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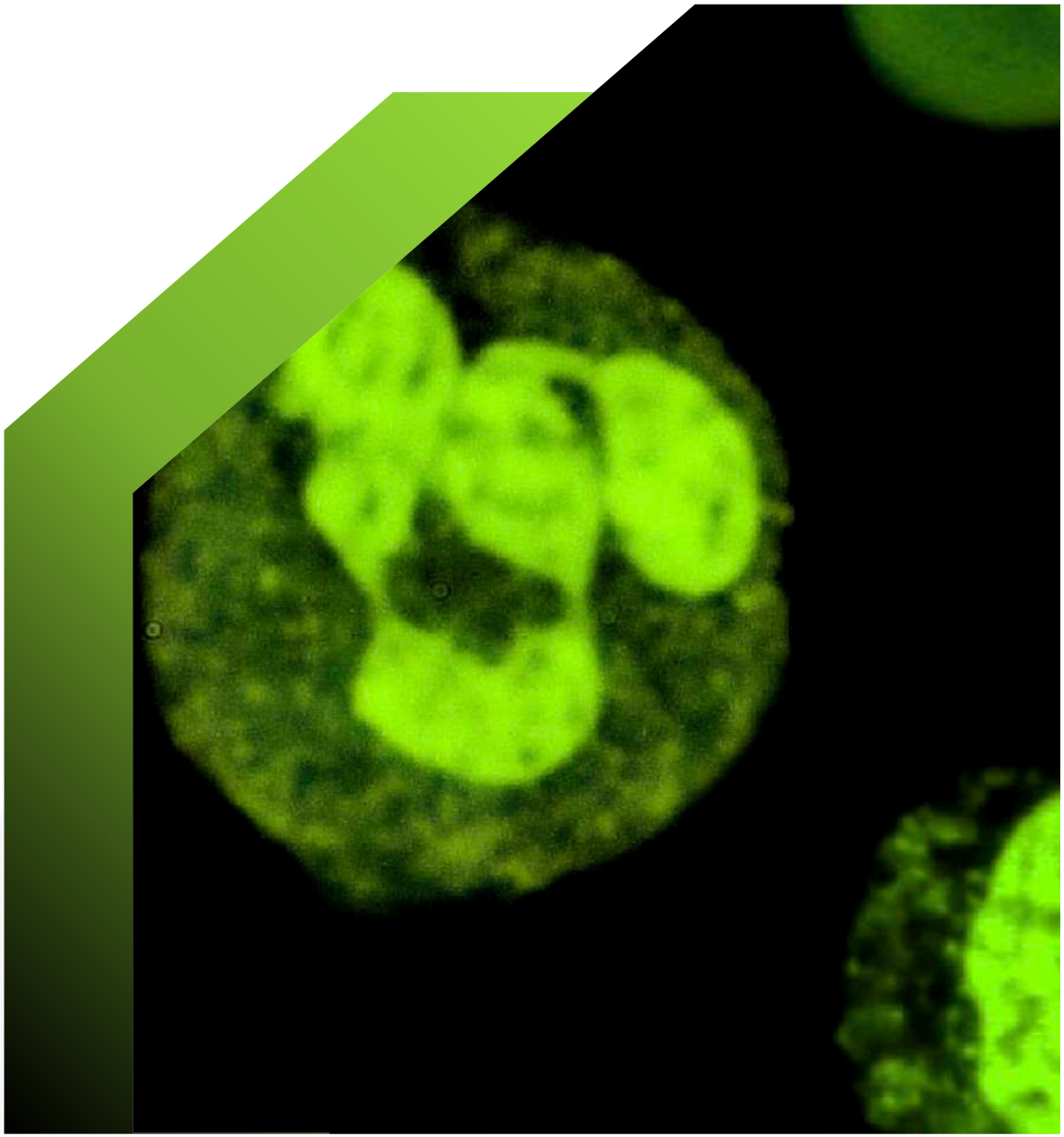
**Off-the-shelf, universal, macrophage reprogramming cell therapies for life-threatening diseases**



NASDAQ Ticker: ENLV

# Forward-Looking Statements

These slides and the accompanying oral presentation contain forward-looking statements and information. Forward-looking statements are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry's actual results, levels or activity, performance or achievements to be materially different from those anticipated by such statements. The use of words such as "may", "might", "will", "should", "could", "expect", "plan", "anticipate", "believe", "estimate", "project", "intend", "future", "potential" or "continue", and other similar expressions are intended to identify forward looking statements. For example, all statements we make regarding (i) the initiation, timing, cost, progress and results of our preclinical and clinical studies and our research and development programs, (ii) our ability to advance product candidates into, and successfully complete, clinical studies, (iii) the timing or likelihood of regulatory filings and approvals, (iv) our ability to develop, manufacture and commercialize our product candidates and to improve the manufacturing process, (v) the rate and degree of market acceptance of our product candidates, (vi) the size and growth potential of the markets for our product candidates and our ability to serve those markets, and (vii) our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates, are forward looking. All forward-looking statements are based on current estimates, assumptions and expectations by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. Any forward-looking statement speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law. This presentation is not, and nothing in it should be construed as, an offer, invitation or recommendation in respect of our securities, or an offer, invitation or recommendation to sell, or a solicitation of an offer to buy, any of our securities in any jurisdiction. Neither this presentation nor anything in it shall form the basis of any contract or commitment.

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immune rebalancing

## Enlivex: next-generation cell therapies

**PAST**

- Autologous
- Not scalable
- High COGS

- Engineered T-cells

**FUTURE**

- Off-the-shelf
- Scalable
- Low COGS

**&**

- New cell modalities
  - NKs
  - RBCs
  - Macrophages

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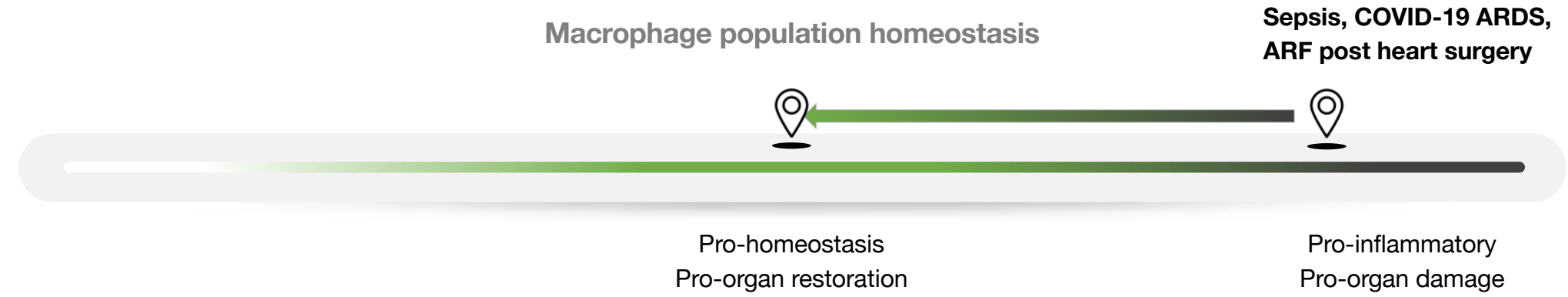
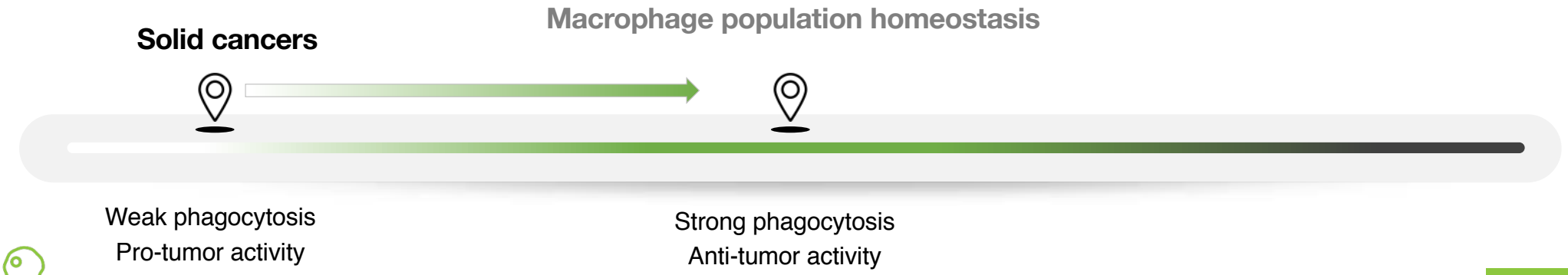
# Macrophage homeostasis implies proper function for its specific tissue, environment and challenge

## Reprogramming imbalanced macrophage populations can lead to disease resolution

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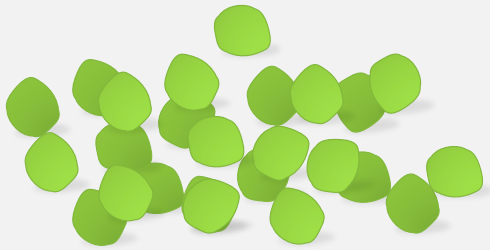
# Allocetra™ Mechanism of Action

## Restoring immune homeostasis through reprogramming of macrophages

# Allocetra™ for macrophage reprogramming

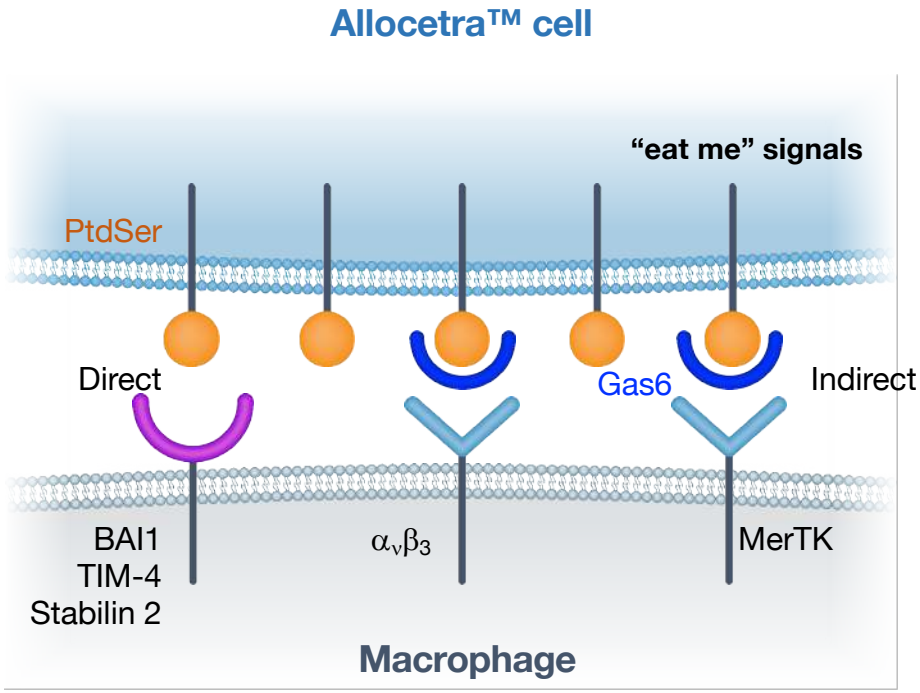
## Proprietary, universal, off-the-shelf, macrophage-reprogramming cells

