Nasdaq

Ticker: ENLV

ENLIVEX

immune rebalancing

Beyond CD47, SIRPα, IL-6 & TNF-α

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

February 2021

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. This presentation is not intended to be relied upon as advice to investors or potential investors and does not take into account the investment objectives, financial situation or needs of any investor.

Macrophage reprogramming

Paradigm shift – homeostasis instead of “anti-inflammatory (M2)” or “”pro-inflammatory (M1)”

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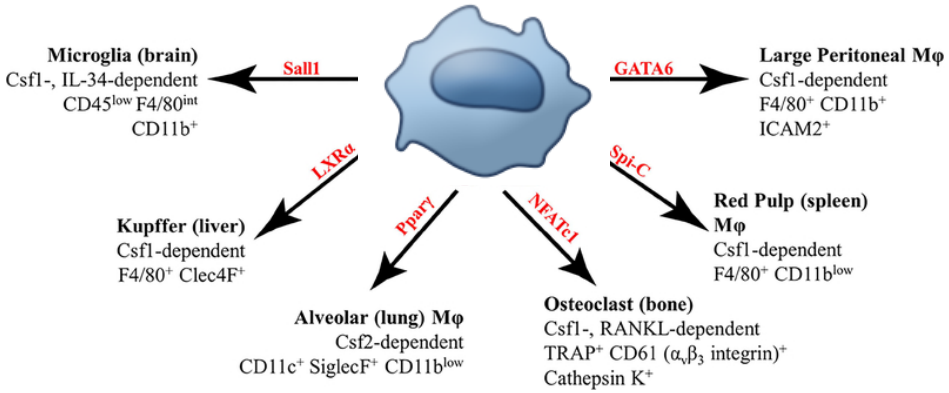
Macrophages are tissue-resident or infiltrated immune cells critical for innate immunity

- Macrophages' function is a sum of their designation, the local environment in which they reside, and the type of situation or pathogen to which they are exposed
- Reprogrammed out of their homeostatic state, macrophages contribute to the pathophysiology of multiple diseases including cancer and various inflammatory disorders

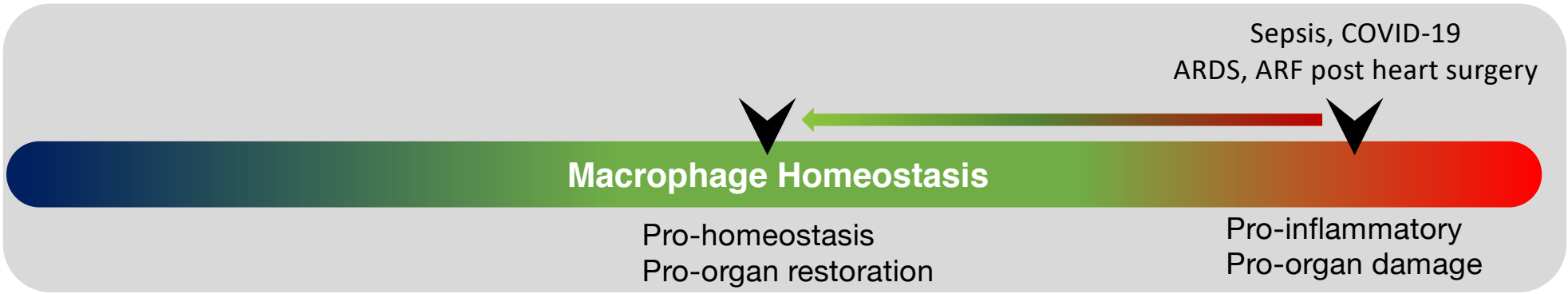
Key Tissue Resident Macrophages (murine)

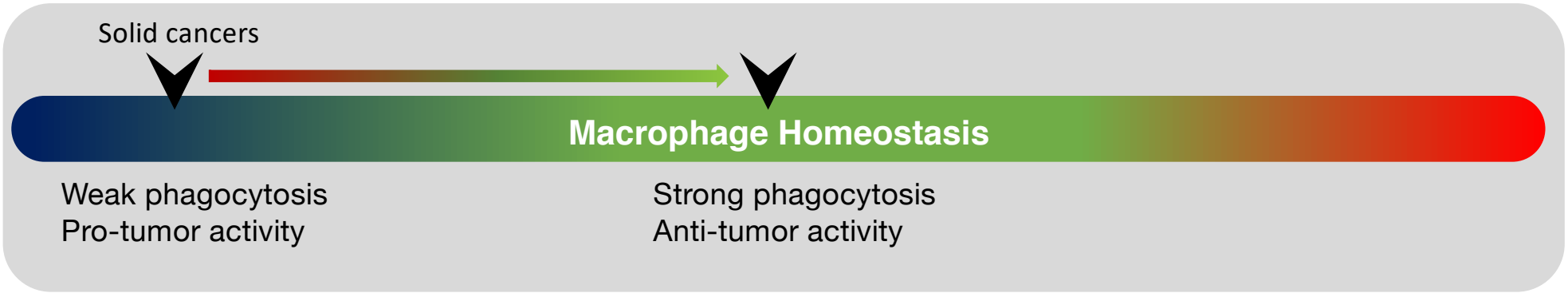


Williams et al.; J Am Coll Cardiol. 2018 Oct 30; 72(18): 2166–2180.

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

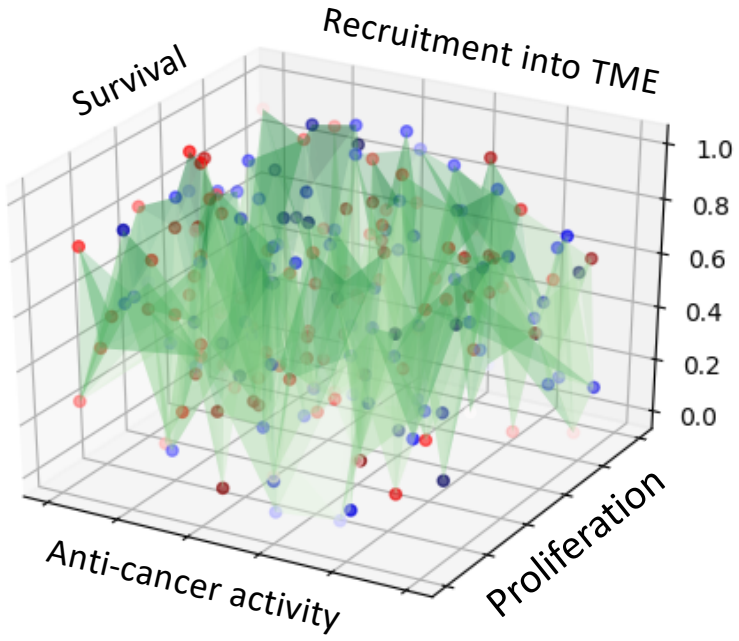
Reprogramming imbalanced macrophage populations can lead to disease resolution



