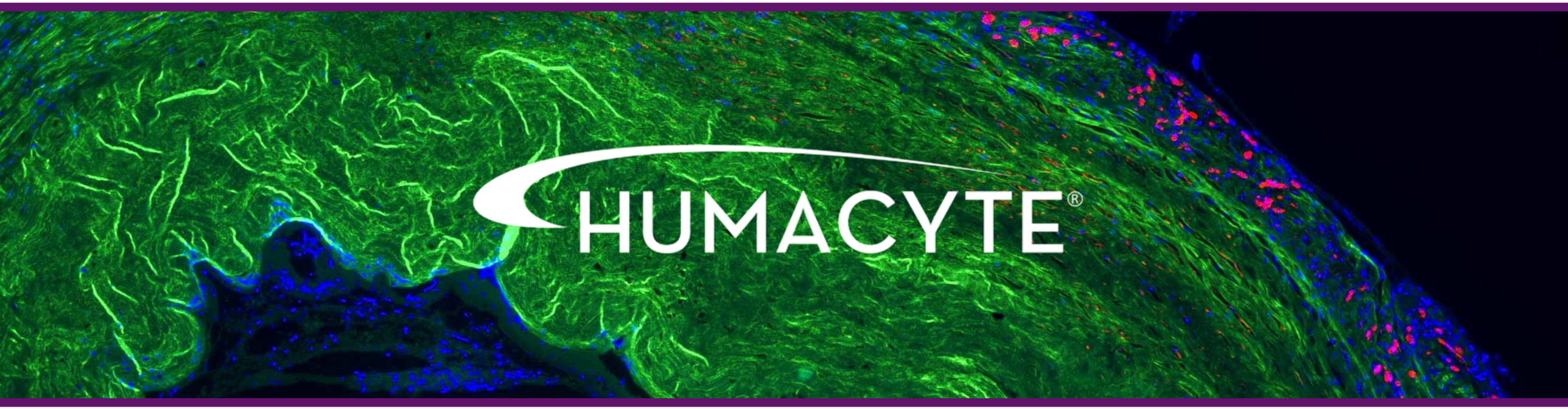


“The Humacyte Graft – Longer Term Patency with a Bioengineered Tissue Graft”

Jeffrey H. Lawson, MD, PHD

Chief Surgical Officer, Humacyte Incorporated
Adjunct Professor of Surgery, Duke University Medical Center

