CEL-SCI
Empowering Immune Defenses

# Multikine (Leukocyte Interleukin, Inj.) Cancer Immunotherapy

Activating the immune system of cancer patients before surgery and radiation and creating a non-toxic cancer drug

April 2023

NYSE: CVM


**CEL-SCI Corporation**

**Geert Kersten**
Chief Executive Officer

8229 Boone Boulevard, Suite 802
Vienna, VA 22182, USA
Phone: **(703) 506-9460**

NYSE American: **CVM**

# Forward Looking Statements

This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. You can generally identify these forward-looking statements by forward-looking words such as “anticipates,” “believes,” “expects,” “intends,” “future,” “could,” “estimates,” “plans,” “would,” “should,” “potential,” “continues” and similar words or expressions (as well as other words or expressions referencing future events, conditions or circumstances). These forward-looking statements involve risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements, including, but not limited to: the progress and timing of, and the amount of expenses associated with, our research, development and commercialization activities for our product candidates, including Multikine; the success of our clinical studies for our product candidates; our ability to obtain U.S. and foreign regulatory approval for our product candidates and the ability of our product candidates to meet existing or future regulatory standards; our expectations regarding federal, state and foreign regulatory requirements; the therapeutic benefits and effectiveness of our product candidates; the safety profile and related adverse events of our product candidates; our ability to manufacture sufficient amounts of Multikine or our other product candidates for use in our clinical studies or, if approved, for commercialization activities following such regulatory approvals; our plans with respect to collaborations and licenses related to the development, manufacture or sale of our product candidates; our expectations as to future financial performance, expense levels and liquidity sources; our ability to compete with other companies that are or may be developing or selling products that are competitive with our product candidates; anticipated trends and challenges in our potential markets; and our ability to attract, retain and motivate key personnel.

All forward-looking statements contained herein are expressly qualified in their entirety by this cautionary statement, the risk factors set forth under the heading “Risk Factors” and elsewhere in our public filings, and in the documents incorporated or deemed to be incorporated by reference therein. The forward-looking statements contained in this presentation speak only as of their respective dates. Except to the extent required by applicable laws and regulations, we undertake no obligation to update these forward-looking statements to reflect new information, events or circumstances after the date of this presentation. In light of these risks and uncertainties, the forward-looking events and circumstances described in this presentation may not occur and actual results could differ materially from those anticipated or implied in such forward-looking statements. Accordingly, you are cautioned not to place undue reliance on these forward-looking statements.

Multikine is the trademark that CEL-SCI has registered for this investigational therapy, and this proprietary name is subject to FDA review in connection with CEL-SCI’s future anticipated regulatory submission for approval. Multikine has not been licensed or approved for sale, barter or exchange by the FDA or any other regulatory agency. Similarly, its safety or efficacy has not been established for any use. Each page of this presentation must be looked at in the context of the whole presentation, not by itself, and is merely meant to be a summary of the full and detailed information concerning the Company in its public filings and its website.

# CEL-SCI Management Team

Geert R. Kersten
*Director and CEO*

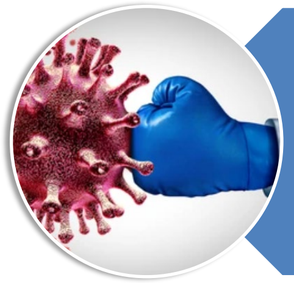
- CEO since 1995; joined in 1987
- 30+ years pioneering field of cancer immunotherapy
- Previously worked at the law firm of Finley & Kumble and Source Capital, an investment bank
- Undergraduate degree Accounting, MBA from George Washington and JD from American University

Eyal Talor, Ph.D.
*Chief Scientific Officer*

- CSO since 2009; joined in 1993
- 29+ years of managing clinical R&D development for immunotherapy application
- Served as Director of Clinical Laboratories; and as R&D Director at CBL
- Author of over 30 publications
- Ph.D. at University of Ottawa and Post Doc and Faculty at Johns Hopkins

| | Officer Title | Joined CVM | Years of Exp. | Background |
|---|---|---|---|---|
|  | Patricia B. Prichep<br>SVP of Operations | 1992 | 40+ | • Former Manager of Quality and Productivity for the NASD<br>• BA from the University of Bridgeport |
|  | Daniel Zimmerman, Ph.D.<br>SVP of Cellular Immunology | 1996 | 40+ | • Author of over 40 scientific publications and dozen patents<br>• Former Senior Staff Fellow at NIH<br>• PhD and Masters U. of Florida; BS Emory and Henry College |
|  | John Cipriano<br>SVP of Regulatory Affairs | 2004 | 48+ | • Former FDA Deputy Director of Biologics IND Division<br>• BS Massachusetts College of Pharmacy and MS (Medicinal Chemist) Purdue University |
|  | William Jones<br>VP of Quality Assurance | 1999 | 30+ | • QA positions at Novartis in US and Europe<br>• Former GMP compliance officer at NCI's Frederick facility<br>• BS from George Mason and MS from Hood College |

# Our Goal was to Create a Cancer Medicine that Activates the Immune System and is Not Toxic



## The immune system is key to our fight against cancer.

- Activate it to fight cancer BEFORE surgery and radiation have damaged it.
- Cancer immunotherapy drugs are typically given after those first treatments.

