# Vasomune Therapeutics

Host-directed therapeutics targeting vascular leak, by boosting vascular endothelial stabilization

Harold Kim, PhD, CSO

Vāsomune therapeutics

## Disclaimer/Conflict of Interest

**H Kim** holds an equity position with Vasomune Therapeutics Inc.

**H Kim, A Weaver, Y Takasu and BE Jahns** have no other conflicts of interest.

## **Hemorrhagic Shock & Polytrauma:** The Critical Window for Intervention

### Military Combat Injury
- Combined injury
- Blast / crush / blood loss
- Hemorrhage, tissue damage, shock remains a leading cause of preventable death

### Polytrauma + Shock
- Systemic vascular instability
- Early, rapid hemodynamic shifts
- Endothelial dysfunction, capillary leak, microvascular collapse; highly unstable physiology

### The Golden Hour
- Peak vascular vulnerability and maximum therapeutic responsiveness
- Vascular stabilization to reduce capillary leak, improve perfusion and organ function

### Operational Goals
- To stabilize physiology
- Extend survivability window
- Enable evacuation
- Transition to higher-level care
- Bridge to trauma units

Early vascular stabilization during the Golden Hour to improve survival from shock and polytrauma.





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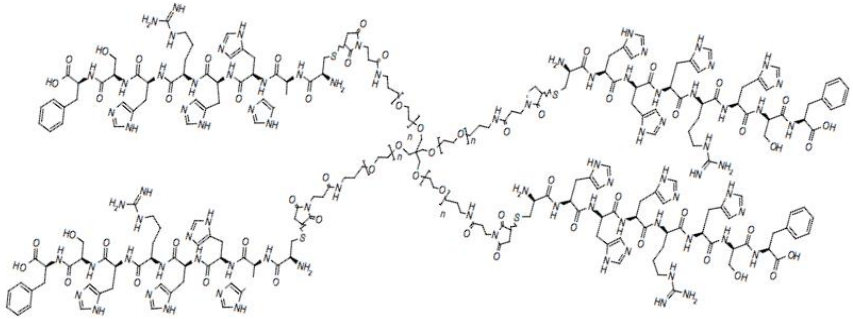
# **Pegevongitide:** Tetrameric PEGylated Peptide that Exhibits Potency, Stability and Manufacturability



Pegevongitide (AV-001) is the cGMP version of Vasculotide

Pegevongitide is a fully synthetic 4-arm branched PEGylated peptide of 14.5 kDa

AV-001 has wide therapeutic window:
MFD > 200-fold PAD

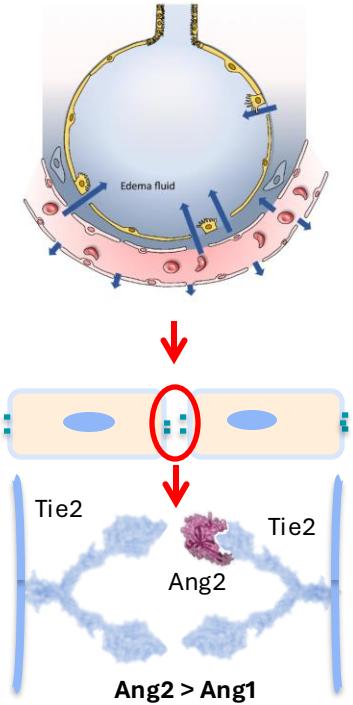
AV-001 exhibits nanomolar affinity:
Kd: 1.9-2.8 nM; EC50: 10.2 nM

AV-001 is highly specific, with negligible inhibition or stimulation of 128 secondary targets