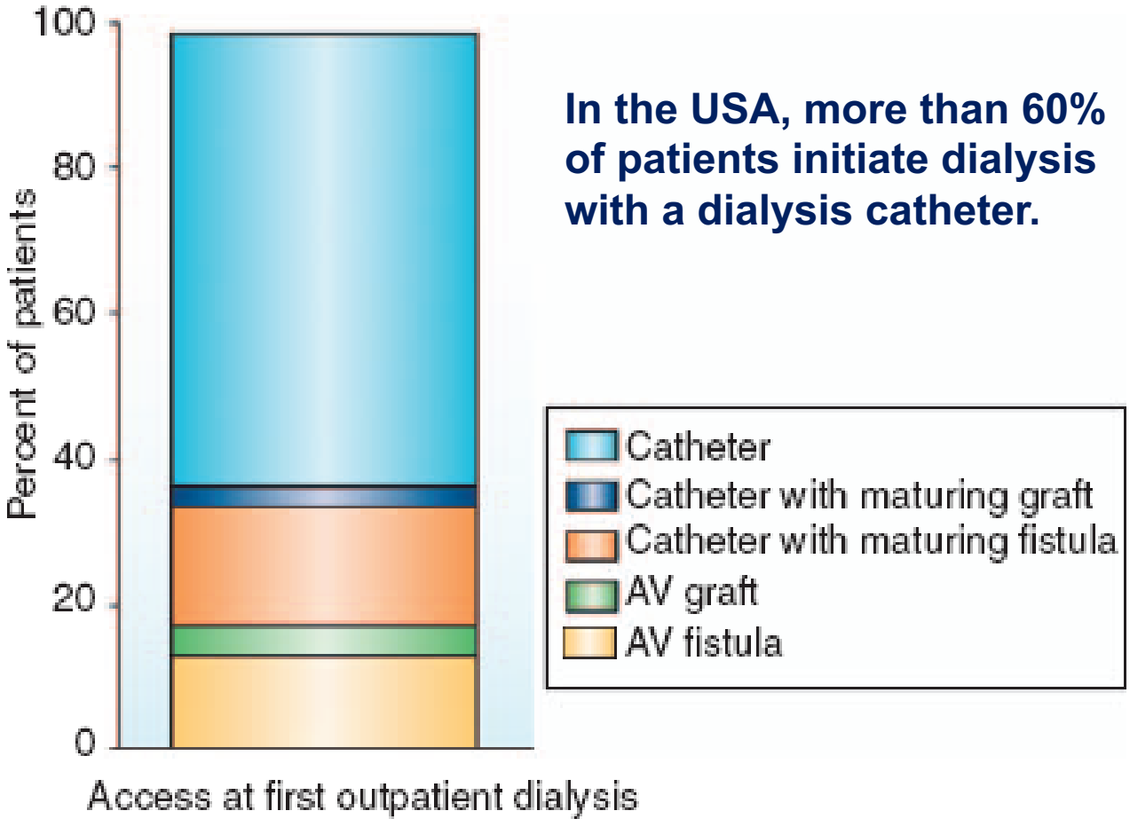
Humacyte Incorporated

CONFLICTS OF INTEREST & DISCLOSURES

Dr. Lawson is the Chief Surgical Officer 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.

VASCULAR ACCESS AT INITIATION OF DIALYSIS



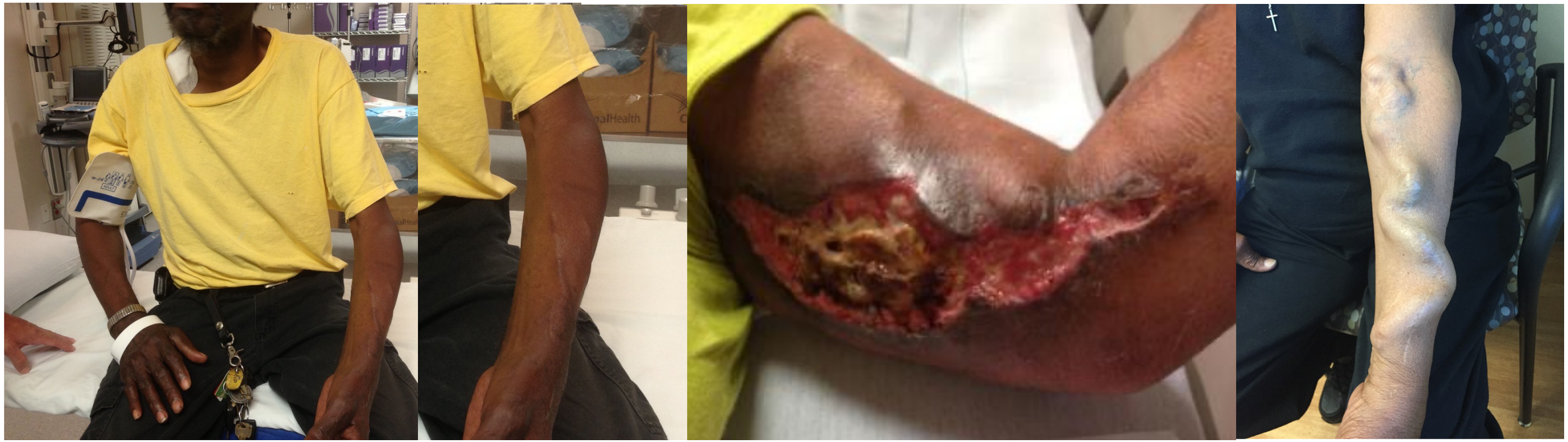
In the USA, more than 60% of patients initiate dialysis with a dialysis catheter.

1) *Hakim, Kidney International (2009) 76, 1040–1048*

MANY MODES OF AV FISTULA FAILURE

Maturation – Hemodialysis Fistula Maturation Study noted that only 61% of fistulas are use-able for dialysis at 6 months [1].