## Our immunotherapy is called Multikine*

"Multikine" is a copy of the pro-inflammatory cytokine immune response that our bodies produce when under attack.

Given by injection for 3 weeks right after diagnosis, before surgery and radiation.

# The First Non-Toxic Cancer Medicine

- 10-year study in head & neck cancer for treatment naïve  patients receiving Multikine followed by surgery and radiotherapy (lower risk for recurrence)
- 14.1% absolute 5-year overall survival benefit (MK 62.7% and Control 48.6% at 5 years)
- Near 4-year median survival benefit
- 5 patients had no tumor left in just 3 weeks – before surgery
- 16% of patients had a partial or complete tumor response in just 3 weeks, no responses in control
- Any patient with a tumor response has a significantly improved overall survival
- No toxicity was added to overall standard of care treatment
- Even the leading cancer drugs Keytruda and Opdivo have not been successful in advanced primary head and neck cancer patients (2022 and 2021)
- The last FDA approval for advanced primary head and neck cancer was over 50 years ago

# Pursuing FDA Approval for Patients in the Treatment Arm Receiving Surgery and Radiation

Considerations for FDA approval:

- pre-specified in the protocol and the Statistical Analysis Plan before Database lock
- treatment arm was determined per NCCN guidelines by treating physicians, not by CEL-SCI
- no patients were excluded from the analysis
- the number of patients in this treatment arm (n=380) is significant (with 80% Power) and the number of patients who would benefit each year is large (about 210,000)

Protocol criterion of 10% overall survival: study showed 14.1%


Protocol criterion of p-value=<0.05: in study was 0.0478


Protocol criterion of 0.721 hazard ratio: in study was 0.68


No toxicity was added to the overall treatment

# What is Multikine?

Multikine is a consistent mixture of cytokines. Research at the US National Institutes of Health (NIH) has shown that the cytokines (shown in yellow) are the ones that are required to reject a tumor.

IL-1 α | IL-1β | IL-2 | IL-3 | TNF-α | IFN-γ | GM-CSF

*Major cytokines and other cellular products in Multikine*

IL-6 | IL-8 | TNF-β | G-CSF | RANTES | MIP-1α | MIP-1β

# How Does Multikine Work?

Multikine is injected 5 days a week for 3 consecutive weeks before any other cancer therapy around the tumor and near adjacent lymph nodes 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—destroy the cancer.

=

**THE GOAL:**

Activate an anti-tumor immune response and increase survival.

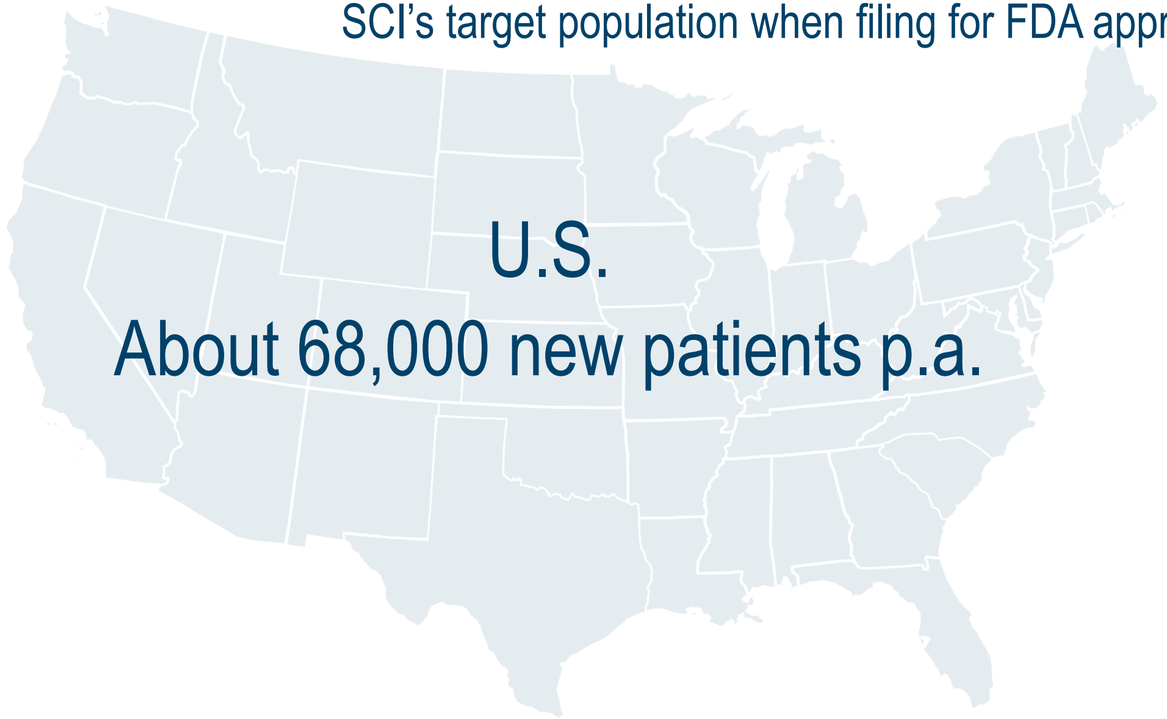
# Why was locally advanced (stages III and IV) primary (not yet treated) head and neck cancer selected as the first indication?