### Allocetra™ characteristics



- Mononuclear cells collected from healthy donors
- Modified through a proprietary process to:
  - Express PtdSer (“eat me” signal) on their surface
    - Enabling engulfment into macrophages via binding to BAI, TIM4, and stabilin 2, annexin V
  - Yet maintain their membrane in-tact
- Universal, off-the-shelf

### Allocetra™ delivery into macrophages via engulfment

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# Allocetra™ for macrophage reprogramming

## Pipeline of reprogrammable macrophage-modulated indications

| Indication | Global Market Size | Pre-Clinical | Phase Ib | Phase IIb | Support for EU Conditional Marketing Approval Submission | Post EU Marketing US Phase 3 |
|---|---|---|---|---|---|---|
| **Organ failure associated with Sepsis** | $33B | | Completed | Phase II Initiated Q1 2021 | Completion of Phase II Q3 2023 | |
| **Advanced-stage solid tumors with peritoneal metastases, in combination with chemotherapy** | $4B | | Phase Ib Q2 2022 | | | |
| **Advanced-stage solid tumors with peritoneal metastases, stand-alone + in combination with anti-PD1** | $4B | | Phase I/II Q3 2022 | | | |

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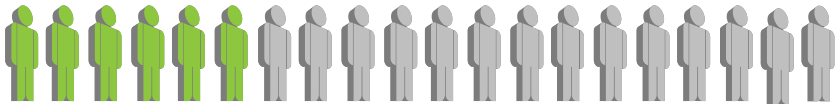
# Allocetra™

## Reprogramming macrophages responsible for organ failure in sepsis

# Sepsis is the 3rd leading cause of death in the U.S. – $33B target market*

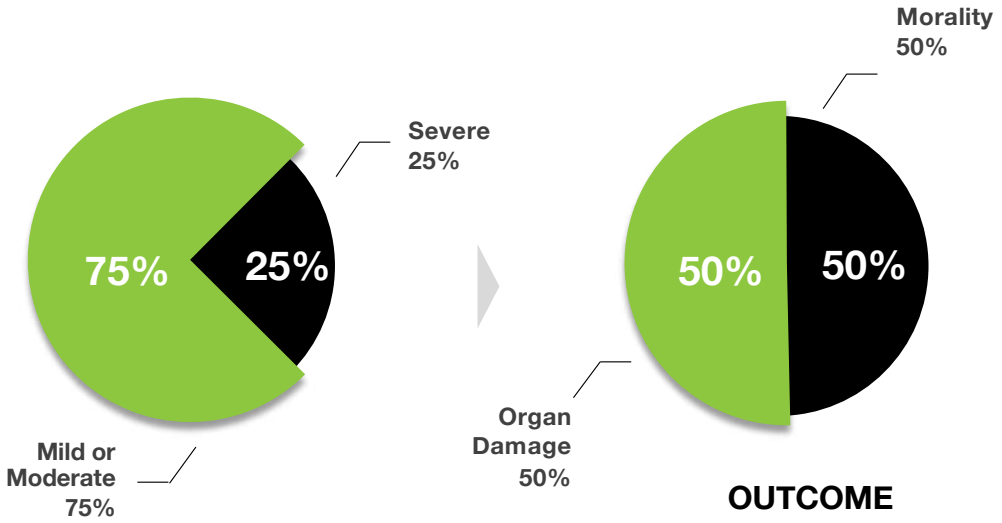
## There are currently no FDA approved drugs for the treatment of sepsis



Each year, at least **1.7 million** adults in America develop sepsis. Nearly **270,000** Americans die as a result of sepsis each year.

**1 in 3** One in three patients who die in a hospital have sepsis.

### SEPSIS CATEGORIES




**$50,000 x 675,000 Patients PA (global) = $33B Total Addressable Market**

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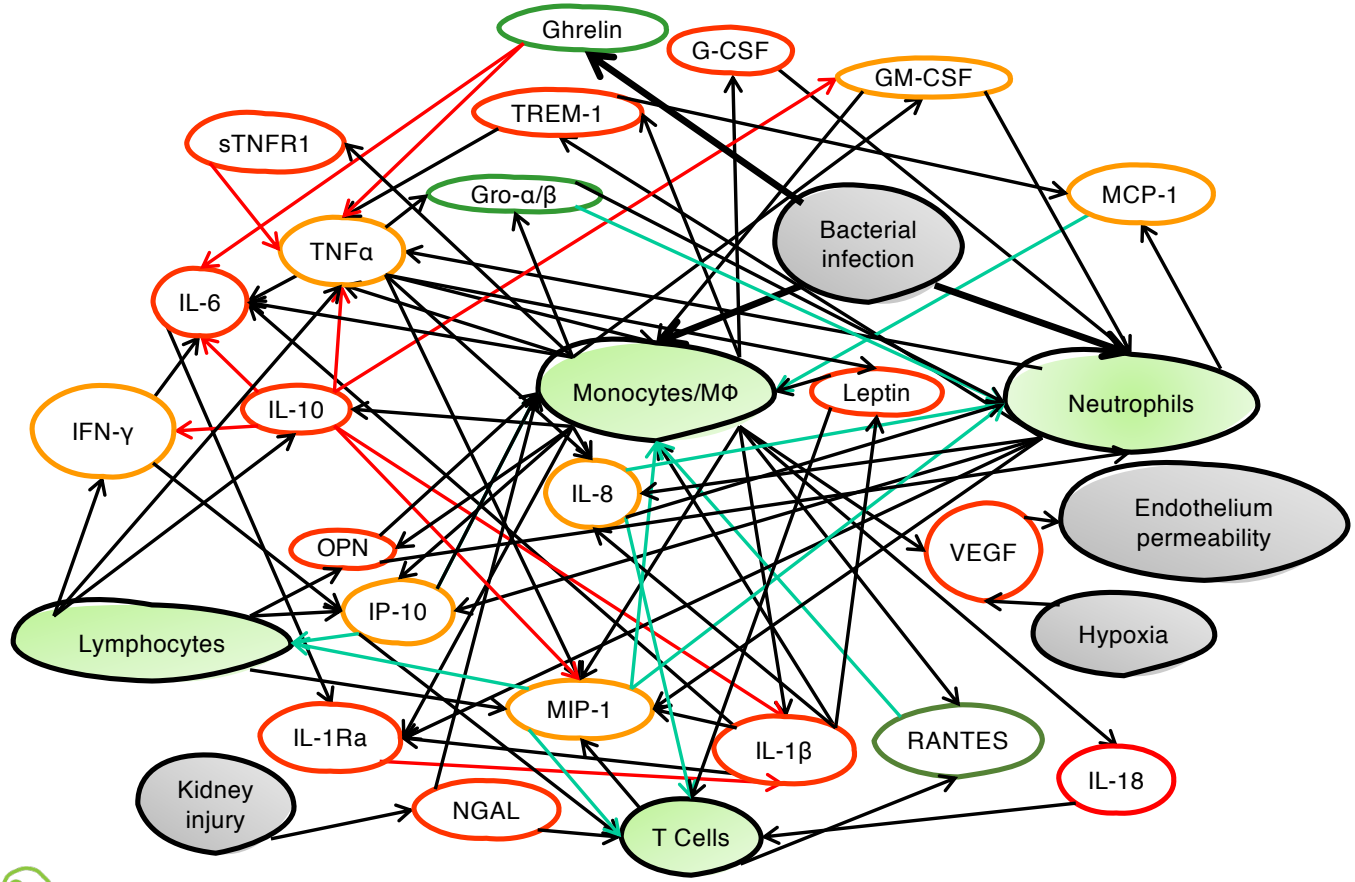
* U.S. & EU

# Cytokine/Chemokine network in sepsis: the impossible task of resolving sepsis with inhibition of a certain cytokine or signaling pathway




MΦ: Macrophages

- Activation
- Inhibition
- Chemotaxis
- Downregulated in most of the patients
- Downregulated in 50% of the patients
- Upregulated in most patients

**Macrophage reprogramming to "manufacturer settings" is required to obtain sepsis resolution**

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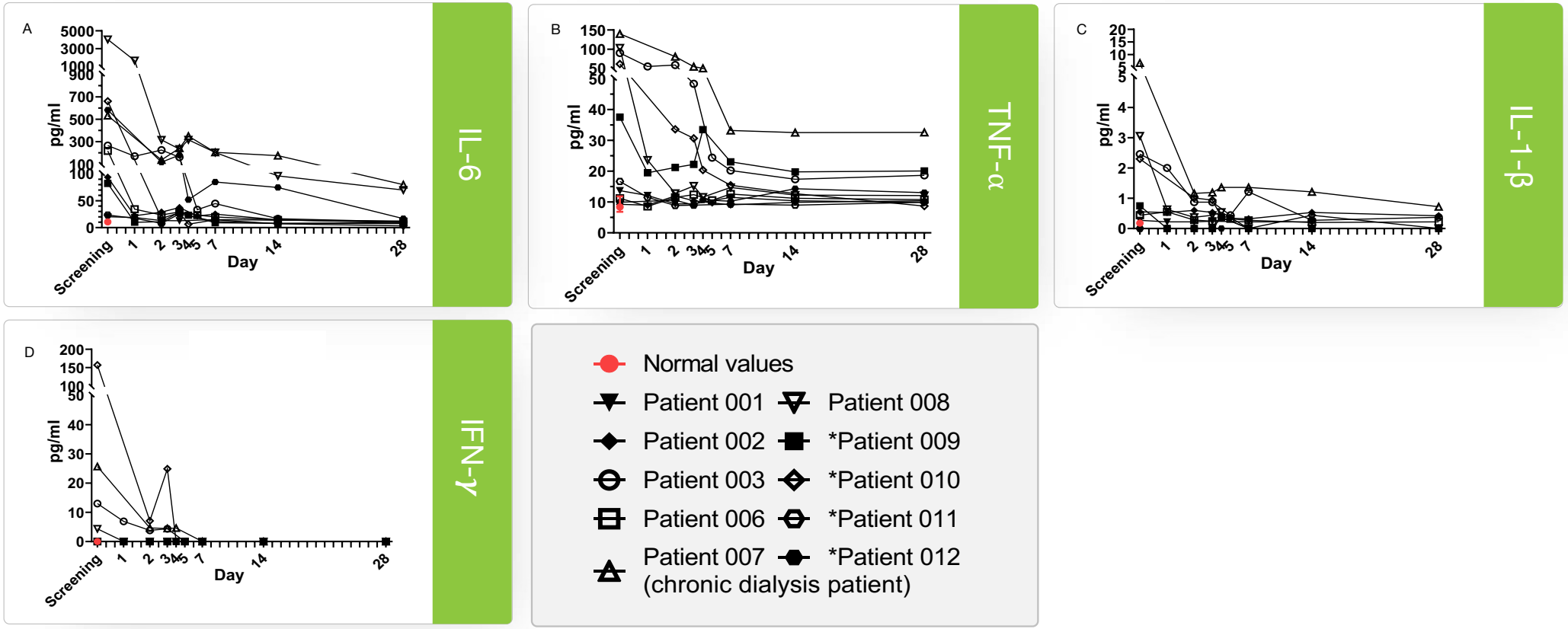
# Allocetra™

