# Humacyte

# Universally Implantable Regenerative Human Tissue

# Disclaimer

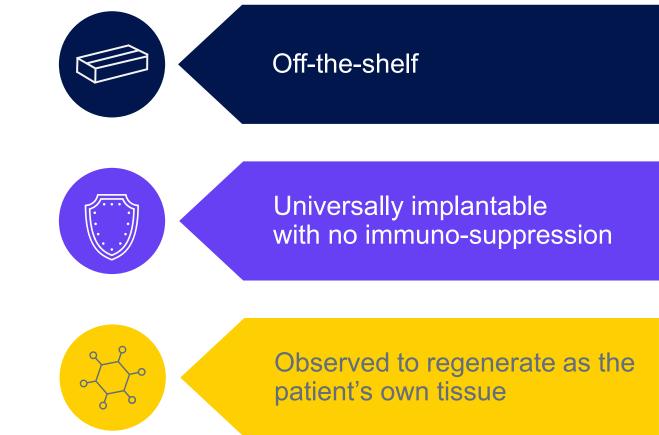


These slides and the accompanying oral presentation contain forward-looking statements. All statements, other than statements of historical fact, included in these slides and the accompanying oral presentation are forward-looking statements reflecting management's current beliefs and expectations. In 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 our plans and ability to commercialize our bioengineered acellular tissue engineered vessels ("ATEV™s") in the United States under the brand name Symvess™ in vascular trauma repair; the anticipated commercialization of our ATEVs and our ability to manufacture ATEVs and other product candidates in sufficient quantities to satisfy our clinical trial and commercial needs; our plans and ability to execute product development, process development and preclinical development efforts successfully and on our anticipated timelines; our plans, anticipated timelines and ability to obtain marketing approval from the U.S. Food and Drug Administration ("FDA") and other regulatory authorities, including the European Medicines Agency, for our ATEVs in other indications and other product candidates; our ability to design, initiate and successfully complete clinical trials and other studies for our product candidates and our plans and expectations regarding our ongoing or planned preclinical and clinical trials; the outcome of our ongoing discussions with the FDA concerning the design of our clinical trials; our anticipated growth rate and market opportunities; the potential liquidity and trading of our securities; our ability to raise additional capital in the future; our ability to use our proprietary scientific technology platform to build a pipeline of additional product candidates; the anticipated characteristics and performance of our ATEVs; the expected size of the target populations and addressable markets for our product candidates; the anticipated benefits of our ATEVs relative to existing alternatives; our assessment of the competitive landscape; the degree of market acceptance of ATEVs and the availability of third-party coverage and reimbursement; the implementation of our business model and strategic plans for our business; our expectations regarding our strategic partnership with Fresenius Medical Care Holdings, Inc. to sell, market and distribute our 6 millimeter ATEV for certain specified indications and in specified markets; the performance of other third parties on which we rely, including our third-party manufacturers, our licensors, our suppliers and the organizations conducting our clinical trials; our ability to obtain and maintain intellectual property protection for our product candidates as well as our ability to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights of others; our ability to maintain the confidentiality of our trade secrets, particularly with respect to our manufacturing process; our compliance with applicable laws and regulatory requirements, including FDA regulations, healthcare laws and regulations, and anti-corruption laws; our ability to attract, retain and motivate qualified personnel and to manage our growth effectively; our future financial performance and capital requirements; our ability to implement and maintain effective internal controls; and the impact of the overall global economy and increasing interest rates and inflation on our business. 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Any forward-looking statements contained herein are based on assumptions that we believe to be reasonable as of the date hereof. Except as required by law, we assume no obligation to update these forward-looking statements, even if new information becomes available in the future. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy, nor shall there be any sale of our securities, in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to the reregistration or gualification  $_{\rm 2}$  under the securities laws of any such state or other jurisdiction.

### Humacyte is a Leader the Field of Regenerative Medicine: Bioengineered Tissues & Organs







**Category-Defining Innovation that Creates New Tissues** 

# **Universally Implantable Regenerative Human Tissue**





# Humacyte Leadership & Board

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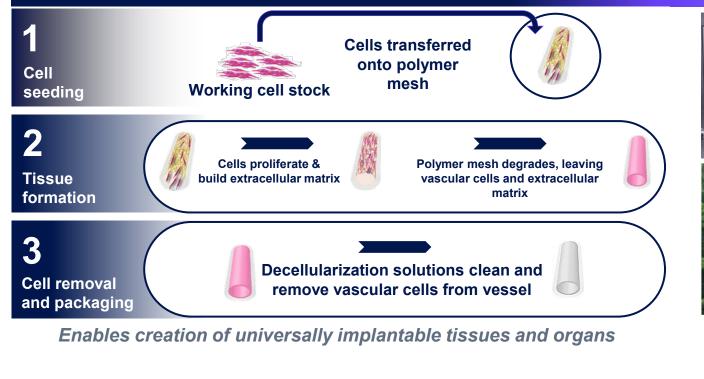
Leadership Team	Board of Directors	Prior Experience
Leadersnip leamImage: Shamik Parikh, MD Chief Medical OfficerImage: Shamik Parikh, MD Chief Regulatory Chief Regulatory Chief Corporate Development OfficerImage: Shamik Parikh, MD Chief Corporate Chief Regulatory Chief Corporate Chief Corporate Development OfficerImage: Shamik Parikh, MD Chief Corporate Chief Regulatory Chief Corporate Chief Corporate <td>Ebard of Directors Kathleen Sebelius Chair of the Board John P. Bamforth, PhD Emery N. Brown, MD, PhD Michael T. Constantino Brady W. Dougan Charles Bruce Green, MD Keith Anthony Jones, M.D., Laura E. Niklason, MD, PhD Todd M. Pope Diane Seimetz, PhD</td> <td><image/><image/><image/><image/><image/><image/><image/><image/><image/><image/></td>	Ebard of Directors Kathleen Sebelius Chair of the Board John P. Bamforth, PhD Emery N. Brown, MD, PhD Michael T. Constantino Brady W. Dougan Charles Bruce Green, MD Keith Anthony Jones, M.D., Laura E. Niklason, MD, PhD Todd M. Pope Diane Seimetz, PhD	<image/>
Sabrina Osborne Chief People Officer Officer	Max Wallace, JD Susan Windham-Bannister, PhD	Yale University School of Medicine