- Last FDA approval of a therapy for advanced primary head and neck cancer was over 50 years ago.
- It represents a severe unmet medical need.
- Multikine was awarded Orphan Drug Status in the US.
- Head and neck cancer is a prevalent debilitating cancer - worldwide.
- Only one standard of care for advanced primary head and neck cancer throughout the world.

**If approved, Multikine should become the first treatment given to patients scheduled for surgery and deemed for subsequent radiotherapy, but not chemotherapy.**

# Head and Neck Cancer Populations

Worldwide about **890,000** new head and neck cancer patients are diagnosed per year. CEL-SCI's target population when filing for FDA approval is about **210,000** patients - globally



U.S.
About 68,000 new patients p.a.

Europe
About 150,000 new patients p.a.

- 90% of head and neck cancers are squamous cell carcinomas
- About 66% of those are advanced primary
- Of the advanced primary about 40% are prescribed surgery and radiation therapy as standard of care
- We plan to apply for FDA approval for that market of about **210,000 annual cases** globally
- Our global study spanned over 20 countries; FDA approval expected to lead to approval in many countries

Multikine

# A Severe Unmet Medical Need

The last FDA approval for advanced primary head and neck cancer was in the late 1950's.

| Recent failures to develop effective SCCHN treatments | | | |
|---|---|---|---|
| **Manufacturer** | *Drug* | *Trial* | *Outcome* |
| **Pfizer & Merck** | Bavencio | JAVELIN 100 | Terminated March 2020 |
| **AstraZeneca** | Durvalumab | KESTREL | Failed February 2021 |
| **Boehringer Ingelheim** | Afatinib | LUX-Head&Neck 2 | Failed June 2019 |
| **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 |

"There have been limited advances for patients with locally advanced head and neck squamous cell carcinoma, and unfortunately, these results suggest that this disease remains very challenging to treat," said Dr. Eliav Barr, senior vice president, head of global clinical development and chief medical officer, Merck Research Laboratories.

# CEL-SCI Phase 3 Study
# Trial Design &
# Summary Study Results

"Head and neck cancer is possibly the most horrific of all cancers. Not only does it take your life, but it takes your beauty, your voice and your dignity."

— from a discussion with a head and neck oncologist

# We Conducted The Largest and Longest Phase 3 Study in Head and Neck Cancer

1. We enrolled 928 patients in our study in advanced primary head and neck cancer.
2. The study was run in about 100 hospitals in 20 countries on 3 continents at a cost of over $100 m.
3. The study lasted almost 10 years because we had to wait for 298 events (patient deaths) in the 2 main groups. Those patient deaths occurred later than expected since our Multikine significantly improved survival.
4. Our final results showed that our Multikine significantly increased survival, the gold standard for cancer drug approval, in patients who were treated with radiation, but not in patients who were also treated with chemotherapy after surgery.
5. This is the f*irst* ever neoadjuvant treatment (given right after diagnosis and before surgery); a randomized Phase 3 study that showed survival benefit in head and neck cancer.
6. Data was presented at top cancer conferences ASCO, ESMO, and most recently at the European Congress on Head & Neck Oncology (ECHNO) and will be published in leading peer reviewed cancer journals.

ASCO® American Society of Clinical Oncology

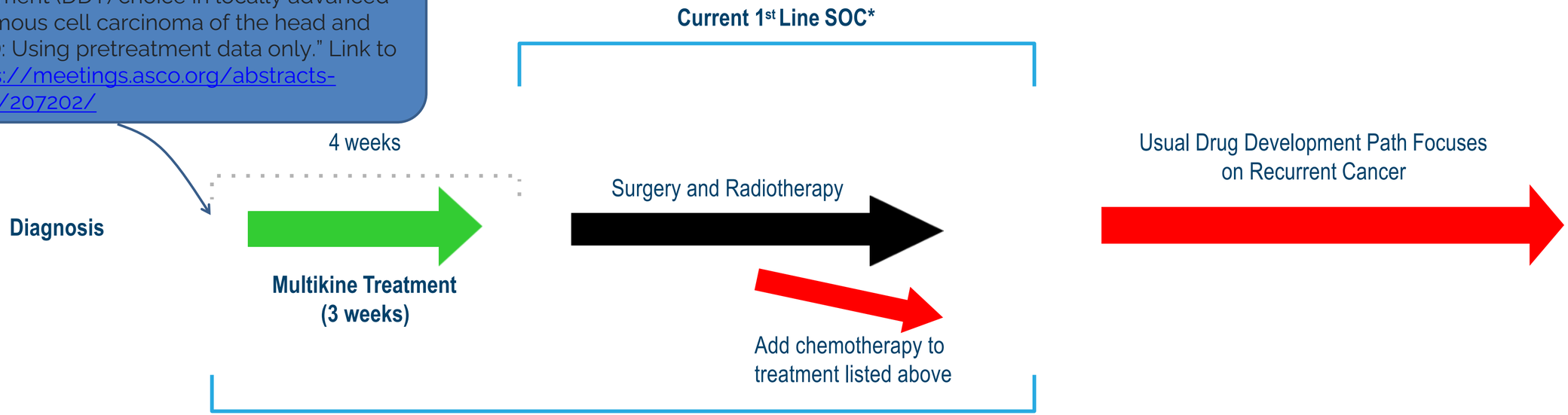
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