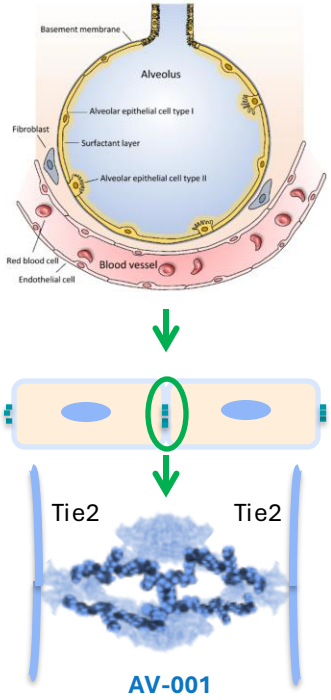
cGMP AV-001 has >6 years stability

**Tie2 and pegevongitide (AV-001/Vasculotide):** Vascular Dysfunction is a foundational mechanism for a variety of devastating disease states

Vascular leak




Vascular stability




**Infectious Disease/Pandemic:**
- Lethal Influenza
- Bacterial Pneumonia
- COVID-19
- Polymicrobial Sepsis

**Neuroscience/Blood-Brain-Barrier/Traumatic Brain Injury:**
- Vascular Dementia
- Occlusive Stroke
- Blood-Brain-Barrier Restoration
- Traumatic Brain Injury

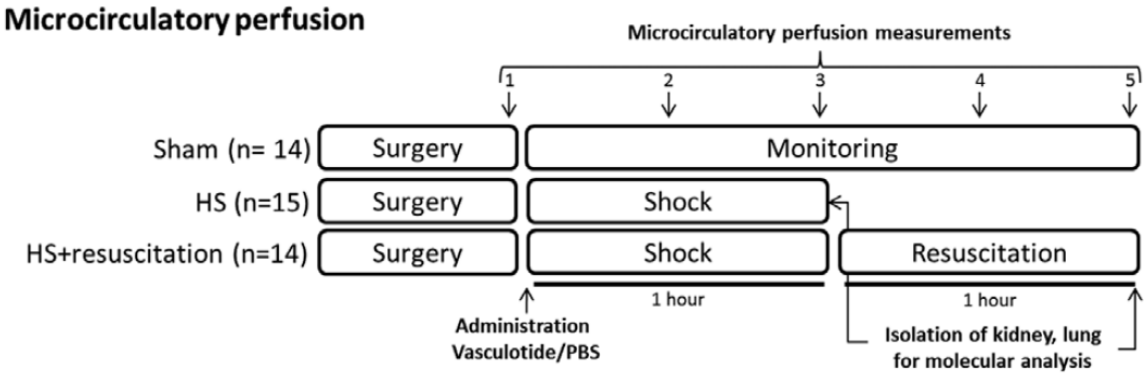
**Radiation and Wound Healing:**
- Wound Healing
- Radiation: Dermal Exposure
- Radiation: Full-Body Irradiation