Maturation failure is a large problem – Small vessels, low blood flow, inadequate vessel remodeling and high prevalence of diabetes and hypertension

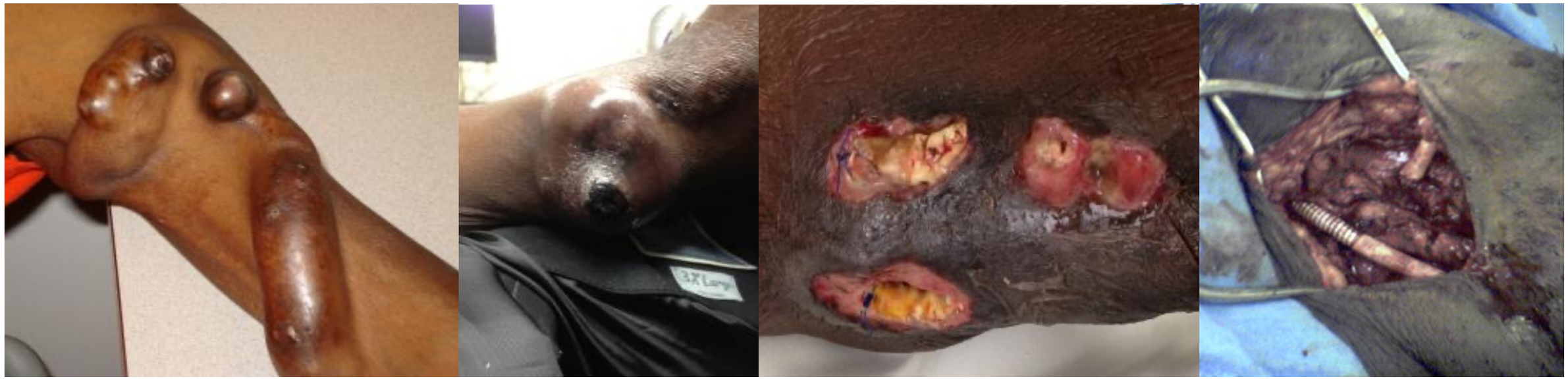


1) Dember et al. JAMA. 2008;299(18):2164-2171

INFECTION AND OTHER MODES OF SYTHETIC (ePTFE) AV GRAFT FAILURE

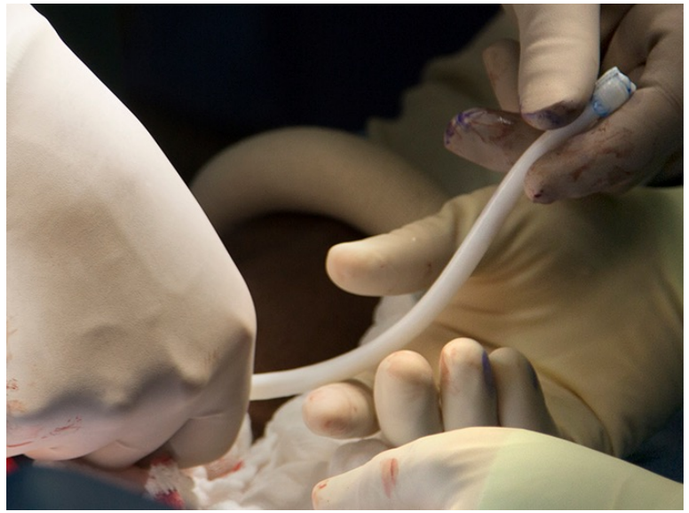
Low Durability and Poor Long-Term Patency

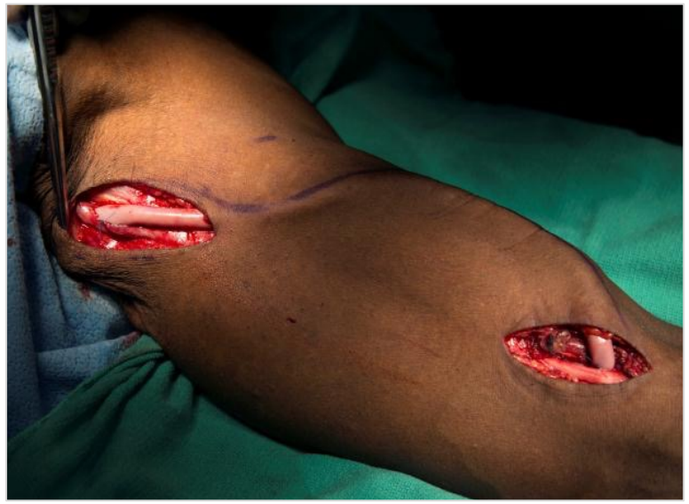
- Only 70% of ePTFE grafts remain functional at one year
- 9% annual rate of infection [1]
- Vein neointimal hyperplasia, stenosis, thrombosis
- Graft wall deterioration



1) Halbert, et al, Kidney306, 2020.