EHNS European Head & Neck Society

# Phase 3 Study Design -Timing of Multikine Treatment Regimen

## Advanced Primary Head and Neck Cancer

•"Novel selection process for assigning risk/disease-directed treatment (DDT) choice in locally advanced primary squamous cell carcinoma of the head and neck (SCCHN): Using pretreatment data only." Link to abstract: https://meetings.asco.org/abstracts-presentations/207202/




**Proposed New 1st Line SOC* for patients receiving Surgery and Radiotherapy only (the black line)**
**CEL-SCI has developed a way of selecting patients destined for surgery and radiation before the surgery (ASCO 2022)**

* Standard of Care

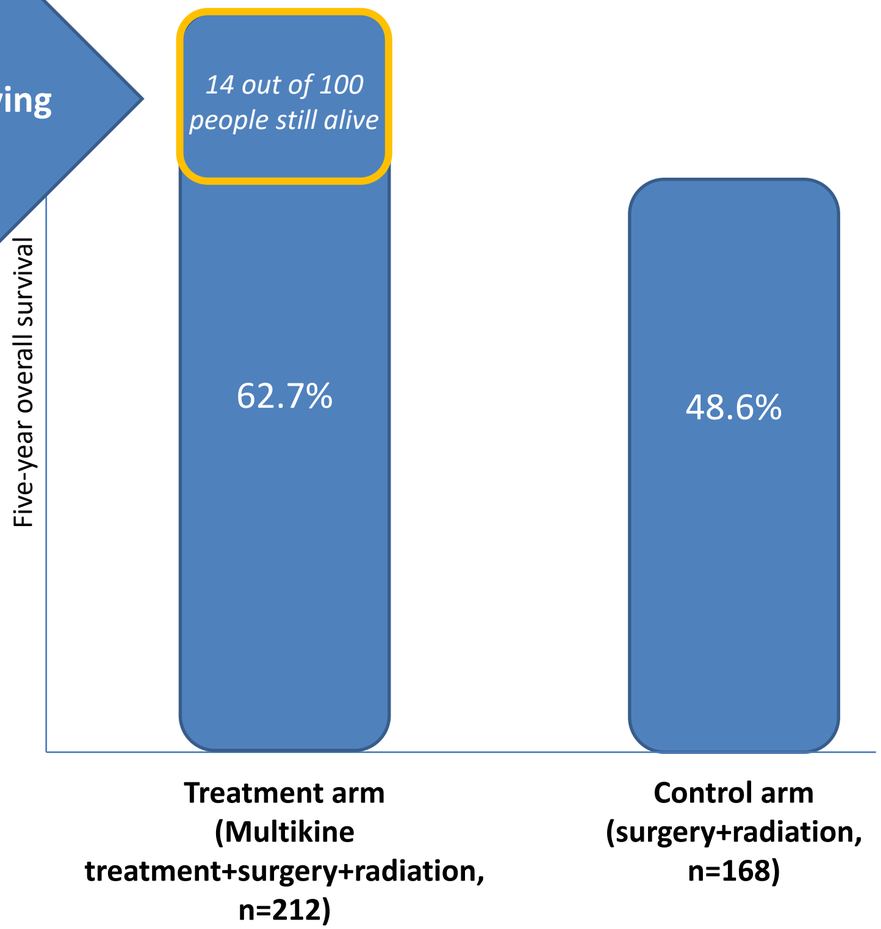
# In the Multikine (MK) + Surgery-plus-radiation treatment arm (n=380, prespecified):

- 14.1% absolute 5-year overall survival benefit
- That means the difference between survival of MK 62.7% and Control 48.6%  at 5 years
- Nearly 4-year median overall survival benefit over Control
- 16.0% of patients saw partial or complete tumor response in the three weeks prior to surgery
- 5 patients had a complete tumor response vs. zero (0) tumor response in control group
- Tumor response → significantly lower death rate
- Histopathology confirmation with 61 markers – benefit to MK over Control
- Confirmatory progression-free survival
- No toxicity was added to the standard of care treatment
- Other very important findings submitted for publication at leading cancer conferences