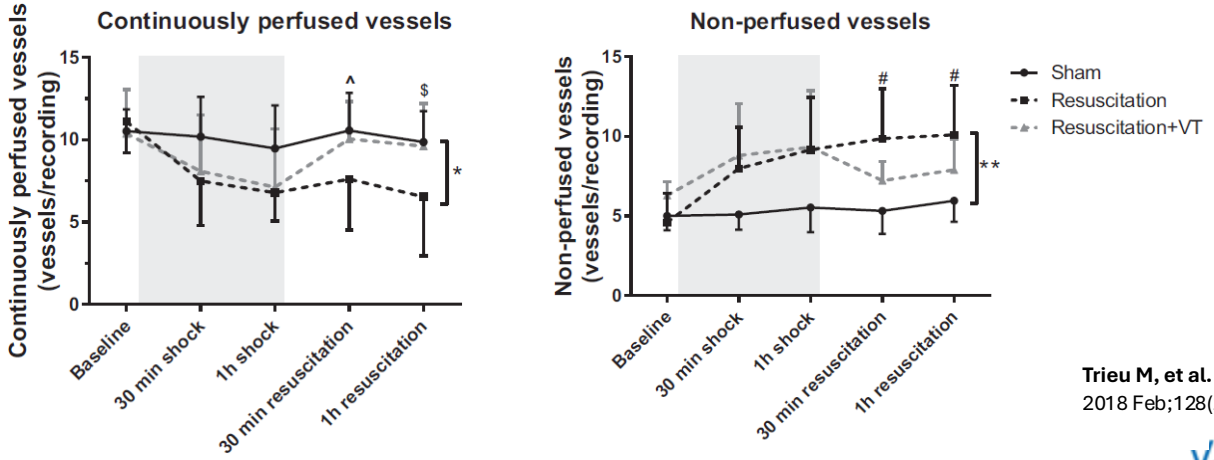
**Biotoxin:**
- Ricin Intoxication

**Shock and Trauma:**
- Severe Burn Injury
- Hemorrhagic Shock
- Polytrauma (Crush+ Fracture+ Hemorrhage)

Leppänen VM et al., Proc Natl Acad Sci U S A. 2017 114(17):4376-4381

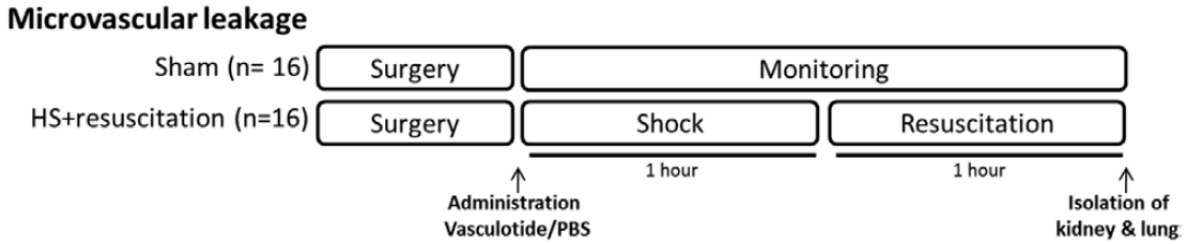
# **Pegevongitide (AV-001; Vasculotide) in Hemorrhagic shock**: Investigating Microcirculatory Dysfunction and Leakage

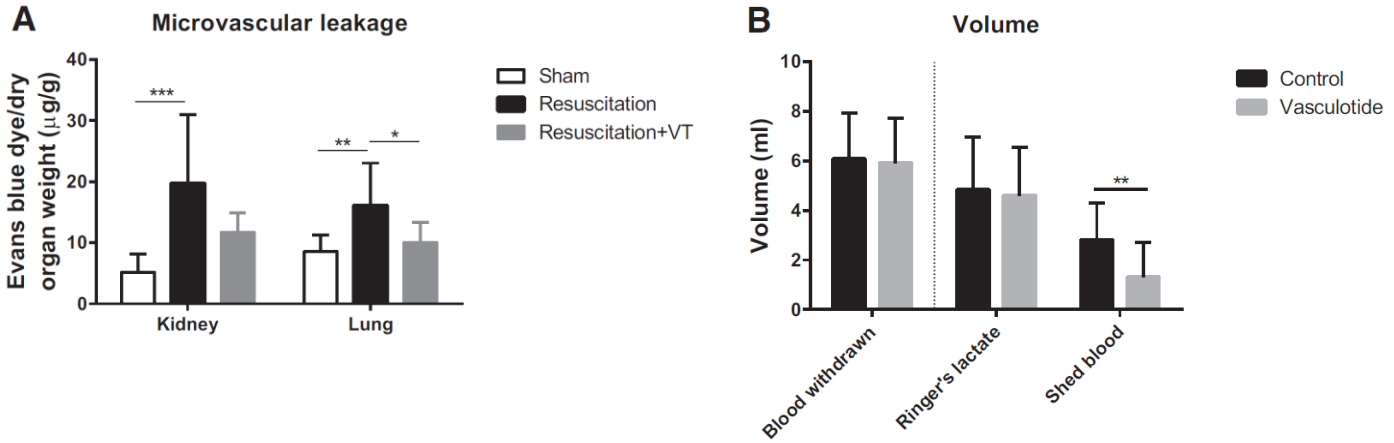



**Trieu M, et al.** Anesthesiology. 2018 Feb;128(2):361-374.

# Prophylactic Administration of Pegevongitide (AV-001; Vasculotide) Reduced Microvascular Leak and Fluid Resusitation Requirements

