFS) benefit in the treatment arm scheduled to receive surgery and radiation.

Reduced Five Year Death Rate from 54% to 22% in Patients Who Were Early Tumor Responders Prior to Any SOC Treatment – impacts Survival

As shown in Figure 27, in the entire lower risk population (N=380), the Kaplan-Meier survival life-table and curve showed overall survival benefit that extended and expanded over time, between Multikine+CIZ treated (Blue line) versus control (Green line), with 4.9% overall survival absolute advantage at 36 months (3-years); 9.5% absolute advantage at 48 months (4-years); and 14.1% absolute advantage at 60 months (5-years), unstratified log rank p=0.0478. This corresponds to a Hazard ratio of 0.68; which equates to a 47% survival prolongation; without adding toxicity to the existing SOC.

Figure 27

OVERALL SURVIVAL (OS) OF THE STUDY LOWER RISK POPULATION (N=380)



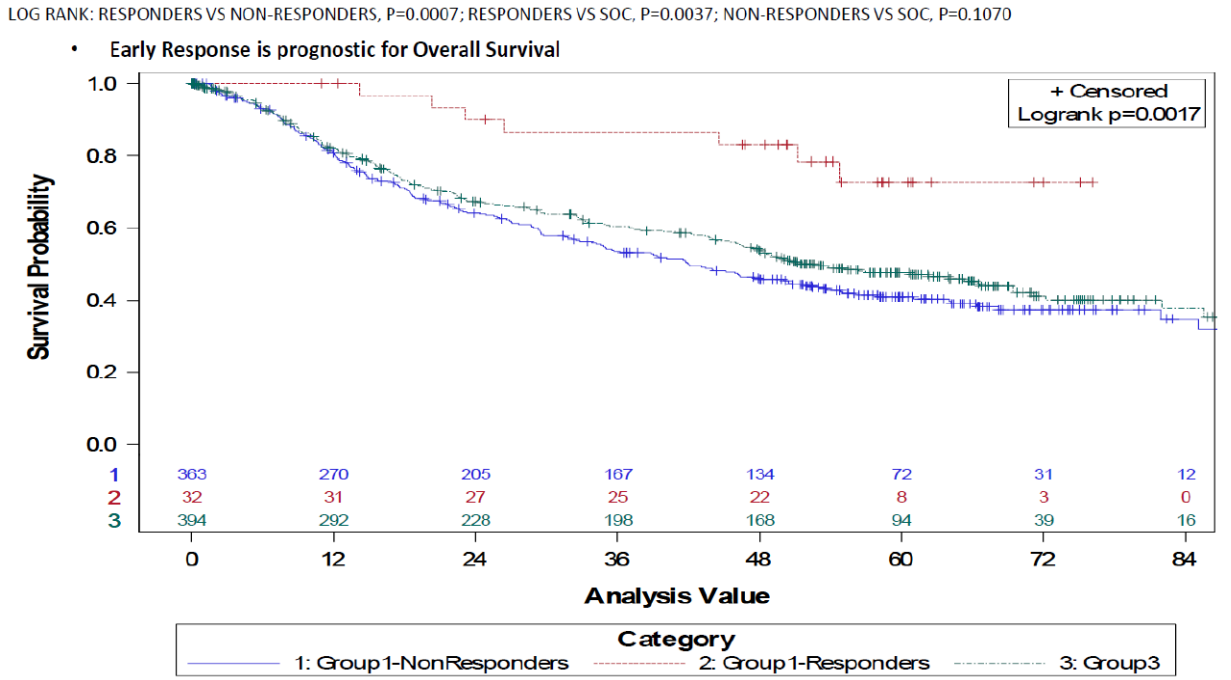
Source: CEL-SCI Corporation.

The Multikine+CIZ+SOC regimen graph (Figure 28, page 44) shows the 32 PSRs (pre-surgery responders documented at surgery by pathology) [Red line] and the remaining 363 non-responders (having less than 30% reduction in tumor burden from entry to surgery) [Blue line] as well as Control – SOC alone [Green line]. There was a highly significant difference between the three survival curves (Log rank two-sided p=0.0017). The Multikine+CIZ-treated responders had superior overall survival to the Multikine+CIZ-treated non-responders (Log rank two-sided p=0.0007) and also superior to the control - SOC alone (Log rank two-sided p=0.0037). There was no statistically significant difference between the Multikine+CIZ-treated non-responders and SOC alone (Log rank two-sided p=0.1070).

The Multikine+CIZ+SOC responders experienced the best overall survival (~80% at 60-months i.e., at five years) in contrast to the survival by SOC alone, which was ~50% at five years. The analysis shown in Figure 28 (page 44) was done for the overall study patients by treatment category (and not by risk category determined after surgery, and not by disease directed therapy – following surgery). Therefore, these data for all groups contain patients who had radiation (lower risk) but also some patients within each group who received chemoradiation (usually given to higher risk patients). In the study's lower-risk patients (n=380; not shown), the Multikine+CIZ+SOC-(Surgery+radiotherapy), non-responders also experienced more favorable survival outcome than SOC alone, indicative of a carryover benefit for Multikine+CIZ+SOC in the lower risk category.

Figure 28

OVERALL SURVIVAL (OS): ITT POPULATION (N=789) OVERALL RESPONDERS VS. NON-RESPONDERS VS. STANDARD OF CARE



Source: CEL-SCI Corporation.

Early Response Conclusions

Early tumor response was highly associated (prognostic and predictive) with survival in the subjects who exhibited early response irrespective of their risk group allocation. These data set the stage for an overall survival advantage confirmation. For the lower risk LI (MK)+CIZ+SOC group, there was a 306% (100 x (1 0.246)/0.246) survival prolongation for 15.2% in this treatment group. Assuming no survival prolongation for the remaining 84.8% in this treatment group, this projects an overall 46.5% survival prolongation (3.06x15.2%); this corresponds to a 0.68 HR (1/1.465), which is exactly what was observed for the LI (MK)+CIZ+SOC group with lower risk classification. The significant 0.68 HR for the lower risk population LI (MK)+CIZ+SOC vs. SOC equates to a 47% survival prolongation, characterized by a five-year 14.1% absolute overall survival advantage, and a 46 month median overall survival advantage over lower risk SOC alone. With approximately 80% of responders surviving for five plus years, a Multikine® response may not only be associated with but could possibly be considered prognostic/predictive of a favorable survival outcome.

CEL-SCI's Multikine® Phase 3 Cancer Study Shows 43% Survival Extension

On March 8, 2023, CEL-SCI reported new data from its pivotal Phase 3 study, the largest study ever conducted in newly diagnosed locally advanced squamous cell carcinoma of the head and neck (SCCHN). A poster presentation titled "Leukocyte Interleukin Injection (LI) immunotherapy followed by radiotherapy extends overall survival (OS) in treatment naïve locally advanced primary squamous cell carcinoma of the head and neck: the IT-MATTERS Study" was delivered by Eyal Talor, Ph.D., CEL-SCI's Chief Scientific Officer (biography on page 8) at the 10th European Congress on Head & Neck Oncology (ECHNO) in Lisbon, Portugal.

A link to the poster can be found at: https://cel-sci.com/wp-content/uploads/2023/03/CEL-SCI-ECHNO-Abstract-77-ePoster-FINAL.pdf.

The Company expects to submit a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) and other regulatory agencies to approve Multikine® in the treatment of newly diagnosed SCCHN in patients deemed at lower risk for recurrence (LR), as defined by National Comprehensive Cancer Network (NCCN) guidelines. The new data presented is significant as it concentrates exclusively on the patient population (n=352) from the IT-MATTERS study for which CEL-SCI is seeking regulatory marketing approval for locally advanced primary head and neck cancer patients scheduled to receive radiotherapy, but not chemotherapy, after surgery.

Per the NCCN guidelines, these LR patients typically are recommended to receive only radiotherapy following surgery. The recommended treatment for higher risk for recurrence (HR) patients is concurrent chemoradiotherapy (chemotherapy and radiotherapy at the same time) after surgery. In the IT-MATTERS study, 44 patients who were determined to be higher risk for recurrence following surgery should have been administered chemoradiotherapy, but received only radiotherapy, and were included in the survival analysis of the IT-MATTERS study initially performed. A more accurate representation of the survival of the intended LR patient population treated with Multikine® would have been obtained had the analysis been performed by excluding these 44 patients.

At the ECHNO 2023 Congress, the Company presented study data demonstrating the survival and death rate advantages of the patients treated with Multikine® over control in the LR population who received only radiotherapy (n=352) following surgery.

Six Different Efficacy Measures Demonstrate Benefits of Adding Multikine® to Standard of Care for Patients Who Have Not Had New Therapy Options in Decades

Key study findings for the intended Multikine® patient population who received radiotherapy following surgery, as recommended by NCCN guidelines, include:

- The overall survival advantage accelerated and increased over time, with the benefit of adding Multikine+CIZ to the treatment regimen compared to Standard of Care (SOC) alone increasing from 2.8% at three years (36 months), to 8.3% at four years (48 months), to 15.6% at five years (60 months)—with a 49.7% survival for control versus 65.3% for the Multikine®-treated group at five years.

- The hazard ratio was 0.70 (95% CI: [0.49 - 1.00]), which represents a 43% survival extension.

- Progression free survival was 8.4% higher at five years for patients treated with Multikine+CIZ+SOC compared to patients treated with SOC control alone.

- 16.5% of these patients were early tumor responders, including complete tumor responders (confirmed by pathology at surgery), following the 3-week treatment with Multikine® compared to 0% responders of patients who were treated with SOC alone.

- Multikine® patients who had an early tumor response had significantly improved survival. Their death rate was only 15.6% versus 48.7% death rate for the control patients.

- Even the patients who did not have an early tumor response had a better survival than the control group patients, with a 43.8% death rate versus 48.7% death rate for control.

FDA Application Process

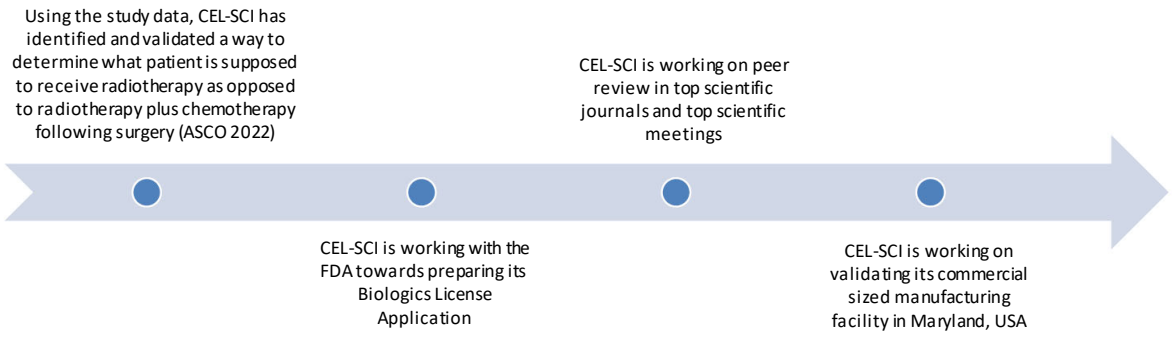
CEL-SCI has retained the services of two leading CROs to help assist in the FDA application process: ICON and Ergomed.

The Company's consultant statistician, Phil Lavin, has a team of experts working with him. Dr. Lavin is a well-known biostatistician with a history supporting clinical trials. He was a member of the Biostatistics faculty at the Harvard School of Public Health and the Department of Surgery at Harvard Medical School, where he was affiliated for over 25 years. He co-founded Boston Biostatistics, which became Aptiv Solutions before it was acquired by ICON plc. He has authored or co-authored over 180 peer reviewed publications in the medical and statistical literature and has innovated a new study design used widely for medical devices. Dr. Lavin has developed solutions for optimum timing of interim analysis, extending labeling for multiple endpoints, and devising composite endpoints and models for interim monitoring of adaptive studies.

Other experts who have been brought on the assist with the FDA application process include: a former FDA Associate Commissioner and congressional insider experienced in strategically resolving regulatory and legislative issues; a former FDA legal counsel; a former FDA clinical reviewer; as well as Key Opinion Leaders (KOLs) in the head and neck cancer community.

Figure 29 summarizes CEL-SCI's steps involved in the FDA approval process.

Figure 29
STEPS IN THE FDA APPROVAL PROCESS



Source: CEL-SCI Corporation.

Upcoming FDA Filing

CEL-SCI has met with the FDA and received their questions and comments. The Company expects to submit a major follow-up package to the FDA very soon, addressing any of its questions or comments. CEL-SCI also expects to file the Clinical Study Report, which is typically filed with a Biologics License Application (BLA). CEL-SCI's treatment is novel and its data is extensive and solid. The Company has been able to identify with high accuracy the patients who are most likely to have great overall survival benefit from Multikine®, which includes over 210,000 patients per year globally. CEL-SCI also continues to validate its manufacturing facility to ensure it will follow the standards for a BLA approval.

Platform for Additional Indications

Although the initial focus is for head and neck cancer, CEL-SCI believes that due to the multi-targeted nature of the candidate's mode of action, Multikine® may reach beyond being a head and neck cancer treatment. Because it functions by mobilizing the immune system to mount a robust anti-tumor response and the specificity of the response comes from the patient's own tumor, CEL-SCI believes that it could also be proven effective for other solid tumors. In this way, Multikine® is similar to a platform technology, creating a foundation from which further applications can be developed.

Initially, the Company plans to capitalize on the full potential of Multikine®'s multi-target capabilities to assess the immunotherapy for treating cervical dysplasia. Specifically, CEL-SCI conducted a Phase I study in women with cervical dysplasia/neoplasia who were co-infected with both Human Immunodeficiency Virus (HIV) and HPV. The presence of HIV causes immunosuppression, which diminishes the body's ability to clear HPV on its own. As a result, women co-infected with both diseases are more likely to develop cervical cancer. Approximately 83% of HIV-positive women are co-infected with HPV (Source: the *Journal of the National Cancer Institute*). This trial returned favorable initial clinical results, showing a decrease by 75% in the number of HPV types in the trial's participants and significant lesion improvement by histology.

Moreover, at two dose levels—200 IU and 400 IU five times per week for two weeks with a two-week break over a six-week period—no severe adverse events related to Multikine® were reported in this trial. The Multikine® regimen was well tolerated by all patients. Future growth in terms of Multikine® could include extending the labeled indications to encompass treatment of other solid tumors, such as breast, skin, bladder, or cervical cancers. CEL-SCI further expects that Multikine® may be used for other indications due to its favorable safety profile (which is unusual for cancer treatments) and potential efficacy.

Development and License Agreements for Multikine®

In order to support its Phase 3 trial of Multikine®, as well as advance its global marketing efforts, the Company has executed key development agreements, including with clinical trial partners (Figure 30) as well as international distribution partners.

Figure 30
PHASE 3 TRIAL PARTNERS

National Institutes of Health, USA	Teva Pharmaceutical Industries Ltd., Israel	Orient Europharma Co. Ltd., Taiwan	Ergomed PLC, UK
Genetic and molecular markers from tumor samples derived from Phase 3 study patients	Licensee for several countries	Licensee for several Far Eastern countries	CRO that completed Phase 3 patient enrollment, contributed up to $12 million towards the cost of the Phase 3 study
About 100 top medical research institutes, universities, and hospitals around the world participating in the Phase 3 study			

Source: CEL-SCI Corporation.

CEL-SCI has also licensed future sales of Multikine®, if approved, to three companies: Teva Pharmaceutical Industries Ltd. in Israel, Turkey, Serbia, and Croatia; Orient Europharma in Taiwan, Singapore, Hong Kong, Malaysia, South Korea, the Philippines, Australia, and New Zealand; and Byron BioPharma, LLC in South Africa. CEL-SCI believes that these companies will have the resources to market Multikine® appropriately in their respective territories, if approved.

COMPETITIVE ADVANTAGES OF MULTIKINE®

A summary of Multikine®'s competitive advantages is provided in Figure 31 and in the accompanying section.

Figure 31
COMPETITIVE ADVANTAGES OF MULTIKINE®

- As a potential first-line treatment for head and neck cancer, it addresses an intact immune system that has not been depleted by earlier treatments
- Combines both passive and active immunotherapy activity into one comprehensive treatment, which means that no external antigens are needed
- Works by enhancing and activating the body's own immune system, with the potential to produce a more robust and sustainable anti-tumor response, while causing a direct, multi-targeted elimination of tumor cells
- May have use in additional solid tumor indications as Multikine® is not tumor specific
- Was shown to be safe and well tolerated
- Does not add toxicity to the current standard of care treatments
- As a non-autologous therapy, Multikine® is ready to use "off-the-shelf" and does not need customization, making large scale manufacturing at a reasonable cost possible
- Granted Orphan Drug status by the FDA

Sources: CEL-SCI Corp., Laryngoscope, Journal of Clinical Oncology, and Crystal Research Associates, LLC.

First-line Treatment

Multikine® is being developed as a first-line treatment to be given to patients before any other therapy options, like surgery, radiation, or chemotherapy, are initiated. Using Multikine® in this manner allows the immunotherapy candidate to augment/stimulate the immune system before it is weakened by surgery, chemotherapy, or radiation, and as a result, still has an intact immune system to stimulate.

Another advantage of using Multikine® as a first-line treatment is that any competing product must be able to accommodate the three-week protocol that Multikine® uses, as any delay of the SOC therapies would be inappropriate and unethical, as administration of existing therapies may potentially be curative on their own. As such, the idea that Multikine® is in competition with the currently FDA approved immunotherapies (e.g., Keytruda®, Opdivo®, CAR-T, and many more) is inaccurate as these therapies are administered over many weeks/months, which would result in a delay in SOC if used as a first line treatment. Further, the extreme toxicities that may be associated with these new products would preclude their use in patients that are potentially curable by the current SOC alone. In addition, if following approval, Multikine® gets accepted as part of a new SOC for its indicated patient population (as is the Company's objective), CEL-SCI believes that developing new competing first-line treatments might be difficult. Any clinical trial of future first-line treatment candidates would not be able to delay SOC therapies to avoid ethical concerns. Thus, if Multikine® is accepted as part of the SOC, that could mean that any competing product might not be able to take its place as a neoadjuvant therapy, making comparisons between Multikine® and any new product in development extremely difficult.

