

# Novel Approaches in Vascular Tissue Engineering

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Humacyte, Inc.

# CONFLICTS OF INTEREST & DISCLOSURES

Dr. Blum is Co-Founder & EVP, Corporate Development and a shareholder in Humacyte, Inc.

None of the data presented in this lecture is intended to be construed as claims for the clinical use, efficacy, or safety of any medical product. The human accellular vessel (HAV) is an investigational product that has not been approved by FDA for any indication.

These slides and the accompanying oral presentation contain forward-looking statements. All statements, other than statements of historical fact, included in these slides and the accompanying oral presentation are forward-looking statements reflecting management's current beliefs and expectations. In some cases, you can identify forward-looking statements by terminology such as "will," "anticipate," "expect," "believe," "intend" and "should" or the negative of these terms or other comparable terminology. Forward-looking statements in these slides and the accompanying oral presentation include, but are not limited to, statements about the initiation, timing, progress and results of our clinical trials; the anticipated characteristics and performance of our human acellular vessels (HAVs), our ability to successfully complete, clinical trials for our HAVs; the anticipated benefits of our HAVs relative to existing alternatives; the commercialization of our HAVs and our ability to manufacture at commercial scale; the implementation of our business model, strategic plans for our business; the scope of protection we are able to establish and maintain for intellectual property rights covering our HAVs and related technology; estimates of our expenses, health economics, future revenues, capital requirements and our needs for additional financing; the timing or likelihood of regulatory filings and approvals; timing, scope and rate of reimbursement for our HAVs; our estimated available market opportunity; our ability to maintain and establish collaborations; our financial performance; developments relating to our competitors and our industry; statements regarding our markets, including the estimated size and anticipated growth in those markets; and statements related to our proposed business combination with a subsidiary of Alpha Healthcare Acquisition Corp. (AHAC), including the timing and structure of the transaction and our ability to recognize the anticipated benefits of the business combination. These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other 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 these forward-looking statements. Except as required by law, we assume no obligation to update these forward-looking statements, even if new information becomes available in the future.

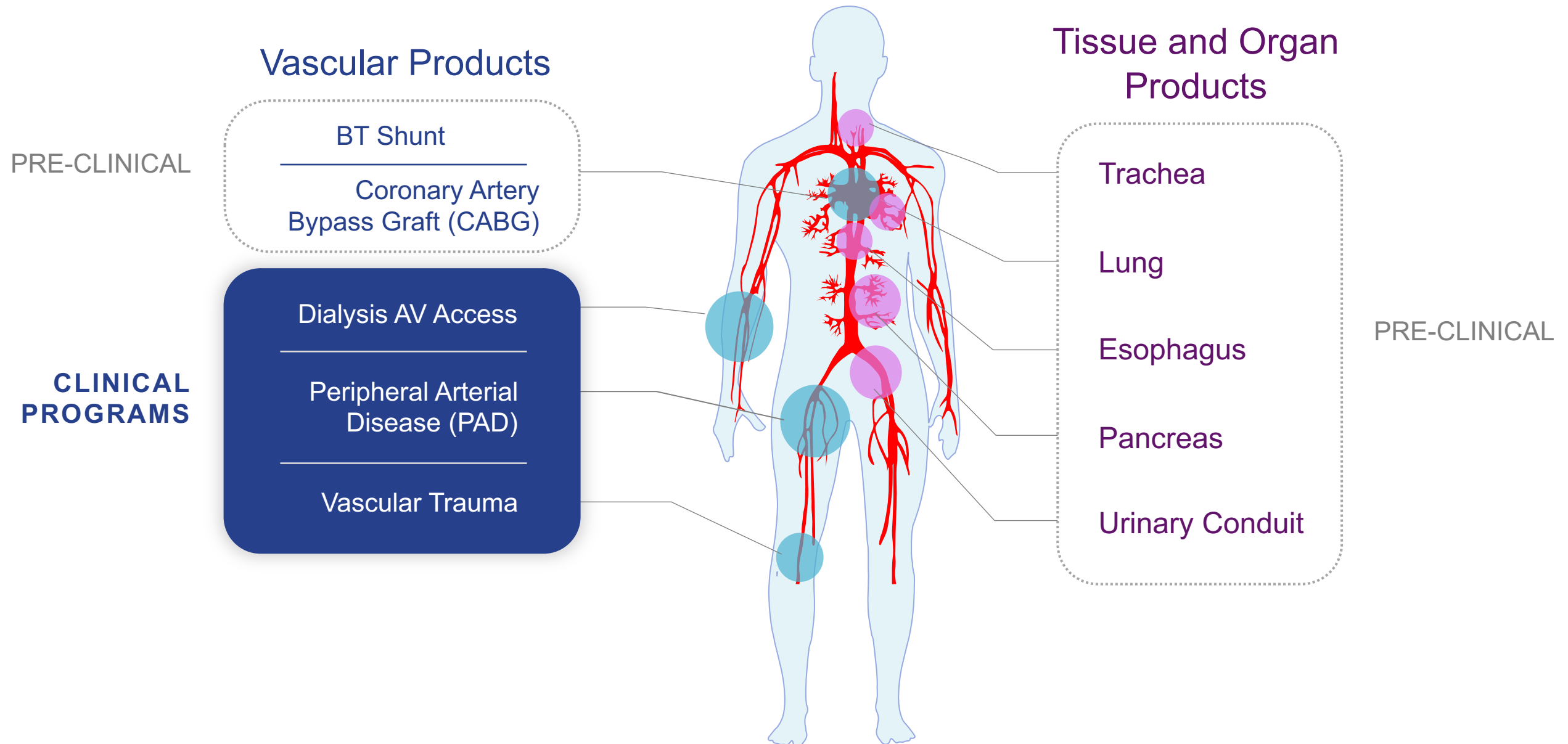


# COMPANY & TECHNOLOGY OVERVIEW

*Humacyte is pioneering the development and manufacture of off-the-shelf, universally implantable, bioengineered human tissues*



# HUMACYTE DEVELOPS BIOENGINEERED TISSUES TO TREAT DISEASES THROUGHOUT THE BODY



# HISTORY DEFINING MILESTONES



**2004**

Founded by Drs. Laura Niklason, Juliana Blum, and Shannon Dahl, Durham, NC



**2013**

First human surgical implantation of HAV at Duke University



**2014**

Humacyte's HAV received Fast Track Designation for Vascular Access in Hemodialysis Program



**2017**

Humacyte Receives Regenerative Medicine Advanced Therapy Expedited Review Designation for HAV