HUMAN ACELLULAR VESSEL (HAV) IN HEMODIALYSIS ACCESS





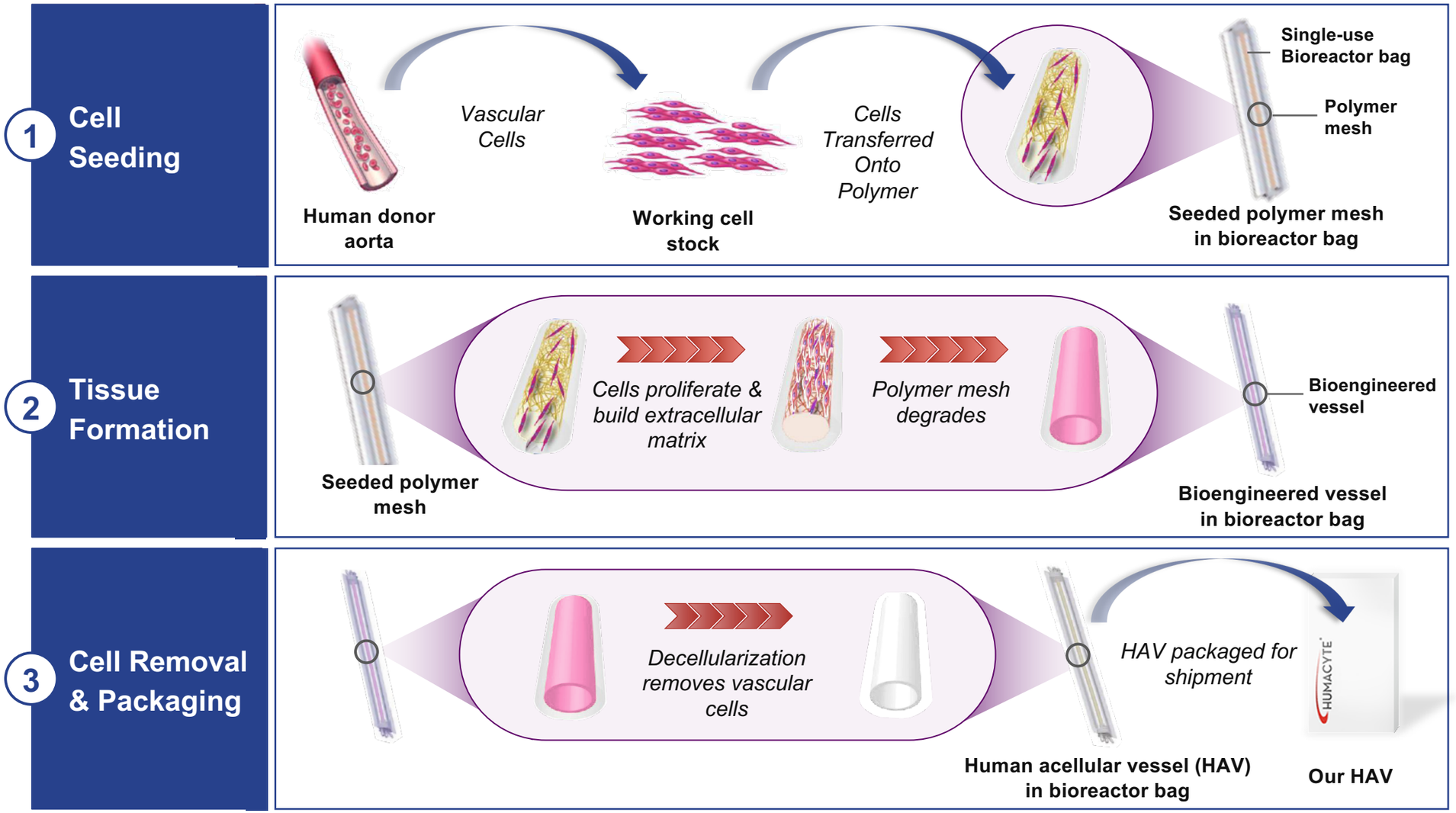
Objective: HAV being developed for dialysis access as an alternative to autologous arteriovenous fistula (AVF).