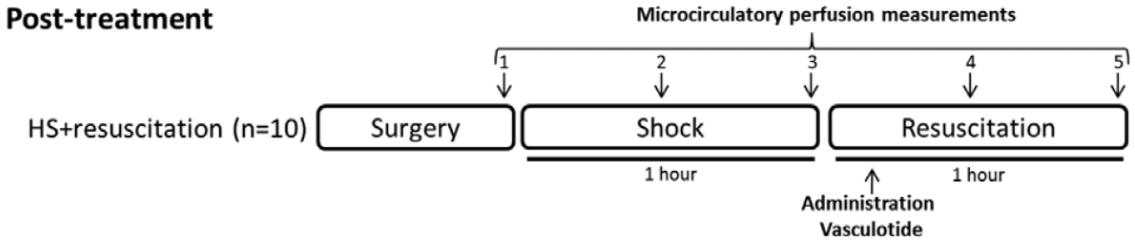


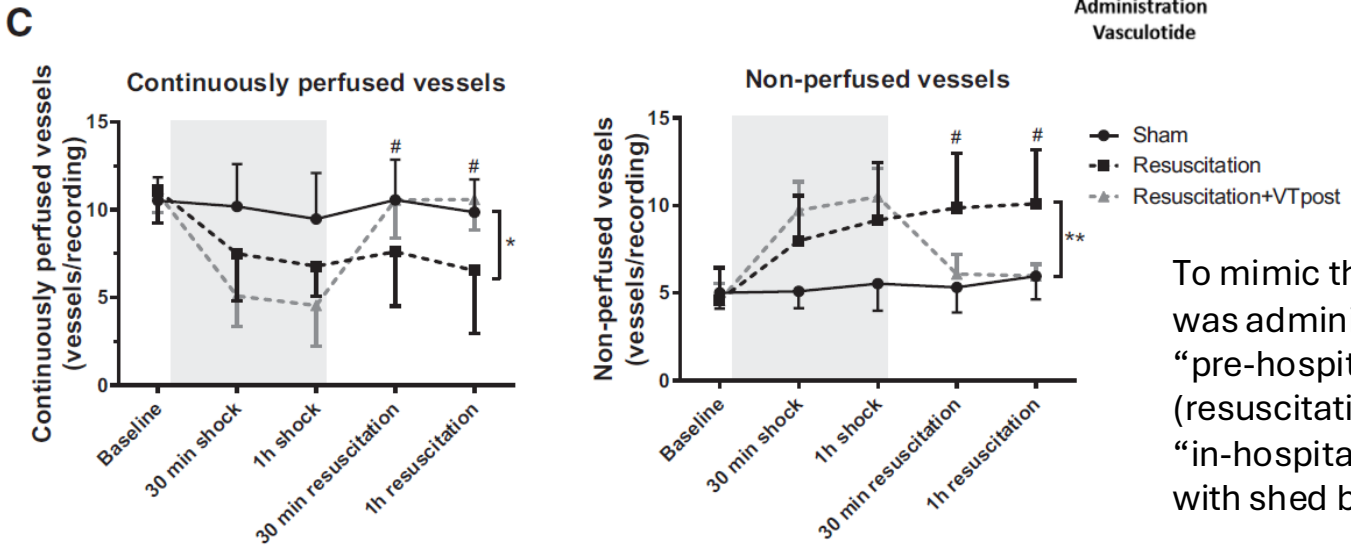




Treatment restored microcirculatory perfusion during fluid resuscitation **significantly attenuated pulmonary microvascular leakage** and **significantly reduced resuscitation volumes required .**