## Phase Ib clinical trial of macrophage reprogramming in sepsis patients

# Reprogrammed macrophages in sepsis patients return to homeostatic state (1)

## Phase Ib clinical trial data, change from screening, pro-inflammatory cytokines

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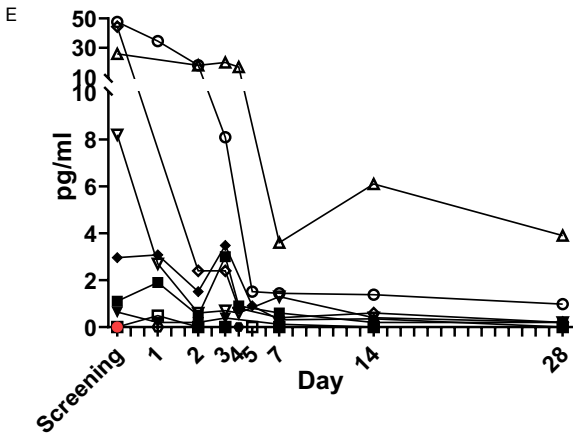
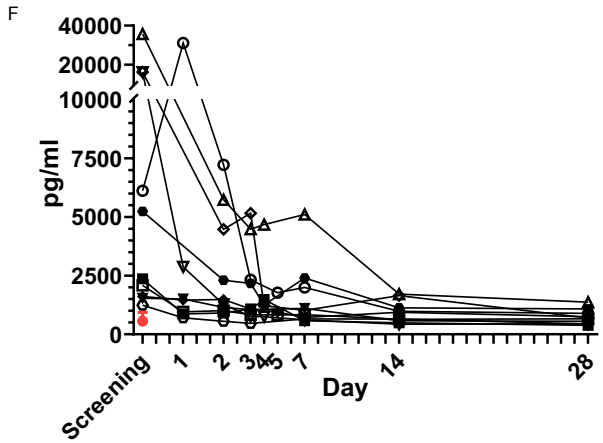
# Reprogrammed macrophages in sepsis patients return to homeostatic state (2)

## Phase Ib clinical trial data, change from screening, anti-inflammatory cytokines

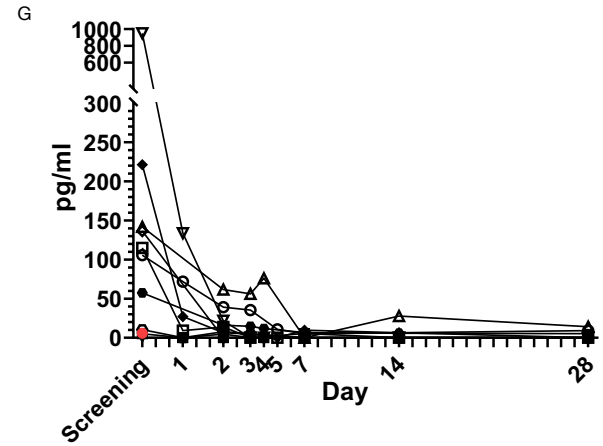
### IL-10

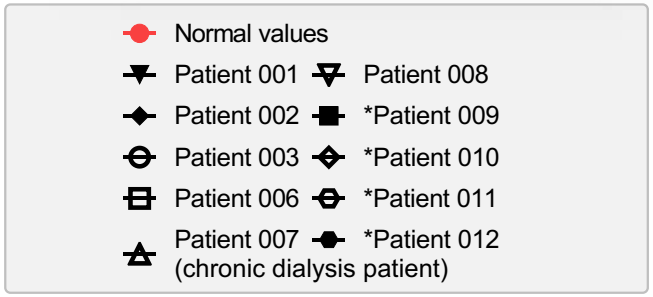



### IL-1Rα




### G-CSF

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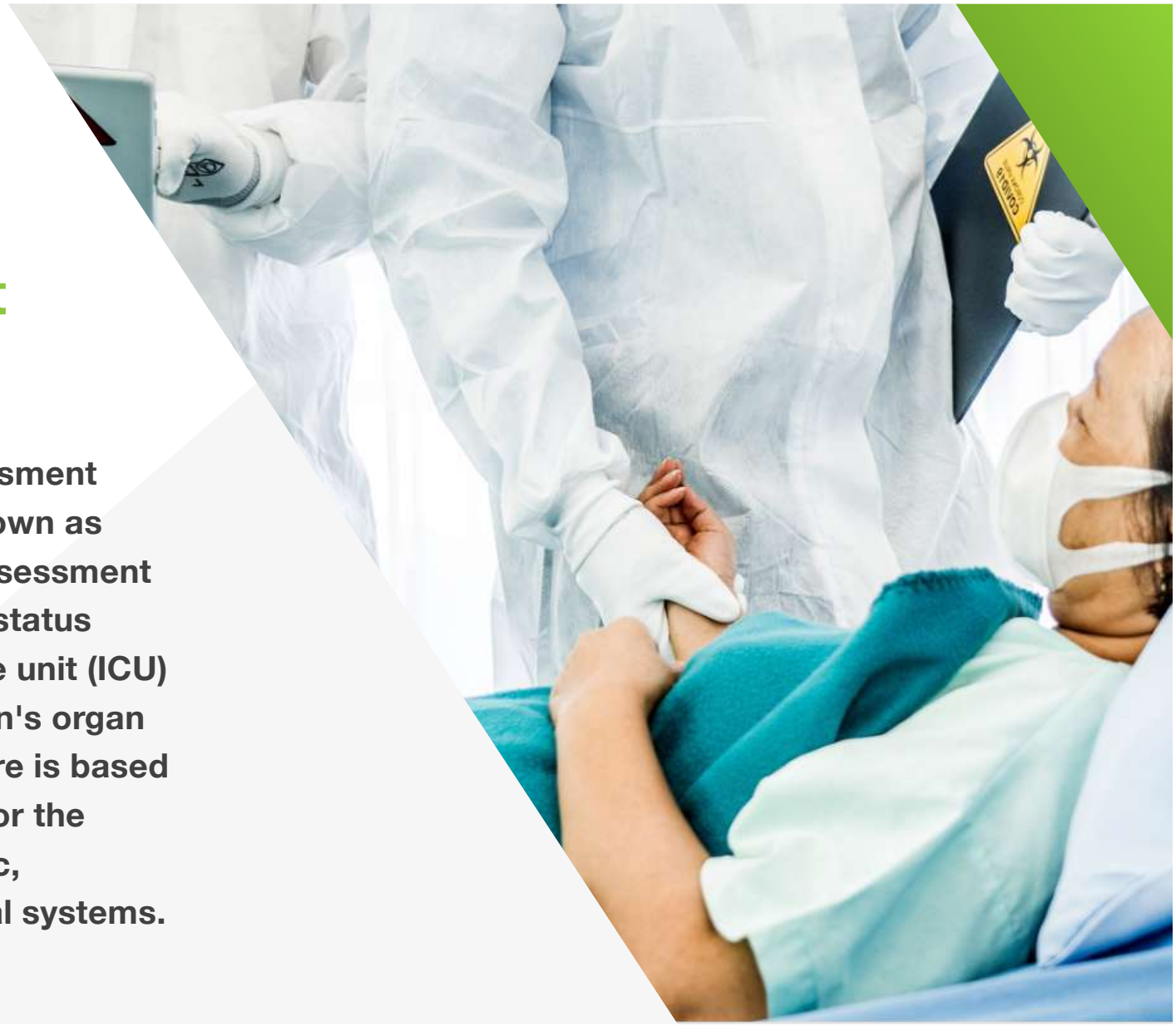
# Sequential Organ Failure Assessment (SOFA) Score

**The sequential organ failure assessment score (SOFA score), previously known as the sepsis-related organ failure assessment score, is used to track a person's status during the stay in an intensive care unit (ICU) to determine the extent of a person's organ function or rate of failure. The score is based on six different scores, one each for the respiratory, cardiovascular, hepatic, coagulation, renal and neurological systems.**



# High degree of matching: treated vs controls

| | Treated (n=10) | Matched Controls (n=37) |
|---|---|---|
| Average age | 71.5 (51-83) | 71.25 (50-83) |
| Male/female | 80/20 | 80/20 |
| Average diagnosis SOFA | 3.4 (2-6) | 3.47 (2-7) |
| Average diagnosis Apache II score | 12.3 (8-21) | 14.25 (5-24) |

| Sepsis source | | |
|---|---|---|
| Pneumonia | 50% | 53% |
| Biliary infections | 30% | 25% |
| Endovascular | 10% | 8.3% |
| UTI | 10% | 14% |

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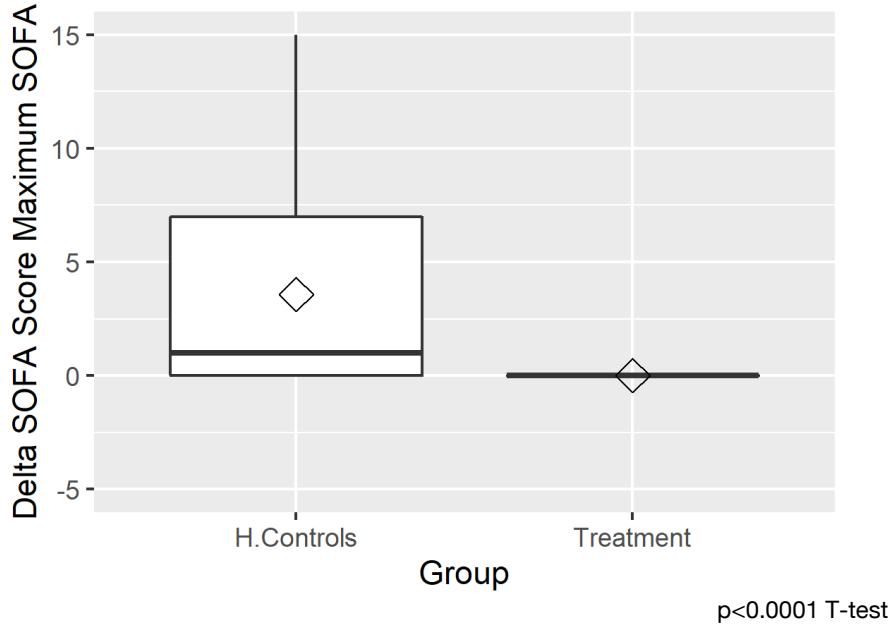
# Allocetra™ macrophage reprogramming leads to improved outcomes for sepsis patients

## Alive and organs recovered on day 28: 100% vs 41%

**Maximal change in SOFA score, diagnosis to day 28**




| | | # | | |
|---|---|---|---|---|
| Total Patients | Controls | 37 | | |
| | Treated | 10 | | |
| Day 28 | | # | % | |
| Died | Controls | 10 | 27% | – |
| | Treated | 0 | 0 | – |
| Alive | | | | |
| Recovery Prospects | Day 28 of SOFA delta vs pre-sepsis baseline | Day 28 alive by category | | Avg. SOFA delta |
| | | # | % | |
| Good | 0-1 | 15 | 41% | 0.6 |
| | | 10 | 100% | 0.1 |
| Fair | 2 | 4 | 11% | 2 |
| | | 0 | 0% | – |
| Poor | ≥3 | 8 | 22% | 5 |
| | | 0 | 0% | – |