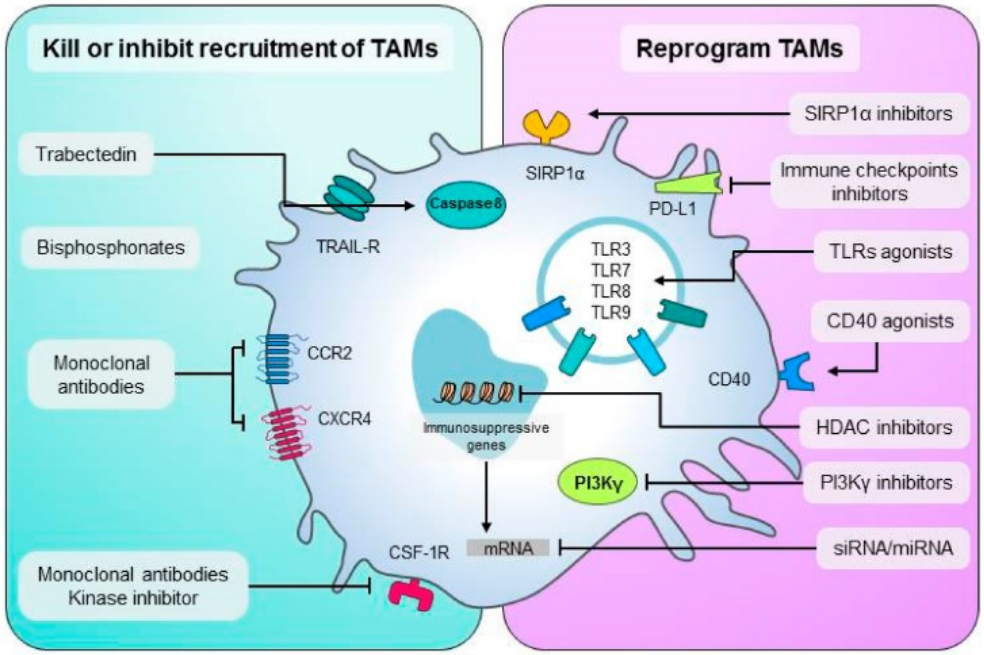


Solid cancer: kill or reprogram non-homeostatic, pro-tumor macrophages (TAMs) in the tumor microenvironment (TME)

Multiple axes for homeostatic macrophage functionality within the tumor microenvironment (TME),