**Trieu M, et al.** Anesthesiology. 2018 Feb;128(2):361-374.

# Pegevongitide (AV-001; Vasculotide) Treatment Increases Microcirculatory Perfusion During Resuscitation from Hemorrhagic shock

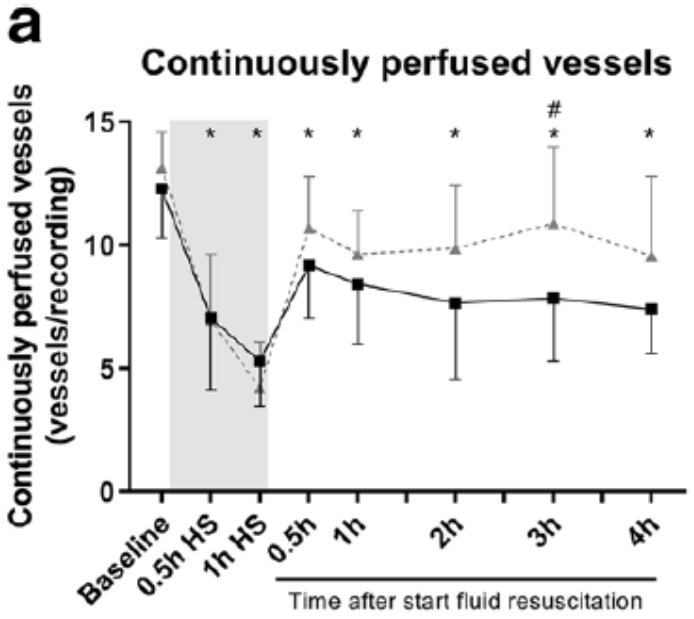


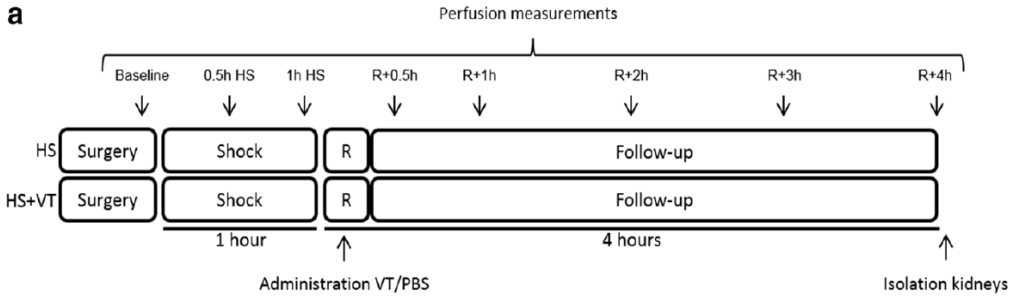




To mimic the clinical setting, drug was administered i.v. between the "pre-hospital" phase (resuscitation with LRS and the "in-hospital" phase (resuscitation with shed blood).

**van Leeuwen ALI, et al.** Intensive Care Med Exp. 2021;9(1):23.

## **Pegevongitide (AV-001; Vasculotide)** Treatment Increases Microcirculatory Perfusion During Resuscitation from Hemorrhagic shock