### **Platform & Manufacturing:** Enable Broad Pipeline of Regenerative Medicine Products



#### **Bioengineering Platform**







Strategically designed with modular capabilities to manufacture products at scale



Our platform technology enables development of a broad range of product candidates

# **Pipeline with Multiple Potential Commercial Launches**



	Preclinical	Phase 1/2	Phase 3	Approved
Vascular Tissue Constructs (ATEV)				
Trauma				Approved by FDA
Dialysis (AV Access)		V007 Phase 3 Trial M	et Co-Primary Endpoints	
	V012 Pha	se 3 Trial in Women Curro	ently Enrolling	
PAD				
Pediatric Heart Disease				
CABG				
Complex Tissue Constructs				
Urinary Conduit				
Tracheal Replacement				
Esophageal Replacement				
Complex Organ Systems				
BioVascular Pancreas (T1D)				
Lung				

## ATEV Observed to Repopulate with Patient's Own Cells Potentially Enabling Infection Resistance & Self-Healing



### **ATEV Overview**



Host cells observed to repopulate the ATEV<sup>1</sup>

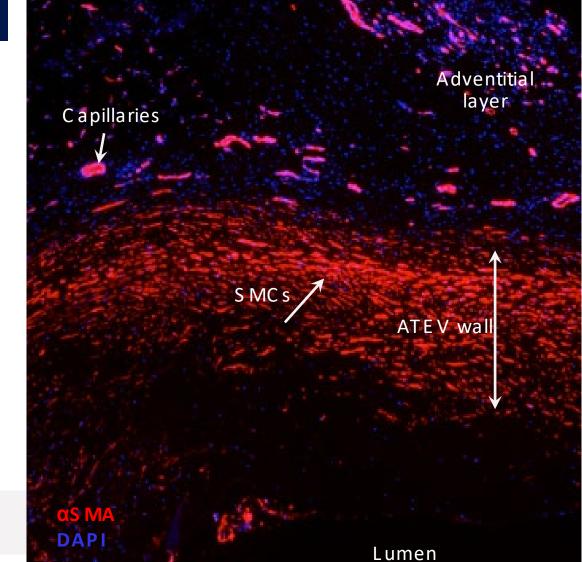


ATEV observed to have low rates of infection



ATEV may have the ability to self-heal

Over 600 patients across multiple indications



### **Benefits of ATEV**



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







No evidence of immunogenicity



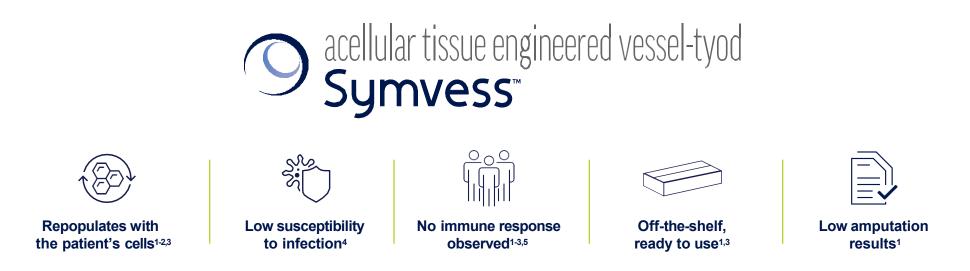
# acellular tissue engineered vessel-tyod

# FDA Approved in Extremity Vascular Trauma



# Symvess is FDA Approved in Extremity Vascular Trauma





### **INDICATION**

SYMVESS is an acellular tissue engineered vessel indicated for use in adults as a vascular conduit for extremity arterial injury when urgent revascularization is needed to avoid imminent limb loss, and autologous vein graft is not feasible.

#### PLEASE SEE ACCOMPANYING FULL PRESCRIBING INFORMATION AT SYMVESS.COM, INCLUDING BOXED WARNING.

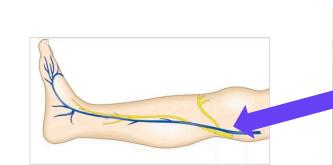
**REFERENCES: 1.** Symvess U.S. Prescribing Information. Durham, NC. Humacyte Global, Inc. **2.** Kirkton RD, et al. Bioengineered human acellular vessels recellularize and evolve into living blood vessels after human implantation. *Sci Transl Med.* 2019;11(485):eaau6934. **3.** Dahl S, et al. Readily available tissue-engineered vascular grafts. *Sci Transl Med.* 2011 Feb 2;3(68):68ra9. **4.** Wang J, et al. Biological mechanisms of infection resistance in tissue engineered blood vessels compared to synthetic expanded polytetrafluoroethylene grafts. *JVS Vasc Sci.* 2023;4:100120. **5.** Moore EE, et al. Bioengineered Human Arteries for the Repair of Vascular Injuries. *JAMA Surg.* 2024 Nov 20:e244893.

## Vascular Trauma Injuries – Symvess Value Proposition



- Common causes of vascular injuries include workplace injuries, car accidents, gunshots and stabbings, and sports injuries
- Symvess address major drawbacks of current treatment options:

Symvess is immediately available, off-the-shelf, and does not require further injuring the patient



Vein is the standard of care, but takes valuable time, delaying revascularization



Prosthetic grafts are quick, but have infection risk and high rates of amputation

Exit wound of a shotgun injury



## **Two Studies Were Used to Support FDA Approval**



### First Study: CLN-PRO-V005 Phase 2/3 Pivotal Trial In U.S. and Israel

- Single-arm, open label study
- Conducted at Level 1 trauma centers
- Arteria injury repair
- Extremity injuries at high risk of contamination / infection

- 69 patients enrolled as of data cut off
- As agreed upon with FDA, focus for BLA filing were 51 patients with extremity injuries