**2018**

FMC & Humacyte Announce Global Partnership Supported by \$150M Equity Investment



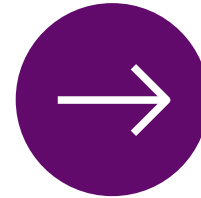
**2019**

Manufacturing facility validation qualification, Durham NC



**2021**

Humacyte goes public on Nasdaq as \$HUMA

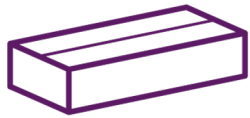


**FUTURE**

Product Launch & Pipeline Development

## KEY FEATURES OF HUMACYTE TECHNOLOGY

### Potential benefits of HAVs evaluated in completed and ongoing clinical trials across multiple indications



Off-the-shelf,  
immediately available  
with 18-month shelf life



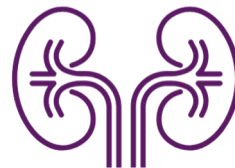
HAV is highly  
resistant to infection



No evidence of  
immunogenicity



Host cells repopulate  
the HAV



For ESRD patients,  
accessible for dialysis  
access within one  
month of implantation



Long-term durability  
is demonstrated in  
ongoing studies

# COMMERCIAL MANUFACTURING SCALE

## Modular Manufacturing System

Bioreactor bag



*Each bioreactor bag contains a single polymer mesh scaffold, seeded with donated human cells*



Growth drawer



*10 bioreactor bags per growth drawer; tubing connects to shared nutritive media*



LUNA200 system



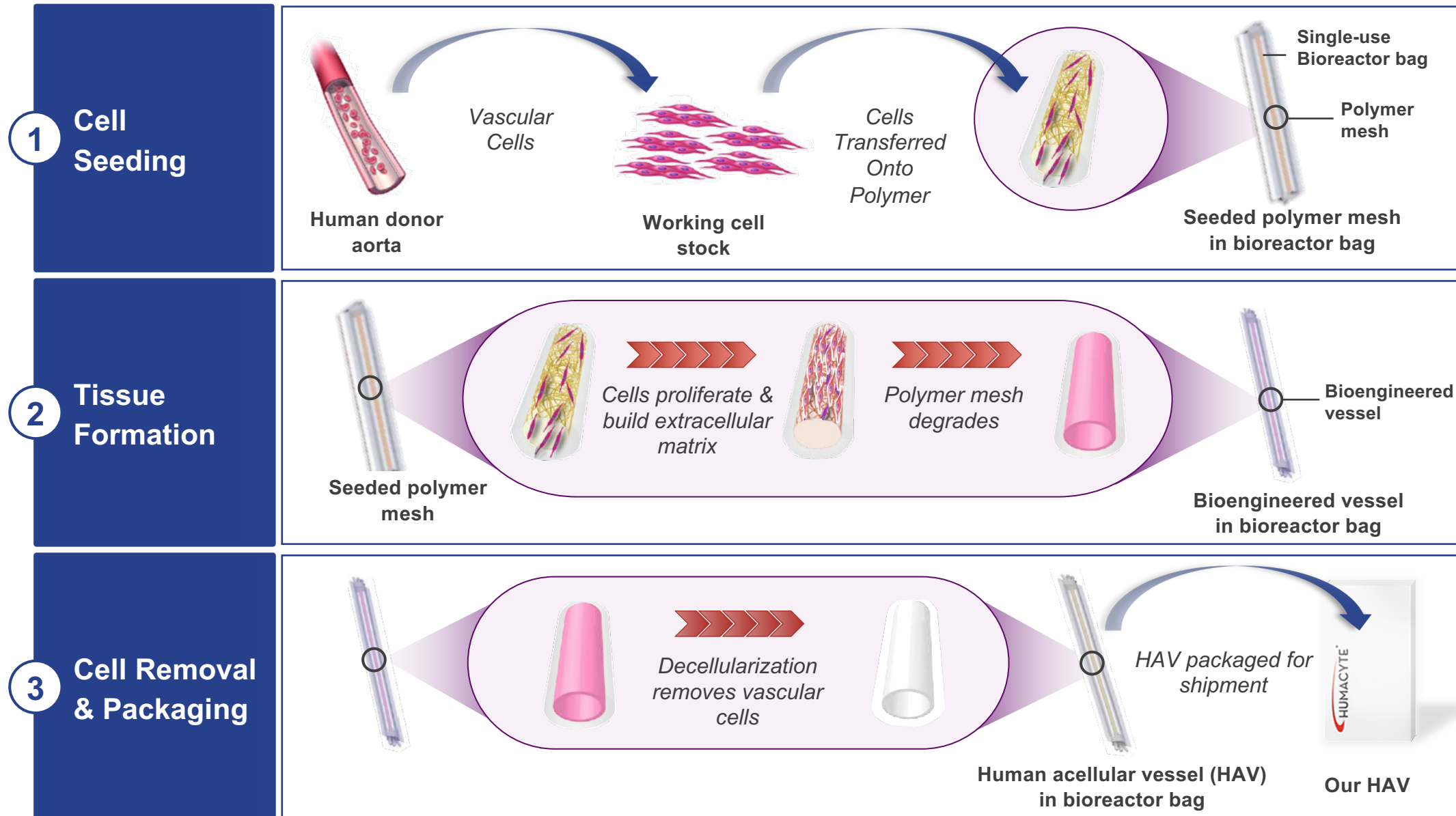
*With 20 growth drawers, each LUNA200 can produce 200 HAVs per batch (or ~1,000 HAVs annually) <sup>1</sup>*

## Commercial 83,000 sq ft Bioprocessing Facility



- Currently operating 8 LUNA200 systems
- Annual Capacity expected to exceed 40,000 HAVs
- Functionally closed system with state-of-the-art process automation