# Phase 3 Trial Results: Summary Of Very Significant Survival Benefit

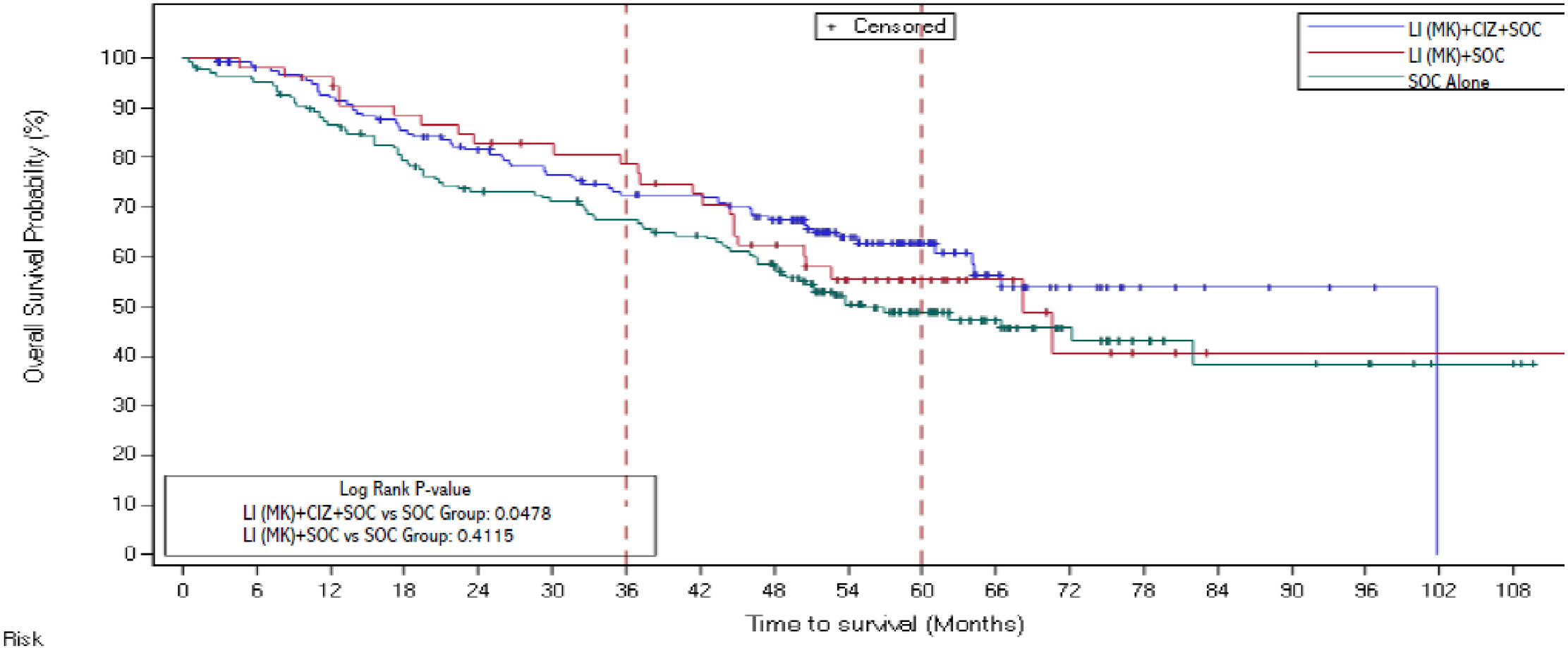
*Ten-year clinical trial of Multikine*
*Five-year overall survival*

**14.1% absolute survival advantage in patients receiving surgery + radiation**



# Overall Survival (OS) of the Study Lower Risk Population (n=380)

Kaplan-Meier (K-M) life tables for the study lower risk population. Group 1 = LI (MK)+CIZ+SOC; Group 2 = LI (MK)+SOC; Group 3 = SOC alone. ULR = Unstratified Logrank, SRL = Stratified Logrank




# at Risk

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| LI (MK)+CIZ+SOC | 158 | 150 | 140 | 129 | 118 | 110 | 102 | 100 | 89 | 61 | 39 | 22 | 13 | 6 | 4 | 3 | 2 | 0 | 0 |
| LI (MK)+SOC | 54 | 53 | 51 | 46 | 43 | 41 | 39 | 35 | 29 | 21 | 14 | 9 | 5 | 3 | 1 | 1 | 1 | 1 | 1 |
| SOC Alone | 168 | 159 | 143 | 129 | 117 | 113 | 106 | 99 | 87 | 61 | 43 | 30 | 18 | 12 | 8 | 8 | 7 | 3 | 2 |

# Overall Survival ITT Lower Risk Entry -> Exit: % Alive 36, 48 and 60 Months (n=380)

| | | Treatment Group | | | Delta |
|---|---|---|---|---|---|
| Population | Milestone | LI (MK)+CIZ+SOC (’1’) | LI (MK)+SOC (‘2’) | SOC (‘3’) | ‘1’ vs ‘3’ |
| ITT (99.5%) | 36 months | 72.4% (64.4%, 78.9%) | 78.8% (65.0%, 87.7%) | 67.5% (59.7%, 74.1%) | 4.9% |
| ITT (99.5%) | 48 months | 67.3% (59.0%, 74.3%) | 62.3% (47.4%, 74.1%) | 57.8% (49.7%, 65.0%) | 9.5% |
| ITT (99.5%) | 60 months | 62.7% (54.0%, 70.2%) | 55.5% (40.5%, 68.2%) | 48.6% (40.4%, 56.4%) | 14.1% |
| **Improving Overall Survival Advantage Over Time** | | | | | |