Active and Passive Immunotherapy Activity

According to CEL-SCI, Multikine® more closely mimics natural immune functions, leveraging both passive and active immunotherapies to produce a more robust and sustainable anti-tumor response, while causing a direct, multi-targeted elimination of tumor cells. The Company believes that available immunotherapies, as well as those currently being developed, are limited by their abilities to target only one or two specific tumor-associated antigens.

Conversely, Multikine®'s multitargeted therapy effect is directed at several targets on the cancer cell and activates multiple cellular components of the immune system in order to fight cancer more effectively. Having multiple elements in its composition enables Multikine® to correct a range of immune deficits and target multiple aspects of the tumor that are required for its destruction. This is unlike mAb therapies or some active immunotherapies, which are directed against and react with one/two specific target/s.

Flexibility and Additional Indications

Because Multikine® is not tumor specific, as it functions by mobilizing the immune system to mount a robust anti-tumor response with the specificity of the response coming from the patient's own tumor, it can be used to address a range of solid tumors and conditions beyond head and neck cancer. The Company believes that Multikine® may also be useful in treating melanoma, cervical dysplasia/neoplasia, and breast, skin, bladder, and prostate cancers.

Safety Profile

During early clinical trials, Multikine® proved to be safe and well tolerated in more than 200 patients, with no severe adverse events associated with its use reported by investigators. Due to its lack of toxicity, it is possible that Multikine® can be combined with other cancer treatments to increase efficacy without added harm to patients (e.g., as an adjunct to radiation and other therapies). This is a significant advantage, as many passive immunotherapies and adjuvants are known to be associated with severe toxicities. Moreover, administering Multikine® in conjunction with other first-line treatments instead of as a monotherapy may benefit late-stage patients.

Non-Autologous Therapy

A significant limitation of the targeted immunotherapies is that many of these are autologous in nature, indicating that they are made from the cancer patient's own tissues and are intended to treat only that patient. This is a costly, labor-intensive process. Multikine® is not an autologous therapy. Multikine® can be mass produced like other pharmaceuticals to exact specifications under cGMP and is an "off-the-shelf" product that can be readily and immediately available and used by physicians for patients.

Multikine®: Orphan Drug Status

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs or biologics intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the U.S., or if it affects more than 200,000 individuals in the U.S., there is no reasonable expectation that the cost of developing and making the drug for this type of disease or condition will be recovered from sales in the U.S. Orphan drug status in the European Union has similar, but not identical, requirements and benefits.

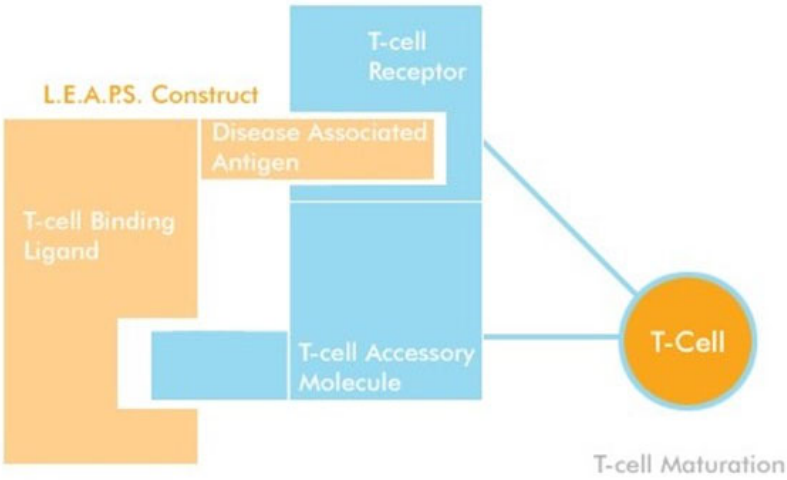
In June 2007, the FDA granted Multikine® Orphan Drug status as a neoadjuvant therapy in patients with SCCHN, establishing another significant competitive advantage for the immunotherapy candidate. As an Orphan Drug, Multikine® should benefit from several policies that standard therapies in development cannot access.

LEAPS™ (Ligand Epitope Antigen Presentation System) Technology

CEL-SCI's second proprietary technology platform, LEAPS™ (Ligand Epitope Antigen Presentation System), is a preclinical technology designed to stimulate the human immune system to fight bacterial, viral, and parasitic infections more effectively, as well as autoimmune conditions, allergies, transplantation rejection, and cancer. LEAPS™ is a patented, T-cell modulation delivery technology designed to stimulate antigen-specific immune responses in T-cells using synthetic peptides. The proprietary peptide immunogens are designed and synthesized by CEL-SCI to target specific disease and conditions.

Administered as a vaccine, the LEAPS™ compound consists of a small T and Immune-cell binding ligand (TCBL/ICBL) linked with a small, disease-associated peptide antigen (Figure 32), and is delivered directly to the recipient's immune system by injection or mucosal absorption. According to the Company, the LEAPS™ technology may provide a new method to treat and prevent certain diseases by enhancing the T-cell responses to that particular antigen, acting earlier in the pathway of the specific disease.

Figure 32
SCHEMATIC REPRESENTATION OF A LEAPS™ CONSTRUCT



Source: CEL-SCI Corporation.

The ability to generate a specific immune response is important because many diseases are often not treated and cured effectively due to the body's selection of the "inappropriate" immune response. The capability to specifically reprogram an immune response may offer a more effective approach than existing vaccines and drugs in attacking an underlying disease.

This platform technology has been shown in several animal models to preferentially direct an immune response to a cellular (e.g. T-cell), humoral (antibody), or mixed pathway. It has the potential to be utilized in diseases for which antigenic **epitope** sequences have already been identified, such as a number of infectious diseases, some cancers, autoimmune diseases, allergic asthma, and select central nervous system (CNS) and other diseases (e.g., Alzheimer's).

THE IMMUNE SYSTEM

The immune system is a network of cells, tissues, and organs that are designed to defend the body against foreign or dangerous substances. Substances that stimulate an immune response in the body are called antigens. Antigens are primarily microorganisms (e.g., bacteria, viruses, and fungi), parasites (e.g., worms), cancer cells, or even transplanted organs and tissues. As the body detects antigens, it produces an immune response aimed at attacking and destroying the substance. This attack involves a variety of **leukocytes** (white blood cells) that work together to destroy invaders. The main leukocytes involved in the immune process are lymphocytes. The two major classes of lymphocytes are B-cells and T-cells, which are also known as B-lymphocytes and T-lymphocytes, respectively.

B-cells

The major function of B-cells is the production of antibodies in response to the presence of antigens. Antibodies are specialized proteins that recognize and bind to one particular antigen. Antibodies binding to a foreign substance are critical as a means of signaling other cells to engulf, kill, or remove that substance from the body. The antibodies attach to foreign antigens to mark them for destruction by T-cells or other immune cells.

T-cells

Unlike B-cells, T-cells do not recognize free-floating antigens. Rather, T-cells' surfaces contain specialized receptors that can detect fragments of antigens on the surface of infected or cancerous cells. T-cells have two major roles in immune defense: (1) direct and regulate immune responses; and (2) directly attack infected cells. Regulation of the immune system is mainly conducted by T-helper (Th) cells (CD4 cells), which is done via the secretion of cytokines. Some cytokines stimulate nearby B-cells to produce antibodies while others activate T-cells, such as the killer T-cell (cytotoxic killer cells), which destroy certain antigens or antigen-infected cells.

T-helper cells differentiate into various effector T-cell subsets, including the well-defined Th1 and Th2 subsets as well as the more recently discovered Th17, Th9, and Th22 subsets (Figure 33). Differentiated T-helper cell subsets secrete different cytokines. Most T-helper cells belong to one of these subsets. However, approximately 10% of Th cells become T-regulatory (T-reg) cells, charged with aiding the regulation of immune system response (Source: Biology-pages.info).

Figure 33
T-HELPER CELLS

	Th1	Th2	Th17	Th9	Th22	Treg
Cytokines Produced	IFNγ	IL-4	IL-17	IL-9	IL-22	IL-10 TGFβ
Function	Intracellular Infections (Cellular)	Extracellular Infections (Humoral)	Extracellular Infections (Humoral)	Extracellular Infections (Humoral)	Extracellular Infections (Humoral)	Regulation

Source: PLOS Pathogens.

LEAPS™ CONSTRUCT

The major goal for preparing a successful vaccine is to elicit the proper immune response to the antigen of interest and avoid excessive inflammation or even suppression of immune responses to achieve the desired outcome. The goal of the LEAPS™ technology is to direct the nature of the immune response to one that is appropriate for the disease to be prevented or treated. As such, the Company's technology aims to remedy situations where the body's immune system has generated an inappropriate response to a particular antigen—reprogramming the immune response to be more effective.

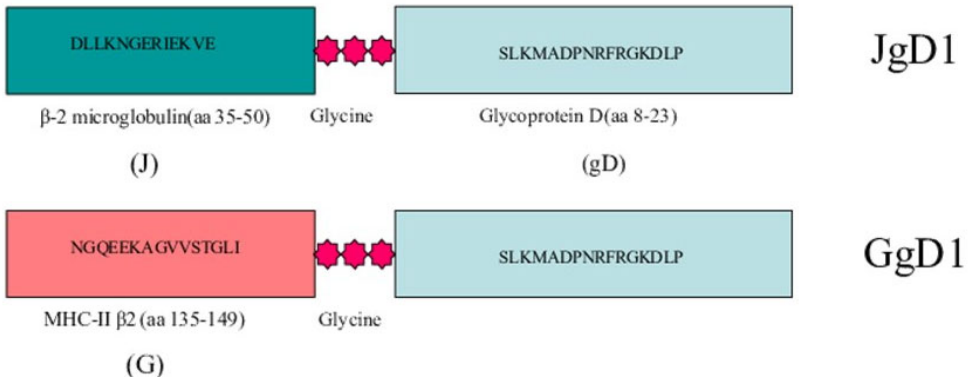
LEAPS™ TCBL/ICBL Epitopes

The concept behind the LEAPS™ technology is to directly mimic cell/cell interactions on the T-cell surface using synthetic peptides. LEAPS™ vaccines consist of a combination of a small peptide, referred to as a T-cell binding ligand (TCBL) or immune cell binding ligand (ICBL), which activates the immune system by targeting or binding to an antigen presenting cell, such as a dendritic cell (example of ICBL) or to a T-cell (TCBL), with another small peptide containing a disease associated epitope. LEAPS™ creates a hetero-conjugate containing both a TCBL and a disease specific epitope, combining adjuvant/activating and antigen/immunizing activities into one relatively small peptide.

When a LEAPS™ formulation attaches to a certain T-cell, it causes that cell to activate a particular immune response. The Company can vary the immune response depending on the type of LEAPS™ construct and TCBL used. Two TCBLs of particular interest for CEL-SCI are TCBL peptides J and G (or the modified and more stable version of G, derG). Conjugates of these appear to activate different sub-sets of T-cells. J is a short fragment from β-microglobulin, which elicits a Th1 response, and G is a modified fragment from MHC II β-chain, which directs to a Th2 response. Figure 34 illustrates examples of the J and G TCBL peptides attached to a Herpes Simple Virus (HSV) epitope (gD).

Figure 34

LEAPS™ TCBL CONSTRUCT EXAMPLES



Source: Journal of Vaccines and Vaccination.

When LEAPS™ stimulates a Th1 response, the Th1 cells react with high cytotoxic T-cell activity relative to the amount of antibody production. Th1 cells secrete IL-2, interferon-γ, and IL-12. Th1 cells kill antigen-presenting cells and are associated with vigorous delayed-type hypersensitivity reactions. Th2 cells, on the other hand, synthesize and secrete IL-4, IL-5, IL-6, and IL-10—cytokines that influence B-cell development and antibody production when LEAPS™ stimulates a Th2 response. Th2 cells cause high antibody production relative to the amount of cytotoxic T-cell activity.

Mechanism of Action

The concept behind the LEAPS™ technology is to directly mimic cell/cell interactions on the T-cell surface using synthetic peptides. When a LEAPS™ formulation attaches to a certain T-cell, it causes that cell to activate a particular immune response, altering only select cytokines specific for each disease model. Thus, the Company believes that its LEAPS™ technology platform has an advantage over other peptide epitope-based technologies because LEAPS™ vaccines can be designed to produce either a cellular response or antibody mediated response (humoral), involving the specific T-cells and immune cells needed for an optimal response for a particular condition.

The combination of a small peptide that activates the immune system with another small peptide from a disease-related protein allows the LEAPS™ vaccines to activate precursors to differentiate and become more mature cells that can initiate and direct appropriate T-cell responses. For example, J-LEAPS™ vaccines (LEAPS™ vaccines using the J conjugate) interact with human monocytes and mouse bone marrow dendritic cells (DC) precursors to promote their maturation into DCs that promote T-cell responses with the Th1 phenotype. DCs are the bridge between the innate and adaptive immune systems. Mature DCs direct the nature of an immune response by producing different cytokine environments while presenting antigen to T-cells. During the development of an adaptive immune response, DCs play an extremely important role in initiating T-helper cells differentiation. Thus, by demonstrating that the J TCBL molecule can activate precursor DCs, it shows that the LEAPS™ technology platform can act earlier in the pathway of the specific disease, recruiting the immune system at the earlier stages.

Results Of Preclinical Studies

The Company and its collaborators have conducted a series of preclinical animal challenge studies in several disease indications, of which key results are summarized on the accompanying pages. Challenge studies entail the administration of a chemical substance or an antigen in order to assess the reaction, whether documenting the occurrence of normal physiological responses or to evoke an immunologic response in a previously sensitized subject. In these studies, the LEAPS™ candidates have demonstrated protection against lethal herpes simplex virus (HSV1) and H1N1 influenza infection as a prophylactic or therapeutic agent. They have also shown some level of efficacy in animals in two autoimmune conditions, curtailing and sometimes preventing disease progression in arthritis and myocarditis animal models.

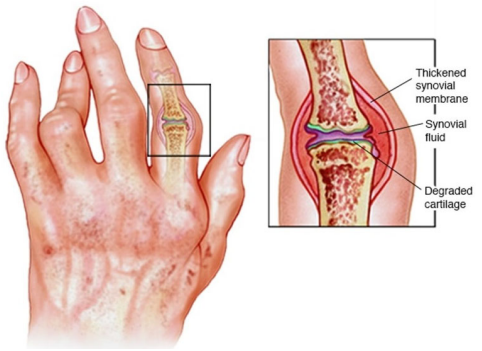
Furthermore, even though the various LEAPS™ vaccine candidates have not yet been given to humans, they have been tested *in vitro* with human cells. In these studies, LEAPS™ constructs have induced similar cytokine responses that were seen in these animal models, which may indicate that the LEAPS™ technology could translate to humans. In addition to the development of product candidates for conditions that currently do not have an available vaccine, CEL-SCI believes that the LEAPS™ technology may even be a significant alternative to vaccines currently available on the market.

PRODUCT CANDIDATES – CEL-2000 AND CEL-4000 FOR RHEUMATOID ARTHITIS

The LEAPS™ technology platform has been used to develop immunoprotective and immunomodulating small peptide vaccines for infectious and autoimmune diseases. Several products are currently in various stages of development at the pre-clinical stage (in animal challenge efficacy studies). In particular, two LEAPS™-based product candidates—CEL-2000 and CEL-4000—have shown the potential to block the progression of autoimmune diseases by immunomodulation of ongoing pathogenic responses.

Rheumatoid arthritis (RA) Overview

Figure 35
RHEUMATOID ARTHRITIS



Source: Mayo Clinic.

Rheumatoid arthritis (RA) is an autoimmune disorder characterized by chronic inflammation and systemic destruction of the peripheral joints. RA affects over 1.3 million Americans and as much as 1% of the worldwide population and is one of the most common autoimmune disorders (Source: RheumatoidArthritis.org). RA occurs when the immune system attacks the synovium, the lining of the membranes that surround the joints. The resulting inflammation causes a painful swelling, which can eventually destroy the joint cartilage and bone, resulting in bone erosion and joint deformity (Figure 35).

RA can affect more than just the joints. The inflammation associated with RA can damage other parts of the body and a wide variety of body systems, including the skin, eyes, lungs, heart, and blood vessels (Source: Mayo Clinic).

RA Mechanisms of Action

RA is a very heterogeneous disease that may have different initiators and be driven by different types of inflammatory responses for each individual. Although the initiating events of RA are unknown, the disease is maintained by pro-inflammatory mediators produced during T-helper (primarily Th1 and Th17) cell-driven autoimmune responses (Source: *Vaccine*, Vol. 35: 4048–4056, 2017).

T-helper cells, generally Th1 or Th17, become actively involved in an inflammatory cascade, featured in the dysregulation of the production of inflammatory and regulatory cytokines. Th17 cells, which produce the inflammatory cytokine IL-17, are involved in inflammation and host defense against extracellular pathogens and have been shown to play an important role in the induction of autoimmune tissue injury. Th1 cells, which secrete IL-2, interferon-γ, and IL-12, kill antigen-presenting cells and are associated with vigorous delayed-type hypersensitivity reactions (immune responses that are exaggerated or inappropriate against an antigen).

Key antigens suggested to be inducers of RA as it relates to the Company's technology are collagen II and **proteoglycan (PG)**, which can induce RA-like disease in mice and elicit potent T-cell responses (Source: *Journal of Clinical and Cellular Immunology*. Vol. 10(1): 574, 2019).

RA Treatments and Vaccines

Current treatment for RA largely focuses on alleviating symptoms (through the use steroids and anti-inflammatory drugs, including NSAIDS) or delaying disease progression through the use of disease-modifying antirheumatic drugs (DMARDs), including biologics. The most recent advances in treatment have come from biologics targeting specific components of the immunological inflammatory pathway. Biologics suppress elements of the immune system in order to curtail the inflammatory process by targeting the cytokines or cell surface receptors that are responsible for maintaining the autoimmune and inflammatory disease processes.