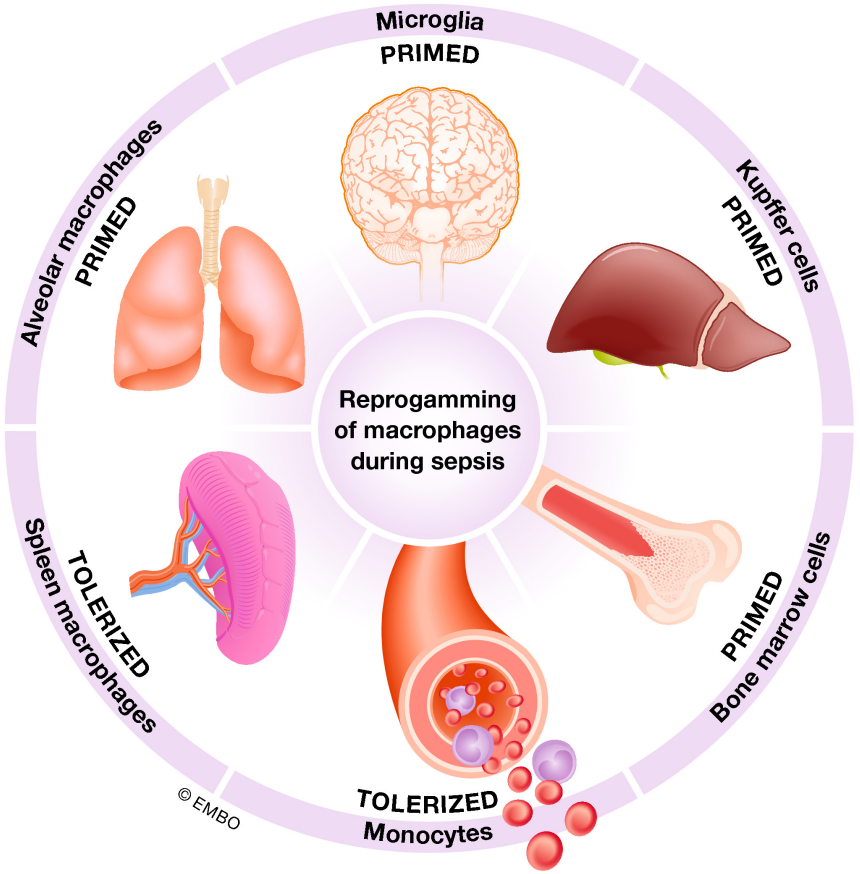


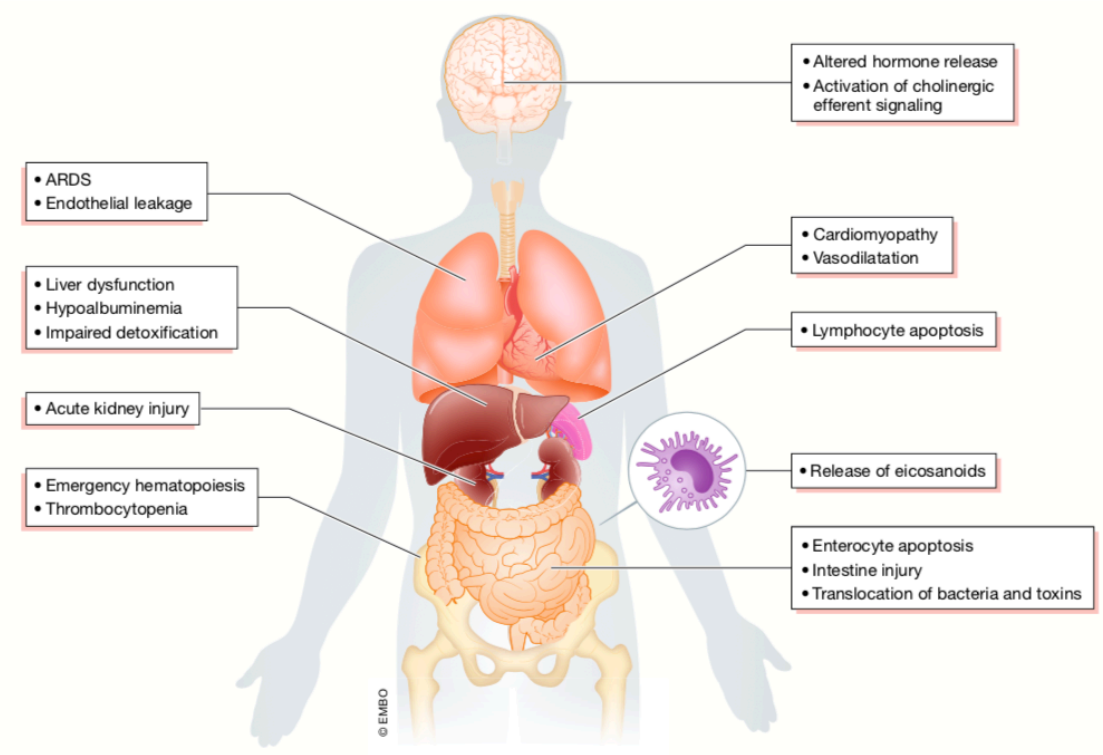
multiple strategies to kill or reprogram non-homeostatic, pro-tumor macrophages (TAMs)



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

Sepsis: negative macrophage reprogramming, no homeostasis





Source: EMBO Molecular Medicine 12:e10128 | 2020

Allocetra™ Mechanism of Action

Restoring immune homeostasis through reprogramming of macrophages

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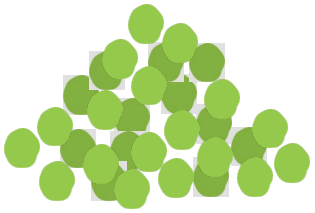
Allocetra™ for macrophage reprogramming

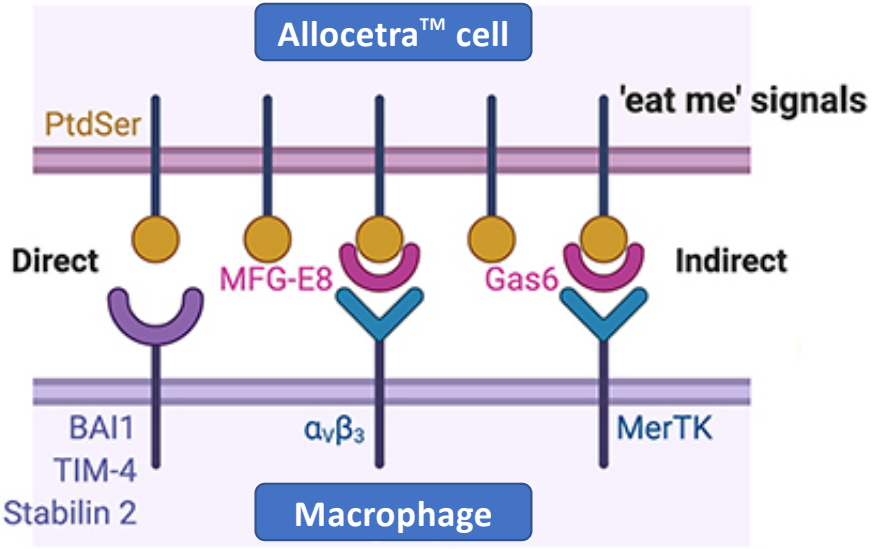
Proprietary, universal, off-the-shelf, macrophage-reprogramming cells

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



Allocetra™ for macrophage reprogramming

Pipeline of reprogrammable macrophage-modulated indications

Indication	Global Market Size	Pre-Clinical	Phase Ib	Phase IIb	EU Conditional Marketing Approval	Post EU Marketing US Phase 3
Organ failure associated with Sepsis	$33B		Completed	Phase IIb Initiation Q1 2021		
ARDS associated with severe/critical COVID-19 / Non-COVID-19 ARDS	$1B (COVID) $15B (ARDS)		Completed COVID-19	Phase II Ongoing COVID-19		
Solid tumors in combination with immune checkpoints	$4B		Q3 2021			

Allocetra™

Reprogramming macrophages responsible for organ failure in sepsis and COVID-19

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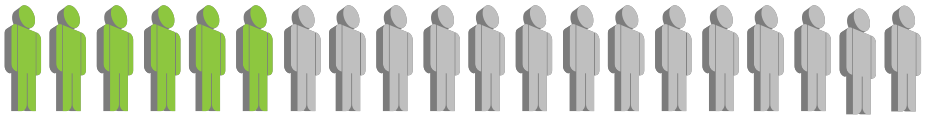
Sepsis is the 3rd leading cause of death in the U.S. – $33B target market*

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



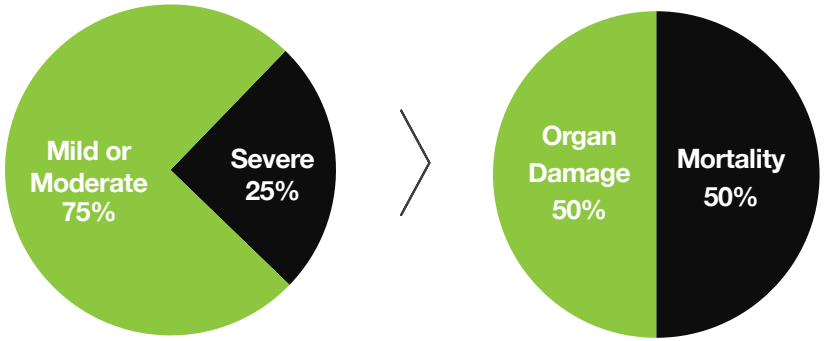
Each year, at least **1.7 million** adults in America develop sepsis.