# Early Tumor Response Rates: Overall and NCCN Risk-based

- Among all 923 subjects and within lower/higher/missing risk populations:

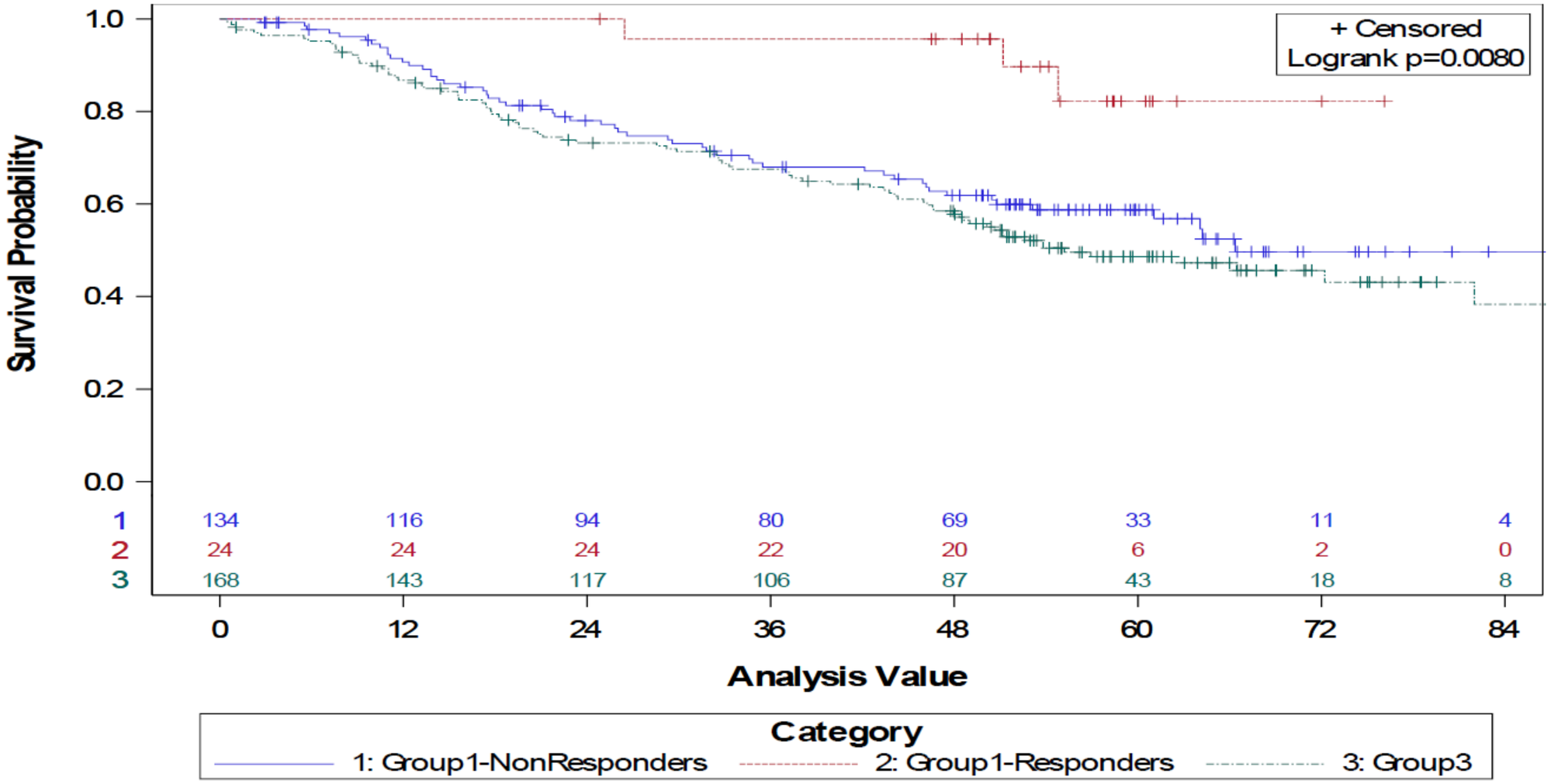
| Metric | LI (MK)+CIZ+SOC (n=395) | LI (MK)+SOC (n=134) | Combined LI (MK) (n=529) | SOC (n=394) |
|---|---|---|---|---|
| Overall ITT | 8.1% (32/395) | 9.7% (13/134) | **8.5% (45/529)** | **0% (0/394)** |
| Lower Risk | 15.2% (24/158) | 18.5% (10/54) | **16.0% (34/212)** | **0% (0/168)** |
| Higher Risk | 3.5% (7/200) | 4.3% (3/69) | **3.7% (10/269)** | **0% (0/198)** |
| Missing Risk | 2.7% (1/37) | 0% (0/11) | **2.1% (1/48)** | **0% (0/28)** |