Although somewhat more selective, this is also an ablative therapy that leaves the patient deficient in certain types of immune protection, increasing the risk of infections and other potentially severe side effects. Since the anti-cytokine and receptor blocking approach is not selective, it can delete essential immune protections against diseases, such as tuberculosis and cancers, putting the treated individual at risk for these diseases. In addition, these therapies are expensive and must be administered by specialists on a regular schedule. Furthermore, DMARDs do not provide a universal therapy for everyone, with their ineffectiveness for 30% to 50% of RA patients demonstrating the need for new approaches to therapy (Source: *Expert Review of Vaccines*, Vol. 14(6):1-18, 2015).

An alternate approach is to actively modulate the ongoing aberrant immune response with a vaccine, so that the immune response no longer promotes disease. Chronic autoimmune diseases result from tissue-damaging inflammation that is initiated by improperly regulated immune responses to self-antigens.

Ideally, an RA therapeutic vaccine would consist of an immune modulation therapy that enhances the regulatory and therapeutic immune response while curtailing the pro-inflammatory responses associated with RA. This method of immune modulation is preferable to anti-cytokine or receptor blocking, as it actively redirects the immune response away from the disease-causing actions, instead of generically removing an important component of the immune system. An additional problem for an RA vaccine is that different approaches may be required for modulating the disease driving T-cell response, since the inflammatory response driving disease (whether Th1 or Th17) may be different in different individuals (Source: *International Immunopharmacology*, Vol.74, 2019).

CEL-2000, a J-LEAPS™ vaccine, blocks the progression of collagen induced arthritis (CIA) by immunomodulation of the Th17 response during RA. CEL-4000, A derG-LEAPS™ vaccine (using a more stable version of the G-TCBL called derG), demonstrated therapeutic efficacy for the proteoglycan (PG)-induced arthritis (PGIA) and PG G1-domain-induced arthritis (GIA) (PGIA/GIA) mouse models of RA by providing antigen specific cessation of Th1 driven disease progression. Figure 36 provides a comparison of both product candidates.

Figure 36
CEL-2000 and CEL-4000 COMPARISON

	TCBL	Epitope	Modulation	Arthritis mouse model
CEL-2000	J	Type II collagen	Th17	Collagen Induced Arthritis (CIA)
CEL-4000	derG	proteoglycan (PG)	Th1	PG-induced arthritis (PGIA) and PG G1-domain-induced arthritis (GIA)

Sources: CEL-SCI Corporation, and Crystal Research Associates, LLC.

Disease progression in the CIA model mimics human disease in terms of joint pathology, inflammation, bone erosion, bone remodeling, cartilage alterations, and pannus formation. The disease in this model is driven by Th17 immune responses, as indicated by the generation of IL17. The PGIA and GIA models in adult female mice are predominantly driven by Th1 responses producing IFNy. The PGIA and GIA models resemble human RA more than other animal models in that disease is induced in older females (Source: *Journal of Clinical and Cellular Immunology*. Vol. 10(1): 574, 2019).

Rheumatoid Arthritis (RA) Vaccine Grants

Research for the development of the LEAPS™ technology as a treatment for RA has been funded via collaborations with the U.S. National Institutes of Health (NIH), U.S. Army, Navy, and universities. In July 2014, CEL-SCI announced that it had been awarded a Phase 1 Small Business Innovation Research (SBIR) grant in the amount of $225,000 from the National Institute of Arthritis Muscoskeletal and Skin Diseases, which is part of the National Institutes of Health. The grant funded the development of CEL-SCI's LEAPS™ technology as a potential treatment for RA.

On September 2017, CEL-SCI was awarded a Phase 2 SBIR grant in the amount of $1.5 million from the National Institute of Arthritis Muscoskeletal and Skin Diseases. This grant provided funding to allow CEL-SCI to advance its first LEAPS™ product candidate, CEL-4000, towards an Investigational New Drug (IND) application, by funding GMP manufacturing, IND enabling studies, and additional mechanism of action studies, among other preclinical development activities.

Product Candidate CEL-2000

Of the different vaccine approaches that have been suggested, the LEAPS™ approach is unique in that the vaccine can be designed to define the direction of the subsequent antigen-specific response toward Th1, Th2, Th17, or Treg cells depending upon the attached TCBL. One such construct is CEL-SCI's product candidate, CEL-2000 (J-CIIx). This LEAPS™ conjugate combines the J-TCBL with an epitope of type II collagen, which is also known to have T-cell responsiveness in human RA patients. The data from animal studies demonstrated that CEL-2000 was effective in the Th17-driven CIA mouse model of RA as a therapy to block the progression of disease after disease initiation, showing that it could be used as an effective treatment against RA associated with the Th17 response, with fewer administrations than those required by other anti-RA treatments currently on the market. The therapeutic effect of CEL-2000 was accompanied by reduced serum levels of pro-inflammatory cytokines.

C-2000 Study Overview
Journal of Vaccines and Vaccinations, Vol. 3:5, 2012.

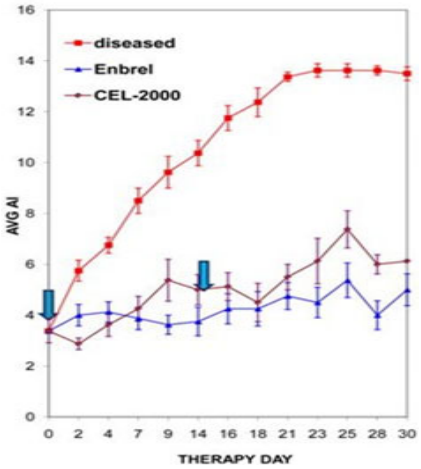
The collagen-induced arthritis (CIA) model was used to demonstrate the ability of a J-LEAPS™ conjugate to therapeutically treat RA. Following the CIA model protocol, mice received two injections of 100µg bovine collagen three weeks apart. Thirty-one days following the first injection, the mice were grouped and assessed via an arthritic index (AI) score. CEL-2000 therapy was initiated after grouping of mice on day 31 of a study, after the onset of disease symptoms. J-LEAPS™ conjugate CEL-2000 (100nmol) was administered on days 0 and 14 after grouping. Control groups were either untreated or treated with TNF-α receptor antagonist, etanercept (Enbrel®), every other day.

Mice with CIA developed notable swelling and inflammation of the paws and ankles, including cell infiltration and destruction of the joints. Mice treated with CEL-2000 had much less swelling of the paws, as measured by an arthritic index (AI) score compared to untreated mice. The efficacy indicated by the favorable AI score was similar to therapy with etanercept (Enbrel®), an anti- TNF-α biologic used in the clinic to treat RA in humans and considered the therapeutic "gold standard", as seen in Figure 37 (page 57). The Figure shows the average AI score of CEL-2000 treated, untreated, and etanercept (Enbrel®)-treated mice following administration of CEL-2000 (arrows). At the end of the study, histopathological examination of ankles and paws following treatment also showed a lack of disease progression due to vaccination that blocked bone or cartilage erosion and damage.

The effect of CEL-2000 on disease progression was also assessed through evaluation of serum cytokine levels taken 10 days after initiation of therapy. Analysis of serum cytokines in treated and untreated mice showed a redirection away from the Th17 response (untreated) and towards a Th1 response (CEL-2000 treated), with a relative decrease in inflammatory cytokines TNF-α and IL-17, IL-6, and increased levels of IFNγ and IL10, a regulatory cytokine. The increase in IL-12p70 but decrease in IL-12p40 suggests a decrease in IL-23, an inducer of the Th17 response. Similar to the therapeutic effect as measured via AI score, serum cytokine results following biweekly CEL-2000 treatments were comparable to those for mice treated every other day with the TNFα antagonist, etanercept (Enbrel®, Figure 38 [page 57]).

Figure 37

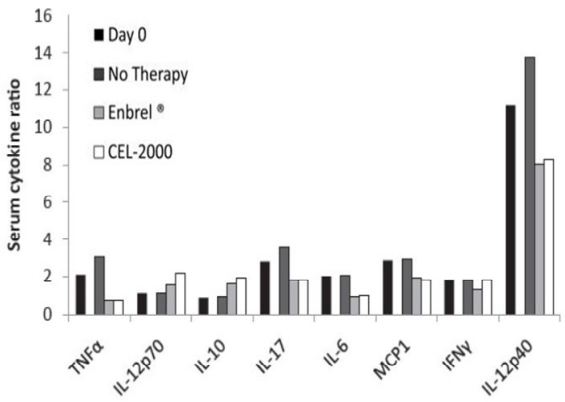
CEL-2000 RA SCORES



Source: Journal of Vaccines and Vaccinations.

Figure 38

CEL-2000 SERUM CYTOKINES



Source: Journal of Vaccines and Vaccinations.

Of note, neither a mixture of the unconjugated J-TCBL nor a DerG version of this vaccine was effective in this RA model.

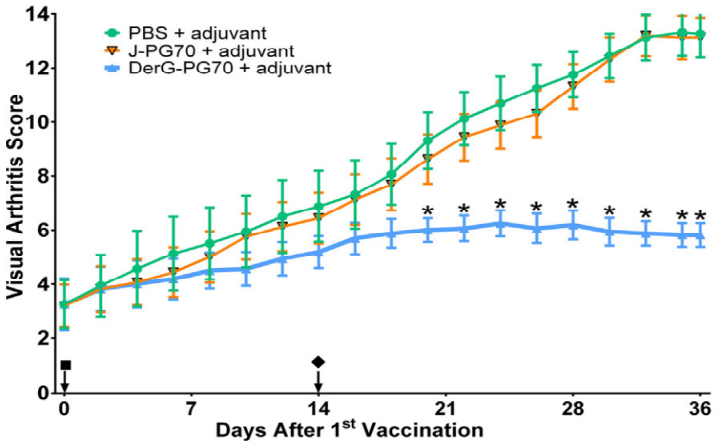
Product Candidate CEL-4000

The second product candidate being studied against RA is CEL-4000 (derG– PG70), consisting of the derG-TCBL and the immunodominant PG peptide (PG70) from human proteoglycan. The preclinical data for CEL-4000 indicates it could be effective against RA cases where a Th1 signature cytokine (IFN-γ) is dominant. CEL-4000 stopped progression of disease and reduced Th1 as well as Th17-related cytokine and inflammatory responses in the Th1 driven PGIA and GIA mouse models of RA. The J-LEAPS™ version of this vaccine (J-PG70) was not effective in this model. The importance of a vaccine's ability to modulate the specific disease-driving proinflammatory immune response within an individual is demonstrated by the difference in efficacy of the J-ICBL (Th1 promoting) and G-ICBL (Th2/ Treg promoting) versions of the CEL-2000 and CEL-4000 LEAPS™ vaccines in the CIA and PGIA/GIA mouse models.

C-4000 Study Overview
Vaccine, Vol. 35: 4048–4056, 2017

In this study, CEL-SCI tested the therapeutic efficacy its LEAPS™ vaccines technology in two Th1 cell-driven mouse models of RA, cartilage proteoglycan (PG)-induced arthritis (PGIA), and PG G1-domain-induced arthritis (GIA). For the study, the immunodominant PG peptide PG70 was attached to a DerG or J immune cell binding peptide, and the DerG-PG70 (CEL-4000) and J-PG70 LEAPS™ vaccines were administered to the mice after the onset of PGIA or GIA symptoms. As indicated by the VA scores, treatment with the DerG-PG70 (CEL-4000) vaccine significantly limited disease progression within three weeks in both PGIA (Figure 39 [page 58]) and GIA models, while J-PG70 had no significant effects compared to control. Importantly, the CEL-4000 vaccine effectively curtailed arthritis symptoms in GIA despite its more aggressive disease course compared to PGIA.

Figure 39
ARTHRITIS SCORE IN PGIA MODEL



Source: Vaccine

In vitro spleen cell-secreted and serum cytokines from CEL-4000-treated mice demonstrated a shift from a pro-inflammatory to an anti-inflammatory/regulatory profile. Treatment of PGIA or GIA mice with the CEL-4000 vaccine led to a reduction of pro-inflammatory Th1 and Th17 cells and an increase in the frequency of anti-inflammatory IL10-producing as well as protective Treg cells in both models.

As in RA, the inflammatory disease in both the PGIA and GIA models is driven and sustained primarily by Th1 but also by Th17 cells and cytokines produced by them. CEL-4000 treatment promoted a more balanced, less inflammatory cytokine responses by increasing Th2 (IL4+ and IL10+) and Treg cells and reducing Th1 and Th17 cells in PGIA, and to a somewhat lesser extent in the GIA system.

CEL-2000 and CEL-4000 – Different Approaches to the Same Goal

The inflammatory response driving RA, whether Th1 or Th17, may be different in different individuals. Failure of some patients to respond to certain therapies may reflect differences in the initiators and responses driving their disease. Thus, different approaches may be required for treating the disease, according to the underlying mechanisms of action for each case.

The importance of LEAPS™' ability to modulate the specific disease-driving pro-inflammatory immune response within an individual is demonstrated by the difference in efficacy of the J-TCBL (Th1 promoting) and derG-TCBL (Th2/Treg promoting) versions of the CEL-2000 and CEL-4000 LEAPS™ vaccines in the CIA and PGIA/GIA mouse models. The CEL-4000 (derG-PG70) vaccine was effective in curtailing progression of RA driven by Th1 responses whereas CEl-2000 (J-CIIx) was effective in blocking the progression of RA in the Th17-driven CIA model.

As such, knowledge of signature T-cell cytokine phenotypes that drive the patient's disease can facilitate the choice of the appropriate experimental LEAPS™ vaccine therapy. These results suggest that once the nature of the inflammatory autoimmune response in a patient with RA has been identified (e.g., by analyzing prominent serum cytokines levels), then this patient could be treated with the appropriate experimental LEAPS™ vaccine with either a J-TCBL to counteract a Th17-driven inflammatory response or a derG-TCBL to counteract a Th1-dominated inflammatory response.

New Epitope Discovery
Journal of Immunology, Vol. 202 (1):133.4, 2019

In May 2019, CEL-SCI announced that a newly discovered LEAPS™ conjugate vaccine acts alone and can complement CEL-4000 therapeutically when administered in combination to an animal model of RA. The data was initially presented at the American Association of Immunologists 103rd Annual Meeting (Immunology 2019).

CEL-4000 (derG-PG70) and a newly discovered LEAPS™ conjugate, derG-PG275Cit, were evaluated alone and in combination in the PGIA and GIA mouse model of RA. Mice were immunized with either one or two different derG LEAPS™ vaccines containing PG epitopes (PG70 or PG275Cit) subcutaneously after signs of arthritis were noted. Mice were examined twice weekly for arthritis progression. At study end, serum antibodies to the vaccine epitopes and splenic T-cell responses to PG G1 domain were determined.

Results showed that new derG LEAPS™ conjugate (derG-PG275Cit), alone or together with CEL-4000 (derG-PG70), modulated the inflammatory response and stopped the progression of RA. derGPG275Cit was effective in providing protection but did not induce significant serum antibodies, whereas CEL-4000 (alone or with derGPG275Cit) induced both protection and antibodies. Results suggest mechanistically different immune responses to the two vaccines. Both derG-LEAPS™ conjugates appears to act on different immune pathways by a different mechanism from each other. In addition, these vaccines incorporate distinct epitopes that are located in distant regions of the PG molecule involved in arthritis induction. Thus, a combination vaccine containing both LEAPS™ conjugates CEL-4000 (derG-PG70) and derG-PG275Cit could offer advantages in case one epitope or another was missing in the disease inducing situation. The combination of the two RA vaccines provided not only broader epitope coverage, but also a greater therapeutic effect than either vaccine alone.

Investment Highlights

- CEL-SCI Corporation ("CEL-SCI" or "the Company") is a late-stage clinical biotechnology company focused on developing immunotherapy products and technologies to treat cancer, autoimmune and infectious diseases that address significant unmet medical needs. The Company aims to develop novel therapies with the potential to activate and utilize the body's own immune system against the disease.

- The Company is focused on developing product candidates based on two innovative technologies: (1) Multikine® (Leukocyte Interleukin, Injection), a next-generation, comprehensive immunotherapy; and (2) LEAPS™ (Ligand Epitope Antigen Presentation System), an immunotherapy vaccine technology platform.

- CEL-SCI's lead product candidate, Multikine®, is an investigational immunotherapy with a completed Phase 3 study for patients with squamous cell carcinoma of the head and neck (SCCHN) (locally advanced primary head and neck cancer), for which the Company has received Orphan Drug Status from the FDA. CEL-SCI intends to demonstrate that Multikine® could become an integral first-line component of the current standard of care (SOC) regimen due to its effectiveness and safety profile. Multikine® has also been studied for the treatment of cervical dysplasia in human immunodeficiency virus (HIV) and human papillomavirus (HPV) co-infected patients.

- Current drug therapies for SCCHN from Merck & Company and Bristol Myers Squibb are approved as a last resort for recurrent head and neck tumors after treatments have failed or for patients who are not candidates for surgery.

- Multikine® modulates the body's immune system through a dual mechanism of action: eliciting the direct killing of tumor cells and micrometastasis, while generating a sustainable anti-tumor response.

- Multikine® is being developed as a first-line treatment for advanced primary head and neck cancer, to be given as a neoadjuvant, prior to surgery and radiation or chemoradiation. The drug has been shown to augment/stimulate the immune system before it is weakened by both the toxic therapies and the cancer itself. Multikine® could become the world's first cancer immunotherapy drug to be administered prior to surgery.

- In its Phase 2 clinical trial for Multikine®, CEL-SCI reported a 10.5% complete response rate (no clinical or pathology evidence of any remaining cancer) and a 33% improvement in overall survival. Most importantly, there was no severe adverse events associated with the use of Multikine®.