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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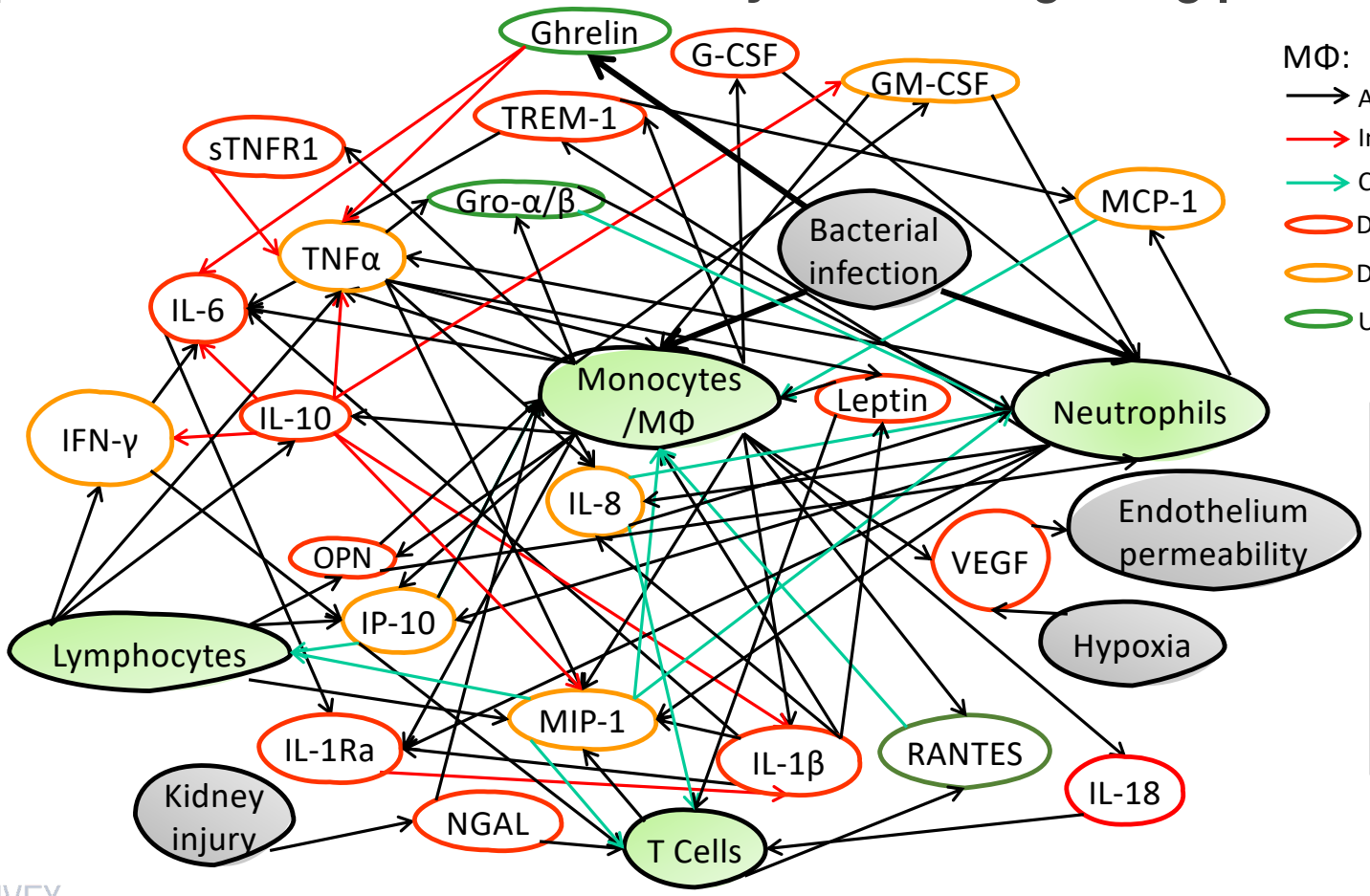
* U.S. & EU

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



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

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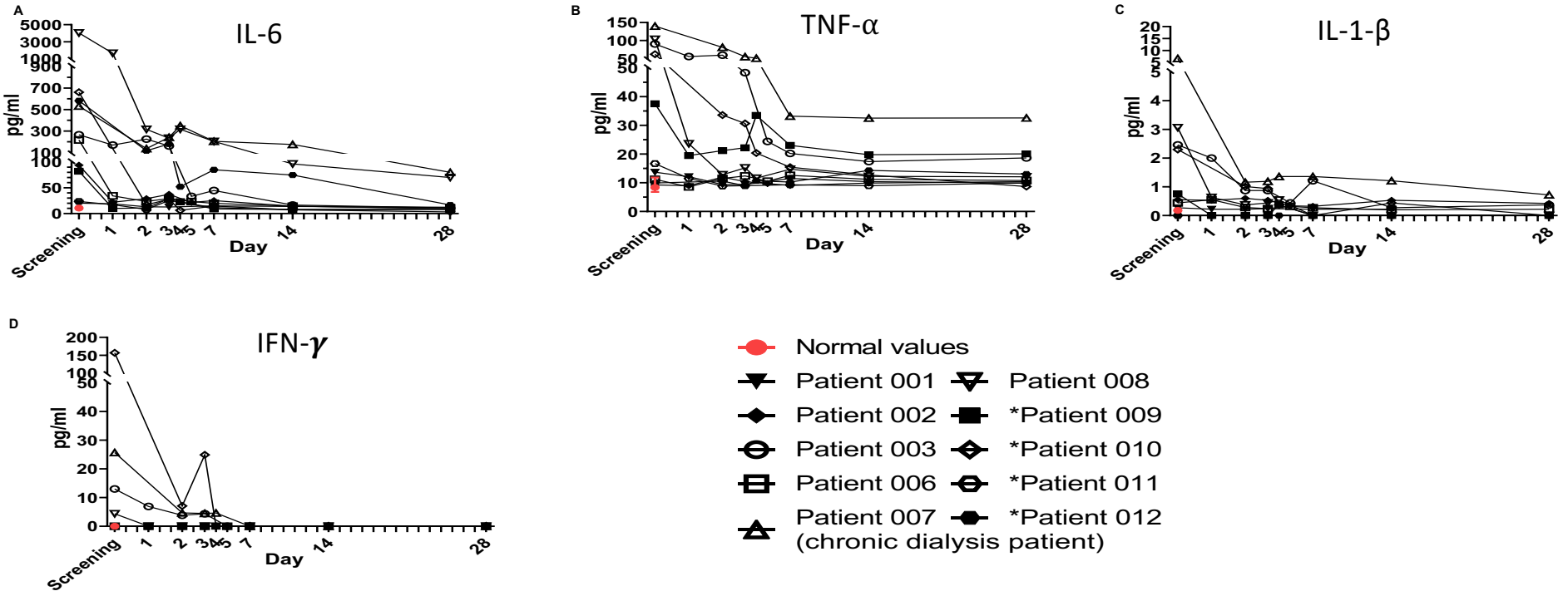
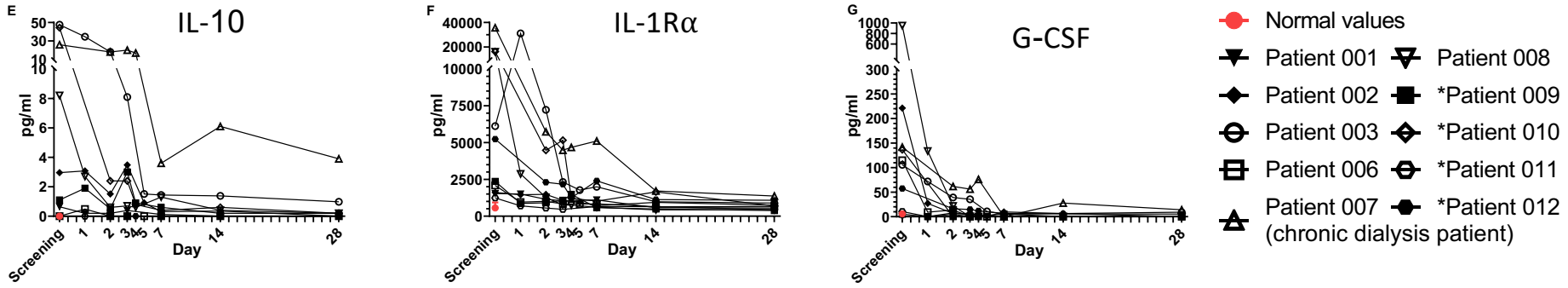
Reprogrammed macrophages in sepsis patients return to homeostatic state (1)