# HUMAN ACELLULAR VESSELS (HAVs)





## READILY AVAILABLE HAVs

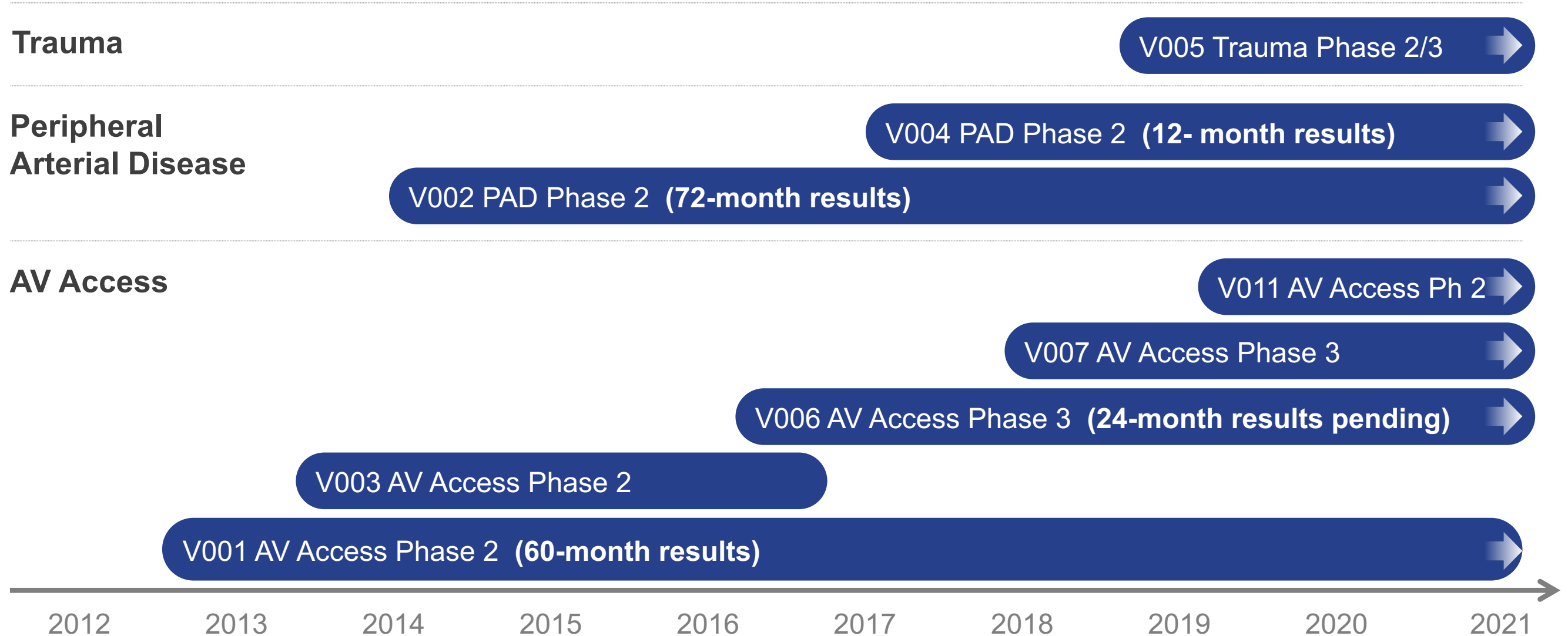


**HAVs are shipped to hospitals for use in operating rooms.  
During surgery, the HAV is removed from its packaging and then implanted into the patient.**

# CLINICAL OVERVIEW - DIALYSIS



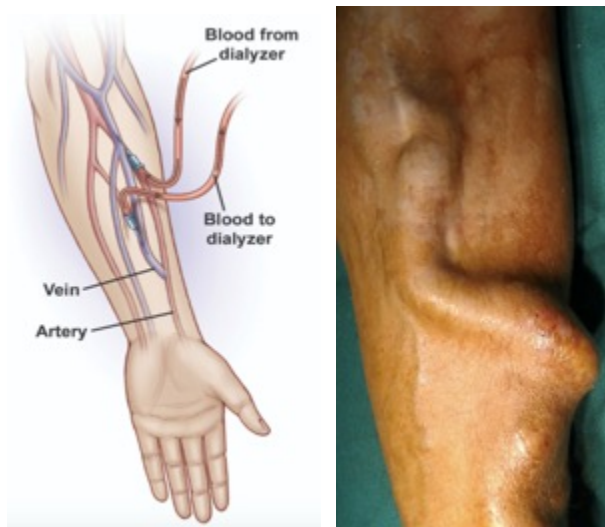
## EXTENSIVE CLINICAL EXPERIENCE ACROSS MULTIPLE CLINICAL TRIALS



**HAVs have been implanted into hundreds of patients over more than 8 years.**

# THE HAV in DIALYSIS: ADDRESSING RECURRENT INFECTIONS AND FISTULA FAILURE

## AV Fistula



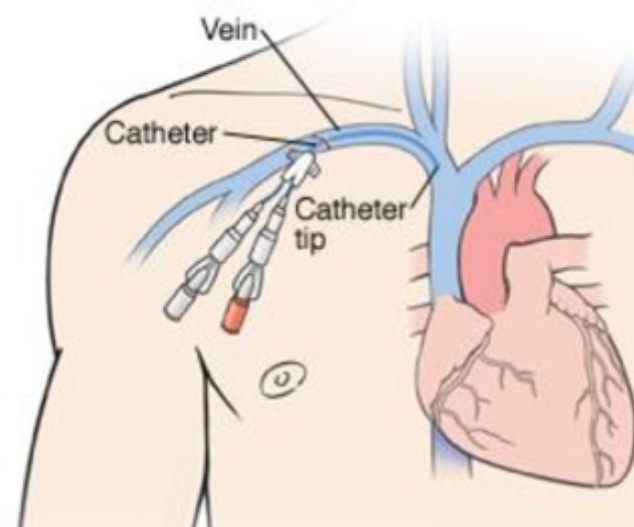
### Standard of Care

- Major risks associated with catheter during wait for fistula maturation
- ~40% of fistulas fail

### Humacyte HAV

- HAV usable within 1 month vs 3-6 months for fistulas
- Decreased catheter contact time in patients awaiting fistula maturation

## Catheter



- High blood stream infection rates (up to 200% per patient-year)

Infection rate for:

- Catheters: up to 200% per patient year<sup>1</sup>
- HAV: 1% per patient year<sup>2</sup>

## Synthetic Graft



- 10-15% annual infection rate: sepsis, hospitalization, death
- Not durable: ~50% fail in 2 years<sup>1</sup>

- 10-15x lower rate of infection versus ePTFE
- Excellent Durability: used for dialysis for ~7 years

<sup>1</sup>Lawson, J.H, et al, The Lancet 2016; 387: 2026-2034.

<sup>2</sup>Halbert, R.J., et al, Kidney360 2020; doi: 10.34067/KID.003502020.



