vascular therapies

Reducing Surgical Stenosis

vascular therapies

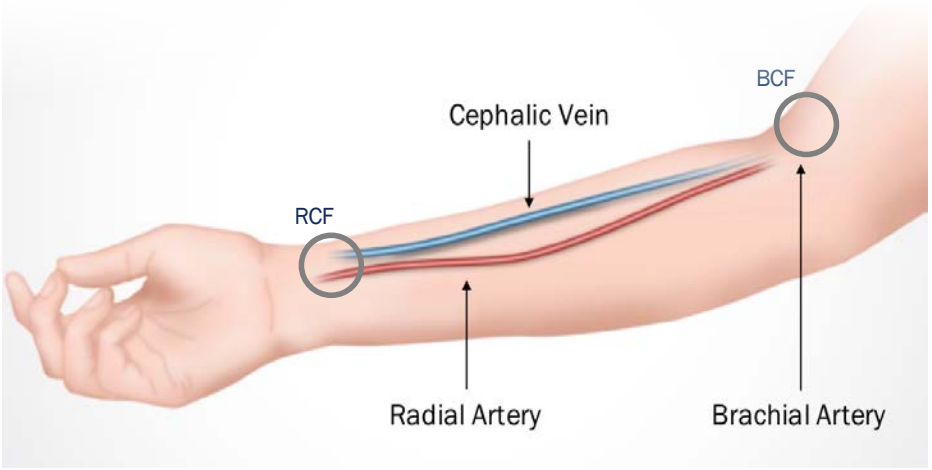
Clinical stage private company that has developed a bioresorbable Sirolimus vascular wrap to reduce vascular surgery stenosis

- **Sirogen™** initial indications AV fistulas and AV Grafts for hemodialysis patients. **Global TAM of $4.5+ billion**
- Favorable regulatory pathway: **Fast Track Status** and **Orphan Drug** designation
- Compelling HECON study with estimated 3-year **cost savings of $25K per patient**
- ACCESS 1 clinical trial missed the original endpoints. **ACCESS 2 trial designed to leverage positive findings from ACCESS 1 and has a high probability of success**
- **$25M financing** to enroll ACCESS 2 trial, review AVF results, AVG IND approval, manufacturing process controls and 1-year stability testing

Initial Indication - AV Fistulas (AVF)

Preferred Vascular Access for Patients requiring Hemodialysis

AVF are created by a **surgical or endovascular procedure to connect the vein and artery** near the wrist or elbow



Radio-cephalic (RCF) or Brachio-cephalic (BCF)