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



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

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



Sequential Organ Failure Assessment (SOFA) Score

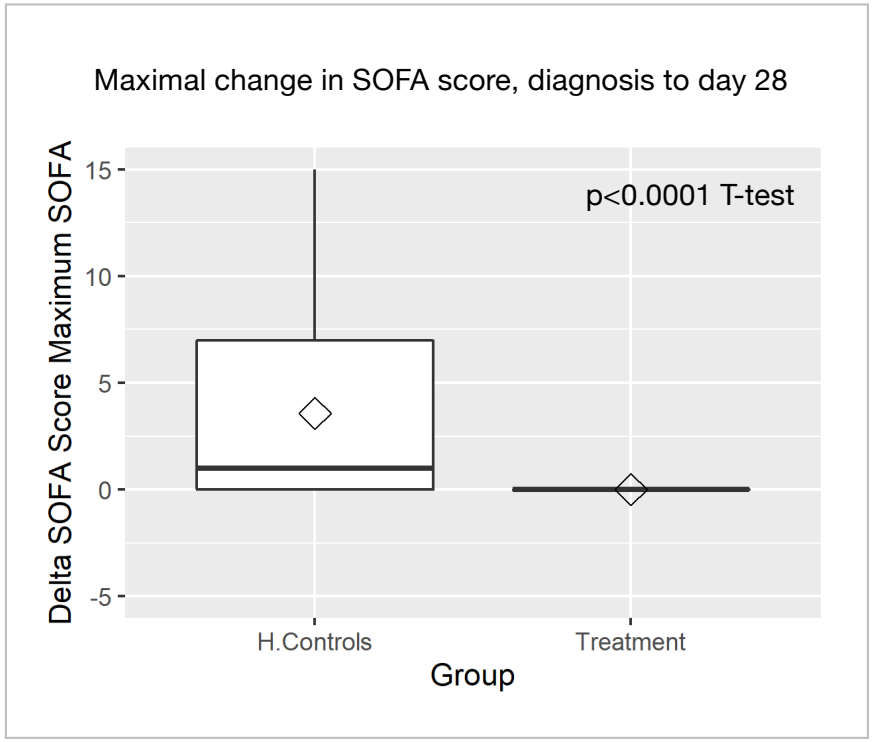
The sequential organ failure assessment score (SOFA score), previously known as the sepsis-related organ failure assessment score, is used to track a person's status during the stay in an intensive care unit (ICU) to determine the extent of a person's organ function or rate of failure. The score is based 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%

Allocetra™ macrophage reprogramming leads to improved outcomes for sepsis patients

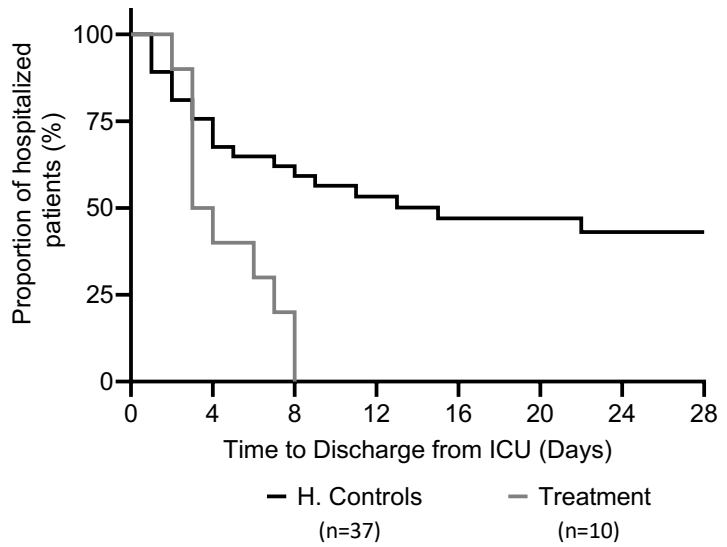


		#		
Total patients	Controls	37		
	Treated	10		
Day 28		#	%	
Died	Controls	10	27%	--
	Treated	0	0	--
Alive				
Recovery prospects	Day 28 SOFA delta vs pre-sepsis baseline	Day 28 alive by category #	%	Avg. SOFA delta
Good	0-1	15	41%	0.6
		10	100%	0.1
Fair	2	4	11%	2
		0	0%	--
Poor	>=3	8	22%	5
		0	0%	--