# Overall Survival: ITT Population

## Surgery plus radiotherapy (LR) (N= 380) Responders vs Non-Responders vs SOC

LOG RANK: LR-RESPONDERS VS LR-NON-RESPONDERS, P=0.0104; LR-RESPONDERS VS LR-SOC, P=0.002; LR-NON-RESPONDERS VS LR-SOC, P=0.2853

- **Early response is prognostic with a carryover effect observed for non-responders**



# 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<br>vs<br>54.1% (262/484) Early non-Responders<br>2-Sided Fisher Exact p-Value [**p<0.0001**] | **HR=0.301**<br>[0.16, 0.566] |
| Combined Lower Risk LI (MK) treated (n=212) | 34/212 (**16.0%**) | 17.6% (6/34) Early Responders<br>vs<br>42.7% (76/178) Early non-Responders<br>2-Sided Fisher Exact p-Value [**p=0.0067**] | **HR=0.348**<br>[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<br>vs<br>41.0% (55/134) Early non-Responders<br>2-Sided Fisher Exact p-Value [**p=0.0101**] | **HR=0.246**<br>[0.077, 0.787] |

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

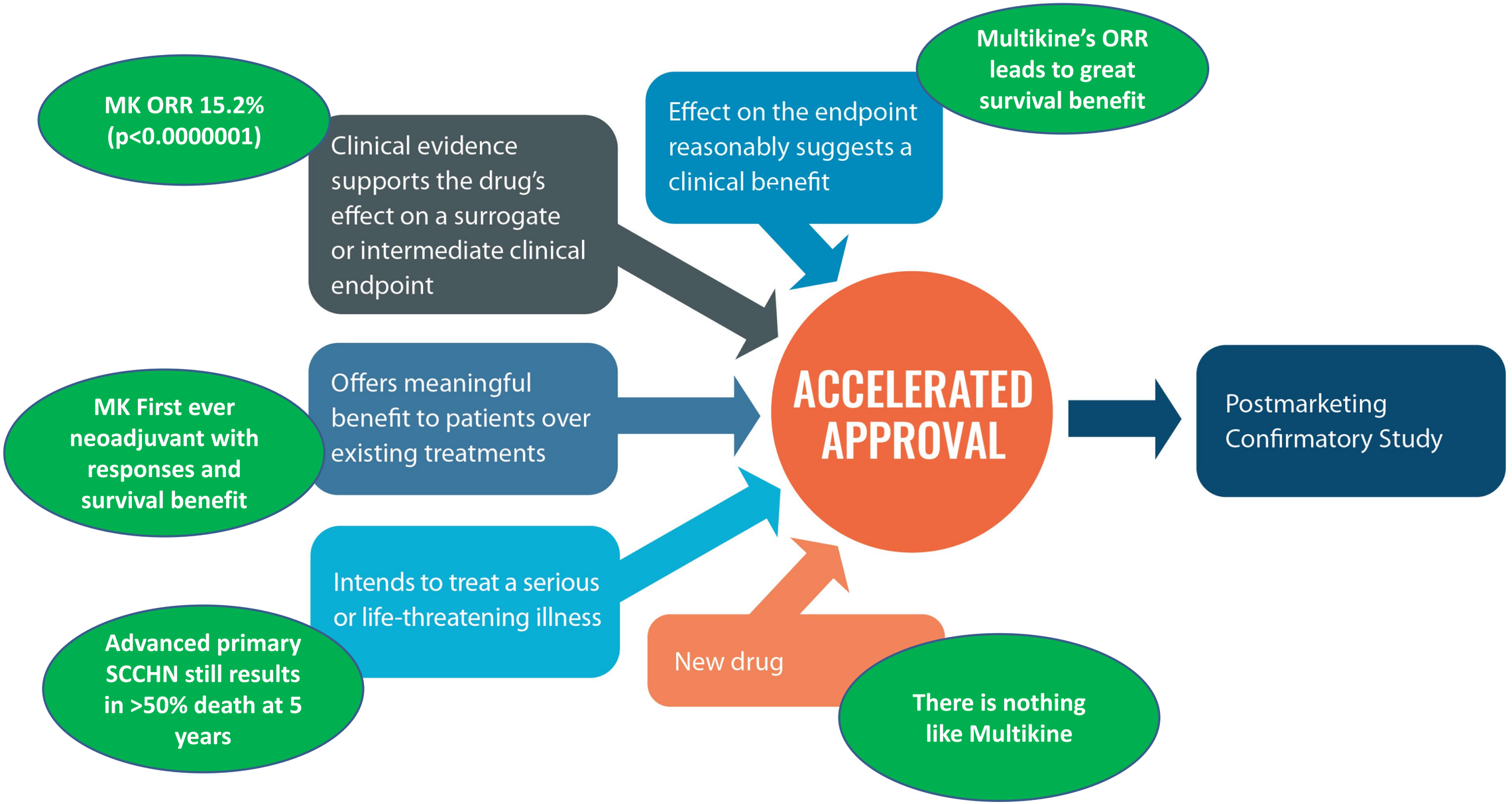
# Early Response Conclusions

- Early response was prognostic and predictive of survival in early response subjects irrespective of their risk group.
- For the lower risk MK+CIZ+SOC group, early responders had 306% survival prolongation for 15.2% in this treatment group.
- Overall early responders had 46.5% survival prolongation (3.06x15.2%); if no other survival contribution from then remaining.
- This corresponds to a 0.68 HR (1/1.465), which is exactly what was observed for the total ITT MK+CIZ+SOC group with lower risk classification (n=158).[22]
- The significant 0.68 HR for ITT MK+CIZ+SOC vs. SOC equates to a 47% survival prolongation.
- Characterized by a 5-year 14.1% absolute OS advantage, and a 46.5-month median OS advantage over surgery plus radiotherapy SOC alone (control).
- Thus, a MK early tumor response is not only prognostic, but also predicts a favorable survival outcome.

# Who is Working with us on the FDA Application, other than our Own Team?

1. **We have retained the services of two leading CROs to help:  ICON and Ergomed**
2. **Phil Lavin, our statistician, has a team of experts working with us:**
   - Dr. Lavin is a well-known biostatistician with a long history supporting clinical trials
   - 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
   - Co-founded Boston Biostatistics which became Aptiv Solutions before it was acquired by ICON plc
   - Authored or co-authored over 180 peer-reviewed publications in the medical and statistical literature
   - Innovated a new study design used widely for medical devices (quasi-non-inferiority design)
   - 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
   - Served as the Lead Biostatistician for >80 original FDA approvals to date
3. **A former FDA Associate Commissioner and congressional insider experienced in strategically resolving regulatory and legislative issues**
4. **A former FDA legal counsel**
5. **A former FDA clinical reviewer**