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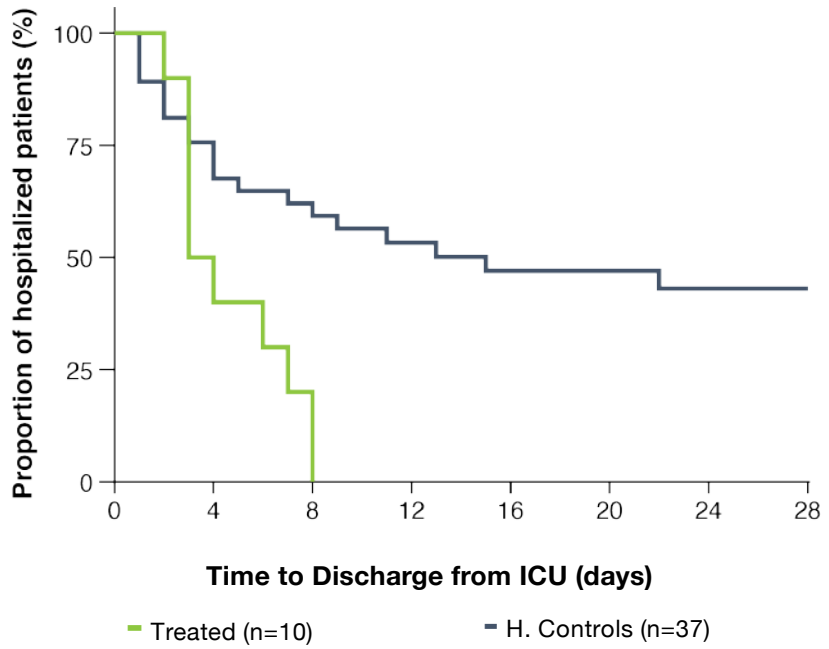
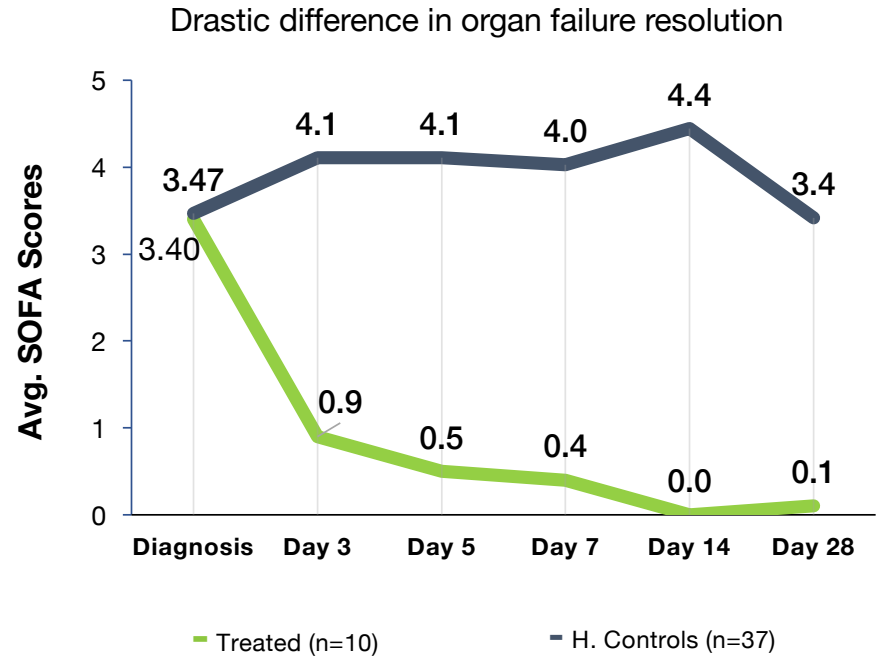
# Allocetra™ macrophage reprogramming leads to improved outcomes for sepsis patients

## Statistically significant improvement in hospitalization and SOFA vs. matched controls

### Time to ICU discharge




### Average SOFA score during 28 days

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# Clinical summary of macrophage reprogramming in sepsis Phase Ib: complete recovery from any organ failure for all 10 patients and 100% 28-day survival

## Sepsis clinical characteristics and organ recovery

| | |
|---|---|
| **Organ Dysfunction** | Each patient had at least 2 organ dysfunctions, maximum of 5 |
| **Kidney** | 3/9 patients (33%) had new-onset acute kidney injury, all have completely recovered to baseline kidney function |
| **Lungs** | 5/10 (50%) of patients had lung involvement, no patient required mechanical ventilation, all patients recovered to normal saturation and no oxygen supplement upon discharge |
| **Cardiovascular** | 3/10 (30%) of patients had mean arterial pressure <70 but none needed vasopressors |
| **Hematological** | 8/10 patients (80%) had significant thrombocytopenia, with complete recovery in all. |
| **Liver** | 4/10 patients (40%, of which 3 had biliary tract infection) had hyperbilirubinemia, with complete recovery in all.<br>5/10 patients had elevated liver enzymes (AST ALT) >3 above normal range, with complete recovery in all. |

# Sepsis

## Allocetra™ macrophage reprogramming Phase IIb clinical plan

| | Sepsis Phase IIb |
|---|---|
| **Addressable global market** | $33 Billion market (severe Sepsis only) |
| **Type** | Controlled, randomized, multi-center (10 centers) |
| **Patients** | 80-160, SOFA < 10, Source: pneumonia, biliary, urinal tract, and peritoneal infections |
| **Duration** | 28 days / patient |
| **Recruitment** | 12 Months |
| **End-points** | Safety, Change in SOFA score |
| **Secondary** | Mortality |
| **First patient dosed** | Q2/2021 |

- **COVID-19 BUSINESS OPPORTUNITY IS DE-PRIORITIZED**
- **CLINICAL DATA PROVIDED TO DEMONSTRATE SAFETY AND EFFECT IN ANOTHER INFECTIOUS DISEASE INDICATIONS**

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## Allocetra™

**Phase Ib & II Clinical Trials in COVID-19 Patients in Severe or Critical Condition**

## Despite strong clinical results, COVID-19 business opportunity is de-prioritized

- Primary reasons:
  - Availability of therapeutics for mild/moderate patients
  - Dominance of Omicron variants, who seem to cause less severe disease in most patients
  - Regulators “step-back” and reluctance to provide emergency use authorizations, requirements for large Phase IIIs

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Patient classification as defined by the NIH classification guide

# Allocetra™: Positive Phase Ib and top line Phase II results in COVID-19

| Clinical Trial | # Patients enrolled | Disease Severity | Clinical Outcome | | Hospitalization Post Administration of Allocetra™ | |
|---|---|---|---|---|---|---|
| | | | Recovered Day 28 | Mortality Day 28 | Discharged Day 28 | Duration (days, avg.) |
| **Phase Ib** | 5 | 2 Severe, 3 Critical | 5/5 (100%) | 0/5 (0%) | 5/5 (100%) | 6.6 |
| **Phase II** | 16 | 9 Severe, 7 Critical | 14/16 (87.5%) | 0/16 (0%) | 14/16 (87.5%) | 5.3 |
| **Total** | 21 | 11 Severe, 10 Critical | 19/21 (90.5%) | 0/21 (0%) | 19/21 (90.5%) | 5.6 |

- 0/21 (0%) mortality on day-28
- 19/21 (90.5%) patients recovered and were discharged from the hospital by day-28
- Average duration of hospitalization post administration of Allocetra™ for discharged patients was 5.6 days
- 2/21 (9.5%) patients, both of whom had critical illness at the time of Allocetra™ treatment, were hospitalized in the ICU on a respirator on day-28

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Patient classification as defined by the NIH classification guide

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# Allocetra™

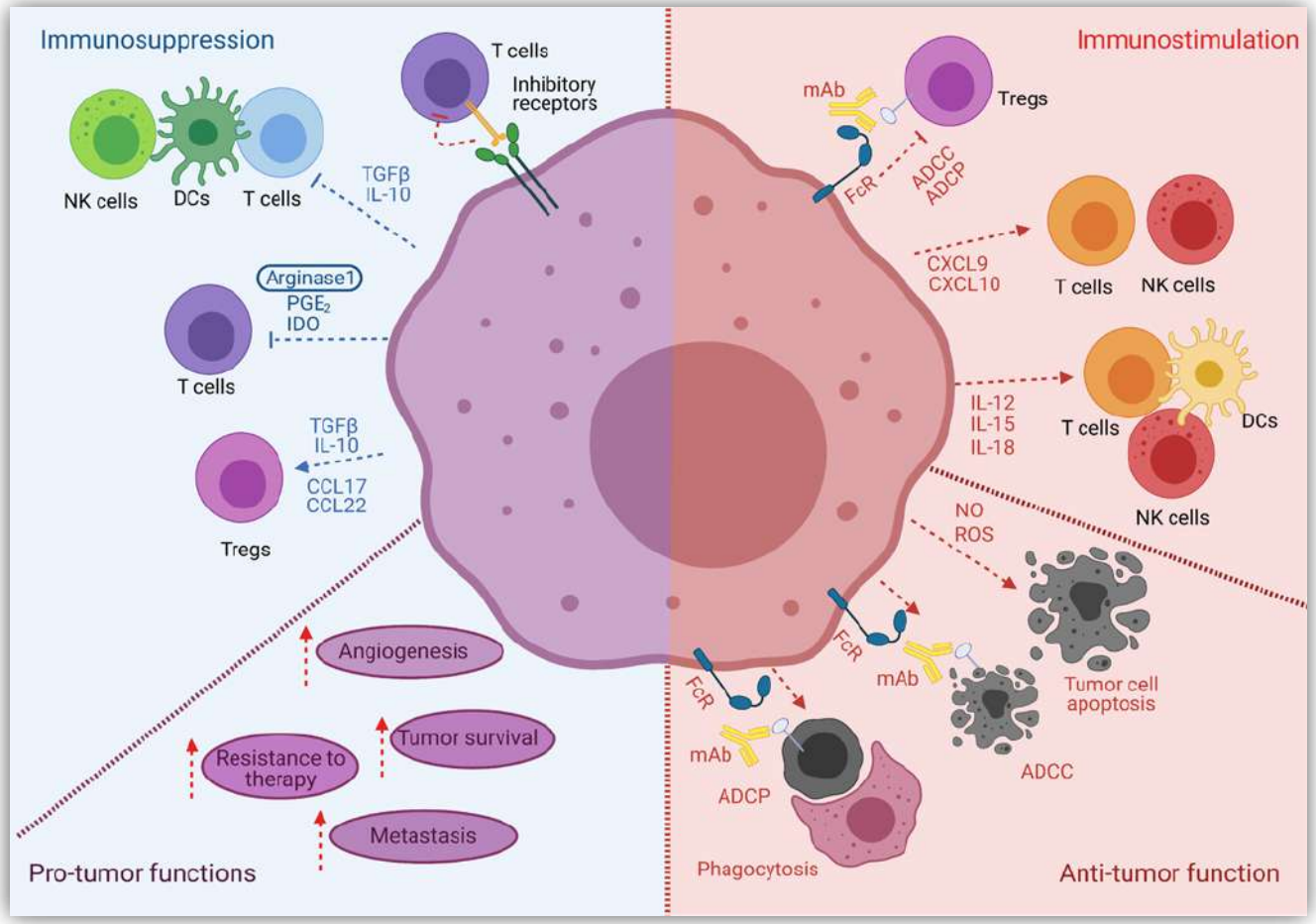
## Macrophage reprogramming in solid tumor microenvironment