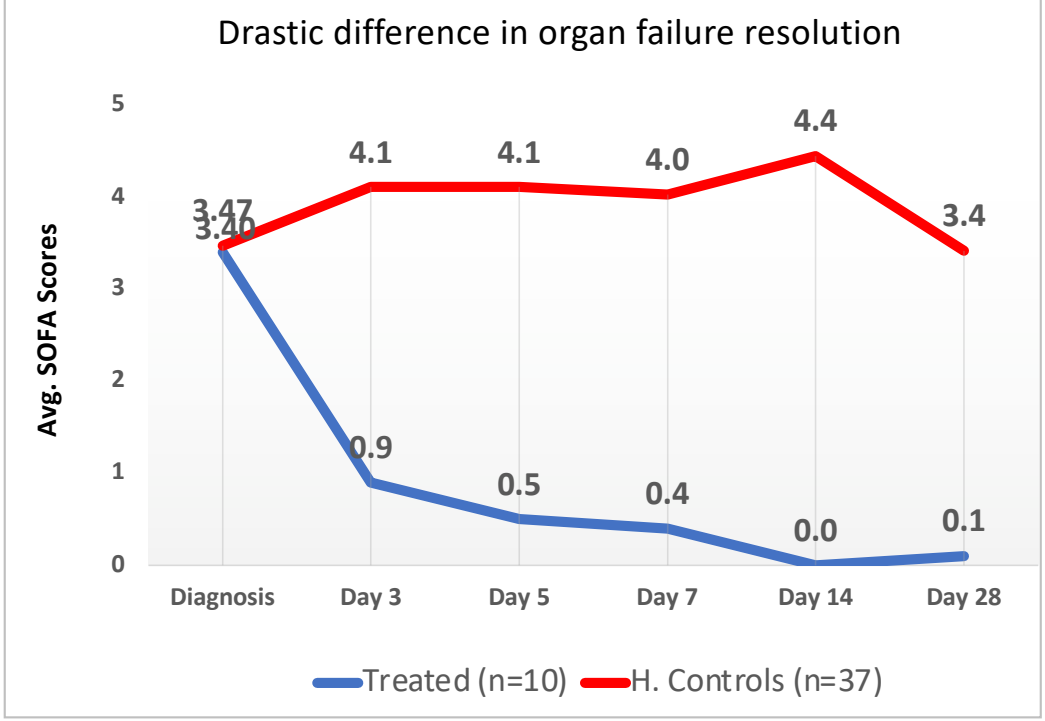
Allocetra™ macrophage reprogramming leads to improved outcomes for sepsis patients

Statistically significant improvement in hospitalization and SOFA vs. matched controls

Time to ICU discharge



Average SOFA score during 28 days



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. 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	120-160, SOFA < 10, Pneumonia-sourced
Duration	28 days / patient
Recruitment	12 Months
End-points	Safety, Change in SOFA score
Secondary	Mortality
First patient dosed	Expected Q1/2021

Allocetra™

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

Allocetra™: positive Phase Ib and interim Phase II results in COVID-19

- **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**

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

Patient classification as defined by the NIH classification guide

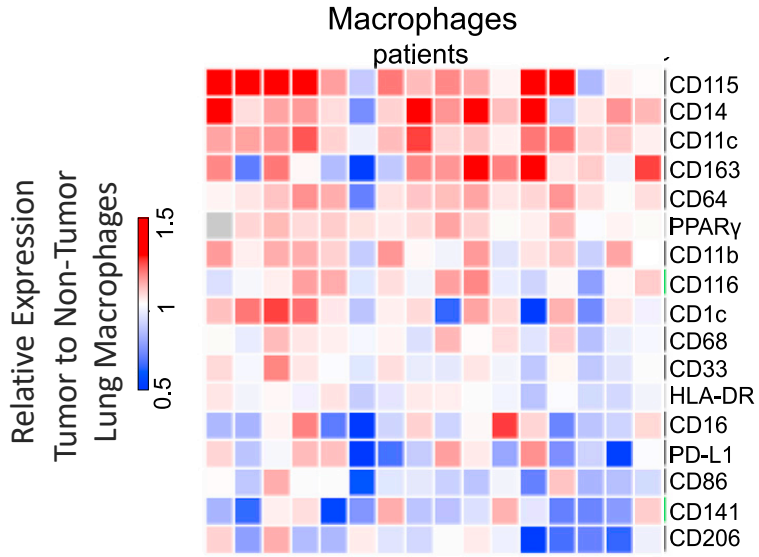
Allocetra™

Macrophage reprogramming
in solid tumor microenvironment

Unique & differentiated
value proposition

The TME is loaded with pro-tumor macrophages (TAMs), which are macrophages reprogrammed by the tumor and have a drastically different gene expression

Gene expression varies drastically in TAMs vs anti-cancer macrophages*



TAMs are macrophages that were reprogrammed by the cancer cells out of their homeostatic state and into a pro-tumor state

* Innate Immune Landscape in Early Lung Adenocarcinoma by Paired Single-Cell Analyses
Lavin et al., 2017, Cell 169, 750–765

Allocetra™: novel reprogramming of pro-tumor macrophages

Key company universe Macrophage properties	Novartis, BMS, Amgen Syndax	47, Trillium ALX, Celgene Surface	Infinity, Arcus MedImmune Corvus, Pfizer	Celgene Nektar, GSK	Celldex AbbVie MedImmune	Enlivex
Programming method	Inhibit or trigger surface target	Inhibit or trigger surface target	Inhibit or trigger surface target	Inhibit or trigger surface target	Inhibit or trigger surface target	Reprogramming to homeostatic state
Desired functionality change						
Recruitment ↑	CSF1-CSF1R	🚫	🚫	🚫	🚫	✓
Proliferation ↑	🚫	🚫	🚫	TLRs	CD40	✓
Survival ↑	CSF1R	🚫	🚫	🚫	🚫	✓
Anti-tumor activity ↑	CSF1-CSF1R	CD47-SIRPα	PI3Kγ, A2AR , CD73, GM-CSF, M-CSF	TLRs	CD40	✓
Safety & tolerability profile (potential negative effect on non-TAM macrophages)	Effect on non-cancer macrophages?	Effect on red blood cells, non-cancer macrophages?	Effect on non-cancer macrophages?	Effect on non-cancer macrophages?	Effect on non-cancer macrophages?	No negative effect on non-cancer macrophages