- Multikine® has completed the largest and longest ever pivotal Phase 3 clinical trial (IT-MATTER) on three continents. The drug is the first of its kind with substantial survival benefit in a randomized Phase 3 trial in locally advanced primary SCCHN.

    - CEL-SCI published and presented data from its pivotal randomized controlled Phase 3 Multikine® head and neck cancer clinical trial at two prominent cancer conferences: 2022 ASCO Annual Meeting in Chicago, Illinois and 2022 European Society for Medical Oncology (ESMO) annual Congress in Paris, France. Additional results from the Phase 3 clinical trial of Multikine® in advanced primary head and neck cancer were posted to the U.S. government clinical trial website.

    - In CEL-SCI's Phase 3 study, Multikine® produced a very significant 14.1 percentage five-year survival benefit (62.7% versus 48.6%) as well as a nearly four-year overall survival benefit in the treatment arm receiving Multikine® prior to surgery plus radiotherapy, as compared to the control group receiving only surgery plus radiotherapy.

    - On March 8, 2023, CEL-SCI reported new data from its Phase 3 study in a poster presentation titled "Leukocyte Interleukin Injection (LI) immunotherapy followed by radiotherapy extends overall survival (OS) in treatment naïve locally advanced primary squamous cell carcinoma of the head & neck: the IT-MATTERS Study" at the 10th European Congress on Head & Neck Oncology (ECHNO) in Lisbon, Portugal.

- The Company is primarily focused on completing and submitting a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) for approval of Multikine® in treating advanced primary head and neck cancer.

- CEL-SCI's second proprietary technology platform, LEAPS™, is a vaccine technology platform designed to stimulate the immune system to fight bacterial, viral, and parasitic infections more effectively, as well as autoimmune conditions, transplant rejection, and cancer. Research for the development of the LEAPS™ technology as a treatment for RA has been funded in part via two Small Business Innovation Research (SBIR) grants from the National Institutes of Health totaling $1.725 million.

    - The inflammatory response driving RA may be different in different individuals, with failure of some patients to respond to certain therapies reflecting these differences. The LEAPS™ platform can be designed to produce a specific natural immune response depending on the type of construct used. Thus, once the nature of the inflammatory response has been identified, the patient can be treated with the appropriate LEAPS™ vaccine.

- The Company operates a dedicated state-of-the art manufacturing facility with over 73,000 square feet of manufacturing and research and development (R&D) space, noting that the production capacity has been doubled to meet anticipated market demand for Multikine® once it receives regulatory approval. The Phase 3 trial was supplied from this facility, reducing regulatory risks at time of approval.

    - CEL-SCI's manufacturing facility is being validated following the completion of its commercial scale build out during the first quarter of 2022. The construction was designed to ensure the facility will be compliant with both FDA GMP and European regulations.

- CEL-SCI has added highly experienced individuals to its team, including scientists, biostatisticians, regulatory counsel who worked at the FDA, an oncologist who worked at the FDA as a clinical reviewer, and more than half a dozen independent oncologists to its Scientific Advisory Board, including key opinion leaders from major U.S. medical centers. Biographies of these key individuals are provided on pages 8-11.

- As of December 31, 2022, CEL-SCI's cash position was $18 million.

Competition

The development and commercialization of new drug and biologic products is highly competitive. CEL-SCI faces competition from leading pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

MULTIKINE® COMPETITIVE LANDSCAPE

According to the Company, the most common misconception with regard to Multikine® is that it is in competition with all of the FDA approved immunotherapies (e.g., Keytruda®, Opdivo®, and other checkpoint inhibitors). In contrast to Multikine®, these immunotherapies are indicated only for patients whose cancers have recurred following standard of care (SOC) treatment or those patients with cancer where surgery is no longer an option. Similarly, none of the other treatment options for head and neck cancer, such as targeted therapies (e.g., EGFR inhibitors like Erbitux® [cetuximab]), and monoclonal antibodies have been approved by FDA as neoadjuvants for the indication sought for Multikine® immunotherapy. Furthermore, the extreme toxicities that are associated with some of these other products would preclude their use in pre-SOC settings. For perspective, no severe adverse events associated with the use of Multikine® were recorded during its clinical trials, where Multikine® proved to be safe and well tolerated in more than 200 patients.

Multikine® is being developed as a first-line treatment to be given to patients following initial definitive diagnosis and before any other therapy options, administered over three-weeks within the four-week period that normally occurs between diagnosis and surgery. Any new therapy must be able to accommodate this protocol, as any delay of the intent to cure SOC treatment would be unethical. However, if following approval, Multikine® gets accepted as part of a new SOC (as is the Company's objective), CEL-SCI believes that development of competing treatments might be difficult. Any clinical trial of future first-line candidates would not be able to delay SOC therapies, which would include Multikine® as its initial treatment, to avoid ethical concerns, and which would mean that they might not be able to take Multikine®'s place as part of the SOC, making comparisons with Multikine® extremely difficult. In addition, Multikine® is a complex biologic requiring special manufacturing, and the Company has spent over 10 years developing and validating its manufacturing process. This signifies a significant barrier to entry for any future similar or generic competitive technologies. A clinical trial of interest to CEL-SCI is from Merck Sharp & Dohme Corp, described below.

pembrolizumab—Merck Sharp & Dohme Corp. (NCT03765918)

A Phase 3 study is assessing the effectiveness of pembrolizumab (Pembro) given prior to surgery and pembrolizumab in combination with SOC radiotherapy given post-surgery in treating naïve participants with newly diagnosed Stage 3 and 4, advanced head and neck squamous cell carcinoma. The Phase 3 study, which started in 2018, is estimated to be completed in 2026.

LEAPS™ COMPETITIVE LANDSCAPE

Multiple drug classes are available for the treatment of rheumatoid arthritis (RA), with the global market for RA therapeutics estimated at $48.3 billion in the year 2022 and projected to reach $66.7 billion by 2030, growing at a CAGR of 4.1% over the period 2022-2030. The RA therapeutics market in the U.S. is estimated at $13.2 billion in the year 2022 (Source: ReportLinker, *Global Rheumatoid Arthritis Therapeutics Industry*, January 2023). A popular treatment strategy for RA involves pharmacotherapy with disease-modifying antirheumatic drugs (DMARDs), supported by non-steroidal anti-inflammatory drugs (NSAIDs) and/or corticosteroids to provide pain relief and control inflammation. Common DMARDs include methotrexate (Trexall, Otrexup, Rasuvo), leflunomide (Arava), and hydroxychloroquine (Plaquenil). However, the ability of these treatment regimens to suppress disease progression and joint destruction is limited for a large number of patients.

Biological agents are a newer class of DMARDs that can target parts of the immune system that triggers inflammation to cause joint and tissue damage. Biological agents include inhibitors of tumor necrosis factor (TNF), which block the activity of key inflammatory mediators, giving rise to the main characteristics of RA; as well as checkpoint inhibitors, which inhibit the production of inflammatory cytokines. However, since this drug suppresses parts of the immune system, they enhance the possibility of infections and other diseases. These include infliximab (Remicade®), adalimumab (Humira®), etanercept (Enbrel®), golimumab (Simponi®), certolizumab pegol (Cimzia®), abatacept (Orencia®), and rituximab (Rituxan®), among others. In addition, Janus Kinase (JAK) inhibitors, such as Tofacitinib (Xeljanz), Filgotinib, and baricitinib are recently approved by the FDA.

The Company faces competition from vaccine technology platforms and vaccine-centric companies that could be developing competing technologies in some of the same indications pursued by CEL-SCI. The list is not intended to be an exhaustive collection, but rather is believed to be representative of the type of competition CEL-SCI may encounter as it seeks to further develop and commercialize its product candidates.

Merck & Co, Inc. (MRK-NYSE)

Merck provides healthcare solutions worldwide. The company offers therapeutic and preventive products, including its vaccines for HPV (Gardasil®), Ebola (Erbevo®), and Rotovirus (Rotateq®). In addition, the company its developing its check point inhibitor, Keytruda®, for multiple oncology targets, in addition to its current indications, which include melanoma, small cell lung cancer, and head and neck squamous cell carcinoma, among others. The company is headquartered in Kenilworth, New Jersey.

Sanofi (SNY-NASDAQ)

Sanofi is a diversified global healthcare company with extensive lines of prescription medicines and vaccines, as well as consumer health products. Its product offerings include the vaccines Flublok® and Fluzone® for influenza, as well as therapeutic products Kevzara® for RA and Libtayo® for metastatic cutaneous squamous cell carcinoma. Sanofi is headquartered in Paris, France.

Historical Financial Results

Figures 40, 41, and 42 provide CEL-SCI's Condensed Statements of Operations, Condensed Balance Sheets, and Condensed Statements of Cash Flows for the period ending December 31, 2022.

Figure 40
CONDENSED STATEMENTS OF OPERATIONS
THREE MONTHS ENDED DECEMBER 31, 2022 and 2021
(UNAUDITED)

	2022	2021
Operating expenses:		
Research and development	$ 5,392,546	$ 6,083,167
General and administrative	2,258,003	2,760,208
Total operating expenses	7,650,549	8,843,375
Operating loss	(7,650,549)	(8,843,375)
Other expense	(50,171)	–
Gain on derivative instruments	–	364,596
Other non-operating gains	–	(30,793)
Interest expense, net	(152,789)	(273,034)
Net loss	(7,853,509)	(8,782,606)
Modification of warrants	(171,552)	–
Net loss available to common shareholders	$ (8,025,061)	$ (8,782,606)
Net loss per common share – basic	$ (0.18)	$ (0.20)
Weighted average common shares outstanding - basic	43,440,387	43,077,961
Net loss per common share - diluted	$ (0.18)	$ (0.20)
Weighted average common shares outstanding - diluted	44,440,387	43,083,420

Source: Cel-SCI Corporation.

Figure 41
CONDENSED BALANCE SHEETS

ASSETS	DECEMBER 31, 2022 (UNAUDITED)	SEPTEMBER 30, 2022
Current assets:		
Cash and cash equivalents	$ 18,017,319	$ 22,672,138
Prepaid expenses	538,291	762,063
Supplies used for R&D and manufacturing	1,848,720	2,001,715
Total current assets	20,404,330	25,435,916
Finance lease right of use assets	10,486,344	10,937,797
Operating lease right of use assets	1,839,418	1,884,464
Property and equipment, net	11,520,968	11,889,029
Patent costs, net	202,070	212,201
Supplies used for R&D and manufacturing	104,607	164,299
Total assets	$ 44,557,737	$ 50,523,706
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,599,812	$ 1,618,290
Accrued expenses	800,838	842,492
Due to employees	550,575	471,488
Lease liabilities, current portion	1,790,716	1,731,481
Total current liabilities	4,741,941	4,663,751
Finance lease obligations, net of current portion	11,295,512	11,721,368
Operating lease obligations, net of current portion	1,803,663	1,850,380
Other liabilities	125,000	125,000
Total liabilities	17,966,116	18,360,499
Commitments and contingencies		
STOCKHOLDERS' EQUITY		
Preferred stock, $.01 par value-200,000 shares authorized; -0- shares issued and outstanding	–	–
Common stock, $.01 par value - 600,000,000 shares authorized; 43,725,636 and 43,448,317 shares issued and outstanding at December 31, 2022 and September 30, 2022, respectively	437,256	434,484
Additional paid-in capital	488,904,967	486,625,816
Accumulated deficit	(462,750,602)	(454,897,093)
Total stockholders' equity	26,591,621	32,163,207
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY	$ 44,557,737	$ 50,523,706

Source: Cel-SCI Corporation.

Figure 42
CONDENSED STATEMENTS OF CASH FLOWS
THREE MONTHS ENDED DECEMBER 31, 2022 and 2021
(UNAUDITED)

	2022	2021
Net loss	$ (7,853,509)	$ (8,782,606)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	988,543	887,930
Non-cash lease expense	5,078	24,997
Share-based payments for services	148,858	218,318
Equity-based compensation	1,692,831	3,262,296
Common stock contributed to 401(k) plan	50,178	52,555
Gain on short-term investments	—	(615)
Loss on patent impairment	—	30,793
Gain on derivative instruments	—	(364,596)
(Increase)/decrease in assets:		
Prepaid expenses	111,537	144,542
Supplies used for R&D and manufacturing	212,687	(61,139)
Increase/(decrease) in liabilities:		
Accounts payable	(115,285)	(523,152)
Accrued expenses	13,346	95,685
Due to employees	79,087	209,046
Net cash used in operating activities	(4,666,649)	(4,805,946)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Proceeds from maturity of US treasury bills	—	6,152,000
Purchases of property and equipment	(53,580)	(17,036)
Expenditures for patent costs	—	(22,741)
Net cash (used in) provided by investing activities	(53,580)	6,112,223
CASH FLOWS FROM FINANCING ACTIVITIES:		
Payments of stock issuance costs	(9,010)	(32,800)
Proceeds from exercises of warrants and options	447,291	117,200
Payments on obligations under finance lease	(372,871)	(340,908)
Net cash provided by (used in) financing activities	65,410	(256,508)
NET (DECREASE) INCREASE IN CASH AND CASH EQUIVALENTS	(4,654,819)	1,049,769
CASH AND CASH EQUIVALENTS, BEGINNING OF PERIOD	22,672,138	36,060,148
CASH AND CASH EQUIVALENTS, END OF PERIOD	$ 18,017,319	$ 37,109,917

Source: Cel-SCI Corporation.

Recent Events

March 8, 2023—CEL-SCI Corporation reported new data from its pivotal Phase 3 study, the largest study ever conducted in newly diagnosed locally advanced squamous cell carcinoma of the head and neck (SCCHN). A poster presentation titled "Leukocyte Interleukin Injection (LI) immunotherapy followed by radiotherapy extends overall survival (OS) in treatment naïve locally advanced primary squamous cell carcinoma of the head & neck: the IT-MATTERS Study" was delivered by Eyal Talor, Ph.D., CEL-SCI's Chief Scientific Officer on March 8, 2023 at the 10th European Congress on Head & Neck Oncology (ECHNO) in Lisbon, Portugal.

March 3, 2023—Announced it will present new data from its pivotal Phase 3 study, the largest study ever conducted in newly diagnosed locally advanced squamous cell carcinoma of the head and neck (SCCHN), on March 8, 2023 at the 10th European Congress on Head & Neck Oncology in Lisbon, Portugal.

December 28, 2022—Reported financial results for the fiscal year ended September 30, 2022, as well as key clinical and corporate developments.

November 22, 2022—Issued a letter to its shareholders.

October 17, 2022—Announced the availability to the public of an oral presentation delivered by Dr. Philip Lavin of groundbreaking tumor response and increased overall survival in head and neck cancer. This presentation includes data presented at the European Society for Medical Oncology (ESMO) Annual Congress on September 10, 2022 in Paris, France. https://youtu.be/zMoFtweVGzs.

September 12, 2022—Announced two poster presentations were delivered at the European Society for Medical Oncology (ESMO) annual Congress on September 10, 2022 in Paris, France. Data presented (two separate poster presentations) were from the Company's pivotal Phase 3 study, the largest study ever conducted in newly diagnosed locally advanced squamous cell carcinoma of the head and neck.

September 7, 2022—Issued a letter to its shareholders.

August 19, 2022—Announced Phase 3 Multikine® head and neck cancer results posted on Clinicaltrials.gov.

August 15, 2022—Reported financial results for the quarter ended June 30, 2022, as well as key clinical and corporate developments.

August 8, 2022—Announced the appointment of Dr. Gail K. Naughton to its Board of Directors.

July 14, 2022—Announced that Geert Kersten, Chief Executive Officer, will be on Reddit AMA ("Ask Me Anything") today at 12:30 PM ET to discuss Multikine® and the Company's recent publications at ASCO 2022.

June 8, 2022—Announced that Geert Kersten, Chief Executive Officer, is scheduled to present at the LD Micro Invitational XII Conference June 8, 2022 at 4:30 p.m. EDT. The Conference is taking place in person at the Four Seasons in Westlake Village, CA from June 7-9, 2022.

June 7, 2022—Announced that its abstract and poster titled "Leukocyte interleukin injection (LI) immunotherapy extends overall survival (OS) in treatment-naive low-risk (LR) locally advanced primary squamous cell carcinoma of the head and neck: The IT-MATTERS study" was presented on June 6, 2022 at the American Society of Clinical Oncology (ASCO)'s 2022 ASCO Annual Meeting in Chicago, Illinois.

May 27, 2022—Announced the American Society of Clinical Oncology (ASCO) has published two abstracts related to CEL-SCI's pivotal Phase 3 Multikine® (Leukocyte Interleukin, Inj.) head and neck cancer clinical trial. The poster will be presented by CEL-SCI's Chief Scientific Officer, Eyal Talor, Ph.D., at the 2022 ASCO Annual Meeting was held June 3-7, 2022 in Chicago, Illinois.

May 16, 2022—Reported financial results for the quarter ended March 31, 2022, as well as key clinical and corporate developments.

April 22, 2022—Announced that two abstracts related to CEL-SCI's pivotal Phase 3 head and neck cancer clinical trial were accepted at the American Society of Clinical Oncology (ASCO) meeting held June 3-7, 2022 in Chicago, IL. After a two-year hiatus, ASCO comes alive in June 2022 under the theme, "Advancing Equitable Cancer Care Through Innovation." ASCO is the largest cancer meeting in the world, bringing together thousands of cancer experts from academia, industry, patient advocacy, and policy

February 14, 2022—Reported financial results for the quarter ended December 31, 2021, as well as key clinical and corporate developments.

December 22, 2021—Reported financial results for the fiscal year ended September 30, 2021, as well as key clinical and corporate developments.

October 22, 2021—Announced the Company had completed the expansion of its existing dedicated Multikine* cGMP manufacturing facility. The expansion was undertaken in anticipation of filing a Biologics License Application (BLA) which, if approved, will allow Multikine® produced in the facility to be commercially distributed. The construction, which began in 2020, expanded the facility and added various upgrades to ensure it will be in compliance with all requirements of the FDA's Current Good Manufacturing Practice (GMP) regulations. The facility's production capacity has been doubled to meet anticipated market demand for Multikine® once it is licensed. The renovations also anticipate that additional personnel will be required to staff a second manufacturing shift to meet the eventual market demand for Multikine®. Following an $11 million investment to increase production, CEL-SCI staff recently moved back into the renovated facility.