Potential benefits of HAV evaluated in completed and ongoing clinical trials include:

- Off-the-shelf
- Usable within one month after implantation
- Potential for decreased catheter contact time as compared to patients awaiting fistula maturation
- HAV appears to be highly resistant to infection
- HAV has no evidence of immunogenicity
- Host cells repopulate the HAV
- Long-term durability in ongoing studies.

6

BIOENGINEERED HUMAN ACELLUAR VESSELS (HAVs)



HAV Clinical Experience

- First implants in 2012
- Over 430 patients
- 800 patient-years
- 8 clinical trials
- 3 investigational indications
- 60 clinical sites
- Over 100 surgeons have implanted the HAV into patients

7

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 [1].
- **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* [1]

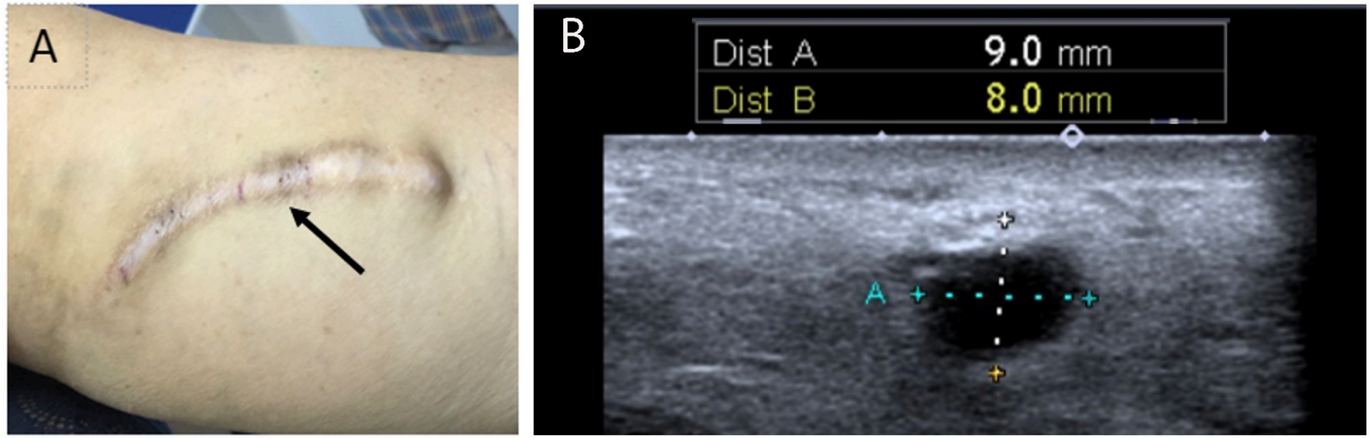
Phase 2 HAV Results vs. Historical Fistula & ePTFE Data

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

[1] Lawson, J.H. et al. The Lancet 2016; 387: 2026-2034.
[2] Halbert, R.J, et al . Kidney360 December 2020, 1 : 1437-1446
[3] Allon, M., et al. American J Kidney Disease 2018; 71: 677-689.
[4] Arhuidese, I.J., et al. Journal Vascular Surgery 2018; 68: 1166-1174
[5] Al-Jaishi, A.A., et al. JASN 2017; 28: 1839-1850.