# HAV IN HEMODIALYSIS ACCESS: PHASE 2 STUDY THROUGH 12 MONTHS

- **Methods:** Six centers in the US and Poland, HAV implanted in patients who were in need of dialysis access and who were suitable for arteriovenous grafting <sup>1</sup>.
- **Subjects:** 60 patients, mean follow-up 16 months
  - Age = 59 ± 10y;
  - 77% Caucasian;
  - 90% with hypertension;
  - 43% diabetic;
  - Prior AV accesses: 3.6 ± 2.1.
- **Safety Outcomes:**
  - No aneurysmal degeneration;
  - No clinical rejection;
  - Multiple subjects subsequently received successful kidney transplants.
- **Results:**
  - 12 month HAV outcomes published in *The Lancet* <sup>1</sup>

Volume 387, No. 10032, p2026-2034  
Published in issue: May 14, 2016

## Phase 2 HAV Results vs. Historical Fistula & ePTFE Data

Conduit	6-month Secondary Patency	12-month Secondary Patency	Infection Rate per patient-year
<b>HAV Phase 2</b>	<b>97% (85-98%)</b>	<b>89% (74-93%)</b>	<b>1.3%</b>
<b>Historical Fistula</b> <sup>2,3,4</sup>	<b>61%</b> <sup>3</sup> (useable for dialysis)	<b>59.5%</b> <sup>4</sup>	<b>4.0%</b> <sup>5</sup>
<b>Historical ePTFE</b> <sup>5</sup>	<b>80% (75-84%)</b>	<b>70%(64-75%)</b>	<b>9.0%</b>

<sup>1</sup> Lawson, J.H. et al. The Lancet 2016; 387: 2026-2034.

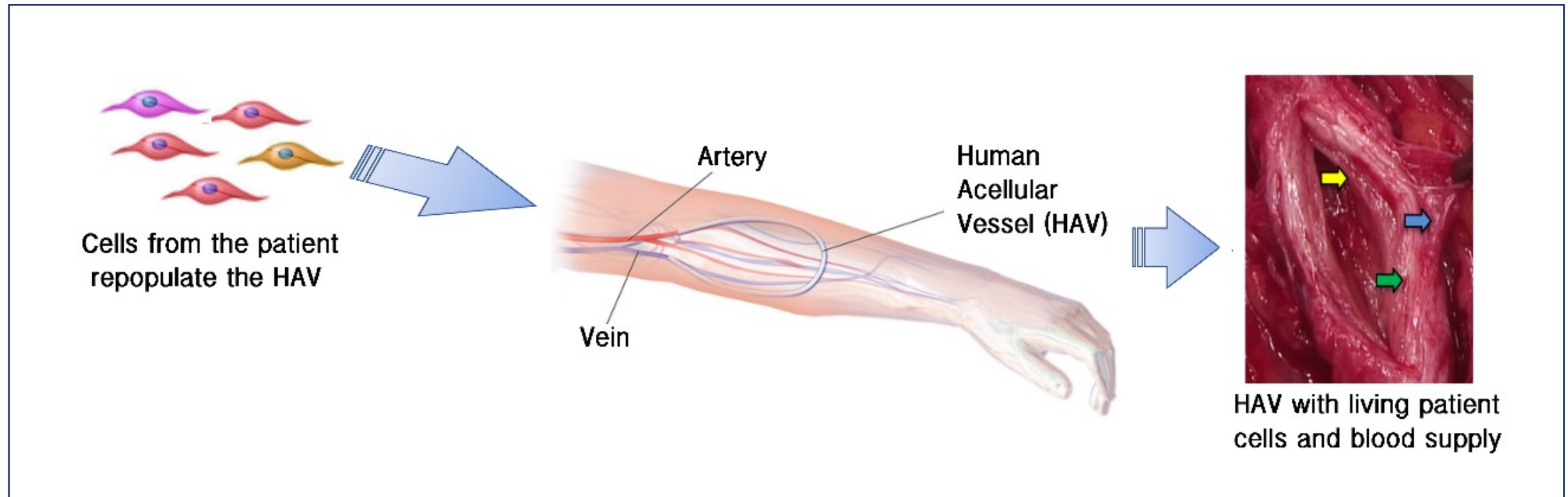
<sup>2</sup> Halbert, R.J. et al. Kidney360 December 2020, 1 : 1437-1446

<sup>3</sup> Allon, M., et al. American J Kidney Disease 2018; 71: 677-689.

<sup>4</sup> Arhuidese, I.J., et al. Journal Vascular Surgery 2018; 68: 1166-1174

<sup>5</sup> Al-Jaishi, A.A., et al. JASN 2017; 28: 1839-1850.

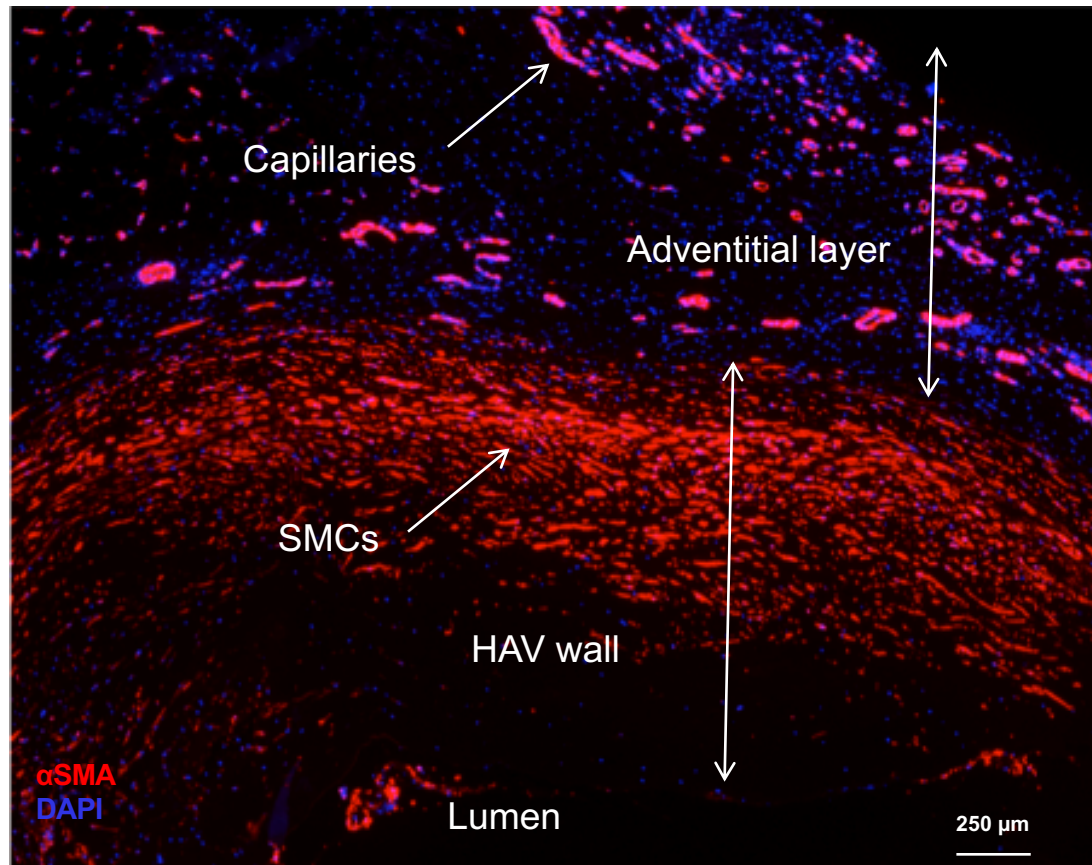
## CLINICAL EVIDENCE THE HAV REGENERATES WITH PATIENT CELLS



After implantation, clinical data has shown cells from the patient gradually repopulate the HAV, producing a tissue that has living cells and its own blood supply.