August 16, 2021—Reported financial results for the quarter ended June 30, 2021, as well as key clinical and corporate developments.

Risks and Disclosures

This Executive Informational Overview® (EIO) has been prepared by CEL-SCI Corporation ("CEL-SCI" or "the Company") with the assistance of Crystal Research Associates, LLC ("CRA") based upon information provided by the Company. CRA has not independently verified such information. Some of the information in this EIO relates to future events or future business and financial performance. Such statements constitute forward-looking information within the meaning of the Private Securities Litigation Act of 1995. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in CEL-SCI's statements on its financial and other reports filed from time to time.

The content of this report with respect to CEL-SCI has been compiled primarily from information available to the public released by the Company through news releases, presentations, Annual Reports, and other filings. CEL-SCI is solely responsible for the accuracy of this information. Information as to other companies has been prepared from publicly available information and has not been independently verified by CEL-SCI or CRA. Certain summaries of activities and outcomes have been condensed to aid the reader in gaining a general understanding. CRA assumes no responsibility to update the information contained in this report. In addition, CRA has been compensated by the Company in cash of forty thousand U.S. dollars for its services in creating this report and for updates.

Investors should carefully consider the risks and information about CEL-SCI's business. Investors should not interpret the order in which considerations are presented in this or other filings as an indication of their relative importance. In addition, the risks and uncertainties overviewed herein are not the only risks that the Company faces. Additional risks and uncertainties not presently known to CEL-SCI or that it currently believes to be immaterial may also adversely affect the Company's business. If any of such risks and uncertainties develops into an actual event, CEL-SCI's business, financial condition, and results of operations could be materially and adversely affected, and the trading price of the Company's shares could decline.

This report is published solely for informational purposes and is not to be construed as an offer to sell or the solicitation of an offer to buy any security in any state. Past performance does not guarantee future performance. Additional information about CEL-SCI as well as copies of this report, can be obtained by calling (703) 506-9460.

RISKS RELATED TO CEL-SCI

The Company faces business disruption and related risks resulting from the recent pandemic of COVID-19, which could have a material adverse effect on its business plan.

The development of CEL-SCI's product candidates could be disrupted and materially adversely affected by the ongoing COVID-19 pandemic. CEL-SCI knows that COVID delayed the time to reach data lock for its Phase 3 clinical trial, delayed the expansion of CEL-SCI's manufacturing facility for Multikine, and could potentially affect the regulatory pathway for Multikine® through the FDA and/or other regulatory agencies throughout the world. CEL-SCI is continually assessing its business plans and the impact COVID-19 may have on its ability to seek regulatory approval for Multikine® and conduct the preclinical studies and clinical trials other than CEL-SCI's Phase 3 trial, but there can be no assurance that this analysis will enable it to avoid part or all of any impact from the spread of COVID-19 or its consequences, including downturns in business sentiment generally. The extent to which the COVID-19 pandemic and global efforts to contain its spread will impact CEL-SCI's operations will depend on future developments, which are highly uncertain and cannot be predicted, and include the duration, severity, and scope of the pandemic and the actions taken to contain or treat the COVID-19 pandemic.

CEL-SCI has incurred significant losses since its inception and anticipates that it will continue to incur significant losses for the foreseeable future and may never achieve or maintain profitability.

The Company has a history of net losses, expects to incur substantial losses and have negative operating cash flow for the foreseeable future, and may never achieve or maintain profitability. Since the date of its formation and through September 30, 2022, CEL-SCI incurred net losses of approximately $456 million. The Company has relied principally upon the proceeds from the public and private sales of its securities to finance its activities. To date,

CEL-SCI has not commercialized any products or generated any revenue from the sale of products, and does not expect to generate any product revenue for the foreseeable future, nor does not know whether or when it will generate product revenue or become profitable.

CEL-SCI is heavily dependent on the success of Multikine® for which Phase 3 data has been announced and presented at ASCO 2022 and ESMO 2022. The Company cannot be certain that Multikine® will receive regulatory approval or be successfully commercialized even if CEL-SCI receives regulatory approval. Multikine® is the only product candidate in late-stage clinical development and CEL-SCI's business currently depends heavily on its successful development, regulatory approval, and commercialization. CEL-SCI has no drug products for sale currently and may never be able to develop approved and marketable drug products.

Even if the Company succeeds in developing and commercializing one or more of its product candidates, CEL-SCI expects to continue to incur significant operating and capital expenditures as it:

- continues to undertake preclinical development and clinical trials for product candidates;
- seeks regulatory approvals for product candidates; and
- implements additional internal systems and infrastructure.

To become and remain profitable, CEL-SCI must succeed in developing and commercializing product candidates which must generate significant revenue. This will require it to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of its product candidates, discovering or acquiring additional product candidates, obtaining regulatory approval for these product candidates, and manufacturing, marketing and selling any products for which CEL-SCI may obtain regulatory approval. CEL-SCI is only in the preliminary stages of most of these activities and may never succeed in these activities and, even if it does, may never generate revenue that is significant enough to achieve profitability.

Even if CEL-SCI does achieve profitability, it may not be able to sustain or increase profitability on a quarterly or annual basis. The failure to become and remain profitable could depress the value of CEL-SCI's common stock and could impair its ability to raise capital, expand its business, maintain research and development efforts, diversify product offerings, or even continue in operation. A decline in the value of CEL-SCI's common stock could cause its stockholders to lose all or part of their investment.

CEL-SCI has identified conditions and events that raise substantial doubt about its ability to continue as a going concern.

Primarily as a result of CEL-SCI's losses incurred to date, its expected continued future losses, and the uncertainties associated with obtaining regulatory approval and ultimately commercializing its products, management has identified conditions and events that raise substantial doubt about CEL-SCI's ability to continue as a going concern. CEL-SCI's ability to continue as a going concern is contingent upon, among other factors, the sale of its securities or obtaining alternate financing.

CEL-SCI will require substantial additional capital to remain in operation. A failure to obtain this necessary capital when needed could force the Company to delay, limit, reduce, or terminate the product candidates' development or commercialization efforts.

As of September 30, 2022, CEL-SCI had cash and cash equivalents of approximately $22.7 million. The Company believes that it will continue to expend substantial resources for the foreseeable future developing Multikine, LEAPS, and any other product candidates or technologies that it may develop or acquire. These expenditures will include costs associated with research and development, obtaining regulatory approvals and having the products manufactured, as well as marketing and selling products approved for sale, if any. In addition, other unanticipated costs may arise. CEL-SCI cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of the product candidates.

CEL-SCI's future capital requirements depend on many factors, including:

- the cost of completing Phase 3 clinical development of Multikine® for the treatment of certain head and neck cancers;
- the results of the applications to and meetings with the FDA, the EMA, and other regulatory authorities and the consequential effect on operating costs;
- the cost, timing, and outcome of the efforts to obtain marketing approval for Multikine® in the U.S., Europe, and in other jurisdictions, including the preparation and filing of regulatory submissions for Multikine® with the FDA, the EMA, and other regulatory authorities;
- the scope, progress, results, and costs of additional preclinical, clinical, or other studies for additional indications for Multikine, LEAPS, and other product candidates and technologies that CEL-SCI may develop or acquire;
- the timing of, and the costs involved in, obtaining regulatory approvals for LEAPS™ if clinical studies are successful;
- the cost and timing of future commercialization activities for the products, if any of the product candidates are approved for marketing, including product manufacturing, marketing, sales, and distribution costs;
- the revenue, if any, received from commercial sales of the product candidates for which CEL-SCI receives marketing approval;
- the cost of having the product candidates manufactured for clinical trials and in preparation for commercialization;
- the ability to establish and maintain strategic collaborations, licensing, or other arrangements and the financial terms of such agreements;
- the costs involved in preparing, filing and prosecuting patent applications and maintaining, defending and enforcing its intellectual property rights, including litigation costs, and the outcome of such litigation; and
- the extent to which CEL-SCI acquires or in-licenses other products or technologies.

CEL-SCI will need to raise additional funds in order to continue its operations and additional funds may not be available when CEL-SCI needs them on terms that are acceptable to the Company, or at all. If adequate funds are not available to CEL-SCI on a timely basis, it may be required to delay, limit, reduce, or terminate preclinical studies, clinical trials, or other development activities for Multikine, LEAPS, or any other product candidates or technologies that CEL-SCI develops or acquires, or delay, limit, reduce, or terminate its sales and marketing activities that may be necessary to commercialize its product candidates. Due to recurring losses from operations and future liquidity needs, there is substantial doubt about CEL-SCI's ability to continue as a going concern without additional capital becoming available. The substantial doubt about CEL-SCI's ability to continue as a going concern could have an adverse impact on CEL-SCI's ability to execute its business plan, result in the reluctance on the part of certain suppliers to do business with it, or adversely affect the Company's ability to raise additional debt or equity capital.

The costs of the product candidates' development and clinical trials are difficult to estimate and will be very high for many years, preventing CEL-SCI from making a profit for the foreseeable future, if ever.

Clinical and other studies necessary to obtain approval of a new drug or biologic can be time consuming and costly, especially in the U.S., but also in foreign countries. The estimates of the costs associated with future clinical trials and research may be substantially lower than what CEL-SCI actually experiences. It is impossible to predict what CEL-SCI will face in the development of a product candidate, such as Multikine. The purpose of clinical trials is to

provide both CEL-SCI and regulatory authorities with safety and efficacy data in humans. The difficult and often complex steps necessary to obtain regulatory approval, especially that of the FDA and the EMA, involve significant costs and may require several years to complete. CEL-SCI expects that it will need substantial additional financing over an extended period of time in order to fund the costs of future clinical trials, related research, and general and administrative expenses.

CEL-SCI's LEAPS™ technology may not result in a viable drug candidate

Using CEL-SCI's LEAPS™ technology, the Company also developing a LEAPS™ immunotherapy for the potential treatment of Rheumatoid Arthritis. However, the development of this technology is in a preliminary stage. There can be no assurance that the LEAPS™ technology will be successful in treating any disease. CEL-SCI's primary focus at present is seeking the approval of Multikine® for the treatment of head and neck cancer.

An adverse determination in any future legal proceedings could have a material adverse effect on CEL-SCI.

CEL-SCI may be the target of claims asserting violations of securities fraud and derivative actions, or other litigation or arbitration proceedings in the future. Any future litigation could result in substantial costs and divert management's attention and resources. These legal proceedings may result in large judgments or settlements against CEL-SCI, any of which could have a material adverse effect on its business, operating results, financial condition, and liquidity.

Compliance with changing regulations concerning corporate governance and public disclosure may result in additional expenses.

Changing laws, regulations, and standards relating to corporate governance and public disclosure may create uncertainty regarding compliance matters. New or changed laws, regulations, and standards are subject to varying interpretations in many cases. As a result, their application in practice may evolve over time. CEL-SCI is committed to maintaining high standards of corporate governance and public disclosure. Complying with evolving interpretations of new or changing legal requirements may cause the Company to incur higher costs as CEL-SCI revises current practices, policies, and procedures, and may divert management's time and attention from potential revenue-generating activities to compliance matters. If the efforts to comply with new or changed laws, regulations, and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, CEL-SCI's reputation may also be harmed. Further, CEL-SCI's Board members, Chief Executive Officer, and other executive officers could face an increased risk of personal liability in connection with the performance of their duties. As a result, the Company may have difficulty attracting and retaining qualified board members and executive officers, which could harm its business.

CEL-SCI has not established a definite plan for the marketing of Multikine®, if approved.

CEL-SCI has not established a definitive plan for marketing Multikine® nor has the Company established a price structure for any of its product candidates, if approved. However, CEL-SCI intends, if it is in a position to do so, to sell Multikine® itself in certain markets where it is approved and/or to enter into written marketing agreements with various third parties with established sales forces in such markets. The sales forces in turn would, CEL-SCI believes, focus on selling Multikine® to targeted cancer centers, physicians, and clinics involved in the treatment of head and neck cancer. CEL-SCI has already licensed future sales of Multikine®, if approved, to three companies: Teva Pharmaceutical Industries Ltd. in Israel, Turkey, Serbia, and Croatia; Orient Europharma in Taiwan, Singapore, Hong Kong, Malaysia, South Korea, the Philippines, Australia, and New Zealand; and Byron BioPharma, LLC in South Africa. CEL-SCI believes that these companies will have the resources to market Multikine® appropriately in their respective territories, if approved, but there is no guarantee that they will. There is no assurance that CEL-SCI will be able to find qualified third-party partners to market its products in other areas, on terms that are favorable to CEL-SCI or at all.

CEL-SCI may encounter problems, delays, and additional expenses in developing marketing plans with third parties. In addition, even if Multikine, if approved, is cost-effective and demonstrated to increase overall patient survival, CEL-SCI may experience other limitations involving its proposed sale, such as uncertainty of third-party coverage and reimbursement. There is no assurance that CEL-SCI can successfully market Multikine, if approved, or any other product candidates it may develop.

CEL-SCI hopes to expand its clinical development capabilities in the future, and any difficulties hiring or retaining key personnel or managing this growth could disrupt its operations.

CEL-SCI is highly dependent on the principal members of its management and development staff. The Company expects to expand its clinical development and manufacturing capabilities, which will involve hiring additional employees. Future growth will require it to continue to implement and improve its managerial, operational, and financial systems and continue to retain, recruit, and train additional qualified personnel, which may impose a strain on its administrative and its operational infrastructure. The competition for qualified personnel in the biopharmaceutical field is intense. CEL-SCI is highly dependent on its ability to attract, retain, and motivate highly qualified management and specialized personnel required for clinical development. Due to limited resources, CEL-SCI may not be able to effectively manage the expansion of its operations or recruit and train additional qualified personnel. If CEL-SCI is unable to retain key personnel or manage its future growth effectively, it may not be able to implement its business plan.

If product liability or patient injury lawsuits are brought against CEL-SCI, the Company may incur substantial liabilities and may be required to limit clinical testing or future commercialization of Multikine® or its other product candidates.

CEL-SCI faces an inherent risk of product liability as a result of the clinical testing of Multikine® and other product candidates and will face an even greater risk if CEL-SCI is able to commercialize any of its product candidates. For example, CEL-SCI may be sued if its Multikine® or LEAPS™ product candidates, or any other future product candidates, allegedly cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing or, if approved, marketing, sale, or during administration to patients. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product candidate, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts.

Furthermore, Multikine® is made, in part, from components of human blood. There are inherent risks associated with products that involve human blood, such as possible contamination with viruses, including hepatitis or HIV. Any possible contamination could cause injuries to patients who receive contaminated Multikine, or could require CEL-SCI to destroy batches of Multikine, thereby subjecting CEL-SCI to possible financial losses, lawsuits, and harm to its business.

If CEL-SCI cannot successfully defend itself against product liability claims, it may incur substantial liabilities or be required to limit or cease the clinical testing or commercialization of its product candidates, if approved. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for Multikine® or other product candidates, if approved and commercialized, or clinical holds or suspension of the IND while the candidates are still in clinical development;
- injury to CEL-SCI's reputation;
- withdrawal of existing, or failure to enroll additional, clinical trial participants;
- costs to defend any related litigation;
- a diversion of management's time and resources;

- substantial monetary awards to trial participants or patients;
- recalls of approved products, withdrawal of BLA approvals or new labeling, marketing or promotional restrictions;
- loss of revenue;
- inability to commercialize Multikine® or other product candidates; and
- a decline in the price of CEL-SCI's common stock.

Although CEL-SCI has product liability insurance for Multikine® in the amount of $10 million, the successful prosecution of a product liability case against CEL-SCI could have a materially adverse effect upon its business if the amount of any judgment exceeds the insurance coverage. Any claim that may be brought against CEL-SCI could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by CEL-SCI's insurance or that is in excess of the limits of the insurance coverage. CEL-SCI's insurance policies also have various exclusions, and the Company may be subject to a claim for which CEL-SCI has no coverage. CEL-SCI may have to pay any amounts awarded by a court or negotiated in a settlement that exceed the coverage limitations or that are not covered by its insurance, and CEL-SCI may not have, or be able to obtain, sufficient capital to pay such amounts. CEL-SCI commenced the Phase 3 clinical trial for Multikine® in December 2010. Although no claims have been brought to date, participants in the clinical trials could bring civil actions against CEL-SCI for any unanticipated harmful effects allegedly arising from the use of Multikine® or any other product candidate that CEL-SCI may attempt to develop.

CEL-SCI's commercial success depends, in part, upon attaining significant market acceptance of its product candidates, if approved, among physicians, patients, healthcare payors, and major operators of cancer clinics.

Even if CEL-SCI obtains regulatory approval for its product candidates, any resulting product may not gain market acceptance among physicians, healthcare payors, patients and the medical community, which are critical to commercial success. Market acceptance of any product candidate for which CEL-SCI receives approval depends on a number of factors, including:

- the efficacy and safety of the products as demonstrated in clinical trials;
- the timing of market introduction of such product as well as competitive products;
- the clinical indications for which the biological product is approved;
- the approval, availability, market acceptance, and reimbursement for the companion diagnostic, if appropriate or necessary;
- acceptance by physicians, major operators of cancer clinics, and patients of the biologic as a safe and effective treatment;
- the potential and perceived advantages of such product candidate over alternative treatments, especially with respect to patient subsets that are targeted with such product;
- the safety of such product seen in a broader patient group, including its use outside the approved indications;
- the cost of treatment in relation to alternative treatments;
- the availability of adequate reimbursement and pricing by third-party payors and government authorities;

- relative convenience and ease of administration;
- the prevalence and severity of adverse side effects; and
- the effectiveness of sales and marketing efforts.

If CEL-SCI's product candidates are approved but fail to achieve an adequate level of acceptance by physicians, healthcare payors, and patients, the Company will not be able to generate significant revenues, and CEL-SCI may not become or remain profitable.