#### Statistical Analysis Plan

#### Historical Benchmark Comparator

 Systematic literature review of synthetic grafts in vascular trauma

#### **Primary Comparison**

> 30-day endpoint of patency

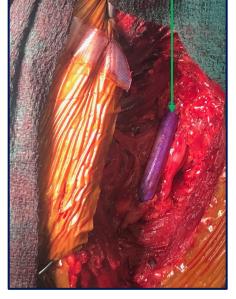
#### Secondary Comparisons

- > 30-day infection rate
- > 30-day amputation rate

### **Examples of Symvess Implants in V005 Study**



Gunshot Wound







**Knee Dislocation** 

## Ukraine Real World Experience of Symvess Use in Vascular Repair



### Second Study: V017 Humanitarian Program in Ukraine

- At request of Ukraine surgeons Humacyte supported humanitarian program for patients injured in conflict
- 19 patients received Symvess
- At suggestion of FDA, patients from humanitarian program were included in BLA filing
  - 17 consented for data collection and study participation
  - 16 patients had extremity trauma repair (one patient required Symvess for latrogenic trauma repair)

### **Case Study of Patient Treated in Ukraine Program**



Ukraine Patient Blast Injury







Pre-op CT Scan Sym Fei

Symvess repair of Femoral artery

Walking once again (Day 113)

## **Symvess Performed Better than Synthetic Graft Benchmark**



- Benchmark for Symvess efficacy was the published performance of prosthetic grafts<sup>1</sup>
- Data from V005 and V017 and the benchmark were included in the BLA file, supporting Symvess approval

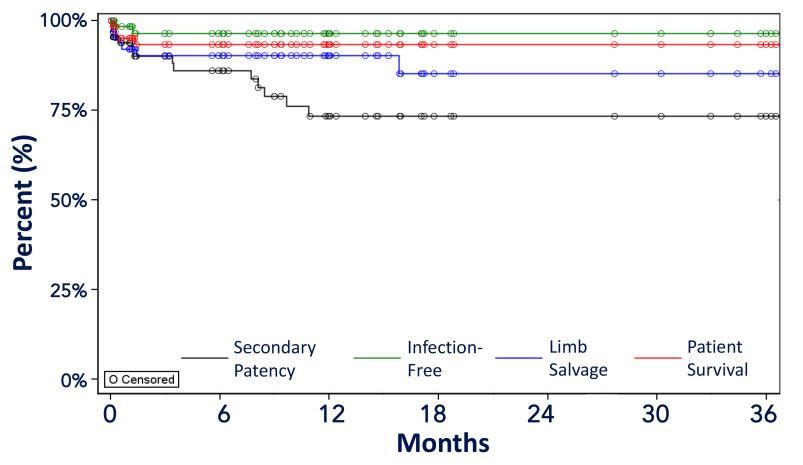
Outcome Day 30	Symvess V005 (n=51) <sup>1</sup>	Symvess V017 (n=16) <sup>1</sup>	Combined Symvess (N=67) <sup>1</sup>	Synthetic Graft Benchmark <sup>1</sup>
Primary Patency	84.3 %	93.8%	87.1%	78.9%
Secondary Patency	90.2%	93.8%	91.5%	78.9%
Conduit Infection rate	2.0%	0%	0.9%	8.4%
Amputation rate	9.8%	0%	4.5%	24.3%
Death rate (all cause)	5.9%	0%	3.5%	3.4%

Humacyte filed the BLA with trauma clinical data based upon the accepted statistical analysis plan. These data were also peer reviewed and published in *JAMA Surgery* on November 20, 2024. In the package insert, the FDA elected to exclude the synthetic graft comparator that was in the statistical analysis plan. The FDA also applied a different imputing methodology for V005 Symvess patients who did not have a day 30 assessment.

<sup>1</sup>Moore EE, et al. Bioengineered Human Arteries for the Repair of Vascular Injuries. JAMA Surg. 2024 Nov 20:e244893. ; Humacyte BLA filed December 11, 2023.

# Symvess was Durable in Trauma Repair in V005 and V017 Studies<sup>1</sup>





- Function of Symvess is durable over 36 months of observation in trauma repair
- Zero reports of late infection, aneurysm, or mechanical failure

<sup>1</sup>Moore EE, et al. Bioengineered Human Arteries for the Repair of Vascular Injuries. JAMA Surg. 2024 Nov 20:e244893...

## Symvess Compares Well to Autologous Vein<sup>1</sup>



- Symvess was compared to Prospective Observational Vascular Injury Trial (PROOVIT) registry
- NOT a head-to-head study. Retrospective comparison to existing registry
- Symvess patients (n=67) were propensity-matched 1:2 to PROOVIT patients (n=134) who were previously treated with vein. Identical injured arteries. Similar injury severity scores (though SYMVESS patients were more severe)
- Symvess outcomes were similar to autologous vein:

Outcome @ Day 30 for Symvess (@ initial hospitalization for Vein – average 16 days of follow up)	V005 + V017 Symvess (N=67)	<i>PROOVIT</i> Autologous Vein (N=134)	P-value
Primary Patency	86.6%	91.8%	0.276
Secondary Patency	91.0%	97.7%	0.077
Amputation rate	7.5%	8.2%	0.852
Conduit Infection rate	1.5%	0.0%	0.333
Death rate (all cause)	4.5%	4.5%	0.991
Reintervention Thrombosis/Stenosis	6.0%	8.2%	0.550

<sup>1</sup>Manuscript under review. Retrospective comparison at 30 days (SYMVESS) or during initial hospitalization (*PROOVIT*).



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# Commercial Launch in Extremity Vascular Trauma



## U.S. Vascular Trauma Market – Total Addressable Market for Symvess



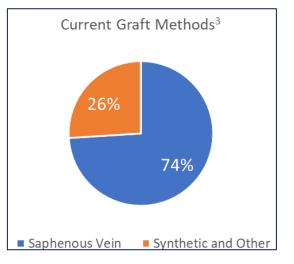
Total Vascular Trauma Patients (All Injuries)<sup>1</sup>

79,000

Emergent Vascular Trauma – 56,000 Iatrogenic Vascular Trauma – 23,000 Target U.S. TAM for Symvess Based on Hospital Claims Data<sup>2</sup>

26,000

Emergent Vascular Trauma – 18,667 Iatrogenic Vascular Trauma – 7,333



Symvess-Eligible Patients	Exclusions
<ul> <li>Type of repair: Bypass, repair, replacement, supplement, destruction or restriction</li> <li>Location: Extremity arteries of interest</li> <li>latrogenic: Arterial injuries co-occurring with other surgeries</li> </ul>	<ul> <li>Vein injury / repair</li> <li>Injuries to torso, head, neck, wrist, hand, ankle, foot</li> <li>Primary repair: Ligation or endovascular repair</li> </ul>

<sup>1</sup>Third-party market research based on procedural volumes (2019) and secondary literature search

<sup>2</sup>Based on analysis of Definitive Healthcare (DHC) Claims Database 2022, claims as of November 2023. Adjusted to reflect estimate the database captures approximately 60% of procedures:

Diagnosis (Dx) Codes: Identify Injury type, location

Procedure Codes: ICD-10 PCS or CPT

<sup>3</sup>Based on analysis of Prospective Observational Vascular Injury Trial (PROOVIT) registry



## Drivers of U.S. Commercial Launch in Vascular Trauma

### **Concentrated Market**

Approximately 200 Level 1 trauma centers in U.S.