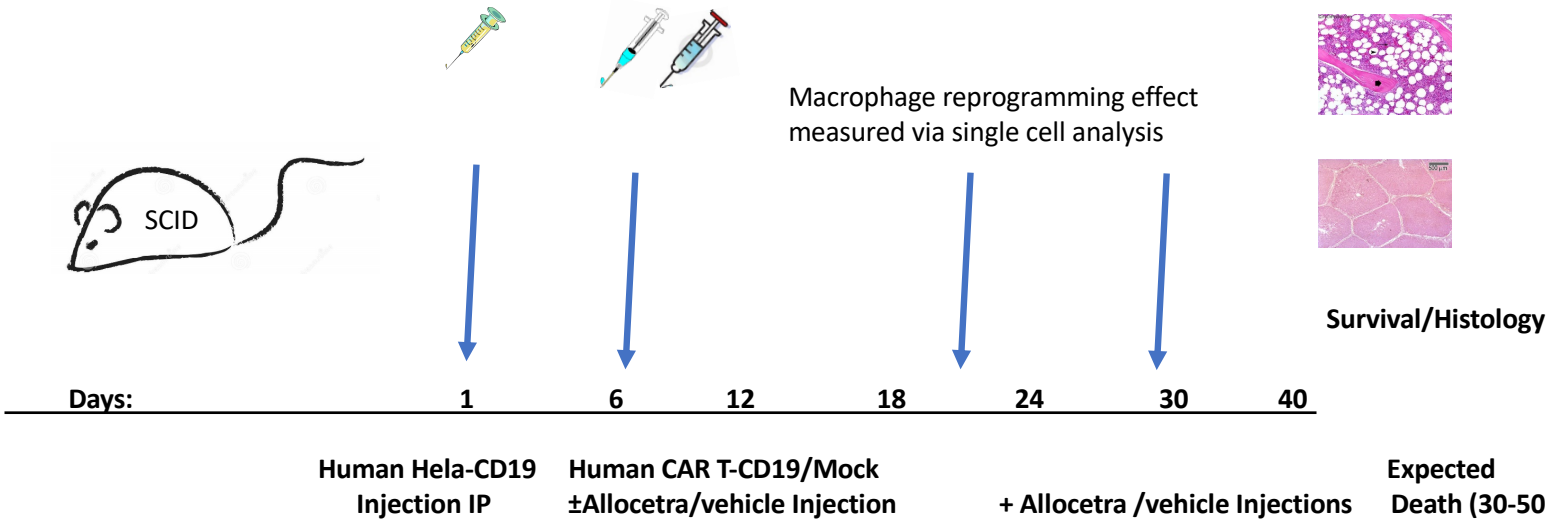
Allocetra™

Macrophage reprogramming in solid tumor microenvironment

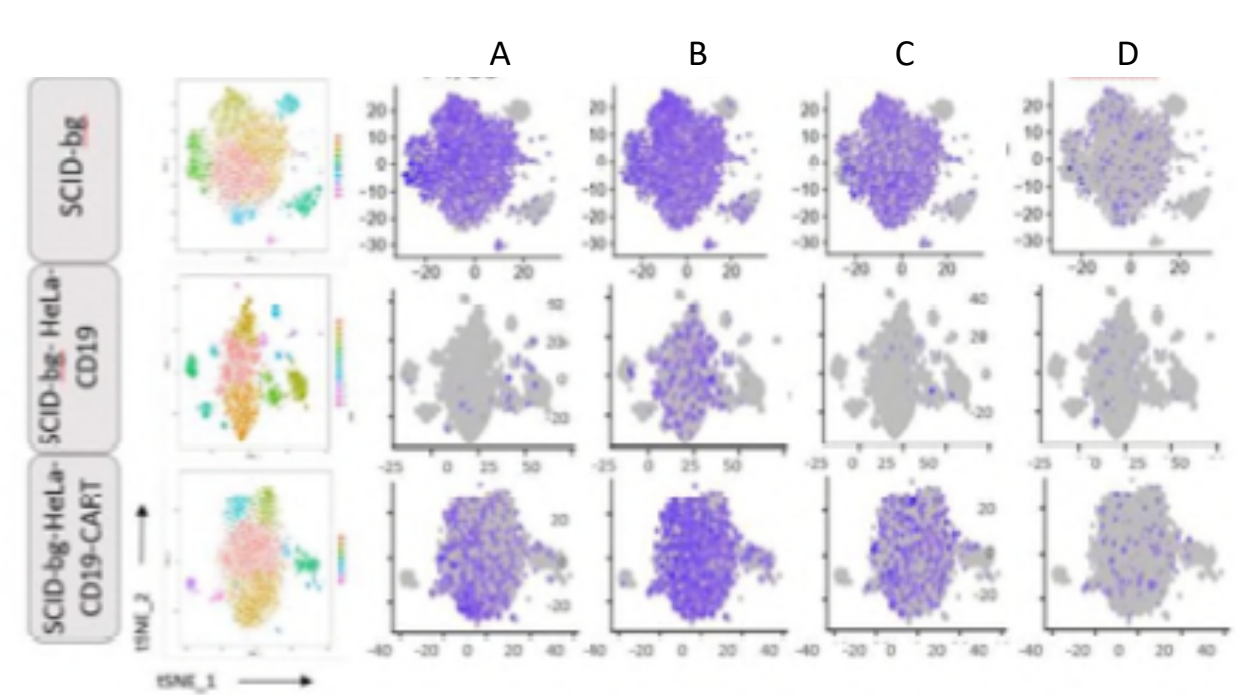
Preclinical data

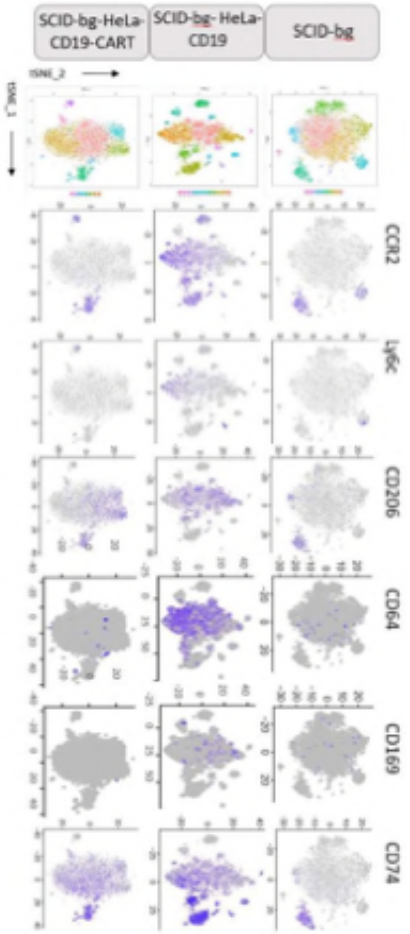
Allocetra™: reprogramming of peritoneal pro-tumor macrophages