Under CEL-SCI's amended bylaws, stockholders that initiate certain proceedings may be obligated to reimburse CEL-SCI and its officers and directors for all fees, costs, and expenses incurred in connection with such proceedings if the claim proves unsuccessful.

On February 18, 2015, CEL-SCI adopted new bylaws which include a fee-shifting provision in Article X for stockholder claims. Article X provides that in the event any stockholder initiates or asserts a claim against CEL-SCI, or any of its officers or directors, including any derivative claim or claim purportedly filed on CEL-SCI's behalf, and the stockholder does not obtain a judgment on the merits that substantially achieves, in substance and amount, the full remedy sought, then the stockholder will be obligated to reimburse CEL-SCI and any of its officers or directors named in the action, for all fees, costs, and expenses of every kind and description that CEL-SCI or its officers or directors may incur in connection with the claim. In adopting Article X, it is the intent that:

- all actions, including federal securities law claims, would be subject to Article X;
- the phrase "a judgment on the merits" means the determination by a court of competent jurisdiction on the matters submitted to the court;
- the phrase "substantially achieves, in both substance and amount" means the plaintiffs in the action would be awarded at least 90% of the relief sought;
- only persons who were stockholders at the time an action was brought would be subject to Article X; and
- in addition to CEL-SCI, only the directors or officers named in the action would be allowed to recover.

The fee-shifting provision contained in Article X of the bylaws is not limited to specific types of actions, but is rather potentially applicable to the fullest extent permitted by law. Fee-shifting bylaws are relatively new and untested. The case law and potential legislative action on fee-shifting bylaws are evolving and there exists considerable uncertainty regarding the validity of, and potential judicial and legislative responses to, such bylaws.

For example, it is unclear whether the ability to invoke the fee-shifting bylaw in connection with claims under the federal securities laws would be pre-empted by federal law. Similarly, it is unclear how courts might apply the standard that a claiming stockholder must obtain a judgment that substantially achieves, in substance and amount, the full remedy sought. The application of the fee-shifting bylaw in connection with such claims, if any, will depend in part on future developments of the law. CEL-SCI cannot assure its shareholders that it will or will not invoke the fee-shifting bylaw in any particular dispute. In addition, given the unsettled state of the law related to fee-shifting bylaws, such as CEL-SCI's, the Company may incur significant additional costs associated with resolving disputes with respect to such bylaw, which could adversely affect CEL-SCI's business and financial condition.

If a stockholder that brings any such claim, suit, action, or proceeding is unable to obtain the required judgment, the attorneys' fees and other litigation expenses that might be shifted to a claiming stockholder are potentially significant. This fee-shifting bylaw may therefore dissuade or discourage stockholders and their attorneys from initiating lawsuits or claims against CEL-SCI or its directors and officers. In addition, it may impact the fees, contingency or otherwise, required by potential plaintiffs' attorneys to represent the stockholders or otherwise discourage plaintiffs' attorneys from representing the stockholders at all. As a result, this bylaw may limit the

ability of stockholders to alter CEL-SCI's management and direction, particularly through litigation or the threat of litigation.

The provision of the amended bylaws requiring exclusive venue in the U.S. District Court for Delaware for certain types of lawsuits may have the effect of discouraging lawsuits against CEL-SCI and its directors and officers.

Article X of CEL-SCI's amended bylaws provides that stockholder claims brought against CEL-SCI, or its officers or directors, including any derivative claim or claim purportedly filed on its behalf, must be brought in the U.S. District Court for the district of Delaware and that with respect to any such claim, the laws of Delaware will apply. The exclusive forum provision may limit a stockholder's ability to bring a claim in a judicial forum the stockholder finds favorable for disputes with CEL-SCI or its directors or officers and may have the effect of discouraging lawsuits with respect to claims that may benefit CEL-SCI or its stockholders.

A provision in the Company's Bylaws regarding shareholder claims may not be enforceable.

Article X of CEL-SCI's bylaws provides that stockholder claims brought against the Company, or our officers or directors, including any derivative claim or claim purportedly filed on our behalf, must be brought in the U.S. District Court for the district of Delaware. Although it is the Company's intent that this provision applies to actions arising under the Securities Act of 1933 and the Securities Exchange Act of 1934, there is uncertainty as to whether a court would enforce this provision since Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations under the Securities Act. In addition, since this provision in the Company's bylaws applies to state law claims, there is uncertainty as to whether any court would enforce this provision.

RISKS RELATED TO CLINICAL DEVELOPMENT, GOVERNMENT APPROVALS, AND THE MARKETING OF BIOPHARMACEUTICAL PRODUCTS

CEL-SCI depends heavily on the success of Multikine, for which Phase 3 data has been presented, while its other candidates are still in preclinical phases. CEL-SCI's product candidates must undergo rigorous preclinical and clinical testing and regulatory approvals, which could be costly and time-consuming and subject CEL-SCI to unanticipated delays or prevent CEL-SCI from marketing any products. If CEL-SCI is unable to advance its product candidates in clinical development, obtain regulatory approval, and ultimately commercialize its product candidates, or experiences significant delays in doing so, its business will be materially harmed.

CEL-SCI currently has no products approved for sale and cannot guarantee that it will ever have marketable products. The Company's product candidates are subject to premarket approval from the FDA in the U.S., the EMA in the European Union, and by comparable agencies in most foreign countries before they can be sold. Before obtaining marketing approval, these product candidates must undergo costly and time consuming preclinical and clinical testing, which could subject CEL-SCI to unanticipated delays and may prevent the Company from marketing the product candidates in the future. There can be no assurance that such approvals will be granted on a timely basis, if at all.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of the product candidates may not be predictive of the results of later-stage clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. CEL-SCI's current and future clinical trials may not be successful.

The Company is in the early development stages for the candidates designed using its LEAPS™ technology and has not yet initiated any clinical studies for any of those product candidates. Clinical trials can be delayed for a variety of reasons, including delays related to:

- the availability of financial resources needed to commence and complete the planned trials;
- obtaining regulatory approval to commence a trial;
- reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining Institutional Review Board, or IRB, approval at each clinical trial site;
- recruiting suitable patients to participate in a trial;
- having patients complete a trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- adding new clinical trial sites; or
- manufacturing sufficient quantities of the product candidate for use in clinical trials.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors, including the competence of the CRO running the study, size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications CEL-SCI is investigating. Furthermore, CEL-SCI relies on CROs and clinical trial sites to ensure the proper and timely conduct of the clinical trials and while the Company has agreements governing their committed activities, CEL-SCI has limited influence over their actual performance.

CEL-SCI could also encounter significant delays and/or need to terminate a development program for a product candidate if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of the product candidates while existing treatments have established safety and efficacy profiles. Furthermore, a clinical trial may be suspended or terminated by CEL-SCI, by one or more of the IRBs for the institutions in which such trials are being conducted, by CEL-SCI upon a final recommendation by the Independent Data Monitoring Committee, or IDMC, with which CEL-SCI agrees for such trial, or by FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or the clinical protocols, as a result of inspection of the clinical trial operations or trial site(s) by FDA or other regulatory authorities, the imposition of a clinical hold or partial clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. The occurrence of any one or more of these events would have significant and severe material consequences for CEL-SCI and could impact CEL-SCI's ability to continue as a going concern.

If CEL-SCI experiences termination of, or delays in the completion of any clinical trial of its product candidates, the commercial prospects for the product candidates will be harmed, and the ability to generate product revenues will be delayed. In addition, any delays in completing the clinical trials will increase the costs, slow the product development and approval process, and jeopardize the ability to commence product sales and generate revenues. Any of these occurrences may harm CEL-SCI's business, prospects, financial condition, and results of operations significantly. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to a delay or the denial of regulatory approval for the product candidates.

CEL-SCI cannot be certain when or under what conditions it will undertake future clinical trials. Early trials for the other product candidates, or the plans for later trials, may not satisfy the requirements of regulatory authorities, such as the FDA. CEL-SCI may fail to find subjects willing to enroll in the trials. Accordingly, the clinical trials relating to the product candidates may not be completed on schedule, the FDA or foreign regulatory agencies may order CEL-SCI to stop or modify research, or these agencies may not ultimately approve any of the product candidates for commercial sale. Varying interpretations of the data obtained from pre-clinical and clinical testing could delay, limit, or prevent regulatory approval of the product candidates. The data collected from the clinical trials may not be sufficient to support regulatory approval of the various product candidates, including Multikine. The failure to adequately demonstrate the safety and efficacy of any of the product candidates would delay or prevent regulatory approval of the product candidates in the U.S., which could prevent CEL-SCI from achieving profitability.

The development and testing of product candidates and the process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. FDA sanctions could include, among other actions, refusal to approve pending applications, withdrawal of an approval, a clinical hold, termination of the Phase 3 study, warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, and payment of civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on CEL-SCI.

The requirements governing the conduct of clinical trials, manufacturing, and marketing of the product candidates, including Multikine, outside the U.S. vary from country to country. Foreign approvals may take longer to obtain than FDA approvals and can require, among other things, additional testing and different trial designs. Foreign regulatory approval processes include all of the risks associated with the FDA approval process. Some of those agencies also must approve prices for products approved for marketing. Approval of a product by the FDA or the EMA does not ensure approval of the same product by the health authorities of other countries. In addition, changes in regulatory requirements for product approval in any country during the clinical trial process and regulatory agency review of each submitted new application may cause delays or rejections.

CEL-SCI has only limited experience in filing and pursuing applications necessary to gain regulatory approvals. The lack of experience may impede its ability to obtain timely approvals from regulatory agencies, if at all. CEL-SCI will not be able to commercialize Multikine® and other product candidates until it has obtained regulatory approval. In addition, regulatory authorities may also limit the types of patients to which CEL-SCI or its third-party partners may market Multikine® (if approved) or the other product candidates. Any failure to obtain or any delay in obtaining required regulatory approvals may adversely affect CEL-SCI's or its third-party partners' ability to successfully market the product candidates after they are approved.

Even if CEL-SCI obtains regulatory approval for its investigational products, it will be subject to stringent, ongoing government regulation.

If CEL-SCI's investigational products receive regulatory approval, either in the U.S. or internationally, those products will be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval and may contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance of the safety and efficacy of the investigational products. CEL-SCI will continue to be subject to extensive regulatory requirements. These regulations are wide-ranging and govern, among other things:

- product design, development, and manufacture;
- product application and use;
- adverse drug experience monitoring reporting;
- product advertising and promotion;

- product manufacturing, including compliance with good manufacturing practices;
- record keeping requirements;
- registration and listing of products with the FDA, EMA, and other state and national agencies;
- product storage and shipping;
- drug sampling and distribution requirements;
- electronic record and signature requirements; and
- labeling changes or modifications.

CEL-SCI and any of its third-party manufacturers or suppliers must continually adhere to federal regulations setting forth human drug and biologic manufacturing requirements, known as current Good Manufacturing Practices (cGMPs), and their foreign equivalents, which are enforced by the FDA, the EMA, and other national regulatory bodies through their facilities inspection programs. If the facilities, or the facilities of the contract manufacturers or suppliers, cannot pass a pre-approval inspection by regulators or fail such inspections in the future, the FDA, EMA, or other national regulators will not approve the marketing applications for the product candidates, or may withdraw any prior approval. In complying with cGMP and foreign regulatory requirements, CEL-SCI and any of its potential third-party manufacturers or suppliers will be obligated to expend time, money, and effort in production, record-keeping, and quality control to ensure that the product candidates meet applicable specifications and other requirements.

If CEL-SCI does not comply with regulatory requirements at any stage, whether before or after marketing approval is obtained, CEL-SCI may be subject to, among other things, license suspension or revocation, criminal prosecution, seizure, injunction, fines, be forced to remove a product from the market, or experience other adverse consequences, including restrictions or delays in obtaining regulatory marketing approval for such products or for other product candidates for which CEL-SCI seeks approval. This could materially harm CEL-SCI's financial results, reputation and stock price. Additionally, CEL-SCI may not be able to obtain the labeling claims necessary or desirable for product promotion. If CEL-SCI or other parties identify adverse effects after any of the products are on the market, or if manufacturing problems occur, regulatory approval may be suspended or withdrawn. CEL-SCI may be required to reformulate products, conduct additional clinical trials, make changes in product labeling or indications of use, or submit additional marketing applications to support any changes. If CEL-SCI encounters any of the foregoing problems, its business and results of operations will be harmed and the market price of its common stock may decline.

The FDA and other governmental authorities' policies may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of CEL-SCI's product candidates. If CEL-SCI is slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if CEL-SCI is not able to maintain regulatory compliance, it may lose any marketing approval that it may have obtained, which would adversely affect its business, prospects, and ability to achieve or sustain profitability. CEL-SCI cannot predict the extent of adverse government regulations, which might arise from future legislative or administrative action. Without government approval, CEL-SCI will be unable to sell any of its product candidates.

CEL-SCI's product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial utility of an approved prescribing label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by its product candidates could cause CEL-SCI or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Results of the clinical trials could reveal a high and unacceptable severity and/or prevalence of these or other side effects. In such an event, the trials could be

suspended or terminated and the FDA or comparable foreign regulatory authorities could order CEL-SCI to cease further development of, or deny approval of, the product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm CEL-SCI's business, financial condition, and prospects significantly.

As well, if one or more of the product candidates receives marketing approval, and CEL-SCI or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including but not limited to the following:

- regulatory authorities may withdraw approvals of such product or require product recalls;
- regulatory authorities may require additional warnings on the label or impose restrictions on product distribution or use;
- regulatory authorities may require CEL-SCI to conduct new post-marketing studies or clinical trials;
- CEL-SCI could receive warning or untitled letters from the FDA or comparable notices of violations from foreign regulatory authorities;
- CEL-SCI may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- CEL-SCI could be sued and held liable for harm caused to patients; and
- CEL-SCI's reputation may suffer.

Any of these events could prevent CEL-SCI from achieving or maintaining market acceptance of a particular product candidate, if approved, and could significantly harm its business, results of operations, and prospects.

CEL-SCI relies on third parties to conduct its preclinical and clinical trials. If these third parties do not successfully carry out their contractual duties and meet regulatory requirements, or meet expected deadlines, CEL-SCI may not be able to obtain regulatory approval for or commercialize the product candidates and its business could be substantially harmed.

CEL-SCI does not have the ability to independently conduct large clinical trials. The Company has relied upon and plans to continue to rely upon third-party CROs to prepare for, conduct, monitor, and manage data for its ongoing preclinical and clinical programs, including the global Phase 3 trial for Multikine. CEL-SCI relies on these parties for all aspects of the execution of its clinical trials and although CEL-SCI diligently oversees and carefully manages the CROs, the Company directly controls only certain aspects of their activities and relies upon them to provide timely, complete, and accurate reports on the conduct of the studies. Although such third parties provide support and represent CEL-SCI for regulatory purposes in the context of the clinical trials, ultimately CEL-SCI is responsible for ensuring that each of the studies is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards, and the reliance on the CROs does not relieve CEL-SCI of its regulatory responsibilities.

The Company and the CROs acting on CEL-SCI's behalf, as well as principal investigators and trial sites, are required to comply with Good Clinical Practice (GCP) and other applicable requirements, which are implemented through regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area (EEA), and comparable foreign regulatory authorities for all of the products in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators, and trial sites. If CEL-SCI or any of the CROs fail to comply with applicable GCPs or other applicable regulations, the clinical data generated in the clinical trials may be determined to be unreliable and CEL-SCI may therefore need to enroll additional subjects in the clinical trials, or the FDA, EMA, or comparable foreign regulatory authorities may require CEL-SCI to perform an additional clinical trial or trials before approving the marketing applications. Moreover, if CEL-SCI or any of the CROs, principal investigators, or trial sites, fail to comply with applicable

regulatory and GCP requirements, CEL-SCI, the CROs, principal investigators, or trial sites may be subject to enforcement actions, such as fines, warning letters, untitled letters, clinical holds, civil or criminal penalties, and/or injunctions. CEL-SCI cannot assure investors that upon inspection by a given regulatory authority, such regulatory authority will determine that any of the clinical trials comply with cGCP regulations. In addition, the clinical trials must be conducted with product produced under cGMP regulations. The failure to comply with these regulations may require CEL-SCI to delay or repeat clinical trials, which would delay the regulatory approval process.

If any of the relationships with the third-party CROs terminate, CEL-SCI may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. In addition, the CROs are not CEL-SCI's employees, and except for remedies available to CEL-SCI under the agreements with such CROs, the Company cannot control whether or not they devote sufficient time and resources to the on-going clinical, nonclinical and preclinical programs. If CROs do not successfully fulfill their regulatory obligations, carry out their contractual duties, or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to the clinical protocols, regulatory requirements or for other reasons, the clinical trials may be extended, delayed, or terminated, and CEL-SCI may not be able to obtain regulatory approval for, or successfully commercialize, the product candidates. As a result, CEL-SCI's results of operations and the commercial prospects for the product candidates would be harmed, the costs could increase and the ability to generate revenues could be delayed.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays may occur, which can materially impact CEL-SCI's ability to meet the desired clinical development timelines. Though CEL-SCI diligently oversees and carefully manages its relationships with the CROs, there can be no assurance that CEL-SCI will not encounter similar challenges or delays in clinical development in the future or that these delays or challenges will not have a material adverse impact on CEL-SCI's business, financial condition, and prospects.

CEL-SCI has obtained orphan drug designation from the FDA for Multikine® for neoadjuvant, or primary, therapy in patients with squamous cell carcinoma of the head and neck, but may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biologic intended to treat a rare disease or condition, which is defined as one occurring in a patient population of fewer than 200,000 in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug or biologic will be recovered from sales in the U.S. In the U.S., orphan drug designation entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity.