Approximately 3,000 vascular surgeons across civilian and military market opportunities

# **Symvess**<sup>m</sup>

acellular tissue engineered vessel-tyod

#### The Right Team

Sales team of ten executives who are experienced in vascular and/or trauma surgery and regenerative therapies

Sales team is complemented by Medical Affairs, market access, and marketing teams

#### **Health Economics**

and infection

**Superior Clinical Results** 

In the civilian and military clinical

studies, Symvess was observed

to have high rates of patency

and low rates of amputation

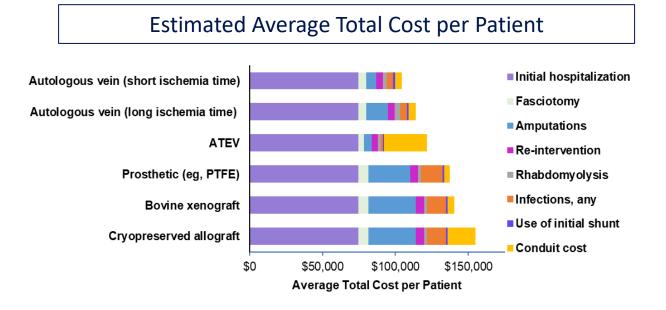
Budget Impact Model projects that the per-patient cost of treating patients with Symvess is estimated to be less than the cost of treating with synthetic grafts and other conduits

## Symvess Pricing Supported by Budget Impact Model



The U.S. launch price of Symvess will be \$29,500 per unit

- A Budget Impact Model supporting Symvess economic benefit was based on:
  - Symvess clinical results
  - Estimated reduction in clinical complications
  - Medical costs incurred by hospitals derived from real-world hospital and claims databases
- The per-patient cost of treating patients with Symvess is estimated to be less than the cost of treating with synthetic grafts and "non-autologous other" conduits
- Major drivers of cost savings were attributed to reductions in the rate of amputation and infection



## **NTAP Reimbursement And CMS Progress**



### **Application Timelines**

- > NTAP Submission: Submitted on October 6, 2024
  - FDA approval required by May 1, 2025
- CMS Townhall Meeting: <u>December 11, 2024</u>
- Opportunity to present and address questions
- IPPS Proposed Rulemaking Process: Spring 2025
  - Opportunity for public comment
- > NTAP Decision: August 2025

### <u>3 Criteria to be Eligible for an NTAP</u>

- ✓ Newness Criterion: must be novel
- Cost Criterion: must be costly, such that the DRG rate is inadequate to cover
- Substantial Clinical Improvement: must be better than existing services

### ICD-10-PCS Codes and NTAP

- ✓ ATEV PCS codes effective October 1, 2024
- ✓ Codes trigger NTAP hospital reimbursement

### **NTAP Implications**

- Enables additional payment to hospitals, specifically for ATEV usage in Medicare beneficiaries
- Also provides a benchmark payment for Medicaid and private payers to imitate
- Covers up to 65% of the cost of ATEV and is active for 2 to 3 years, with the payment going directly to the hospital
- When implemented, this becomes an inflection point in overall product adoption

# AV Access for Dialysis

Humacyte

# AV Access for Hemodialysis Has Limitations



### **Estimate of Permanent Access Procedures Performed in U.S.**

### ~60% AV fistulas

Primary/AV Fistula (Autogenous)

Market targeted by ongoing V007 Phase 3 Trial

### ~20% Catheters

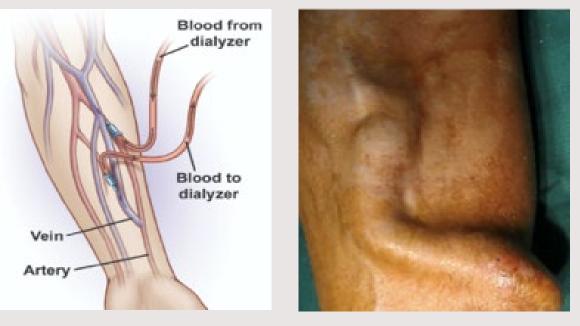
Venous / Temporary Catheter

### ~20% Grafts

### Secondary / Graft



## Limitations of AV Fistulas (Current Standard of Care)



- ~40% of fistulas fail to mature
- Even the fistulas that do mature take 3-6 months to become usable for dialysis
  - Catheter infection rates are up to 200% per patient-year

# **ATEV is Designed to Address Failures in AV Access**

### ATEV provides potential for improved patient outcomes

- ATEV usable for dialysis after only four weeks
- ATEV reduces catheter contact time, thereby reducing risk of catheter infection
- >80% of ATEVs functional for dialysis at 6 months
- ATEV infection rate is comparable to AVF
- Opportunity to reduce cost of access failures and other complications:
  - Access failures and complications
  - Dialysis complications
  - Infections





Strategic collaboration with FMC, the largest provider of renal care services



RMAT designation granted by FDA

## **Current AV Access in Women Work Poorly and is Expensive**

# Partnered with Fresenius / Frenova Renal Research to identify the hemodialysis subpopulations with highest unmet needs

### Analysis of 178,575 adults with in-center hemodialysis established that:

- Women are more likely to use AVG ± CVC for access within 90 days of initiation
  - Women have up to 90% increased risk of AVG ± CVC use, as compared to men
- AVG ± CVC access has much higher complication rates: ~2X higher than AVF
  - Nearly \$3 billion spent by Medicare in 2013 for on access complications/maintenance
  - Top quintile of dialysis patients cost between \$91,841 to >\$155,632 annually to maintain access
- Women are more likely to fail AVF maturation: Cost >\$30,000 in first year
  - Women are 20% more likely to fail AVF maturation
  - Women are 20% more likely to have multiple access failures in the first 6 months
  - Women are 24% more likely to have multiple hospitalizations for access complications
- Some female sub-groups are at especially high risk
  - Example: Obese, diabetic women have excess costs of ~\$27,000 to \$91,000 during the first year