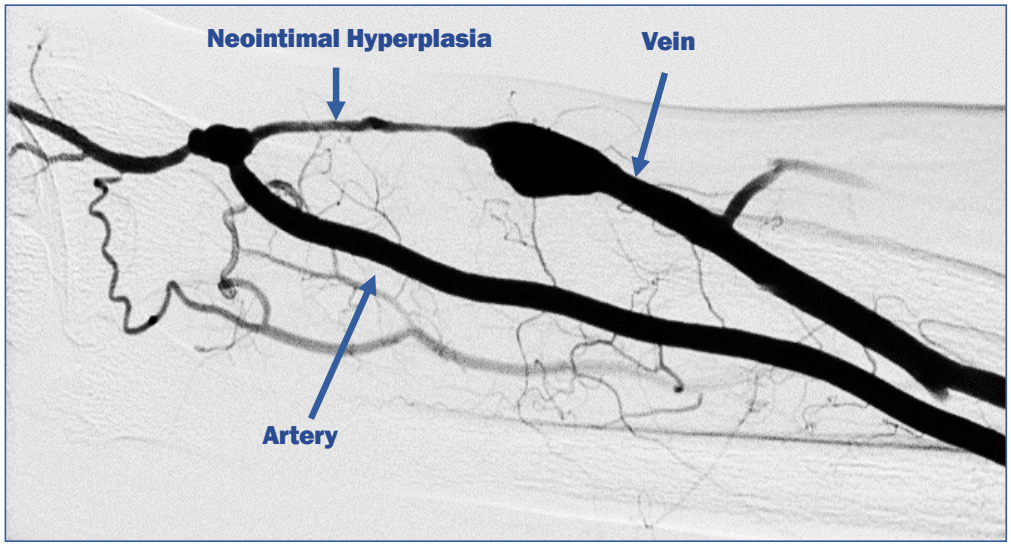
~375,000
annual global procedures

Most procedures **(85%) performed as outpatient**

Performed by **Surgeons and Interventionalists**

Problem: AVFs Have High Failure Rates

AVF fail to "mature" and provide adequate blood flow for dialysis due to a narrowing in the vein (stenosis) resulting from neointimal hyperplasia



AVF maturation failures are common and unpredictable

In ESRD patients age ≥ 65, only

50–60%

of AVF are suitable for hemodialysis at 1-year

Reference

1. USRDS. (2020). United States Renal Data System. 2017 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesdea, MD, 2017, 1–18. Retrieved from https://www.usrds.org
2. Michelle Robin, Prediction of Arteriovenous Fistula Clinical Maturation from Postoperative Ultrasound Measurements: Findings from the Hemodialysis Fistula Maturation Study, 2018 Journal of American Society of Nephrology

Sirolimus is Clinically Proven to Reduce Stenosis

Clinical Investigation and Reports

Lack of Neointimal Proliferation After Implantation of Sirolimus-Coated Stents in Human Coronary Arteries

A Quantitative Coronary Angiography and Three-Dimensional Intravascular Ultrasound Study

J. Eduardo Sousa, MD, PhD; Marco A. Costa, M
Andrea S. Abizaid, MD; Fausto Feres, MD; Ibrai
Rodolfo Staico, MD; Luiz A. Mattos, MD; Amanda G.
Judith Jaeger, BA; Jeffrey J. Popma, MD

Background—Restenosis remains an important limitation of inter
the safety and efficacy of sirolimus (a cell-cycle inhibitor)-coa
Methods and Results—Thirty patients with angina pectoris we
sirolimus-coated stents (slow release [SR], n=15, and fast relea
and patients were discharged without clinical complications. In
3D volumetric intravascular ultrasound data (immediately aft
clinical follow-up was obtained for all patients. There was min
in the SR group and 10.4±3.0% in the FR group, *P*=NS) by ult
late loss, 0.09±0.3 mm [SR] and −0.02±0.3 mm [FR]; in-lesio
No in-stent or edge restenosis (diameter stenosis ≥50%) was
repeat revascularization, myocardial infarction, or death) had
Conclusions—The implantation of sirolimus-coated BX Velocity
proliferation. Additional placebo-controlled trials are required
103:192-195.)

Key Words: stents ■ reste

Restenosis remains a vexing problem of percutaneous intervention. The most promising approach to prevent restenosis has been the application of intracoronary radiation[1]; however, some relevant side effects (edge restenosis and late thrombosis) have been reported.[2,3] Numerous pharmacological approaches to reduce restenosis have failed, possibly due to insufficient local drug concentrations.[4] Delivering medication directly to the site of vascular injury via polymeric-coated stents is a rational approach to achieve adequate local drug delivery.[5,6]

Sirolimus (Rapamune), a natural macrocyclic lactone, is a potent immunosuppressive agent that was developed by Wyeth-Ayerst Laboratories and approved by the Food and Drug Administration for the prophylaxis of renal transplant rejection in 1999.[7] Sirolimus binds to an intracellular receptor protein and elevates p27 levels, which leads to the inhibition

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 2, 2003 VOL. 349 NO. 14

Sirolimus-Eluting Stents versus Standard Stents in Patients with Stenosis in a Native Coronary Artery

Jeffrey W. Moses, M.D., Martin B. Leon, M.D., Jeffrey J. Popma, M.D., Peter J. Fitzgerald, M.D., Ph.D., David R. Holmes, M.D., Charles O'Shaughnessy, M.D., Ronald P. Caputo, M.D., Dean J. Kereiakes, M.D., David O. Williams, M.D., Paul S. Teirstein, M.D., Judith L. Jaeger, B.A., and Richard E. Kuntz, M.D., for the SIRIUS Investigators*

ABSTRACT

BACKGROUND
Preliminary reports of studies involving simple coronary lesions indicate that a sirolimus-eluting stent significantly reduces the risk of restenosis after percutaneous coronary revascularization.