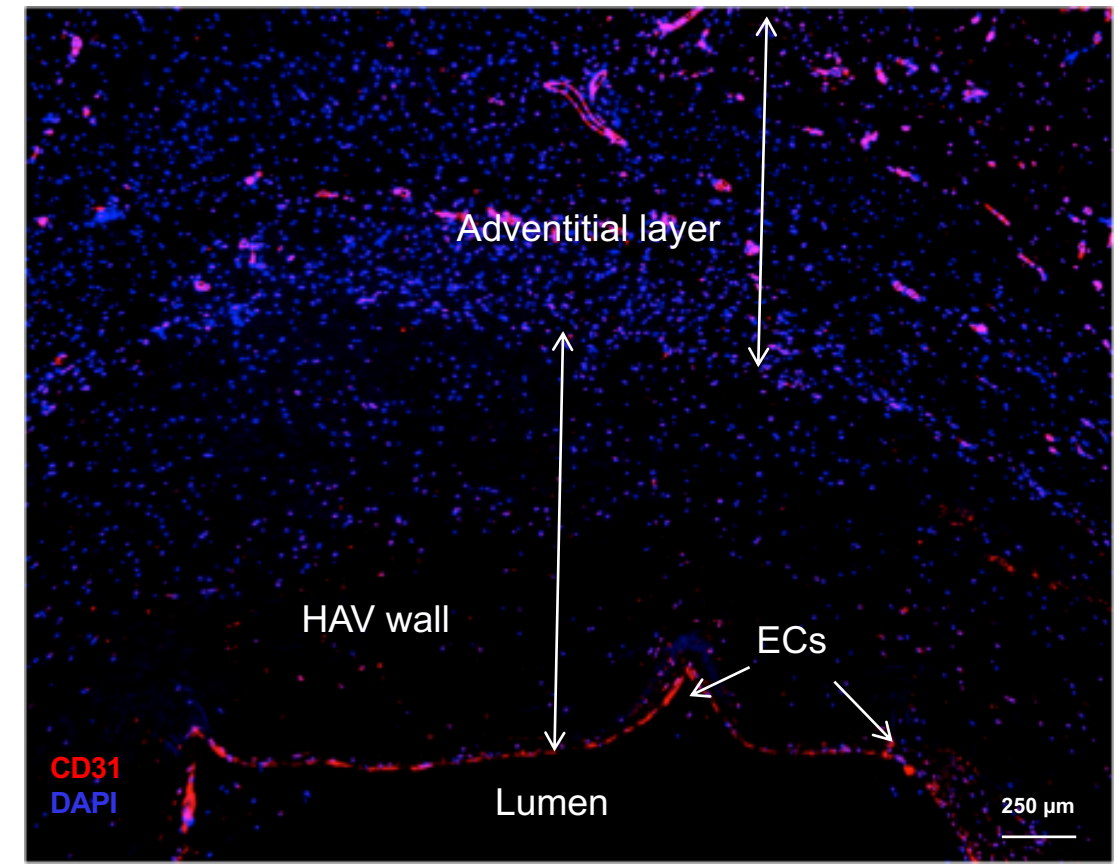
# CLINICAL DATA SHOWS THAT HAV BECOMES LIVING BLOOD VESSEL

Smooth Muscle Cells (Red) Prominent in HAV Wall,  
Adventitial Layer with Capillaries<sup>3</sup>



At 44 weeks

Endothelial Cells (Red)  
Line the HAV Lumen<sup>3</sup>



**Clinical data shows the HAV repopulates with the patient's own cells,  
angiogenesis enables self-maintenance, and self-heals in response to injury.**

<sup>1</sup> Samples were assessed at 16, 18, 22, 27, 37, 44, 55, 97, 100, 121, and 200 weeks.

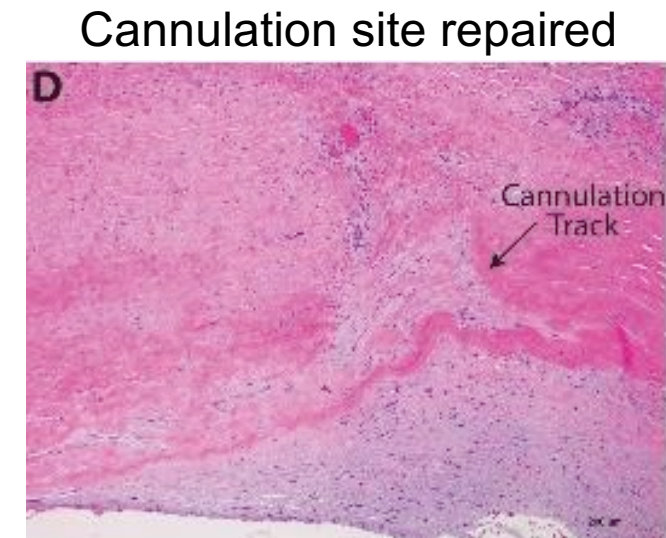
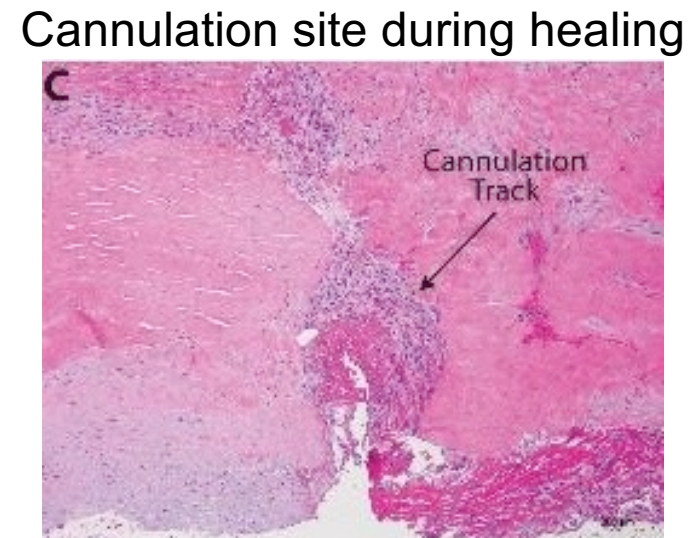
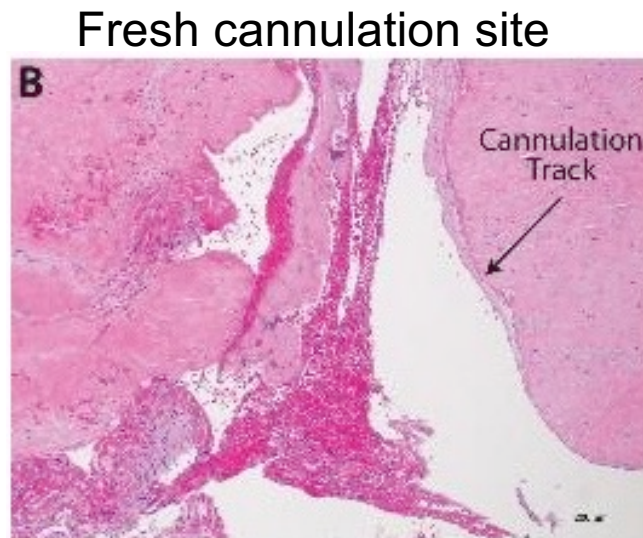
<sup>2</sup> No evidence of chronic inflammation.