Even though CEL-SCI has received orphan drug designation for Multikine® for the treatment of squamous cell carcinoma of the head and neck, the Company may not be the first to obtain marketing approval of a product for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. CEL-SCI believes this to be unlikely since it does not know of any other company with a similar technology in Phase 3 studies. In addition, exclusive marketing rights in the U.S. may be limited if CEL-SCI seeks approval for an indication broader than the orphan-designated indication, or may be lost if the FDA later determines that the request for designation was materially defective or if CEL-SCI is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Further, even if CEL-SCI obtains orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve another drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Biologics carry unique risks and uncertainties, which could have a negative impact on future results of CEL-SCI's operations.

The successful discovery, development, manufacturing, and sale of biological products like CEL-SCI's candidates is a long, costly, and uncertain process. There are unique risks and uncertainties with biologics. For example, access to and supply of necessary biological materials, such as cell lines, may be limited and governmental regulations restrict access to and regulate the transport and use of such materials. In addition, the development, manufacturing, and sale of biologics is subject to regulations that are often more complex and extensive than the regulations applicable to other pharmaceutical products.

Manufacturing biologics, especially in large quantities, is often complex and may require the use of innovative technologies. Such manufacturing also requires facilities specifically designed and validated for this purpose and sophisticated quality assurance and quality control procedures. Biologics are also frequently costly to manufacture because production inputs are derived from living animal or plant material, and some biologics cannot be made synthetically. Failure to successfully discover, develop, manufacture, and sell its biological product candidates would adversely impact CEL-SCI's business and future results of operations.

CEL-SCI may face substantial competition, which may result in others discovering, developing or commercializing competing products more quickly or more successfully than CEL-SCI.

The development and commercialization of new drug and biological products is highly competitive. CEL-SCI expects to face competition with respect to any product candidates that it may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Many of the companies which CEL-SCI may compete with in the future have significantly greater financial resources and expertise in research and development, manufacturing, nonclinical studies, conducting clinical trials, obtaining marketing approvals and marketing approved products than CEL-SCI. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of CEL-SCI's potential competitors. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties may compete with CEL-SCI in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, CEL-SCI's programs.

CEL-SCI may be unable to successfully scale-up manufacturing of its lead product candidate Multikine® in sufficient quality and quantity, which would delay or prevent the Company from commercializing its product, if approved for marketing by the FDA or other regulatory agencies.

In order to commercialize its product candidates, CEL-SCI will need to manufacture them in large quantities. At the present time, the Company is not manufacturing Multikine® while the manufacturing plant for Multikine® is being validated to produce commercial quantities, if approved. The Company may be unable to successfully increase the manufacturing capacity for its lead product candidate, Multikine, due to issues that may arise during scale-up activities.

Further, in order to release product and demonstrate stability of product candidates for future commercial use, CEL-SCI's analytical methods must be validated in accordance with regulatory guidelines. CEL-SCI may not be able to successfully validate or maintain validation of its analytical methods during scale-up or demonstrate adequate purity, stability, or comparability of its biological product candidates in a timely or cost-effective manner, or at all. Even if CEL-SCI believes its manufacturing processes meets all of the regulatory manufacturing requirements, the FDA will review those processes and the manufacturing facility as part of the review of the future BLA for Multikine® when submitted. If CEL-SCI is unable to successfully scale up the manufacture of Multikine® in sufficient quality and quantity, or if CEL-SCI encounters validation issues, the development, testing, and clinical trials of future product candidates, may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product, including Multikine, may be delayed or may not be successfully achieved.

Failure to obtain or maintain adequate coverage and reimbursement for the product candidates, if approved, could limit the ability to market those products and decrease CEL-SCI's ability to generate revenue.

Sales of CEL-SCI's product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of the approved products will be paid by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other third-party payors. CEL-SCI anticipates that government authorities and other third-party payors will continue efforts to contain healthcare costs by limiting the coverage and reimbursement levels for new drugs and biologics. If coverage and reimbursement are not available, or are available only to limited levels, CEL-SCI may not be able to successfully commercialize its product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow CEL-SCI to establish or maintain pricing sufficient to realize a return on its investment. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for CEL-SCI's product candidates.

Moreover, in some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, CEL-SCI may be required to conduct a clinical trial that compares the cost-effectiveness of its product candidate to other available therapies. If reimbursement of its products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, CEL-SCI's business could be harmed, possibly materially.

Even if any product candidate receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community necessary for commercial success.

If CEL-SCI's product candidates do not achieve an adequate level of acceptance, the Company may not generate significant product revenues and CEL-SCI may not become profitable. The degree of market acceptance of its product candidates, including Multikine® if approved for commercial sale, will depend on a number of factors, including:

- the timing of CEL-SCI's receipt of any marketing approvals;
- the terms of any approvals and the countries in which approvals are obtained;
- the efficacy and safety and potential advantages and disadvantages compared to alternative treatments, including future alternative treatments;
- the prevalence and severity of any side effects associated with CEL-SCI's product candidates;
- the indications for which its products are approved and the scope of risk information required to be included in the product labeling;
- adverse publicity about CEL-SCI's products or favorable publicity about competing products;

- the approval of other products for the same indications as CEL-SCI's products;
- CEL-SCI's ability to offer its products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the success of CEL-SCI's physician education programs;
- the strength of CEL-SCI's marketing and distribution support; and
- the availability of third-party coverage and adequate reimbursement.

If any product candidate CEL-SCI commercializes fails to achieve market acceptance, it could have a material and adverse effect on CEL-SCI's business, financial condition, results of operation, and prospects.

CEL-SCI currently has no marketing and sales force. If the Company is unable to establish effective sales or marketing capabilities or enter into agreements with third parties to sell or market its product candidates, CEL-SCI may not be able to effectively sell or market its product candidates, if approved, or generate product revenues.

CEL-SCI currently has no sales and marketing infrastructure due to the fact that all of its product candidates are still in clinical development. To achieve commercial success for any approved product candidate for which CEL-SCI retains sales and marketing responsibilities, CEL-SCI must build its sales, marketing, managerial, and other non-technical capabilities or make arrangements with third parties to perform these services.

For example, CEL-SCI has entered into agreements with certain foreign distributors to commercialize Multikine, if approved, within their respective territories. However, CEL-SCI may determine that there is a need to build its own sales force in the U.S. for the future marketing of Multikine, if approved, rather than seeking a U.S. co-marketing partner or relying on a contracted sales force. There are risks involved with either establishing its own sales and marketing capabilities or entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is costly and time consuming and could delay any product launch. If the commercial launch of a product candidate for which CEL-SCI recruits a sales force and establishes marketing capabilities is delayed or does not occur for any reason, CEL-SCI would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and its investment would be lost if CEL-SCI cannot retain or reposition its sales and marketing personnel.

Factors that may inhibit CEL-SCI's efforts to commercialize its product candidates on its own include:

- CEL-SCI's inability to recruit, hire, retain, and incentivize adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to use and administer CEL-SCI's future products;
- the lack of complementary products to be offered by sales personnel, which may put CEL-SCI at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with establishing an independent sales and marketing organization.

If CEL-SCI does not establish sales and marketing capabilities successfully, either on its own or in collaboration with third parties, it will not be successful in commercializing Multikine, if approved, or any of its other product candidates that receive marketing approval or any such commercialization may experience delays or limitations.

CEL-SCI's business activities may be subject to the Foreign Corrupt Practices Act and similar anti-bribery and anti-corruption laws of other countries in which CEL-SCI operates or will operate in the future.

The Company has conducted and has ongoing studies in international locations and may in the future initiate additional studies in countries other than the U.S. Moreover, CEL-SCI has entered into agreements with foreign distributors to commercialize Multikine, if approved, in various territories outside of the U.S. As a result, CEL-SCI's business activities may be subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery or anti-corruption laws, regulations, or rules of other countries in which CEL-SCI operates. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls.

CEL-SCI's business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the healthcare providers who prescribe biopharmaceuticals are employed by their government, and the purchasers of biopharmaceuticals are government entities; therefore, CEL-SCI's dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the SEC and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of CEL-SCI's employees, agents or contractors conducting business abroad will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against CEL-SCI, its officers or employees, the closing of CEL-SCI's facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs and prohibitions on the conduct of CEL-SCI's business. Any such violations could include prohibitions on CEL-SCI's ability to offer its product candidates, if approved, in one or more countries and could materially damage its reputation, its brand, its future international marketing efforts, its ability to attract and retain employees and its business, prospects, operating results and financial condition.

Healthcare legislative reform measures may have a material adverse effect on CEL-SCI's business and results of operations.

Existing regulatory policies may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of CEL-SCI's product candidates. The Company cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If CEL-SCI is slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if the Company is not able to maintain regulatory compliance, CEL-SCI may lose any marketing approval that it may have obtained and it may not achieve or sustain profitability.

In the U.S., there have been and continue to be a number of legislative initiatives to contain healthcare costs that may result in more limited coverage or downward pressure on the price CEL-SCI may otherwise receive for its product candidates. For example, in March 2010, Congress passed the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, which expanded healthcare coverage through Medicaid expansion and the implementation of the individual mandate for health insurance coverage and which included changes to the coverage and reimbursement of drug products under federal healthcare programs. The ACA contains a number of provisions that affect coverage and reimbursement of drug and biological products and/or that could potentially reduce the demand for pharmaceutical products such as increasing drug rebates under state Medicaid programs for brand name prescription drugs and extending those rebates to Medicaid managed care and assessing a fee on manufacturers and importers of brand name prescription drugs reimbursed under certain government programs, including Medicare and Medicaid.

Tax reform legislation was enacted at the end of 2017 that eliminates the tax penalty established under the ACA for individuals who do not maintain mandated health insurance coverage beginning in 2019. In a May 2018 report, the Congressional Budget Office estimated that, compared to 2018, the number of uninsured will increase by 3 million in 2019 and 6 million in 2028, in part due to the elimination of the individual mandate. The ACA has also been subject to judicial challenge. In December 2018, a federal district court, in a challenge brought by a number of state attorneys general, found the ACA unconstitutional in its entirety because, once Congress repealed the individual mandate provision, there was no longer a basis to rely on Congressional taxing authority to support enactment of the law. Pending appeals, which could take some time, the ACA is still operational in all respects.

CEL-SCI's industry continues to face potential changes in the legal and regulatory landscape on the federal, state, and international levels. Additional legislative actions to control U.S. healthcare or other costs have passed. The Budget Control Act, as amended, resulted in the imposition of 2% reductions in Medicare (but not Medicaid) payments to providers in 2013 and will remain in effect through 2027 unless additional Congressional action is taken. There has also been increasing and considerable public and government interest in the U.S. with respect to specialty drug pricing practices, including proposed federal and state legislation designed to bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, put in place limits and caps on pharmaceutical prices, request rebates for certain pharmaceutical products, and reform government program reimbursement methodologies for drugs. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what biopharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. In markets outside of the U.S., reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and control the prices of medicinal products for human use.

CEL-SCI expects that current or future healthcare reform measures may result in more rigorous coverage criteria and in additional downward pressure on the price that it receives for any approved product, including Multikine, if it is approved for commercialization. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent CEL-SCI from being able to generate revenue, attain profitability, or commercialize its product candidates.

Legislative and regulatory proposals also have been made to expand post-approval requirements and restrict sales and promotional activities for biotechnology products. CEL-SCI cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance, or interpretations for biological products will be changed, or what the impact of such changes on the marketing approvals of its product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval and decision-making processes may significantly delay or prevent marketing approval, as well as subject CEL-SCI to more stringent product labeling and post-marketing testing and other requirements.

Foreign governments often impose strict price controls, which may adversely affect CEL-SCI's future profitability.

CEL-SCI intends to seek approval to market its lead investigational product, Multikine, in both the United States and foreign jurisdictions. If CEL-SCI obtains approval in one or more foreign jurisdictions, CEL-SCI will be subject to rules and regulations in those jurisdictions relating to Multikine. In some foreign countries, particularly in the European Union, prescription drug pricing is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug candidate. Coverage and reimbursement decisions in one foreign jurisdiction may impact decisions in other countries. To obtain reimbursement or pricing approval in some countries, CEL-SCI may be required to conduct clinical trials that demonstrate the product candidate is more effective than current treatments and that compare the cost-effectiveness of Multikine® to other available therapies. If reimbursement of Multikine® is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, CEL-SCI may be unable to achieve or sustain profitability.

If CEL-SCI fails to comply with environmental, health and safety laws and regulations, it could become subject to fines or penalties or incur costs that could harm its business.

CEL-SCI is subject to numerous environmental, health, and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment, and disposal of hazardous materials and wastes generated in its biologic manufacturing facility. The Company cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from its use of hazardous materials, including radioactive materials used in its research laboratory, CEL-SCI could be held liable for any resulting damages, and the amount of the liability could exceed its resources. CEL-SCI also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

RISKS RELATED TO INTELLECTUAL PROPERTY

CEL-SCI may not be able to achieve or maintain a competitive position, and other technological developments may result in its proprietary technologies becoming uneconomical or obsolete.

CEL-SCI is involved in a biomedical field that is undergoing rapid and significant technological change. The pace of change continues to accelerate. The successful development of product candidates from the compounds, compositions, and processes, through research financed by CEL-SCI or as a result of possible third-party licensing arrangements with pharmaceutical or other companies, is not assured. The Company may fail to apply for patents on important technologies or product candidates in a timely fashion, or at all.

Many companies are working on drugs designed to cure or treat cancer. Many of these companies have financial, research and development, and marketing resources which are much greater than CEL-SCI's and are capable of providing significant long-term competition either by establishing in-house research groups or by forming collaborative ventures with other entities. In addition, smaller companies and non-profit institutions are active in research relating to cancer and infectious diseases. The future market share of Multikine® or the other product candidates, if approved, will be reduced or eliminated if the competitors develop and obtain approval for products that are safer or more effective than CEL-SCI'S product candidates. Moreover, the patent positions of pharmaceutical companies are highly uncertain and involve complex legal and factual questions for which important legal principles are often evolving and remain unresolved. As a result, the validity and enforceability of patents cannot be predicted with certainty. In addition, CEL-SCI does not know whether:

- the Company was the first to make the inventions covered by each of its issued patents and pending patent applications;
- CEL-SCI was the first to file patent applications for these inventions;
- others will independently develop similar or alternative technologies or duplicate any of the Company's technologies;
- any of the pending patent applications will result in issued patents;
- any of the patents will be valid or enforceable;
- any patents issued to CEL-SCI or its collaboration partners will provide CEL-SCI with any competitive advantages or will be challenged by third parties;
- the Company will be able to develop additional proprietary technologies that are patentable;
- the U.S. government will exercise any of its statutory rights to CEL-SCI's intellectual property that was developed with government funding; or
- its business may infringe the patents or other proprietary rights of others.

CEL-SCI's patents might not protect its technology from competitors, in which case the Company may not have any advantage over competitors in selling any products that the Company may develop.

CEL-SCI's commercial success will depend, in part, on its ability to obtain additional patents and protect its existing patent position, as well as its ability to maintain adequate intellectual property protection for the technologies, product candidates, and any future products in the U.S. and other countries. If CEL-SCI does not adequately protect its technology, product candidates, and future products, competitors may be able to use or practice them and erode or negate any competitive advantage CEL-SCI may have, which could harm CEL-SCI's business and its ability to achieve profitability. The laws of some foreign countries do not protect the proprietary rights to the same extent or in the same manner as U.S. laws, and the Company may encounter significant problems in protecting and defending its proprietary rights in these countries. CEL-SCI will be able to protect its proprietary rights from unauthorized use by third parties only to the extent that its proprietary technologies, product candidates, and any future products are covered by valid and enforceable patents or are effectively maintained as trade secrets.

Certain aspects of CEL-SCI's technologies are covered by U.S. and foreign patents. In addition, CEL-SCI has a number of new patent applications pending. There is no assurance that the applications, which are pending or which may be filed in the future, will result in the issuance of any patents. Furthermore, there is no assurance as to the breadth and degree of protection any issued patents might afford CEL-SCI. Disputes may arise between CEL-SCI and others as to the scope and validity of these or other patents. Any defense of the patents could prove costly and time consuming and there can be no assurance that CEL-SCI will be in a position, or will deem it advisable, to carry on such a defense. A suit for patent infringement could result in increasing costs, delaying or halting development, or even forcing CEL-SCI to abandon a product candidate. Other private and public concerns, including universities, may have filed applications for, may have been issued, or may obtain additional patents and other proprietary rights to technology potentially useful or necessary to CEL-SCI. The Company is not currently aware of any such patents, but the scope and validity of such patents, if any, and the cost and availability of such rights are impossible to predict.

Much of CEL-SCI's intellectual property is protected as trade secrets or confidential know-how, not as a patent.

CEL-SCI considers proprietary trade secrets and/or confidential and unpatented know-how to be important to its business. Much of the intellectual property pertains to the Company's manufacturing methodologies, certain aspects of which may not be suitable for patent filings and must be protected as trade secrets and/or confidential know-how. This type of information must be protected diligently by CEL-SCI to protect its disclosure to competitors, since legal protections after disclosure may be minimal or non-existent. Accordingly, much of the value of this intellectual property is dependent upon the Company's ability to keep its trade secrets and know-how confidential.

To protect this type of information against disclosure or appropriation by competitors, CEL-SCI's policy is to require its employees, consultants, contractors, and advisors to enter into confidentiality agreements with the Company. However, current or former employees, consultants, contractors, and advisers may unintentionally or willfully disclose the confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Enforcing a claim that a third party obtained illegally, and is using, trade secrets and/or confidential know-how is costly, time consuming, and unpredictable. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction.

In addition, in some cases a regulator considering the application for product candidate approval may require the disclosure of some or all of the proprietary information. In such a case, the Company must decide whether to disclose the information or forego approval in a particular country. If CEL-SCI is unable to market its product candidates in key countries, CEL-SCI's opportunities and value may suffer.

Failure to obtain or maintain trade secrets and/or confidential know-how trade protection could adversely affect CEL-SCI'S competitive position. Moreover, competitors may independently develop substantially equivalent proprietary information and may even apply for patent protection in respect of the same. If successful in obtaining such patent protection, competitors could limit the use of such trade secrets and/or confidential know-how.