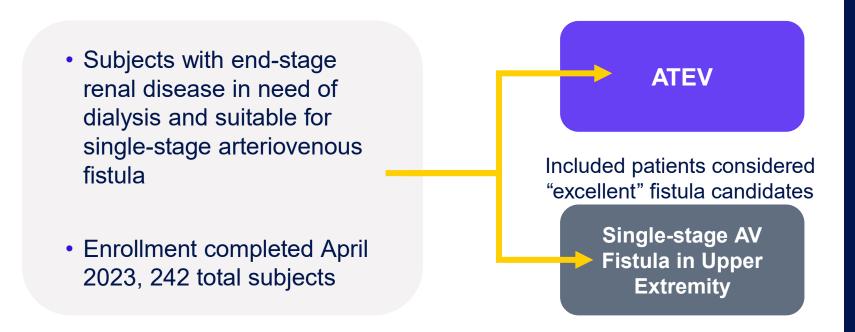






# V007 Phase 3 Trial: ATEV vs. Fistula

V007 Phase 3 Trial Design: 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



Results presented at American Society of Nephrology's *Kidney Week 2024* 



## > Endpoints

- Efficacy: Useability for dialysis and patency during the first year
- > Safety: interventions, infections, etc.

# > Duration

> Subjects followed for 24 months after implantation

> Sites> 30 centers in the U.S.





# ATEV demonstrated superior function and patency at six and 12 months (co-primary endpoints) compared to autogenous fistula, the current standard of care for hemodialysis

<b>Co-Primary Endpoints</b>	ATEV (N=37)	AVF (N=33)	p-value	
Functional Patency at Month 6	<b>81.3</b> %	66.4%	0.0071	
Secondary Patency at Month 12	<b>68.3</b> %	<b>62.2</b> %		
			Difference	p-value
Duration of Use Over First 12 Months	7.5 months	<b>6.1</b> months	<b>1.4</b> months	0.0162

- More adverse events were reported in patients on the ATEV treatment arm than those on the AV fistula treatment arm:
  - More thromboses in the ATEV group, but virtually all were resolved
  - A number serious events occurred more frequently in the AVF arm:
    - Two ruptures of AVF (a potentially fatal event), none for ATEV
    - Substantially more "steal" (ischemia of the hand), surgical revisions, and balloon-assisted maturation in the AVF group compared to the ATEV group



### ATEV showed superior function and patency in subgroups with historically poor outcomes

Females	ATEV (N=37)	AVF (N=33)	p-value	
Functional Patency at Month 6	<b>89.2</b> %	<b>54.5</b> %	<0.0001	
Secondary Patency at Month 12	<b>81.1</b> %	<b>48.5</b> %	<0.0001	
			Difference	p-value
Duration of Use Over First 12 Months	<b>8.3</b> months	<b>5.0</b> months	<b>3.3</b> months	0.0011
<b>Obese (BMI ≥ 30)</b>	ATEV (N=51)	AVF (N=42)	p-value	
Functional Patency at Month 6	<b>80.4</b> %	<b>52.4</b> %	<0.0001	
Secondary Patency at Month 12	<b>72.5</b> %	<b>47.6</b> %		
			Difference	p-value
Duration of Use Over First 12 Months	7.7 months	<b>4.5</b> months	<b>3.2</b> months	0.0051



Diabetic	ATEV (N=82)	AVF (N=83)	p-value	
Functional Patency at Month 6	<b>81,7</b> %	<b>61.4</b> %	0.0024	
Secondary Patency at Month 12	<b>68.3</b> %	<b>59.0</b> %		
			Difference	p-value
Duration of Use Over First 12 Months	7.4 months	<b>5.5</b> months	<b>1.9</b> months	0.0155

Females, and males with BMI ≥ 30 and diabetes	ATEV (N=56)	AVF (N=54)	p-value	
Functional Patency at Month 6	<b>85.7</b> %	<b>51.9</b> %	<0.0001	
Secondary Patency at Month 12	<b>76.8</b> %	<b>46.3</b> %		
			Difference	p-value
Duration of Use Over First 12 Months	<b>8.0</b> months	4.5 months	<b>3.5</b> months	0.0002

## **Planned Supplemental BLA Strategy**

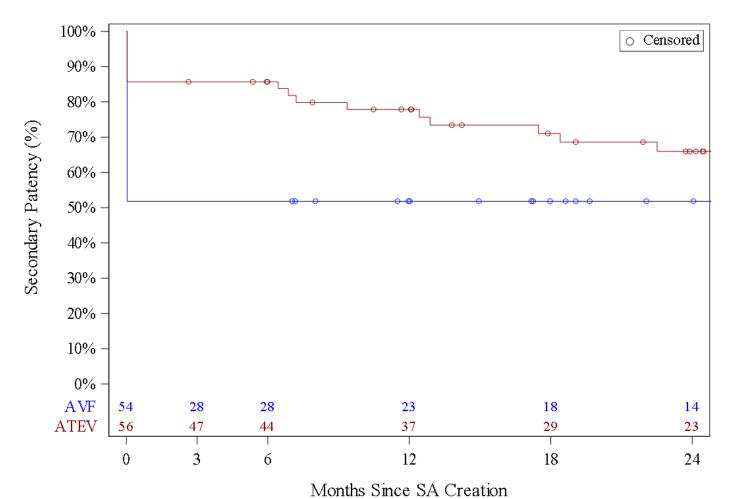


### Our current thinking, subject to modification based on FDA discussions...

- File supplemental BLA based primarily on V007 study results:
  - Planned supplemental BLA filling in 2<sup>nd</sup> half of 2025
- Target subgroups in which the ATEV showed the best results in the V007 study:
  - All females, and males with two risk factors (BMI  $\ge$  30 kg/m2 and diabetes)
  - This collection of subgroups encompasses over 50% of dialysis patients
- Anticipate using two-year results from V007 study which will be available in April 2025
  - Two-year results from 70% of the patients in V007 are already available on show durability of ATEV as illustrated on following slide