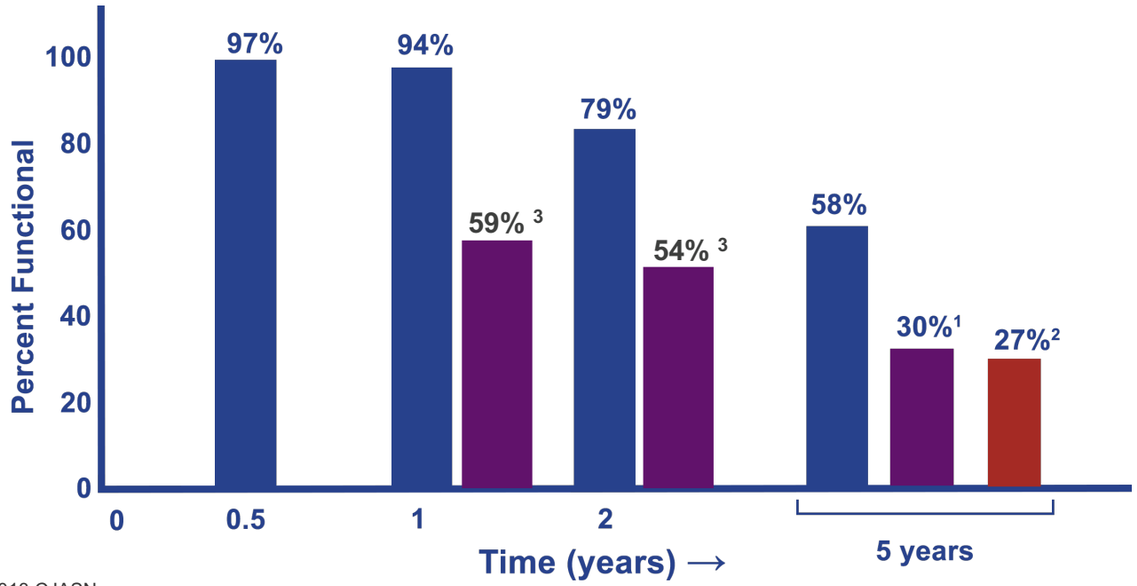
8

HAV IN HEMODIALYSIS ACCESS:
PHASE 2 STUDY ≥ 5 YEARS, LONG TERM DURABILITY



A) Patient with access site utilized for 6 years (arrow).

B) Ultrasound of HAV from same patient.



HAV Fistula ePTFE

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

[1] Lok, et al; 2013 CJASN
[2] Kakisis et al; 2017, JVS
[3] Arhuidese, et al, 2018; JVS.

HAV REPOPULATES WITH CELLS FROM THE PATIENT OVER TIME [1]