## Unique & differentiated value proposition

# Tumor-associated macrophages: pro-tumor, immunosuppressive activities

Immunosuppressive functions[1]
- inhibit T cell, DC and NK cell activation
- suppress anti-tumor T cell functions through inhibitory

Direct pro-tumor functions
- Promote resistance to therapy, angiogenesis, tumor cell survival and metastasization

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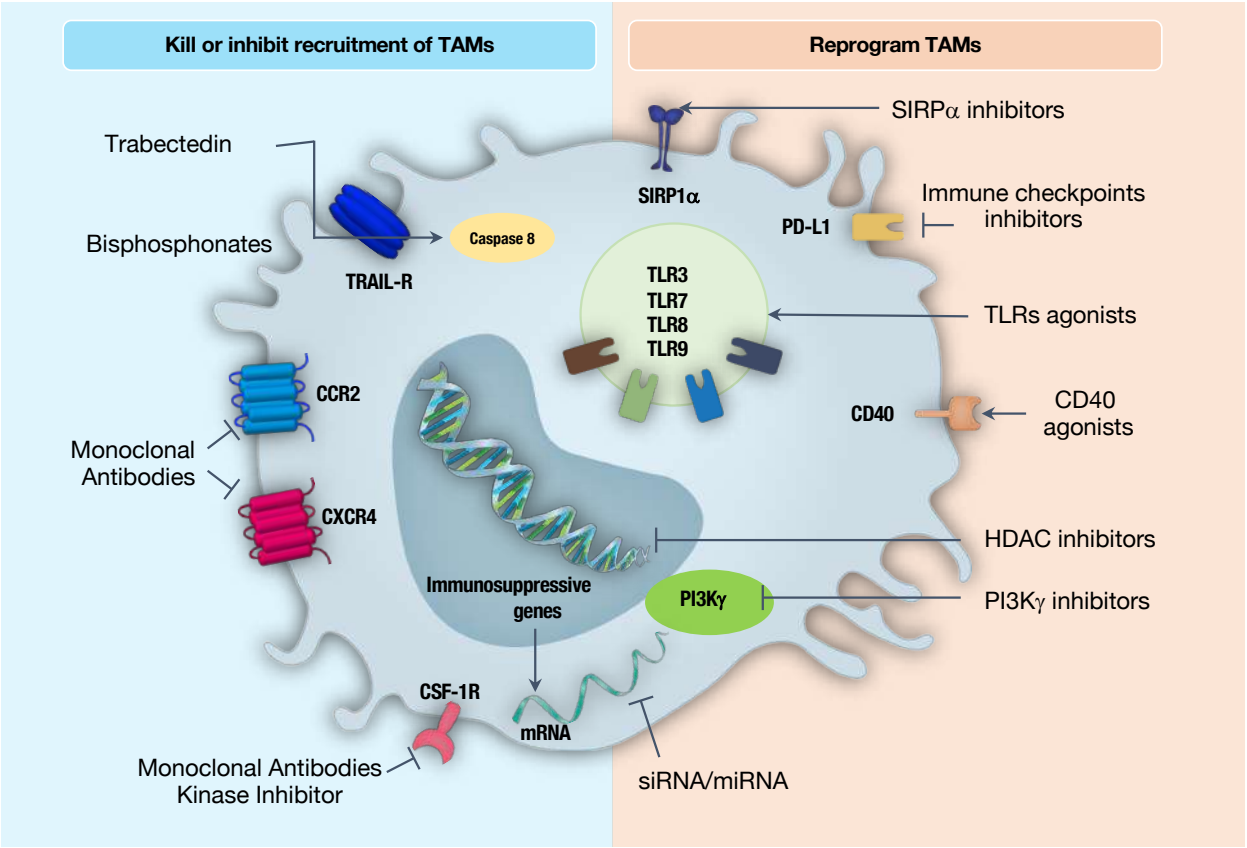
[1] Turning enemies into allies-reprogramming tumor-associated macrophages for cancer therapy, Molgora et al., Med (N Y). 2021 June 11;

# Effective solid cancer therapy requires changes to macrophages in the TME

## Multiple strategies to kill or reprogram non-homeostatic, pro-tumor macrophages (TAMs)[1]




[1] Adapted from Current Strategies to Target Tumor-Associated-Macrophages to Improve Anti-Tumor Immune Responses, Anfray et al., Cells 2020, 9, 46

# The Enlivex differentiation: Balance of resident macrophages vs bloodborne infiltrating macrophages and the effect on anti-tumor activity

**Cancer-induced changes to macrophage sub-populations:**

- **Elimination of resident macrophages**
- **Accumulation of pro-tumor TAMs originating from infiltrating macrophages**

**Allocetra™ therapy, in combination with anti-cancer agents/therapies**

- **Repopulation of resident macrophages**
- **Depletion of pro-tumor TAMs originating from infiltrating macrophages**

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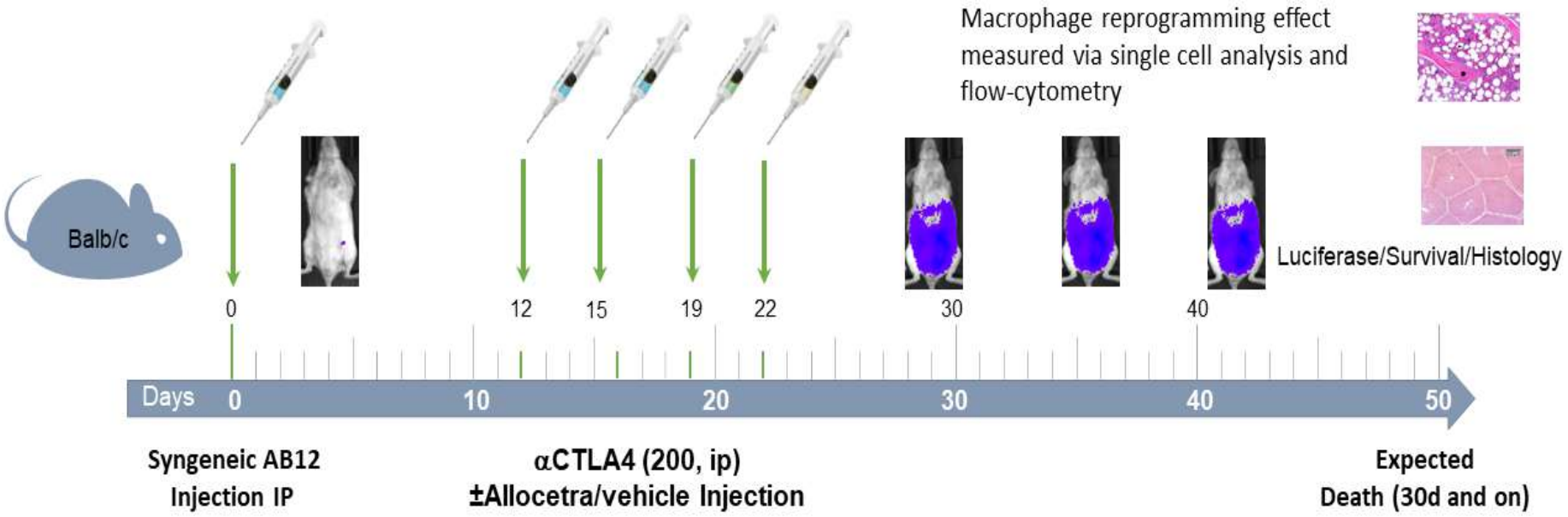
# Allocetra™

## Macrophage reprogramming in solid tumor microenvironment

## Preclinical data

# Synergistic effect of Allocetra™ + anti-CTLA4 in peritoneal mesothelioma solid tumor

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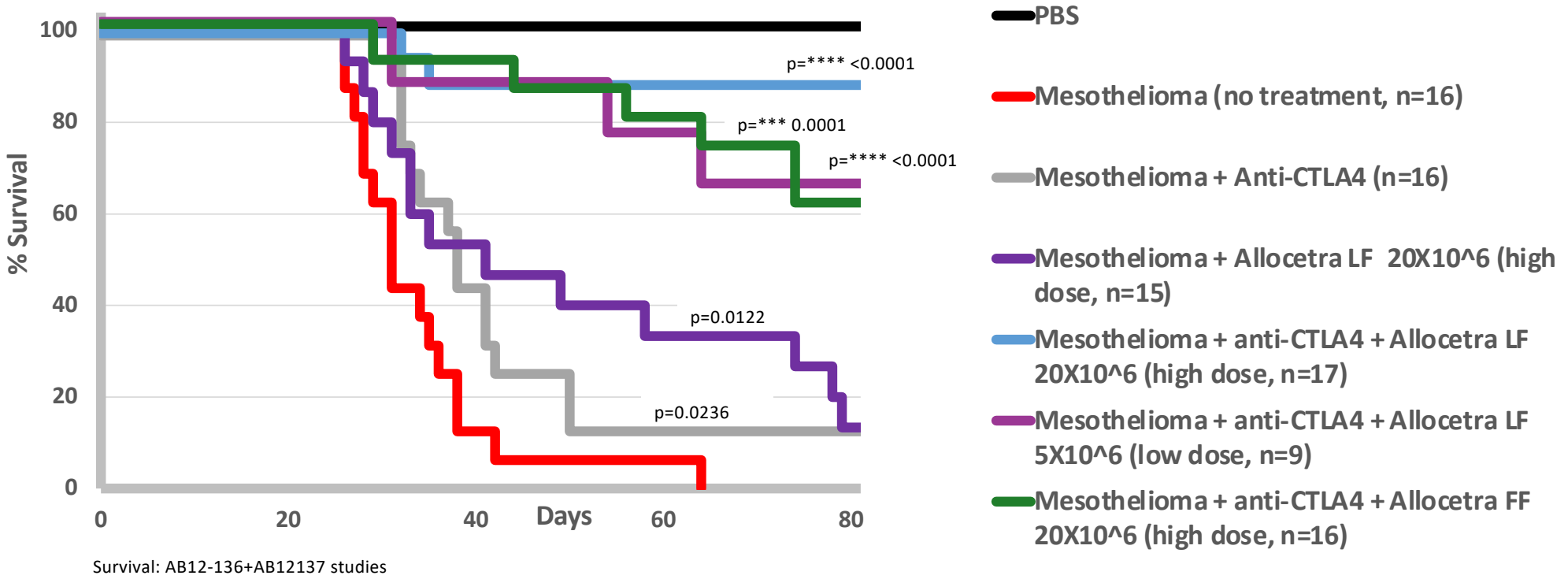
# Synergistic effect of Allocetra™ + anti-CTLA4 in peritoneal mesothelioma solid tumor

- **Superior survival of the anti-CTLA4+Allocetra combinations, dose response demonstrated**
- **Weak, although statistically-significant, survival effect of stand-alone anti-CTLA4, Allocetra**