<sup>3</sup> Explant from 01-001-V003, 44 weeks after implantation.



# CLINICAL EVIDENCE OF HEALING

Low  
magnification of  
3 cannulation  
sites



Repopulation with host vascular cells and angiogenesis enable healing



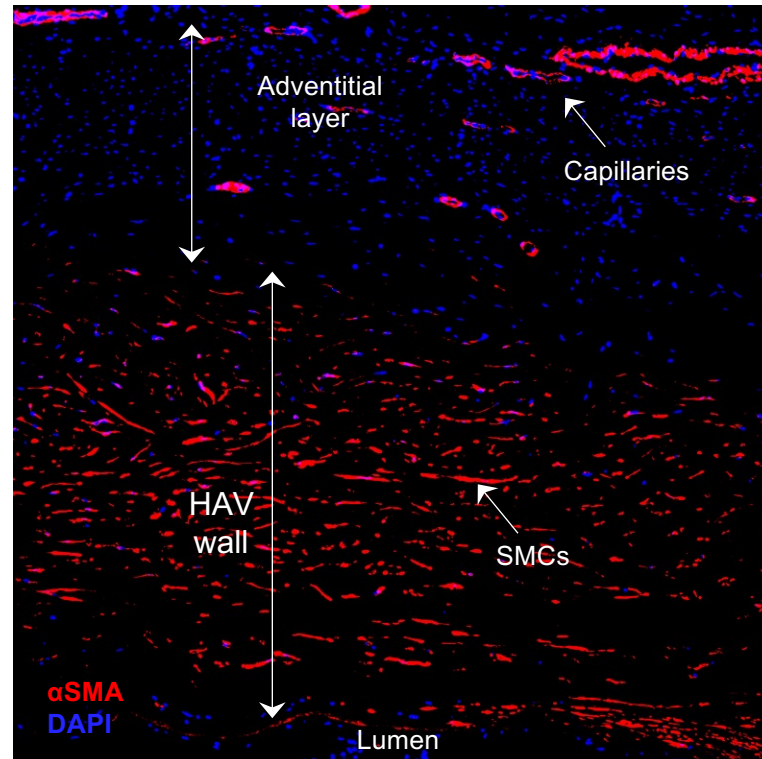
**Clinical data<sup>1</sup> suggests after cannulation, HAV potentially heals to close the cannulation injury site.  
In contrast, PTFE has permanent cannulation injury with no healing.**

<sup>1</sup> HUMACYL® Patient CLN-PRO-V003 01-001 histology Phase II trial, 2014. unpublished data. A section of an implanted Humacyte graft removed at 11 months. All images are Hematoxylin & Eosin stain (H&E) (n=1)