# ATEV has shown superior long-term patency to date in the expected target population (all females and males with BMI $\ge$ 30 kg/m2 and diabetes)



The 24-month results reflect data from the 70% of patients who had reached their 24-month visit as of 12-month data cut off. 100% of patients will have reached their 24-month visit by April 2025



# ATEV has shown no increased safety events per year of usability in the expected target population (all females and males with BMI $\geq$ 30 kg/m2 and diabetes)

	AT	ATEV		AVF	
12-Month Safety Summary	Subjects (%) n=54	Events per Patient Year		Subjects (%) n=56	Events per Patient Year
Treatment Emergent Adverse Events	96.3%	14.8		98.2%	21.8
Serios Adverse Events	77.8%	4.2		67.9%	6.1
Adverse Events of Special Interest:					
CEC SA-related infections	7.4%	0.1		5.5%	0.1
Thrombosis	51.9%	1.2		12.5%	0.3
Stenosis	64.8%	3.0		51.8%	2.9
Clinically significant Steel Syndrome	1.9%	0.0		3.6%	0.1
Rupture of SA	0.0%	0.0		3.6%	0.1
Leading to SA revision or ligation	11.1%	0.2		28.6%	1.2
Leading to SA excision	5.6%	0.2		3.6%	0.1

## V012 (HUMAXX) Trial in Women Dialysis Patients



### Trial comparing Humacyte's (ATEV<sup>™</sup>) to AVF in women

To Compare the Efficacy and Safety of the ATEV With AVF in Female Patients With End-Stage Renal Disease Requiring Hemodialysis (HUMAXX)

Female patients currently receiving hemodialysis via catheter and who are candidates for creation of an AVF or implantation of an ATEV.

#### • Enrollment:

- Target 100 total subjects
- 60 patients enrolled as of December 31, 2024
- 1:1 Prospective randomization
- ATEV vs. Autogenous fistula

#### **Comparators:**

Surgically created AV Fistula in the upper extremity

### **Follow-up Duration:**

12 months without regard of patency status.

24 months (if access not abandoned)

#### **Objectives:**

- **Primary Efficacy:** Total days free from indwelling catheter ("catheter-free days") until 365 days, or until access abandonment, whichever occurs first.
- **Primary Safety:** Number and severity of infections related to all accesses (including catheters) from access creation until 365 days.

## Strategic Value of V012 Study



## Women are 43% of the US dialysis population and many struggle with access

# V012 was designed in consultation with nephrologists and FDA to quantify value of ATEV vs. AVF for women

- V012 is focused on catheter exposure in women:
  - Captures failures of AVFs
  - Catheters are the most expensive access for dialysis
- V012 was designed in consultation with FDA:
  - Agency acknowledges that women have high unmet need in dialysis
  - Agency notes that women suffer high rates of fistula failure
- V012 captures important access complications and adds to health economic narrative:
  - No study has quantified AVF access complications specifically in women
  - Will provide strong health economic data on ATEV
  - Should provide additional support for reimbursement in women

# **Peripheral Arterial Disease (PAD)**

# Humacyte

# **Peripheral Artery Disease (PAD)**

### Critical Limb Threatening Ischemia

### Treatment Requires Restoration of Blood Flow

## Can progress to multiple leg arteries, further reducing circulation

- Tissue does not receive enough
   blood flow to survive
- If untreated, leads to tissue loss, gangrene, and ultimately amputation

# • Non-surgical, catheter-based intervention

Surgical bypass



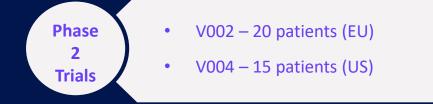




For the 40% of PAD patients who do not have an ipsilateral saphenous vein for arterial bypass, ATEV may represent a promising means of revascularization and limb salvage



## **Current Clinical Experience with ATEV in Peripheral Arterial Disease**



Over 20 U.S. patients with critical limb ischemia treated under FDA Expanded Access program



EA

Investigator-sponsored IND

- 29 patients with severe PAD at risk of limb loss
- Patients did no have saphenous vein available

<sup>1</sup>Piotr Gutowski, et al, 6-Year Outcomes of a Phase 2 Study of Human-Tissue Engineered Blood Vessels for Peripheral Arterial Bypass, JVS: Vascular Science (2023)

 Six-year results from V002 published in Journal of Vascular Surgery – Vascular Science<sup>1</sup>

- Publication of First Eight Expanded Access Cases in Annals of Vascular Surgery<sup>2</sup>
- Outcomes published in *Midwestern* Vascular Surgical Society showing 86% limb salvage rate



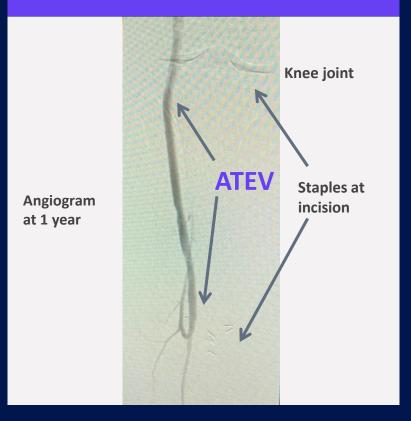
#### **Expanded Access: Restoring Mobility with ATEV**

- The ATEV was used under compassionate use program in 70-year-old patient with severe vascular disease
- No vein was available to perform a bypass, as the vein was previously harvested for a CABG
- A right distal superficial femoral artery-to-peroneal artery bypass was performed using an ATEV
- The patient's postoperative course was unremarkable
- At 1-year follow-up the angiography showed a patent ATEV without significant stenosis at the distal anastomosis
- Four years after ATEV implantation, the patient continues to do well and is walking.