METHODS
We conducted a randomized, double-blind trial comparing a sirolimus-eluting stent with a standard stent in 1058 patients at 53 centers in the United States who had a newly diagnosed lesion in a native coronary artery. The coronary disease in these patients was complex because of the frequent presence of diabetes (in 26 percent of patients), the high percentage of patients with longer lesions (mean, 14.4 mm), and small vessels (mean, 2.80 mm). The primary end point was failure of the target vessel (a composite of death from cardiac causes, myocardial infarction, and repeated percutaneous or surgical revascularization of the target vessel) within 270 days.

RESULTS
The rate of failure of the target vessel was reduced from 21.0 percent with a standard stent to 8.6 percent with a sirolimus-eluting stent (P<0.001) — a reduction that was driven largely by a decrease in the frequency of the need for revascularization of the target lesion (16.6 percent in the standard-stent group vs. 4.1 percent in the sirolimus-stent group, P<0.001). The frequency of neointimal hyperplasia within the stent was also decreased in the group that received sirolimus-eluting stents, as assessed by both angiography and intravascular ultrasonography. Subgroup analyses revealed a reduction in the rates of angiographic restenosis and target-lesion revascularization in all subgroups examined.

CONCLUSIONS
In this randomized clinical trial involving patients with complex coronary lesions, the use of a sirolimus-eluting stent had a consistent treatment effect, reducing the rates of restenosis and associated clinical events in all subgroups analyzed.

From the Lenox Hill Heart and Vascular Institute of New York, New York (J.W.M., M.B.L.); Brigham and Women's Hospital, Boston (J.J.P., R.E.K.); Stanford University Medical Center, Stanford, Calif. (P.J.F.); the Mayo Clinic, Rochester, Minn. (D.R.H.); the North Ohio Heart Center, Elyria (C.O.); Saint Joseph's Hospital, Syracuse, N.Y. (R.P.C.); the Christ Hospital–Lindner Research Center, Cincinnati (D.J.K.); Rhode Island Hospital, Providence (D.O.W.); the Scripps Clinic, La Jolla, Calif. (P.S.T.); and Cordis (Johnson & Johnson), Warren, N.J. (J.L.J.). Address reprint requests to Dr. Moses at the Cardiovascular Research Foundation and Lenox Hill Heart and Vascular Institute of New York City, 130 E. 77th St., Black Hall, 9th Fl., New York, NY 10021, or at jmoses@lenoxhill.net.