Survival: AB12-136+AB12137 studies

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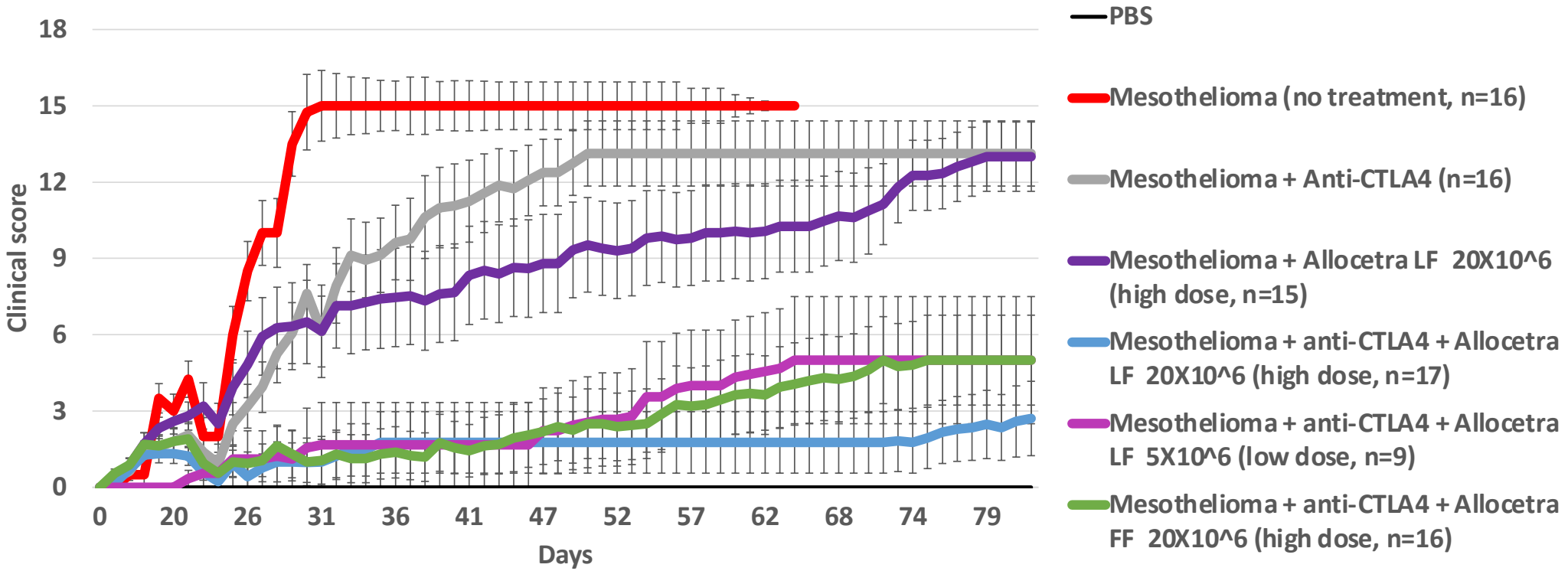
# Synergistic effect of Allocetra™ + anti-CTLA4 in peritoneal mesothelioma solid tumor

- **Clinical score observations support superior clinical and survival effect of the anti-CTLA4+Allocetra combinations**

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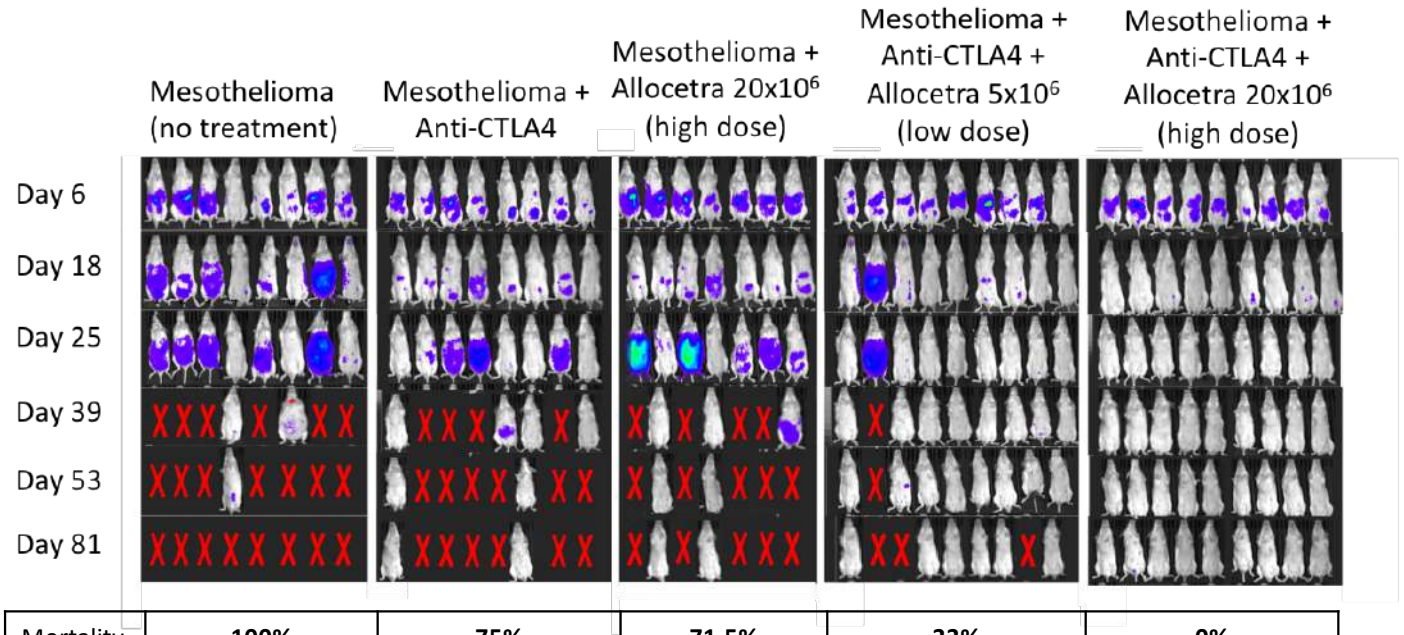
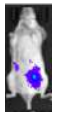
Clinical scores: AB12-136+AB12137 studies

# Synergistic effect of Allocetra™ + anti-CTLA4 in peritoneal mesothelioma solid tumor




| Mortality | **100%** | **75%** | **71.5%** | **33%** | **0%** |
|---|---|---|---|---|---|
| Survival | 0% | 25% | 28.5% | 67% | 100% |
| Complete cure | 0% | 25% | 28.5% | 67% | 100% |

**Legend**

Initial cancer spread 

advanced cancer spread 

mouse dead ✗

mouse alive 

IVIS imageing, AB12-137 study

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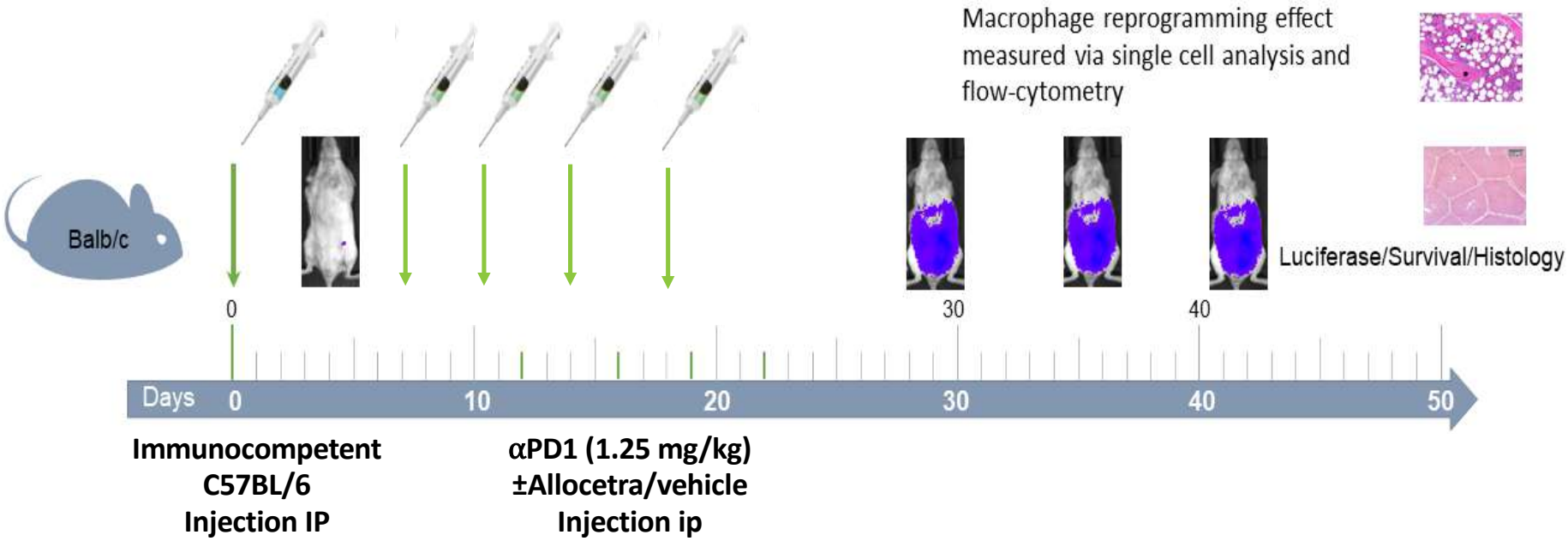
# Synergistic effect of Allocetra™ + anti-PD1 in ovarian cancer solid tumor model

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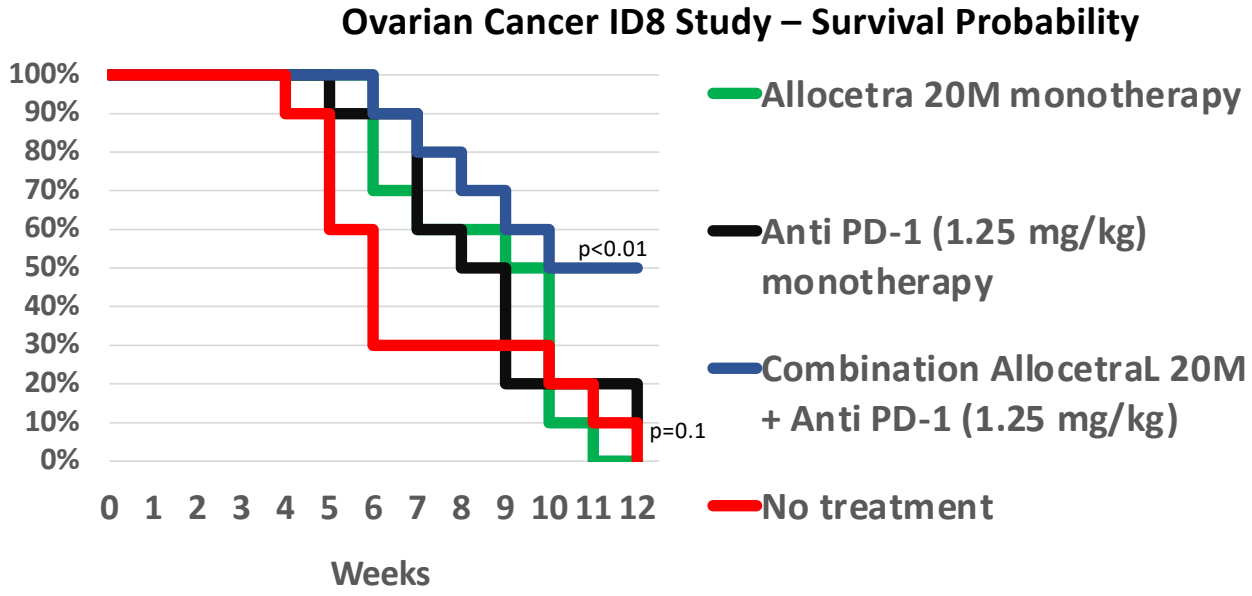
# Synergistic effect of Allocetra™ + anti-PD1 in ovarian cancer