This case was included in ATEV results in critical limb ischemia presented at VESS meeting in January 2022

Bypass performed using the ATEV in patient with severe vascular disease





# Pipeline: Cardiac Bypass



## Potentially Transforming CABG Care: Greater Durability, Less Morbidity



- Saphenous Vein Graft (SVG)
  - Harvesting SVG from the patient is painful and complicated:
    - 41% have persistent numbness
    - 32% develop infection
    - 23% have persistent swelling; worse in obese and diabetic patients; 2x worse in women
  - SVGs do not last long enough: ~33% of patients will require one or more regrafting procedures during their lifetimes

#### Humacyte's ATEV

- Does not require tissue harvest from the patient
- Immediately available and avoids morbidity of vein harvest
- Particularly important to avoid vein harvest in diabetics, women, and the overweight
- Durable and highly uniform in diameter and quality





#### Surgeons know what they are getting each time



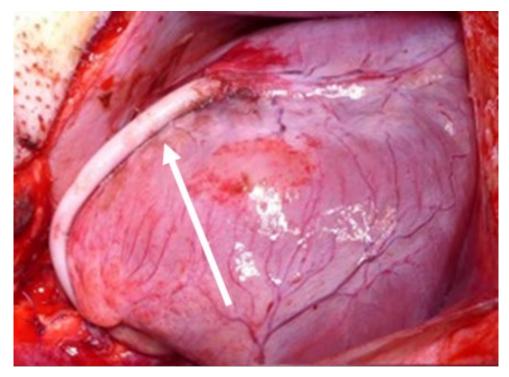
## **CABG Preclinical Results**



#### Next Steps in CABG Development

Proceeding to IND enabling nonclinical studies to support first-inhuman clinical trials

- Testing of ATEV in baboon model has transitioned to right coronary artery (RCA) as distal target
- Results showing ATEV maintained patency and exhibited host-cell remodeling through six months



Humacyte ATEV in Baboon



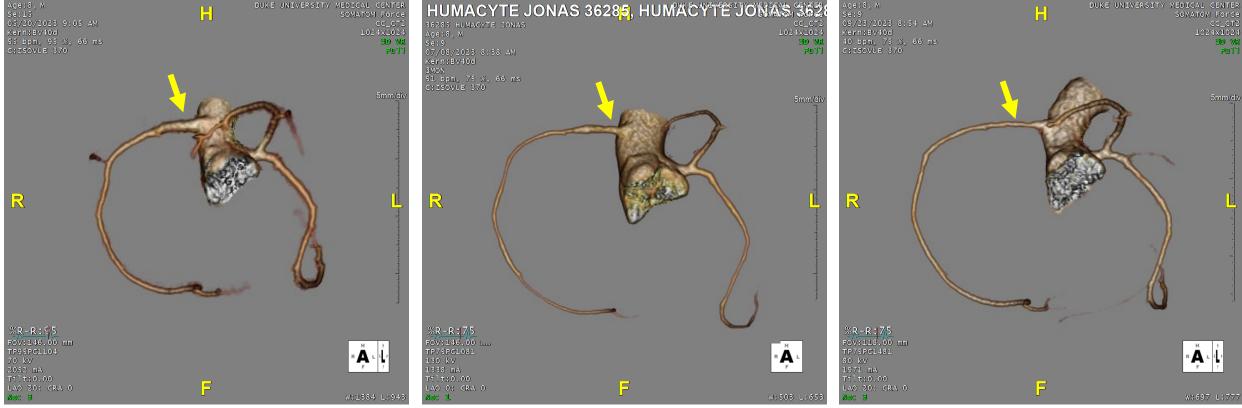
## **Primate – CABG Angiography – Adaptive Remodeling**



## 1 Month

3 Months





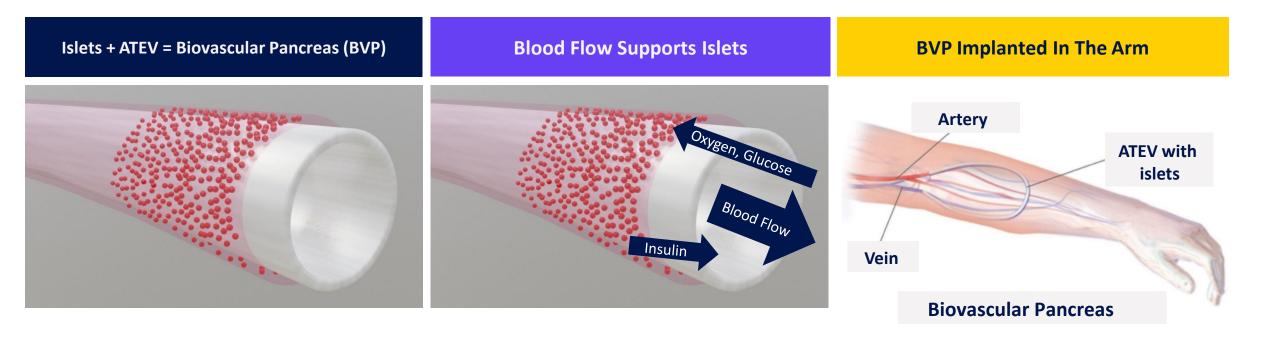
#### Jonas – Left Ventricular Function (%)

Pre-Op	<u>1-Month</u>	<u>3-Month</u>	<u>6-Month</u>
70%	73%	74%	73%

# **Pipeline: BioVascular Pancreas**

#### **Biovascular Pancreas May Deliver Curative Islets to Diabetics**



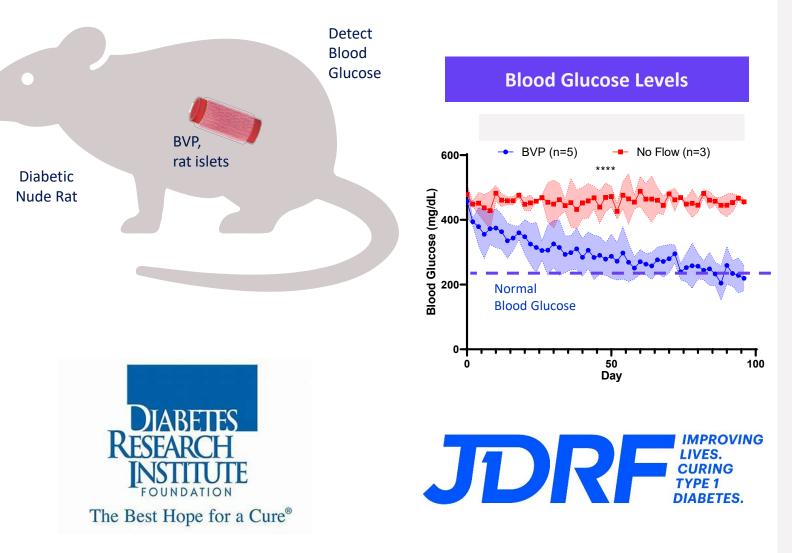


- Islets die after injection into the liver, due to lack of oxygen and nutrients
- Humacyte's ATEV is being developed as a means to provide oxygen and nutrients to islets that are coated on the outside: "Biovascular Pancreas" (BVP)
- Once implanted in the vasculature, blood flow supplies oxygen and nutrients to islets
- One 42-cm ATEV is expected to accommodate all the islets in an entire human pancreas