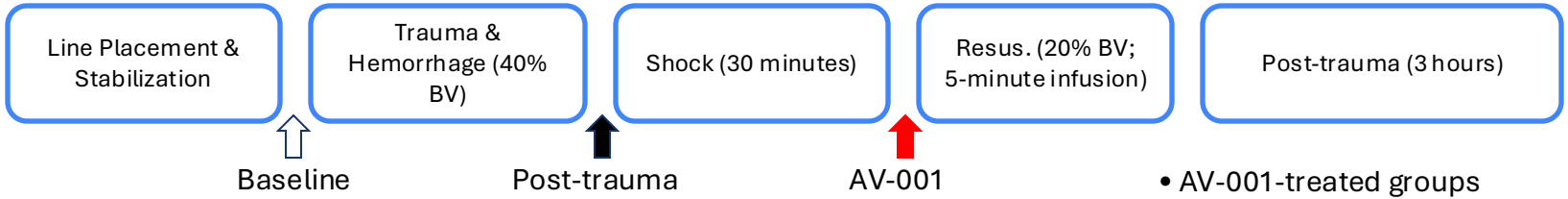



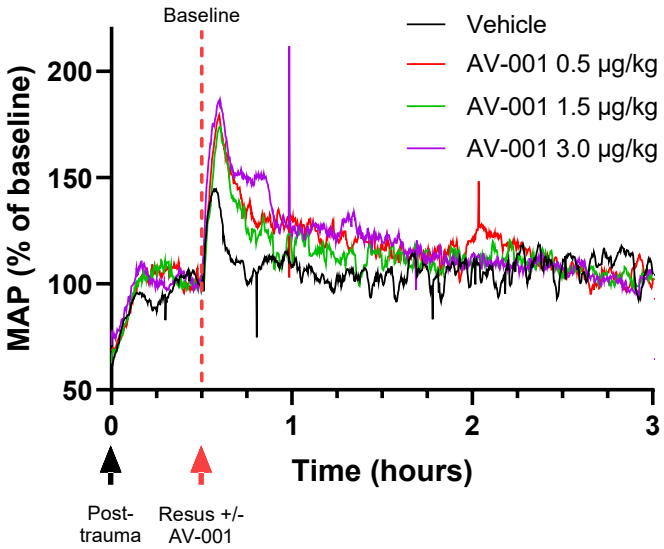

Perfusion was tracked over 4 hours.

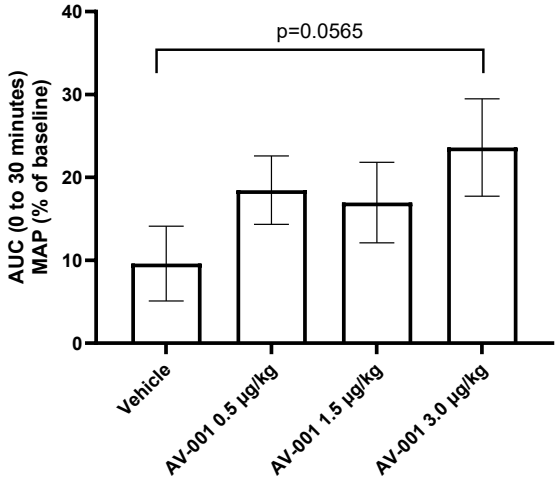
Treatment with pegevongitide restored cremaster perfusion compared to untreated animals.
This was reflected by a significant increase in the number of perfused vessels at 3 h following fluid resuscitation.

**van Leeuwen ALI, et al.** Intensive Care Med Exp. 2021;9(1):23.

# Pegevongitide Modulates Early Post-Resuscitation Hemodynamics in a Polytrauma Hemorrhagic Shock Model




- AV-001-treated groups demonstrated an early increase in MAP relative to vehicle following resuscitation in the first hour post-resuscitation.
- This interval corresponds to a period of maximal physiologic instability following polytrauma, hemorrhage, shock, and reperfusion.
- While per-animal analyses were not statistically significant at n=6/group (p=0.0565), the observed pattern is consistent with an early vascular stabilization effect.

**Weaver et al.,** US Army Institute of Surgical Research 2024.

## Why this matters. Treat early, Stabilize early, Preserve vascular function

| Study | Intervention Timing | Endpoint | Earliest Separation | Statistical Significance |
|---|---|---|---|---|
| Trieu 2018<br>Hemorrhagic shock | At resuscitation | ↑ Microperfusion<br>↓ Edema<br>↓ Resuscitation volume | Early (30–60 min) | Significant at 1 h |
| Van Leeuwen 2021<br>Hemorrhagic shock | At resuscitation | ↑ Microperfusion | Early (30–60 min) | Significant at 3 h |
| Weaver 2024<br>Polytrauma | At resuscitation | ↑ MAP | Early (30–60 min) | p=0.0565 |

Across both hemorrhagic shock and combined injury polytrauma models, the strongest treatment-associated effects are consistently observed during the first 30–60 minutes following resuscitation.