CEL-SCI may be subject to claims challenging the inventorship or ownership of its patents and other intellectual property.

CEL-SCI may also be subject to claims that former employees, collaborators, or other third parties have an ownership interest in its patents or other intellectual property. CEL-SCI may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing the product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If CEL-SCI fails in defending any such claims, in addition to paying monetary damages, it may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on its business. Even if CEL-SCI is successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and employees.

RISKS RELATED TO CEL-SCI'S COMMON STOCK

Future equity offerings or other equity issuances may result in dilution to existing shareholders.

CEL-SCI expects that significant additional capital will be needed in the future to continue its planned operations. To raise additional capital, CEL-SCI may in the future offer additional shares of its common stock or other securities convertible into or exchangeable for its common stock. To the extent CEL-SCI raises additional capital by issuing equity securities, its stockholders may experience substantial dilution and new investors could gain rights superior to existing stockholders.

The exercise of outstanding warrants and options will cause dilution.

As of September 30, 2022, there were outstanding warrants which allow the holders to purchase 1,310,822 shares of common stock, with a weighted average exercise price of $2.97 per share, and outstanding options which allow the holders to purchase up to 12,964,014 shares of common stock, with a weighted average exercise price of $9.06 per share. The exercise of these outstanding warrants and options will cause dilution to holders of our common stock.

Since CEL-SCI does not intend to pay dividends on its common stock, any potential return to investors will result only from any increases in the price of its common stock.

At the present time, CEL-SCI intends to use available funds to finance its operations. Accordingly, while payment of dividends rests within the discretion of its board of directors, no common stock dividends have been declared or paid by CEL-SCI and the Company has no intention of paying any common stock dividends in the foreseeable future. Additionally, any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on CEL-SCI's common stock. Any return to CEL-SCI's shareholders will therefore be limited to appreciation in the price of its common stock, which may never occur. If CEL-SCI's stock price does not increase, its shareholders are unlikely to receive any return on their investments in CEL-SCI's common stock.

The price of CEL-SCI's common stock has been volatile and is likely to continue to be volatile, which could result in substantial losses for shareholders.

CEL-SCI's stock price has been, and is likely to continue to be, volatile. As a result of this volatility, its shareholders may not be able to sell their shares at or above the price they paid. The market price for CEL-SCI's common stock may be influenced by many factors, including:

- actual or anticipated fluctuations in CEL-SCI's financial condition and operating results;
- actual or anticipated changes in CEL-SCI's growth rate relative to competitors;
- competition from existing products or new products or product candidates that may emerge;

- development of new technologies that may make CEL-SCI's technology less attractive;
- changes in physician, hospital, or healthcare provider practices that may make CEL-SCI's product candidates less useful;
- announcements by CEL-SCI, its partners, or competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations, or capital commitments;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- failure to meet or exceed financial estimates and projections of the investment community;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- variations in its financial results or those of companies that are perceived to be similar to CEL-SCI;
- changes to coverage and reimbursement levels by commercial third-party payors and government payors, including Medicare, and any announcements relating to reimbursement levels;
- general economic, industry, and market conditions; and
- the other factors described in this section.

CEL-SCI has identified material weaknesses in its internal control over financial reporting. Failure to achieve and maintain effective internal controls over financial reporting could adversely affect the Company's ability to report its results of operations and financial condition accurately and in a timely manner, which could have an adverse impact on CEL-SCI's business.

CEL-SCI's management is responsible for establishing and maintaining adequate internal control over financial reporting designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement in an entity's annual or interim consolidated financial statements might not be prevented or detected on a timely basis.

Management has noted material weaknesses in its internal control over financial reporting as of September 30, 2022. CEL-SCI's management concluded that material weaknesses existed relating to ineffective information technology general controls in the areas of user access and segregation of duties related to certain information technology systems that support CEL-SCI's financial reporting process and ineffective design of certain management review controls across a significant portion of CEL-SCI's financial statement areas, particularly with regard to the precision of the review and evidence of review procedures performed. Although these control weaknesses did not result in any material misstatement of CEL-SCI's financial statements for the periods presented, they could lead to a material misstatement of account balances or disclosures. As a result, Company management concluded that its internal controls over financial reporting were not effective as of September 30, 2022.

In order to remediate these material weaknesses, CEL-SCI will change certain control activities over financial reporting to include, but are not limited to, the following: (i) evaluating and implementing enhanced process controls around user access management and segregation of duties and (ii) expanding the documentation over user access and system controls and enhancing the level of evidence maintained in management's review controls.

If CEL-SCI is unable to remediate the material weaknesses timely and sufficiently or if the Company identifies future material weaknesses in its internal control over financial reporting or is unable to comply with the requirements of Section 404 in a timely manner or assert that its internal control over financial reporting is effective, CEL-SCI may experience a loss of investor confidence in the accuracy and completeness of its financial statements, incur material misstatements in its financial statements, incur difficulty accessing capital on favorable terms, or at all, be subject to fines, penalties or judgments, incur reputational harm, and the market price of its common stock may be adversely affected.

Glossary

Adjuvant—A secondary treatment in addition to the primary therapy that often speeds or improves the action of the primary therapy.

Antibody—Immune system-related proteins produced by B-cells in response to the presence of antigens. Their function is to recognize and attach to antigens, marking them for other components of the immune system to destroy.

Antigen—A substance that stimulates the production of an antibody when introduced into the body. Antigens include toxins, bacteria, foreign blood cells, and transplanted organs, among other substances.

Apoptosis—Programmed cell death. This physiological process is necessary for the elimination of superfluous, diseased, or damaged cells and the formation of new cells.

Autologous—A treatment in which the donor and recipient are the same person. Autologous immunotherapy normally involves the removal of immune cells from a person, which are altered and later given back to that same person.

Biologic—Vaccines, blood products or derivatives, allergenic products, serums, toxins, antitoxins, and other similar products used to prevent, treat, or cure disease or injury.

Biologics License Application—The biologics license application is a request for permission to introduce or deliver for introduction, a biologic product into interstate commerce (21 CFR 601.2). The BLA is regulated under 21 CFR 600 – 680. A BLA is submitted by any legal person or entity who is engaged in manufacture or an applicant for a license who takes responsibility for compliance with product and establishment standards.

BSL-1—Biosafety level 1, suitable for work with well-characterized agents which do not cause disease in healthy humans.

Cancer Cell Nest—A mass of cells extending from a common center seen in cancerous growths.

CD-4+—T-helper cells (CD-4+) are immune cells that express the CD4 protein on the surface.

CD-8+—Cytotoxic T-cells (CD-8+) are immune cells that express the CD8 protein on the surface. Some CD-8+ cells recognize and kill cancerous cells and those infected by intracellular pathogens (e.g., bacteria, viruses, and mycoplasma).

Cell Cycle—An ordered cycle of complex events, where cells proceed to cell division from a resting state.

Cervical Dysplasia—Dysplasia is the presence of abnormal cells in the cervix that may indicate a precancerous condition. Neoplasia is the pathological process that results in a tumor.

cGMP—Refers to the Current Good Manufacturing Practice regulations enforced by the FDA. cGMPs provide for systems that assure proper design, monitoring, and control of manufacturing processes and facilities.

Checkpoint Inhibitors—A form of cancer immunotherapy that targets immune checkpoints, key regulators of the immune system that, when stimulated, can dampen the immune response to an immunologic stimulus.

Chemokines—Any of a class of cytokines with functions that include attracting white blood cells to sites of infection.

Chemotactic—Pertaining to the attraction and repulsion of living protoplasm to a chemical stimulus.

Collagen Induced Arthritis (CIA)—The collagen-induced arthritis (CIA) mouse model is the most commonly studied autoimmune model of rheumatoid arthritis (RA). Autoimmune arthritis is induced in this model by immunization with an emulsion that includes type II collagen (CII).

Complete Response—The disappearance of all signs of tumor.

Composition of Matter—Relates to chemical compositions and may include mixtures of ingredients as well as new chemical compounds.

Cyclophosphamide—A drug used for immunosuppression and destruction of cancer cells.

Cytokines—Small proteins released by cells that have a specific effect on cell interactions, communications, and behavior. Cytokines include interleukins, lymphokines, and cell signal molecules, such as tumor necrosis factor (TNF) and interferons, which trigger inflammation and respond to infections.

Dendritic Cell (DC)—A special type of antigen-presenting cell that activates T-cells.

Epitope—A region on the surface of an antigen that is capable of eliciting an immune response. An epitope is a site on the surface of an antigen molecule to which a single antibody molecule binds.

Erythropoietin (EPO)—A cytokine that stimulates differentiation of bone marrow stem cells, accelerates cell maturation, and maintains the level of circulating erythrocytes.

European Union Qualified Person (QP)—A technical term used in European Union pharmaceutical regulation. The regulations specify that no batch of medicinal product can be released for sale or supply prior to certification by a QP that the batch is in accordance with the relevant requirements.

First-Line—The first type of therapy given for a condition or disease.

Histopathology—The study of cell and tissue pathology and microscopic changes typical of disease.

Human Epidermal Growth Factor Receptor 2 (HER2+)—A protein involved in normal cell growth. HER2/neu may be made in larger than normal amounts by some types of cancer cells, including breast, ovarian, bladder, pancreatic, and stomach cancers. This may cause cancer cells to grow more quickly and spread to other parts of the body.

Hypersensitivity Immune Reactions—Refers to undesirable reactions produced by the normal immune system, including allergies and autoimmunity.

ICH and EU directives—The European Medicines Agency publishes scientific guidelines on human medicines that are harmonized by the International Council for Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

Immunomodulatory—The modulation or control of the immune system response, caused by either natural or man-made substances. Man-made immunomodulators aim to activate or suppress functions of the body's immune system to achieve a desired therapeutic effect.

Immunotherapy—Also called biologic therapy, is a type of cancer treatment that boosts the body's natural defenses to fight cancer. It uses substances made by the body or in a laboratory to improve or restore immune system functions.

Indomethacin—A drug that belongs to the family of drugs called nonsteroidal anti-inflammatory drugs (NSAIDs). Indomethacin reduces pain, fever, swelling, and redness. It is also being used to reduce tumor-induced suppression of the immune system and to increase the effectiveness of anticancer drugs.

Interferons—A group of signaling proteins made and released by host cells in response to the presence of several viruses. In a typical scenario, a virus-infected cell will release interferons causing nearby cells to heighten their anti-viral defenses.

Interleukins—A group of naturally occurring proteins (*cytokines*) that mediate communication between cells. Interleukins regulate cell growth, differentiation, and motility. They are particularly important in stimulating immune responses, such as inflammation.

Investigational New Drug (IND)—Refers to the Food and Drug Administration's (FDA) program by which a pharmaceutical company obtains permission to ship an experimental drug across state lines (usually to clinical investigators) before a marketing application for the drug has been approved. The FDA reviews the IND for safety to assure that research subjects will not be subjected to unreasonable risk.

Leukocytes—Also known as white blood cells, they are small, colorless cells that circulate in the blood and body fluids and are involved in counteracting foreign substances and disease.

Lymphocytes—A type of leukocyte (white blood cell) that develops from stem cells in the bone marrow and helps protect the body from infection and cancer. There are three main types known as T-cells, B-cells, and natural killer cells. Lymphocytes are part of the body's immune defense and act to recognize antigens, produce antibodies, and destroy cells that could cause damage.

Lymphoproliferative—Referring to the proliferation of the bone marrow cells that give rise to lymphoid cells and reticuloendothelial cells.

Macrophage—A type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells.

Margin—The edge or border of the tissue removed in cancer surgery. The margin is described as "negative" or "clean" when the pathologist does not find any cancer cells at the edge of the tissue, suggesting that all of the cancer has been removed. The margin is described as "positive" or "involved" when the pathologist finds cancer cells at the edge of the tissue, i.e., all cancer has not been removed.

Metastasis—The migration of cancer cells from the original tumor site. Metastasis also is the term used for a secondary cancer growing at a distant site.

Micrometastases—A metastatic tumor cell that is too small to be identified in a scan.

Monoclonal antibodies (mAb)—Any of a class of artificial antibodies produced in the laboratory. Monoclonal antibodies are extremely specific for a particular location in the body. This type of antibody recognizes only one type of antigen and is sometimes used as an immunotherapy to treat diseases such as cancer.

Monocytes—Large white blood cells that ingest other cells and foreign particles. When a monocyte enters tissue, it develops into a macrophage.

Natural killer (NK) cells—Also known as NK cells, they are a type of lymphocyte (a white blood cell) and a component of innate immune system. NK cells play a major role in the host-rejection of both tumors and virally infected cells.

National Comprehensive Cancer Network (NCCN)—An alliance of 32 cancer centers in the United States, most of which are designated by the National Cancer Institute as comprehensive cancer centers.

Necrosis—A type of cell death where cells swell and break open, releasing their contents and damaging neighboring cells thereby provoking inflammation. Necrosis is often caused by infection or the interruption of blood supply.

Neoadjuvant—Treatment given before the primary treatment.

Objective Response Rate—Proportion of patients with reduction in tumor burden of a predefined amount.

Orphan Drug—Designation given to a medication that may treat either a rare disease that affects fewer than 200,000 people or a common disease that has been ignored because it is less prominent in the U.S. than in developing nations.

Perilymphatic—Surrounding or adjacent to a lymphatic node or vessel.

Peritumoral—Surrounding or adjacent to a tumor.

PGIA/GIA—Proteoglycan (PG)-induced arthritis (PGIA) and PG G1-domain-induced arthritis (GIA) are two RA mouse models that use proteoglycan as antigen. The PGIA and GIA models in adult female mice are predominantly driven by Th1 responses and resemble human RA in that disease is induced in older females.

Peptide—Any of various natural or synthetic compounds containing two or more amino acids linked by the carboxyl group of one amino acid to the amino group of another.

Proteoglycan—A compound consisting of a protein bonded to glycosaminoglycan groups, present especially in connective tissue.

Small Business Innovation Research (SBIR)—A U.S. Government program, coordinated by the Small Business Administration, intended to help certain small businesses conduct research and development (R&D). Funding takes the form of contracts or grants**.**

SEER Database—The Surveillance, Epidemiology, and End Results (SEER) Program provides information on cancer statistics in an effort to reduce the cancer burden among the U.S. population. SEER is supported by the Surveillance Research Program (SRP) in NCI's Division of Cancer Control and Population Sciences (DCCPS).

Squamous Cell Carcinoma—Cancer that begins in squamous cells, which are thin, flat cells resembling fish scales. Squamous cells are found in the tissue that forms the surface of the skin, the lining of the hollow organs of the body, and the passages of the respiratory and digestive tracts.

Standard of Care (SOC)—A diagnostic and treatment process that a clinician should follow for a certain type of patient, illness, or clinical circumstance. For head and neck cancer, the standard of care is surgery followed by radiation or concurrent radiation and chemotherapy, depending upon the severity of the cancer and its likelihood of spreading or recurring.

T-cell—A lymphocyte of a type produced or processed by the thymus gland and actively participating in the immune response. There are 3 main types of T-cells: cytotoxic (CD-8), helper (CD-4), and regulatory. Each of them has a different role in the immune response.

T or Immune Cell-Binding Ligand (TCBL/ICBL)—A ligand is a molecule that binds to a site on a target protein to serve a biological purpose. A T-cell or immune cell-binding ligand is a ligand that binds to the T-cell receptor (TCR), a protein complex found on the surface of T-cells, or immune cells, respectively, which produces an immunomodulatory signal or action.

T-cell Transfer Therapy—A type of immunotherapy in which T-cells are taken from the patient's blood or tumor tissue, grown in large numbers in the laboratory, and then given back to the patient to help the immune system fight the cancer. Sometimes, the T-cells are changed in the laboratory with the goal of improving immune functionality and characteristics.

Th1 Response—An acquired immune response characterized by high cytotoxic T-cell activity relative to the amount of antibody production. The Th1 response is promoted by Th1 helper T-cells.

Th2 Response—An acquired immune response characterized by high antibody production relative to the amount of cytotoxic T-lymphocyte activity. The Th2 response is promoted by Th2 helper T-cells.

T-helper (Th) Cells—Immune cells involved in cell-mediated immunity and function as “helpers” by regulating the overall immune response to antigen presence. Also known as CD4+ cells, Th cells help the activity of other immune cells by releasing cytokines, regulating the immune responses.

T-regulatory (T-reg) Cells—Immune cells that have a role in regulating or suppressing other cells in the immune system. T-regs control the immune response to self and foreign particles (antigens) and help prevent excessive reactions and autoimmune disease.

Tumor Necrosis Factor (TNF)—A cytokine with a key role in the body’s immune response by promoting inflammation, controlling the production of other pro-inflammatory molecules, and helping cells heal or repair themselves. TNF-α acts as a cytolytic and cytostatic agent on several cell types. TNF α is a subgroup of molecules capable of initiating signaling cascades that increase cell proliferation, differentiation, and apoptosis.

Tumor Tolerance—A process by which growing tumors, which have mutated proteins and altered antigen expression, prevent elimination by the host immune system.

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About Our Firm: For the past two decades, Crystal Research Associates, LLC has successfully articulated the exceptional stories of small- and mid-cap companies to the Wall Street investor community. Our methods are well-established and diverse, from compiling and disseminating objective, factual information for both institutional and retail investor audiences to capitalizing on our expansive line of targeted distribution channels, which include industry-leading financial data and information providers. Our distribution efforts are accompanied by the use of prominent social media channels and by strategic and targeted appearances on national news programs and print media.

Crystal Research Associates is led by Wall Street veterans, Jeffrey Kraws and Karen Goldfarb. Together, Kraws and Goldfarb have built a unique business model, capitalizing on decades of experience as an award-winning sell-side analyst team to produce institutional-quality industry and market research in a manner that is easily understood by investors and consumers. Our firm's approach has been proven successful over the years as our products are published and available on Bloomberg, Thomson Reuters, S&P Capital IQ, FactSet, and scores of other popular forums.

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