## **Biovascular Pancreas Normalized Glucose in Diabetic Animals**

- Diabetic rodents implanted with BVPs
- All treated animals normalized glucose over time. All shamtreated animals ("No Flow") remained diabetic

### Transplant BVP into Vasculature

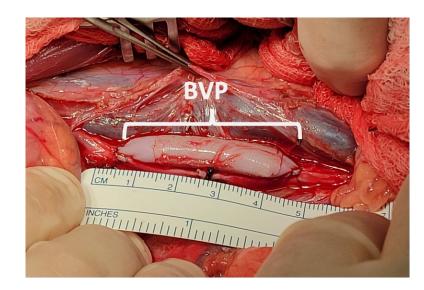




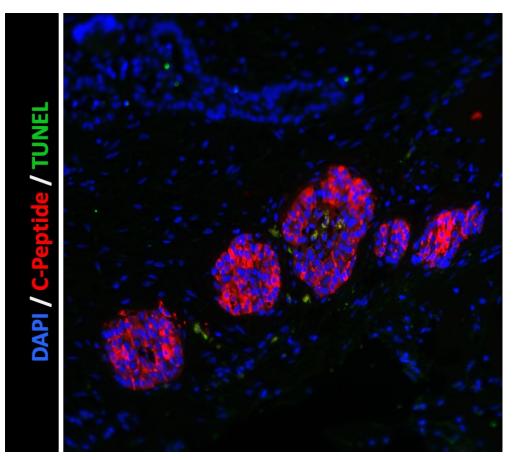
## Primate BVP – Islets Survive, and Produce Insulin



- In this model, the BVP is produced by harvesting islets from one animal, and creating a BVP comprising human ATEV and primate islets
- Animal receives the primate-islet BVP into the aorta
  - 25,600 islet equivalents
  - Corresponds to a potentially curative number of islets in a human



#### Islets survive for weeks after implantation, continue making insulin (c-peptide).



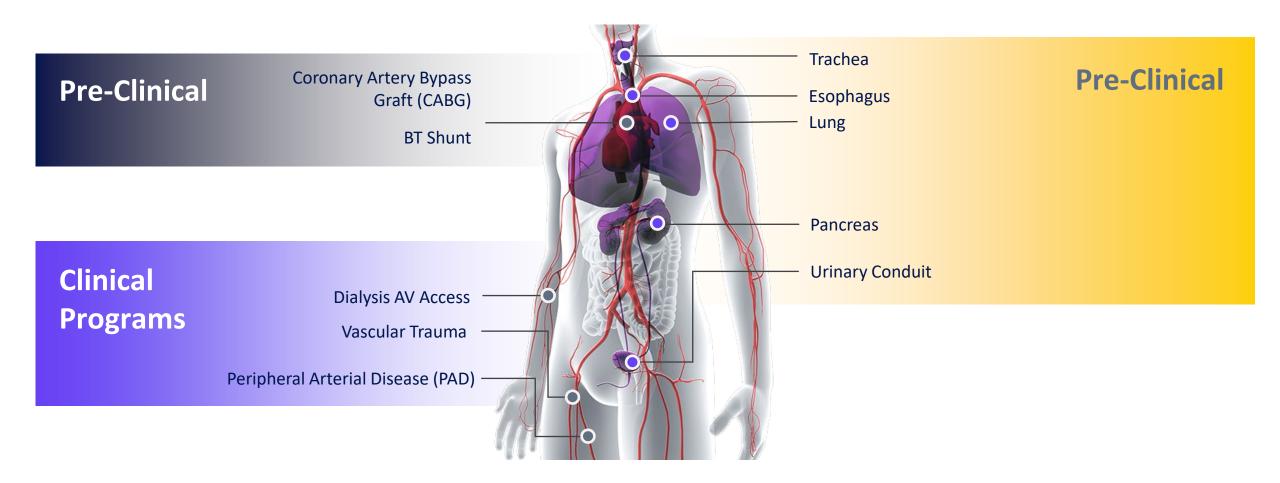
# Milestones

#### **Our Technology Addresses Compelling Unmet Needs in Attractive Markets**



#### Vascular Tissue Constructs

Complex Tissue Constructs and Organ Systems



## **Commercial Manufacturing Scale – LUNA200 System**

#### **Bioreactor bag**

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



#### **Growth drawer**

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



#### LUNA200 System

Each LUNA200 can produce 200 ATEVs per batch (or ~1,000 ATEVs annually) <sup>1</sup>



#### **Commercial 83,000 sq ft Bioprocessing Facility**

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





## **Anticipated 2025 Milestones**



## Completed in 2024

Vascular Trauma (Symvess):

- BLA acceptance and priority review
- BLA approval

V007 ATEV dialysis (AV Access) Phase 3 results – trial met coprimary endpoints

Positive Phase 2 results from PAD trial conducted by Mayo Clinic

*Preclinical BVP results showing survival and function of islets* 

## Planned for 2025

- Vascular Trauma (Symvess):
- U.S. commercial launch
- Multiple publications including Budget impact model
- NTAP reimbursement
- ATEV dialysis (AV Access):
- Completion of enrollment in V012 Phase 3 trial in women
- Submission of Supplemental BLA

- BioVascular Pancreas (BVP) for type-1 diabetes:
- Preclinical results in large animal diabetes model

Cardiac Bypass Surgery (CABG) with of small-diameter ATEV:

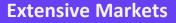
- Preclinical results from large animal studies
- IND submission

Publications & Presentations (Multiple other clinical and preclinical publications and presentations expected for 2025)

## **The Promise of Regenerative Medicine**



Broad platform of universally implantable off-the-shelf bioengineered human tissues and organs



Platform targets extensive markets across multiple indications





Commercial Scale Manufacturing

Existing facilities expected to support anticipated commercial launch with room for modular expansion







## Universally Implantable Regenerative Human Tissue

**Thank You**