6. **Key Opinion Leaders US/International (KOLs) in H&N cancer**

# Steps In The Process For FDA Approval



# Multikine Compares Favorably

| | Multikine Compares Favorably To Two FDA-Approved Drugs (Keytruda and Opdivo) SCCHN | | |
|---|---|---|---|
| | **Multikine** | **Keytruda** | **Opdivo** |
| **Indication** | Newly-diagnosed patients before surgery and radiation | Recurrent or metastatic tumors following the SOC | Recurrent or metastatic tumors following the SOC |
| **Stage of treatment** | First line | Late stage | Late stage |
| **Objective response rate** | 15.2% | 16% | 13.3% |
| **Time to response** | 3 weeks | 3.6 months | 2.1 months |
| **Overall survival benefit** | 46 months | None | 2.4 months |
| **Toxicity** | No toxicity | High toxicity | High toxicity |
| **Marker** | None | PD-L1 | PD-L1 |
| **Study population** | 380 | 174-550 | 361 |
| **FDA pathway** | In process | Accelerated approval | Standard approval |

# State-of-the-Art Facility & Proprietary Manufacturing Process: Potential Barriers to Competition

## cGMP and BSL-1 facility near Washington, DC, USA

- Built specifically for Multikine
- State-of-the art facility
- Over 73,000 $ft^2$ of Manufacturing and R&D space available
- About 45,000 $ft^2$ fully developed
- Proprietary automated cold fill to ensure no loss of biological activity during fill

Well over $100 million spent. Facility was built before the Phase 3 trial started and the capacity was recently doubled in preparation for commercialization.

## Inspected several times by European Qualified Person (QP)

- Inspected by the QP for the manufacture and release of Sterile Medicinal Products (per ICH and EU Directives)

## Significant “know how” developed to manufacture Multikine – Method of Manufacture

- Trade-secret

# Extremely Important for Approval

- No significant safety signals.
- Multikine did not delay surgery or subsequent disease directed therapy.
- We have developed a way to determine the lower risk for recurrence patient population at screening/entry BEFORE surgery.  The information was presented at ASCO in 2022 but has been further refined since. This means that we have the ability to select the patients who will have the greatest benefit from Multikine neoadjuvant treatment.
- Multikine reduced death rate.
- Five year survival benefit.
- Tumor response predicts survival.
- Confirmation of response by histopathology.

# Equity Summary

| | |
|---|---|
| CEL-SCI Corporation | NYSE American: CVM |
| Clinical Trial Stage | Completed Phase 3 cancer immunotherapy study |
| Market Capitalization | ~$123 million |
| Trading Volume | ~ 0.25 million shares per day |
| Shares Outstanding | ~ 43.7 million shares |
| Share Price | ~ $2.83 |
| Cash on Hand | $18 million, per the last quarterly filing |

CEL-SCI
Empowering Immune Defenses

**CEL-SCI Corporation**

**Geert Kersten**
Chief Executive
Officer

8229 Boone Boulevard, Suite 802
Vienna, VA 22182, USA
-
Phone: **(703) 506-9460**

NYSE American: **CVM**