*(study conducted in collaboration with Yale Cancer Center)*

- Superior overall survival, survival duration and lower rate of tumor progression with the anti-PD1+Allocetra combination
- Noticeable and comparable effect on survival duration, weak overall survival effect of stand-alone anti-PD1, Allocetra




| | No treatment | Anti PD-1 (1.25 mg/kg) monotherapy | Allocetra 20M monotherapy | Combination AllocetraL 20M + Anti PD-1 (1.25 mg/kg) |
|---|---|---|---|---|
| Median survival duration (weeks) | 6 | 8.5 | 9.5 | 11 |
| % Survival duration increase vs untreated | -- | 42% | 58% | 83% |
| Overall survival percent | 0% | 10% | 0% | 50% |

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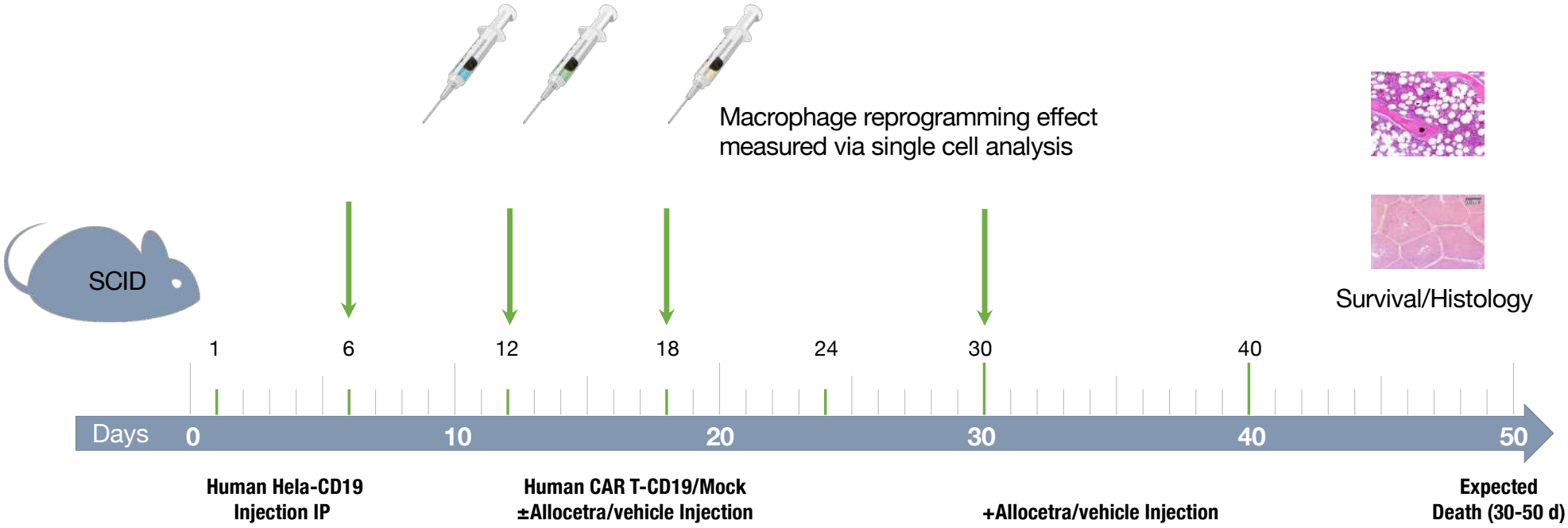
# Allocetra™: reprogramming of peritoneal pro-tumor macrophages

## Preclinical study model: solid tumor engineered to express CD19, making it potentially responsive to CD19 CAR-T

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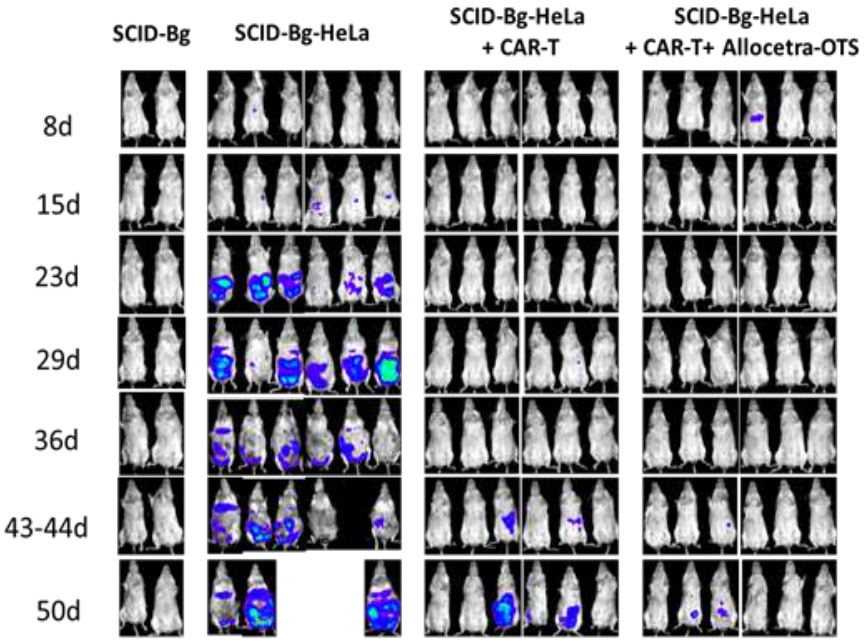
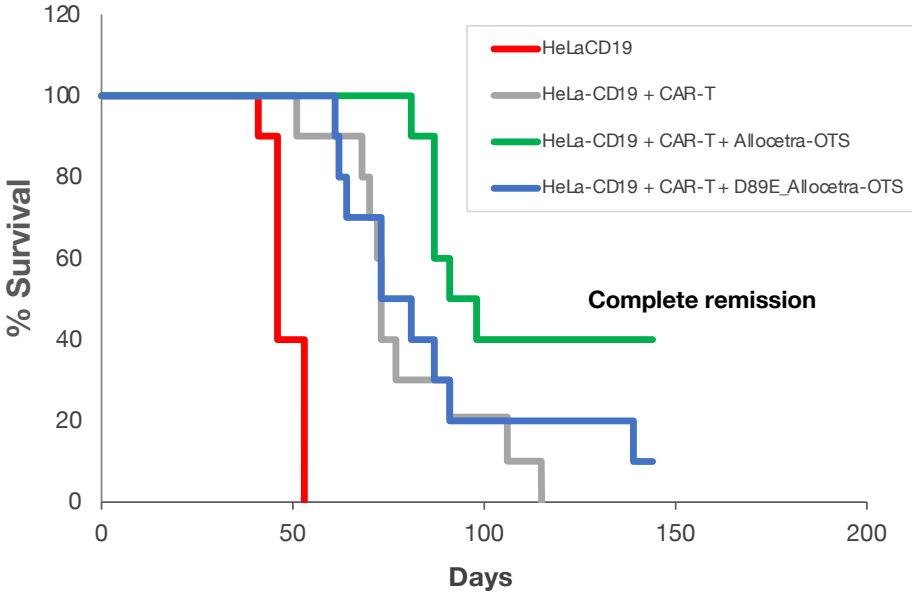
# Allocetra™ macrophage reprogramming synergistic with CD19 CAR-T

## D89* Allocetra (opsonized, not engulfed by macrophages) has no programming nor clinical effect




| Avg. survival, days | | |
|---|---|---|
| No therapy | CAR-T | CAR-T + Allocetra™ |
| 30±5 | 55±11 (p<0.001) | 74±10 (p<0.01) |

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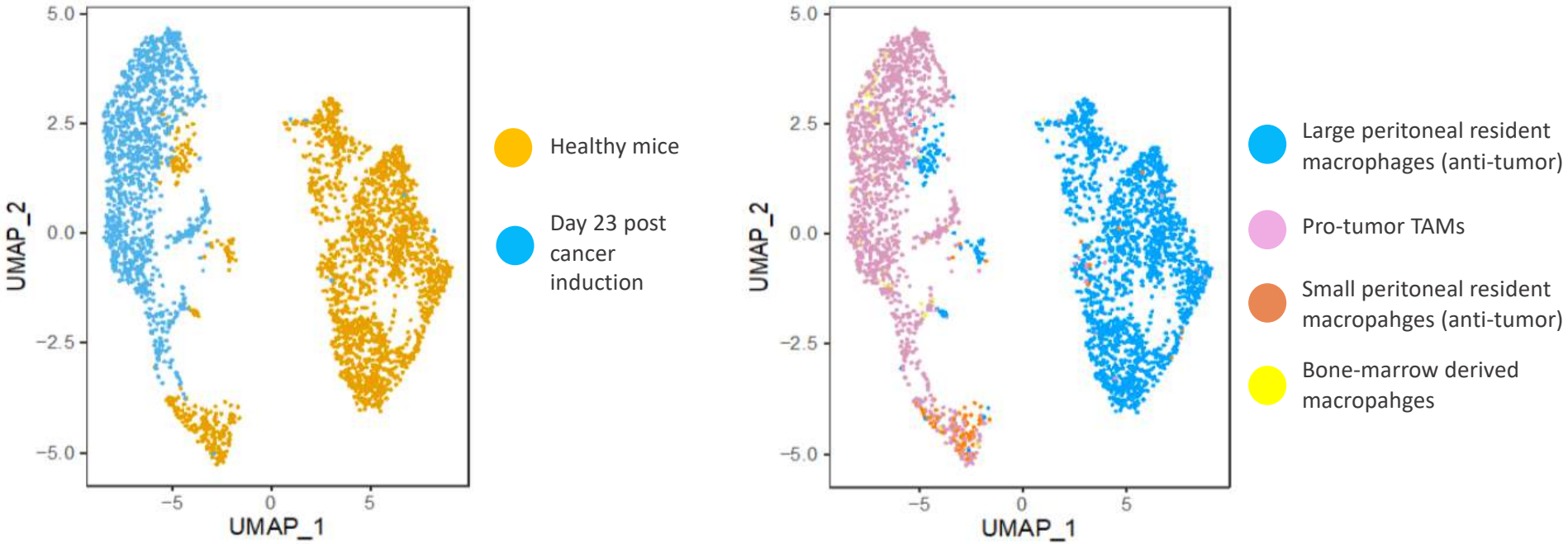
* D89E mutant plasmid was received from N. Nagata, transfected using Lenti X HEK293T cells (Clontech-Takara), and the protein was generated and added to apoptotic cells before intra-peritoneal injection

# The Enlivex differentiation: Balance of resident macrophages vs bloodborne infiltrating macrophages and the effect on anti-tumor activity

**Cancer-induced changes to macrophage sub-populations:**

- **Elimination of resident macrophages**
- **Accumulation of pro-tumor TAMs originating from infiltrating macrophages**

*Peritoneal fluid myeloid cells populations pre/post induction of peritoneal cancer, SCID-bg mice*