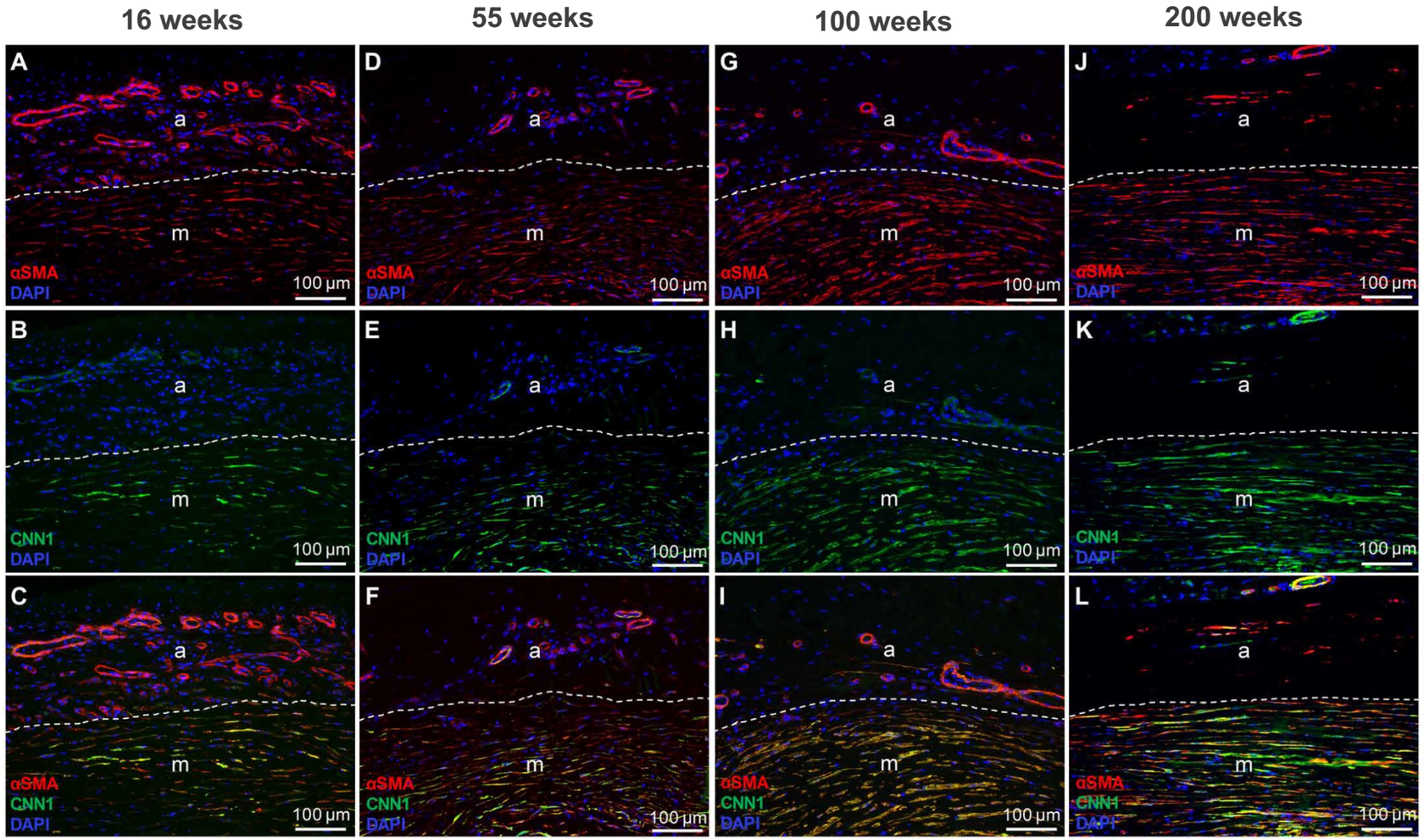
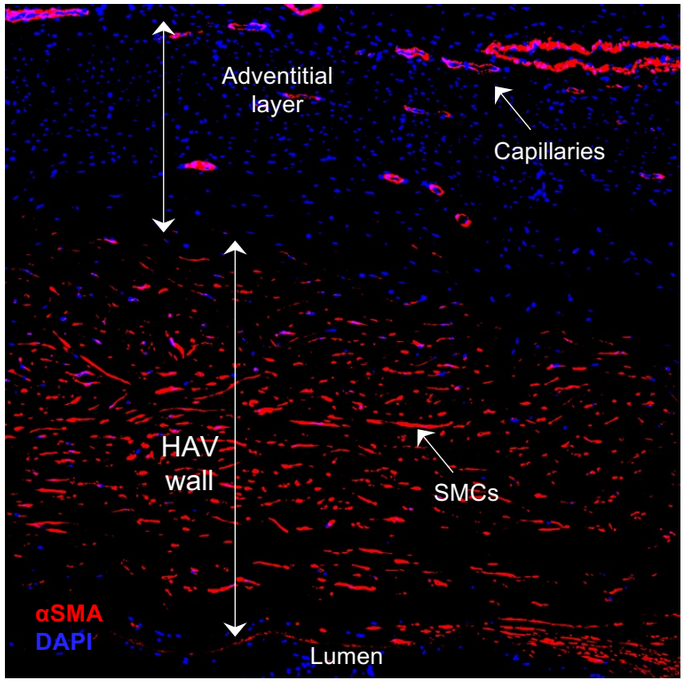


Fig. 4. Infiltration and maturation of aSMA+ host cells within the implanted HAV. Immunofluorescence staining of explanted HAV sections for aSMA (red) and CNN1 (green), a contractile marker of mature SMCs. Developmental maturation indicated by coexpression of CNN1 and aSMA. HAV sections explanted at 16 (**A** to **C**), 55 (**D** to **F**), 100 (**G** to **I**), and 200 (**J** to **L**) weeks after implantation. a, neoadventitia; m, medial layer. The boundary between the neoadventitia and medial layers is delineated by a white dashed line. Nuclei (blue) were counterstained with DAPI.