The consistency of the timing across independent models supports the hypothesis that AV-001 exerts its primary biological activity during the immediate post-resuscitation period.

## Why this matters. Potential Operational Relevance

**Sustain perfusion during the Golden Hour**

**Increase time available for casualty evacuation**

**Bridge patients to damage-control resuscitation**

**Bridge patients to definitive trauma care**

Early vascular stabilization during the golden hour to improve survival from shock and polytrauma.

# **Phase 1** trial demonstrated **on-target activation, safety and tolerability in humans**

**Phase 1 First-In-Human** → Phase 2a Pneumonia/ARDS → FDA Fast Track Designation

**Phase 1 Safety Study Highlights On-Target Activation**

- **NRC IRAP Award 965762: $2.4M CAD**

- N = 48
- Single dose: 4 dose cohorts, 6 active & 2 placebo subjects per cohort, receiving 1.4 µg/kg to 56 µg/kg of AV-001 by IV bolus
- Multiple dose: 2 dose cohorts, 6 active & 2 placebo subjects per cohort, receiving up to 56 µg/kg/day of AV-001 daily for 7 days by IV bolus
- PK and PD amenable to daily dosing
- No evidence of accumulation
- No SUSARS, no AESI, no hypotension, no immunogenicity
- **On-target Tie2 activation**
  - Tie2 phosphorylation on granulocytes via TEL assay

Clinicaltrials.gov: NCT04737486

H. Kim, et al. A Randomized, Double-Blind, Placebo-Controlled Phase1 Single and Multiple-Dose Pharmacokinetic First-In-Human Study of AV-001 in Healthy Subjects for the Treatment of ARDS (abstract). Am J Respir Crit Care Med 2024;209:A5510

On-target Tie2 activation

Excellent safety & tolerability

# **Phase 2a** clinical trial in **pneumonia and Acute Respiratory Distress Syndrome** is nearing completion

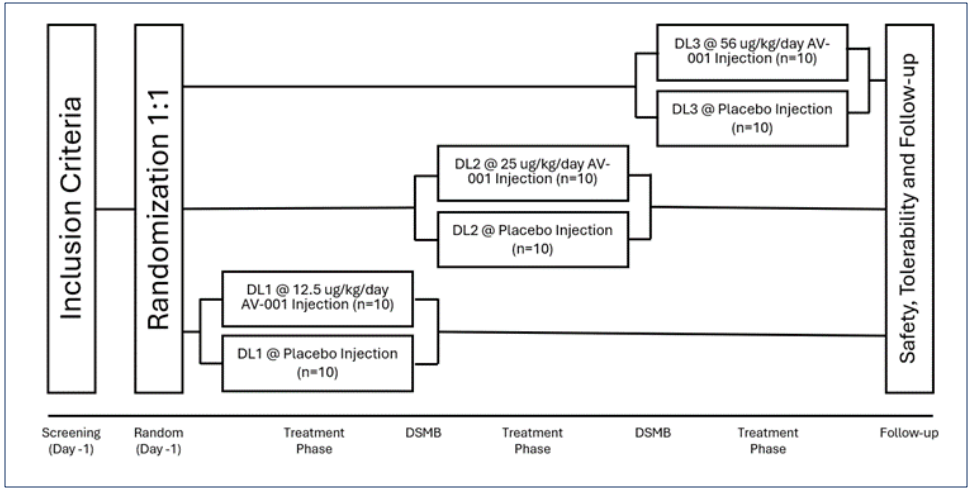
CDMRP DEPARTMENT OF DEFENSE CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

Phase 1 First-In-Human → **Phase 2a Pneumonia/ARDS** → FDA Fast Track Designation