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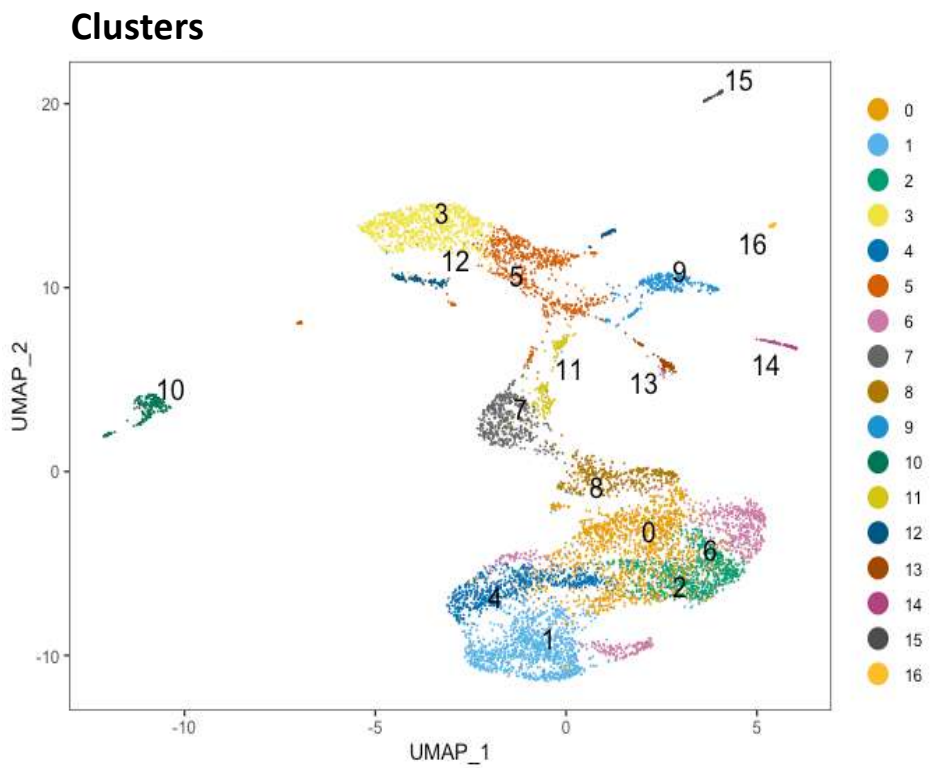
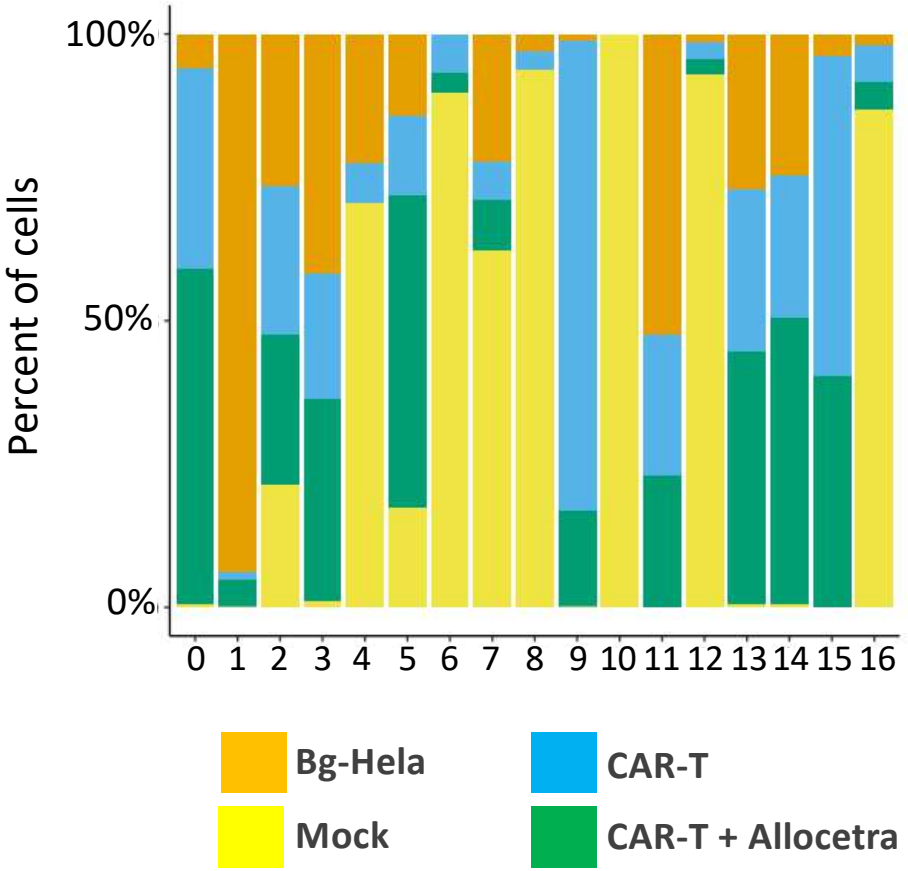
# Peritoneal cell clustering, potential additive effect of Allocetra on top of CAR-T in different cell clusters

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# Allocetra™

## Macrophage reprogramming in solid tumor microenvironment

## Clinical programs

# Phase I/II Clinical Trial Evaluating Allocetra™ + Chemotherapy in Patients with Peritoneal Metastases Arising from Solid Tumors

| | Phase I/II |
|---|---|
| **Addressable global market** | $4 Billion market |
| **Type** | Open-label, single center |
| **Patients** | 12, all-comers with peritoneal metastases |
| **Duration** | 90 days / patient |
| **Expected recruitment** | 12 Months |
| **End-points** | Safety |
| **Secondary** | ORR |
| **First patient expected to be dosed** | Q3/2022 |

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# Allocetra macrophage reprogramming research collaborations

Mount Sinai

Yale University School of Medicine

**Collaborations aim to evaluate the potential of Allocetra™ in combination with immune-checkpoint inhibitors in solid cancer patients that do not respond to stand-alone checkpoint inhibitor therapies**

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# Planned milestones (24 months)

**Q1** 2022

Completion of development of frozen formulation Allocetra™

**Q2** 2022

Regulatory filing for the integration of frozen formulation Allocetra™ into Phase II sepsis and oncology studies

**Q3** 2022

Initiation of Phase I/II in advanced-stage solid tumors patients with peritoneal metastases, stand-alone + in combination with anti-PD1

**Q3** 2022

Initiation of Phase Ib in advanced-stage solid tumors patients with peritoneal metastases, in combination with chemotherapy

**Q1** 2023

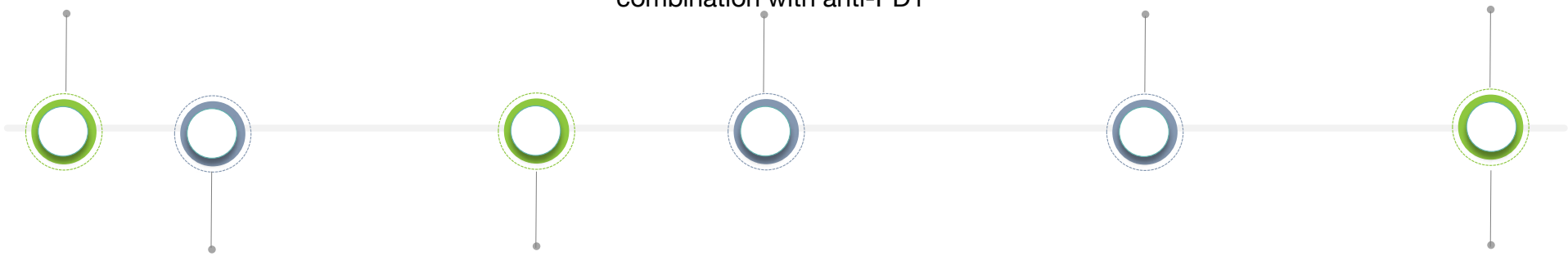
Interim data macrophage reprogramming sepsis Phase II

**Q3** 2023

Top line data macrophage reprogramming sepsis Phase II

**Q3** 2023

Completion of construction of new Allocetra™ manufacturing facility



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## Financial Summary


| | |
|---|---|
| NASDAQ GS | ENLV |
| Cash | $78MM (Mar 31, 2022) |
| Debt | None |
| Shares Outstanding | 18.2 MM |
| Funded Through | Q3 2024 |

# Management

| | |
|---|---|
| **Shai Novik**<br>Executive Chairman | Founder and President of PROLOR Biotech, Sold in 2013 ($560mm transaction). Lead product partnered to Pfizer, $295 million down payment, $275 upon FDA & other regulatory approvals. BLA filed by Pfizer late 2020. |
| **Oren Hershkovitz**<br>CEO | Former Director of CMC, VP R&D and General Manager of OPKO Biologics (PROLOR Biotech). Led multiple clinical programs in Phase I, II and III. Ph.D. in Immunology. |
| **Dror Mevorach**<br>Chief Scientific Officer | Director, Rheumatology Research Centre and Molecular Immunology; and Director, Centre for Rare diseases, Hadassah Medical Center, Jerusalem. |
| **Einat Galamidi**<br>VP Medical | 10 years at Gamida Cell Ltd., where Dr. Galamidi most recently served as Vice President of Clinical Development, and ed clinical development for omidubicel, a cell therapy that successfully completed Phase III in 2020, and the following rolling-BLA submission in 2022. |
| **Odelia Ben-Shitrit**<br>Head of Clinical Operations | Over 20 years of experience in clinical trials and operational management in various therapeutic areas. Former Teva and PAREXEL clinical leader. |
| **Veronique Amor-Baroukh**<br>Head Of CMC | Ph.D., Molecular Cell Biology, Weizmann Institute of Science, Israel. |
| **Shachar Shlosberger**<br>CFO | ~Former PROLOR Biotech Ltd Finance Director where she was responsible for the overall financial operations in Israel and US. A C.P.A., and holds a M.B.A. in Accounting and Business Administration. |

# Board Of Directors

| | |
|---|---|
| **Shai Novik**<br>Executive Chairman | Founder and President of PROLOR Biotech, Sold in 2013 ($560mm transaction). Lead product partnered to Pfizer, $295 million down payment, $275 upon FDA & other regulatory approvals. BLA filed by Pfizer late 2020. |
| **Sangwoo Lee**<br>Director | Executive Director of the Investment Department & Head of U.S. Branch at Korea Investment Partners Co. Ltd |
| **Bernhard Kirschbaum, PhD**<br>Director | Former Executive Vice President & Member of the Board at Merck Serono, and Head of Global Research & Early Development |
| **Gili Hart, Ph.D**<br>Director | Formerly with PROLOR Biotech, led the pre-clinical, clinical and pharmacological activities. CEO of Mitoconix Bio, a biopharmaceutical company developing disease modifying therapies addressing unmet medical needs |
| **Brian Schwartz, M.D.**<br>Director | Former CMO of Arqule through its $2.7 billion acquisition by Merck in 2020. Previously, responsible for the global clinical development of sorafenib (Nexavar®) at Bayer Healthcare. |
| **Abraham Havron, Ph.D.**<br>Director | Former CEO of PROLOR Biotech. Founding team and Director of R&D of Interpharm (Merck Serono) ,VP CMC of BioTechnology General Ltd., and VP of Clal Biotechnology Industries Ltd. |
| **Michel Habib**<br>Director | Managing partner of ALIVE, a medical device VC fund; Former CEO of HBL, former Managing Partner of Agate-MaC Fund, a healthcare VC |

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# Thank You