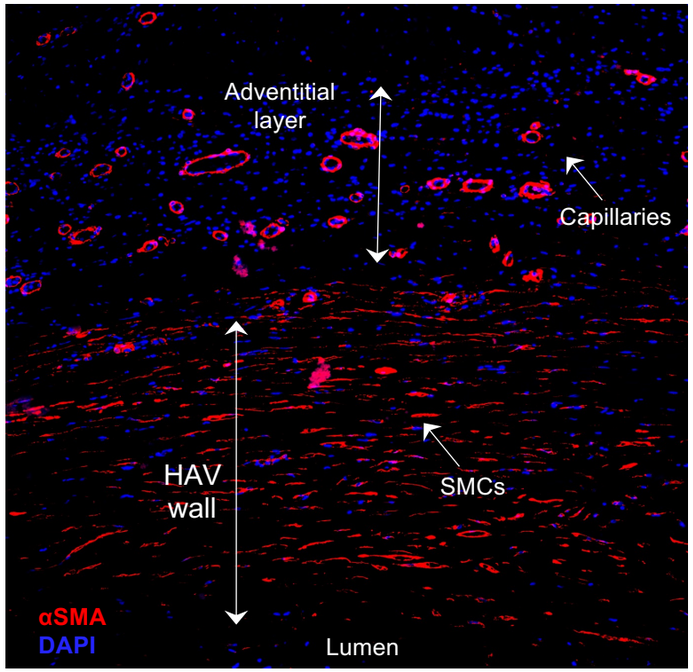
[1] Kirkton, R.D. et al, Sci Trans Med 2019; 11:eaau6934.

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.

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 430 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 [1, 2]

1) Hemodialysis International 2020; 24:36–42
2) Clinical Transplant 2011, Terasaki Foundation Laboratory, Los Angeles, California

NEXT STEPS FOR CLINICAL EVALUATION OF THE HAV

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

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 ***(24-month follow-up anticipated soon)***

- 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.

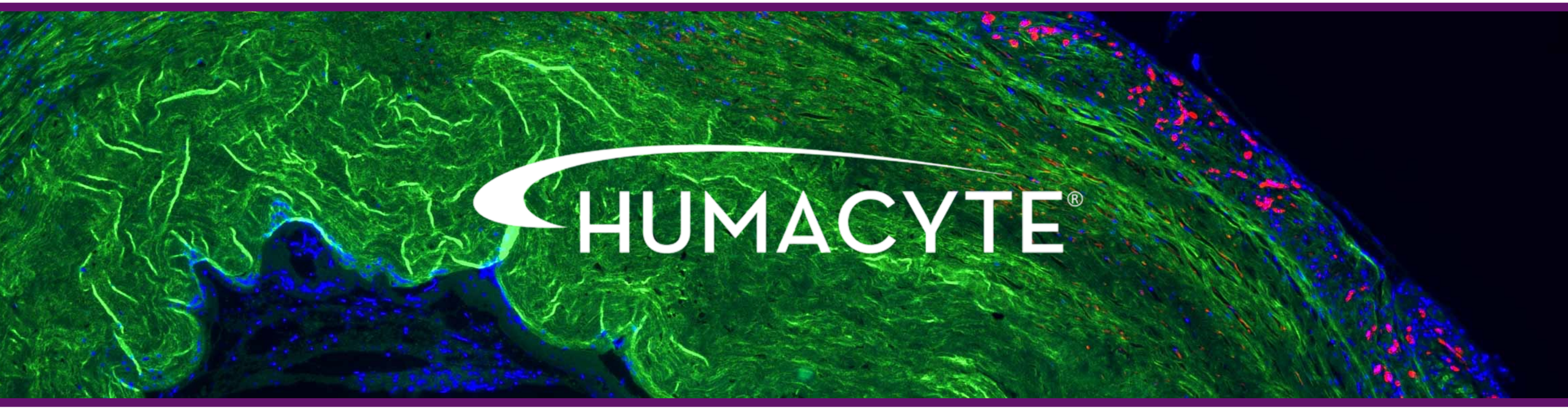
NCT03183245: Compare the Efficacy and Safety of Humacyte's Human Acellular Vessel with that of an **Autologous Arteriovenous Fistula** in Subjects with End-Stage Renal Disease ***(currently enrolling)***

- 30 centers in the US; target 240 total subjects (over 180 subjects enrolled currently).

13

SUMMARY

- Off-the-shelf bioengineered vascular tissues are possible
- They appear to be non immunogenic, integrate with native tissue, repopulate and remodel
- Examined post implant vessels tested appear to have increased strength and limited observable intimal hyperplasia
- Phase II/III clinical trials are ongoing for hemodialysis, PAD and vascular trauma with a highlight on clinical safety and utility of the HAV
- A number of additional clinical cardiovascular programs are in development



“The Humacyte Graft – Longer Term Patency with a Bioengineered Tissue Graft”

Jeffrey H. Lawson, MD, PHD

Chief Surgical Officer, Humacyte Incorporated
Adjunct Professor of Surgery, Duke University Medical Center

Humacyte Incorporated