**Phase 2a Near Completion**

- **CDMRP Award PR191212: $2.8M USD**
- **CDMRP Award PR203503: $6.4M USD**

- 97% enrolled
- 11 sites in US
- Median CPS 5
- Various microbial diagnoses
- Target completion by Q3 2026




Clinicaltrials.gov: NCT05123755

Fast Track for Prevention & Treatment

Pathogen agnostic

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**Summary:** Vasomune is eager to explore opportunities to help fulfill JPEO-CBRND strategic goals to develop **threat agnostic therapy to counter vascular leak**

**Threat agnostic therapeutic with multiple opportunities for intervention**

- Pneumonia/ARDS, specifically, coronaviruses and/or influenza
- Severe burn injury
- Polytrauma
- Cerebrovascular injury

**First-in-class therapy with multiple possible indications**

- Novel Tie2 receptor agonist to activate previously undruggable target
- Mitigates vascular leak by normalizing host vascular response

**Clinical stage asset**

- Broad and favorable preclinical activity profile, and favorable clinical safety profile
- Completed Phase 1, and currently in Phase 2a for pneumonia/ARDS and Phase 2a for cerebrovascular injury
- IND allowance for severe burn injury >40% TBSA

**Robust manufacturing and supply chain**

- Established GMP CMC in place with supply and stability to enable further clinical studies

# Our **leadership team** is complemented by world-class advisors

**Brian Jahns, PharmD**
PRESIDENT, CEO

SVP Commercial and BD, Trillium Therapeutics (NASDAQ: TRIL)

ClinDev & BD, Roche

Biopharma executive, clinical pharmacist, clinical toxicologist

**Harold Kim, PhD**
SCIENTIFIC CO-FOUNDER
CSO

Over 20 years of experience in academia and biotechnology; research fellow in the laboratory of Dr. Daniel Dumont, who discovered the Tie2 receptor.

**Gosia Hodgson, CPA, CA**
CFO

13+ years leadership in accounting and corp dev in biotech, IP management and public accounting

Experience closing >$500M capital transactions, 10 IP licensing deals, one biotech exit

**Shahid Ahmad**
VP, OPERATIONS & PLANNING

20+ in operations and supply chain management

Certified PMP, led >$10M non-dilutive funding initiatives for Vasomune

## Our Advisors and Collaborators

**Daniel Vlock, MD**
CMO

Associate Director, Boehringer Ingelheim and Director, J&J

Faculty, Harvard Medical School

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CLINICAL ADVISOR AND CO-I

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Burn and trauma surgeon and researcher

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Researcher in Molecular Phenotyping ARDS and Precision Medicine in the ICU

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Associate Professor, Critical Care, University of Toronto

**Christopher McIntyre, MD, PhD**
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**Michael V. Callahan, MD, MSPH, DTM&H (UK)**
INVESTIGATOR

Director, Clinical Translation & Mass-Casualty Therapeutics

Massachusetts General Hospital

**Alan J. Weaver Jr., PhD**
INVESTIGATOR

Research Scientist

U.S. Army Institute of Surgical Research Hemorrhage & Vascular Dysfunction

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**References (full AV-001 bibliography available upon request)**


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- Sugiyama MG, et al. The Tie2-agonist vasculotide rescues mice from influenza virus infection. Sci Rep. 2015 Jun 5;5:11030.
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- van Leeuwen ALI et al. The effect of targeting Tie2 on hemorrhagic shock-induced renal perfusion disturbances in rats. Intensive Care Med Exp. 2021 May 17;9(1):23.
- Vasomune study number AV001-IV-011 Data On File


**Regulatory and Clinical:**


- Clinicaltrials.gov: NCT04737486
- Clinicaltrials.gov: NCT05123755
- FDA. IND 152741, Nov 2020.
- FDA. Fast Track Designation AV-001 for the prevention and treatment of ARDS, May 2024.


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