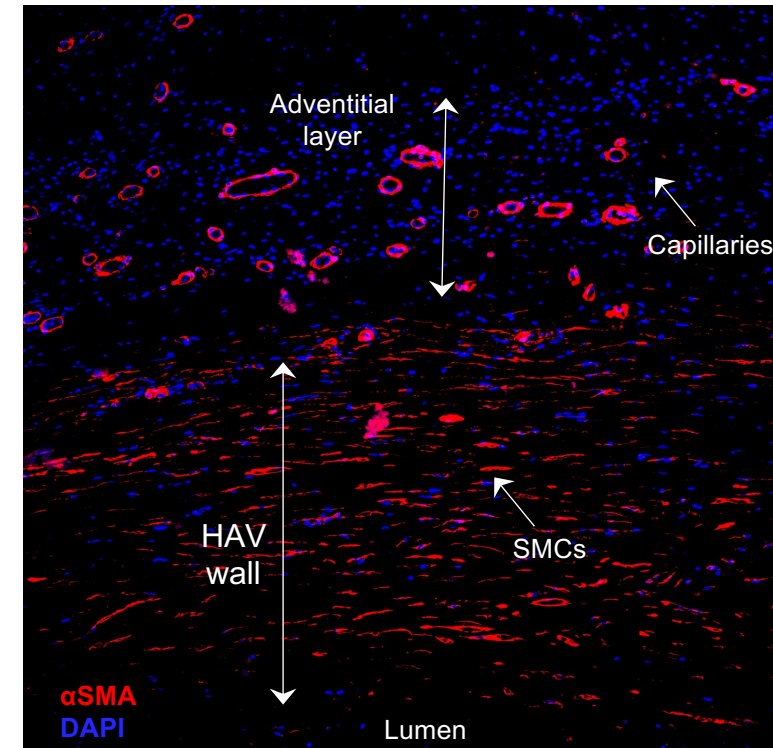


# CLINICAL EVIDENCE SHOWS REMODELING OF THE HAV IS CONSISTENT AND ANGIOGENIC

Subject 3079-012-V006, male, 26 years old.  
67 weeks post-implantation of HAV

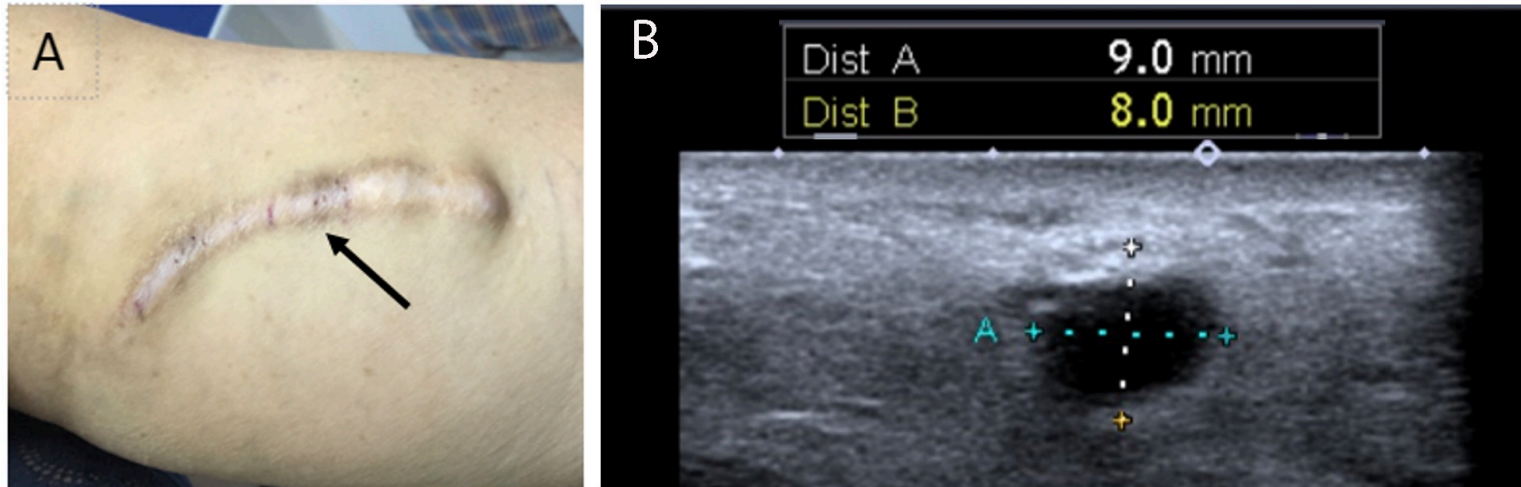


Subject 1006-001-V006, male, 83 years old.  
66 weeks post-implantation of HAV

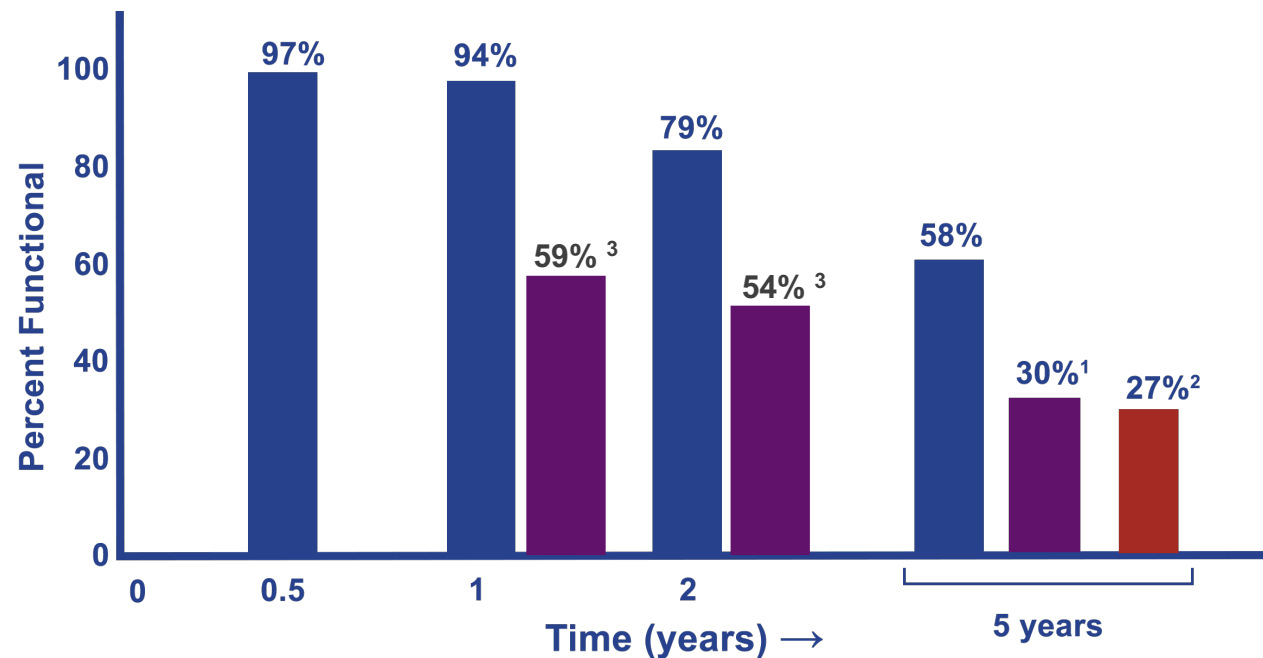


**Patient cells remodel the HAV across a wide range of patient ages.  
Repopulation with vascular cells is combined with robust peri-HAV angiogenesis.**

## HAV IN HEMODIALYSIS ACCESS: PHASE 2 STUDY $\geq 5$ YEARS, LONG TERM DURABILITY



- A) Patient with access site utilized for 6 years (arrow).
- B) Ultrasound of HAV from same patient.



58% secondary patency at 5 years compares well to historical ePTFE and arteriovenous fistulas.

<sup>1</sup> Lok, et al; 2013 CJASN  
<sup>2</sup> Kakisis et al; 2017, JVS  
<sup>3</sup> Arhuidese, et al, 2018; JVS.

## THE HAV DOES NOT STIMULATE INCREASES IN PANEL REACTIVE ANTIBODIES

There have been no reported instances of clinical HAV rejection observed in any patient with more than 460 patients evaluated overall.

Calculated Panel Reactive Antibodies (cPRA) have been measured in many HAV clinical studies to determine potential sensitization, with more than 250 patients evaluated to date.

- Less than 4% of HAV patients reported an increase over baseline values
- Less than 2% of patents reported an increase of more than 20% over baseline

For patients awaiting a transplant, changes in PRA values are closely monitored and evaluated as part of the donor matching and organ allocation considerations

- Patients with increases in PRA levels are viewed as “sensitized” with >20% increase, or “highly sensitized” with >80% increase; and are challenged or less likely to be successfully matched to an immunologically compatible donor candidate <sup>1, 2</sup>

<sup>1</sup> Hemodialysis International 2020; 24:36–42

<sup>2</sup> Clinical Transplant 2011, Terasaki Foundation Laboratory, Los Angeles, California

## NEXT STEPS FOR CLINICAL EVALUATION OF THE HAV IN DIALYSIS

### Phase 2 long-term follow-up results submitted for publication:

**Five-year outcomes in patients with end-stage renal disease who received the bioengineered human acellular vessel for Dialysis Access**