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



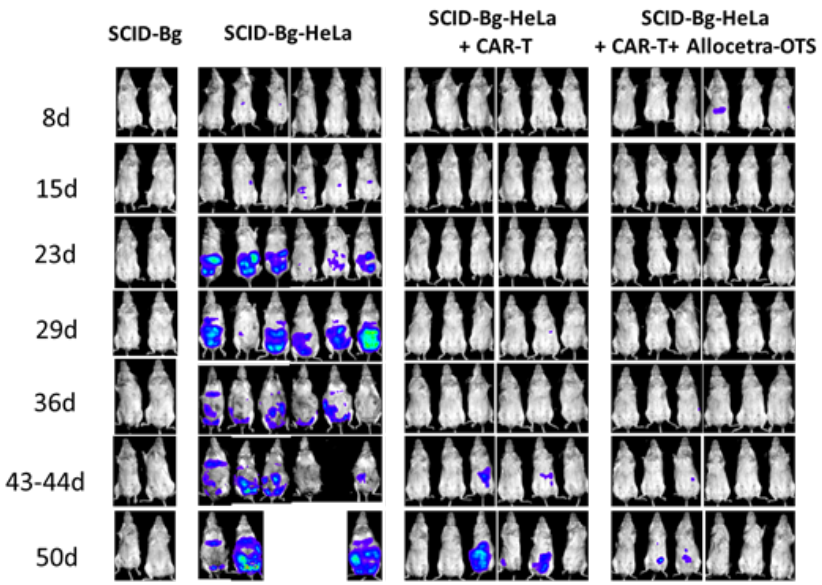
Allocetra™: reprogramming of peritoneal pro-tumor macrophages

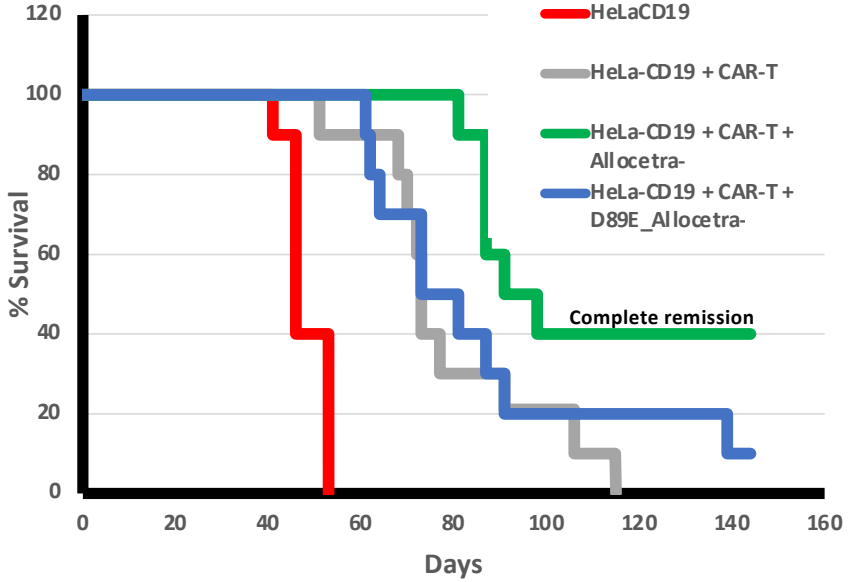




Allocetra macrophage reprogramming synergistic with CD19 CAR-T

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)

* 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

Planned/executed milestones

Q1 2021

Top-line data from macrophage reprogramming COVID-19 Phase II

Q1 2021

Research collaboration: macrophage reprogramming PD-1 combination

Q2 2021

Emergency-use designation for COVID-19 Severe/critical patients

Q3 2021

Initiation of macrophage reprogramming PD-1 combination undisclosed indication Phase Ib

Q3 2021

Interim data macrophage reprogramming sepsis Phase IIb

Q1 2022

Top line data macrophage reprogramming sepsis Phase IIb

Q1 2022

Initiation of macrophage reprogramming PD-1 combination undisclosed indication

Phase Ib

Financial Summary

NASDAQ GS	ENLV
Cash	$36MM (Sep 30, 2020[1])
Debt	None
Shares Outstanding	14.3MM
Funded Through	Q1-2023

[1] Cash balance as reported for Sep 30 2020 plus Q4 warrant exercises

Management

Shai Novik Executive Chairman	Founder of Prolor Biotech, Sold in 2013 ($560mm transaction). Lead product partnered to Pfizer, $295 million down payment, $275 upon FDA approval. Phase III endpoint met Oct 2019.	PROLOR BIOTECH Protein.Longevity.Redefined
Oren Hershkovitz CEO	Former Director of CMC, VP R&D and CEO of OPKO Biologics (PROLOR Biotech). Led multiple clinical programs in Phase I, II and III. Ph.D. in Immunology.	OPKO Biologics
Dror Mevorach Chief Medical & Scientific Officer	Director, Rheumatology Research Centre and Molecular Immunology; and Director, Centre for Rare diseases, Hadassah Medical Center, Jerusalem.	Weill Cornell Medical College
Odelia Ben-Shitrit 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.	teva
Dan Fishelovitch Head Of CMC	Former CMC Director, NeuroDerm Ltd, and Formulation Scientist at Teva Pharmaceutical Industries Ltd. Ph.D. from the faculty of Medicine, Tel-Aviv University in structural Bioinformatics.	parexel
Shachar Shlosberger 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.	NeuroDerm A Mitsubishi Tanabe Pharma Group Company

Board Of Directors

Shai Novik Executive Chairman	Founder of Prolor Biotech, Sold in 2013 ($560mm transaction). Lead product partnered to Pfizer, $295 million down payment, $275 upon FDA approval	**Brian Schwartz, M.D.** 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.
Sangwoo Lee Director	Executive Director of the Investment Department & Head of U.S. Branch at Korea Investment Partners Co. Ltd	**Abraham Havron, Ph.D.** 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.
Bernhard Kirschbaum, PhD Director	Former Executive Vice President & Member of the Board at Merck Serono, Head of Global Research & Early Development	**Baruch Halpert** Director	Over 20 years of experience in VC and Private Equity as an entrepreneur, corporate finance advisor, senior executive and an investor
Gili Hart, Ph.D 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	**Michel Habib** Director	CEO of HBL, former Managing Partner of Agate-MaC Fund, a healthcare VC

Thank You

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