Tomasz Jakimowicz MD PhD<sup>a</sup>; Stanislaw Przywara MD, PhD<sup>b</sup>; Jakub Turek MD<sup>c</sup>; Malgorzata Guziewicz MD PhD<sup>c</sup>; Marek Ilzecki MD, PhD<sup>b</sup>; Michał Macech MD<sup>a</sup>; Wojciech Witkiewicz MD PhD<sup>c</sup>; Norbert Zapotoczny MD<sup>c</sup>; Tomasz Zubilewicz MD PhD<sup>b</sup>; Robert Kirkton PhD<sup>d</sup>; Alison J Pilgrim MD<sup>e</sup>; Heather L Prichard PhD<sup>d</sup>; William Tente MS<sup>d</sup>; Jeffrey H Lawson MD PhD<sup>d,f</sup>; Laura E Niklason MD PhD<sup>d,g</sup>

### Phase 3 studies ongoing:

**NCT02644941 (HUMANITY):** An Assessment of Humacyte's Human Acellular Vessel in Patients Needing Renal Replacement Therapy:  
A Comparison with **ePTFE Grafts** as Conduits for Hemodialysis

- 37 centers in the US, German, UK, Poland, Portugal, and Israel; 355 total subjects;
- 1:1 Prospective randomization HAV (6mm x 42cm) vs. ePTFE grafts.

**NCT03183245:** Compare the Efficacy and Safety of Humacyte's Human Acellular Vessel with that of an **Autologous Arteriovenous Fistula** in Subjects with End-Stage Renal Disease (**currently enrolling**)

- 30 centers in the US; target 240 total subjects (~200 subjects enrolled currently).



# THE ERA OF READILY AVAILABLE, ENGINEERED HUMAN TISSUES HAS ARRIVED

## ***Bioengineered Blood Vessel***

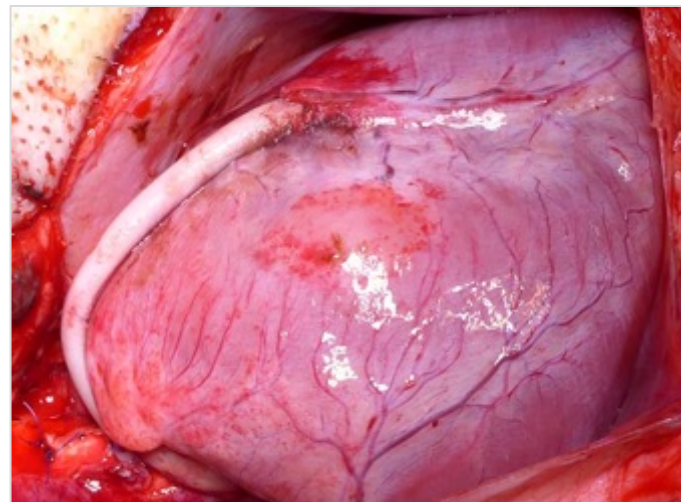
- Hemodialysis
- Vascular Trauma
- PAD



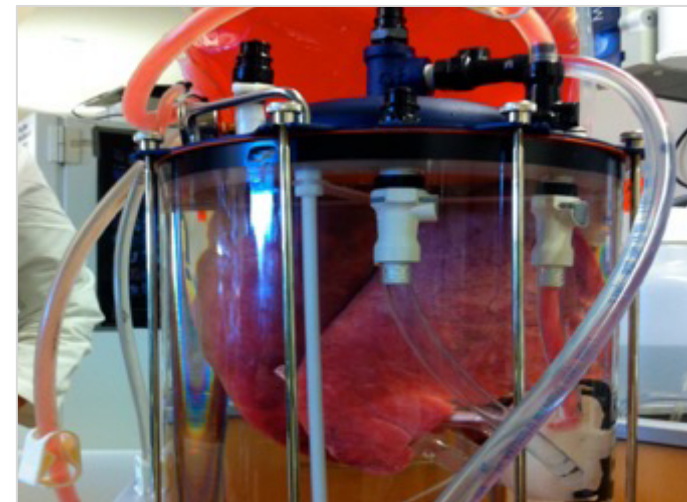
## ***Bioengineered Pancreas***



## ***Bioengineered Human Coronary Artery***



## ***Bioengineered Human Lung***



## SUMMARY

- Breakthrough innovation in large therapeutic areas serving significant unmet medical need is unfolding today
- Proprietary manufacturing technology at commercial scale requires innovation & unique solutions, and is possible
- Focus on completing Phase 3 studies and seeking FDA approval
- Expand the HAV platform and patient opportunities to complex tissues and organs
- Strong partnerships between research & discovery, manufacturing, and commercialization are key to success



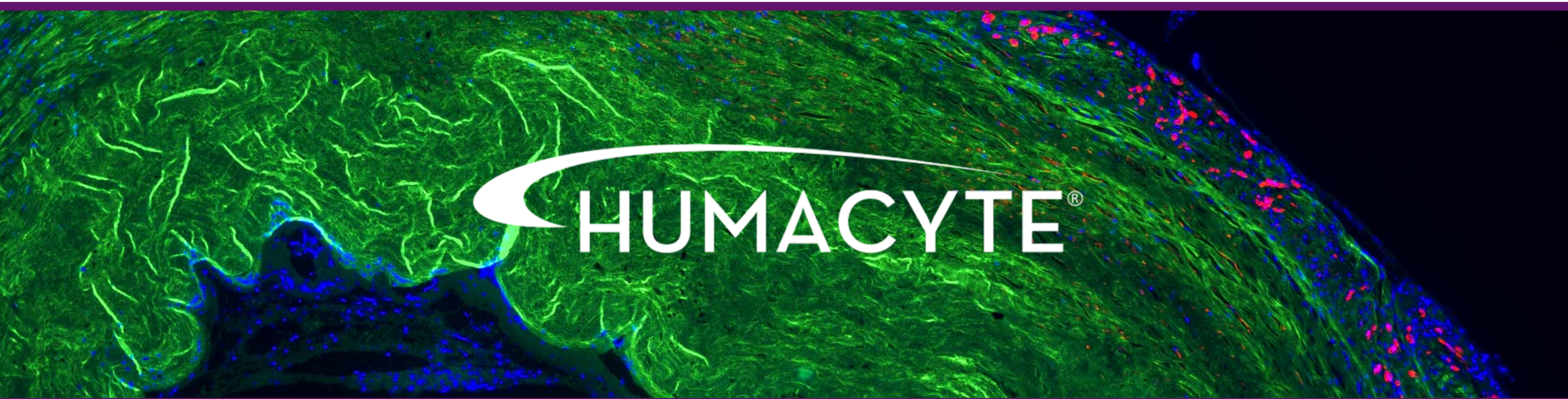


# THANK YOU

*We are committed to bringing first-in-class regenerative medicine products to the marketplace that will improve and save the lives of patients worldwide and transform the practice of medicine.*







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