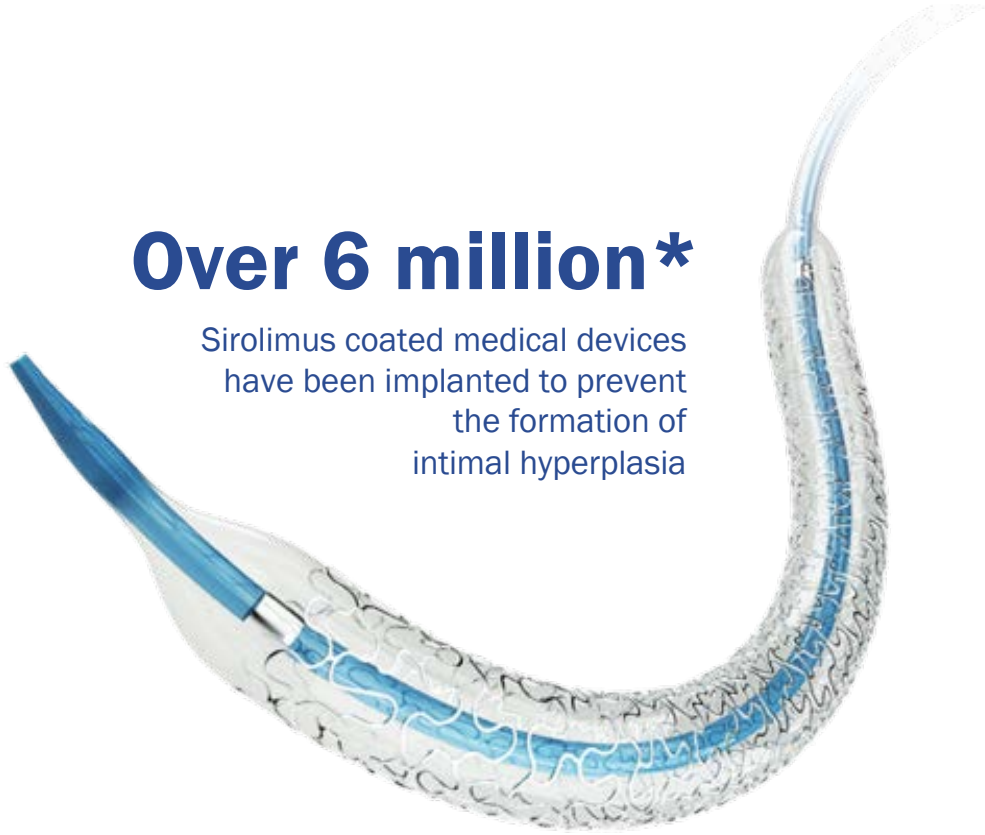
*The SIRIUS investigators are listed in the Appendix.

N Engl J Med 2003;349:1315-23.

1315

Over 6 million*

Sirolimus coated medical devices have been implanted to prevent the formation of intimal hyperplasia



*Estimates based on public information

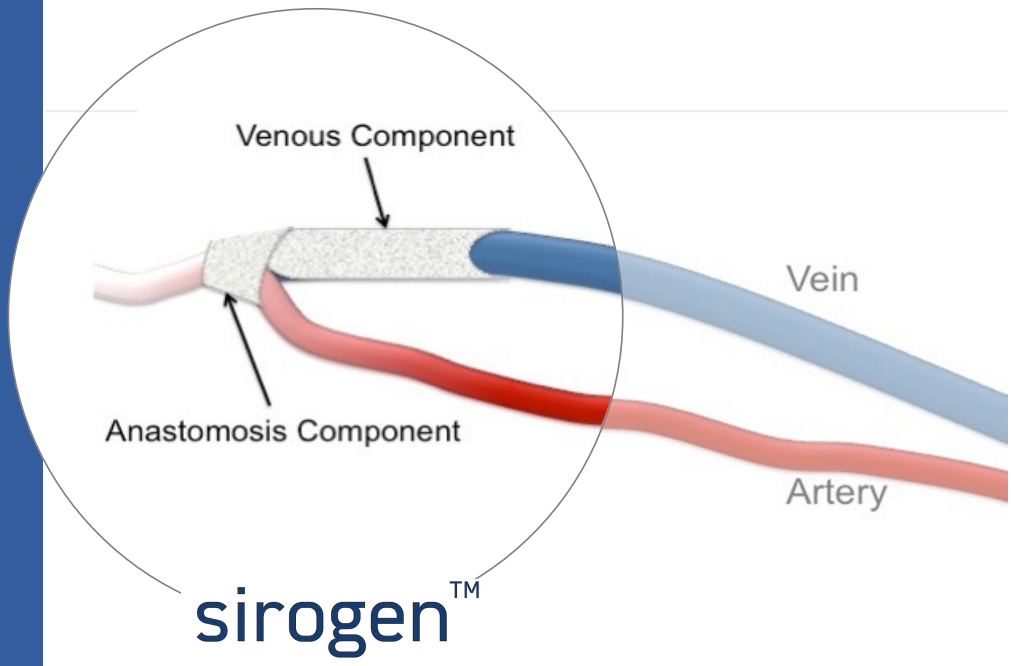
Intraoperative Drug Delivery

sirogen™

Collagen matrix with Sirolimus designed to conform around vein and anastomosis

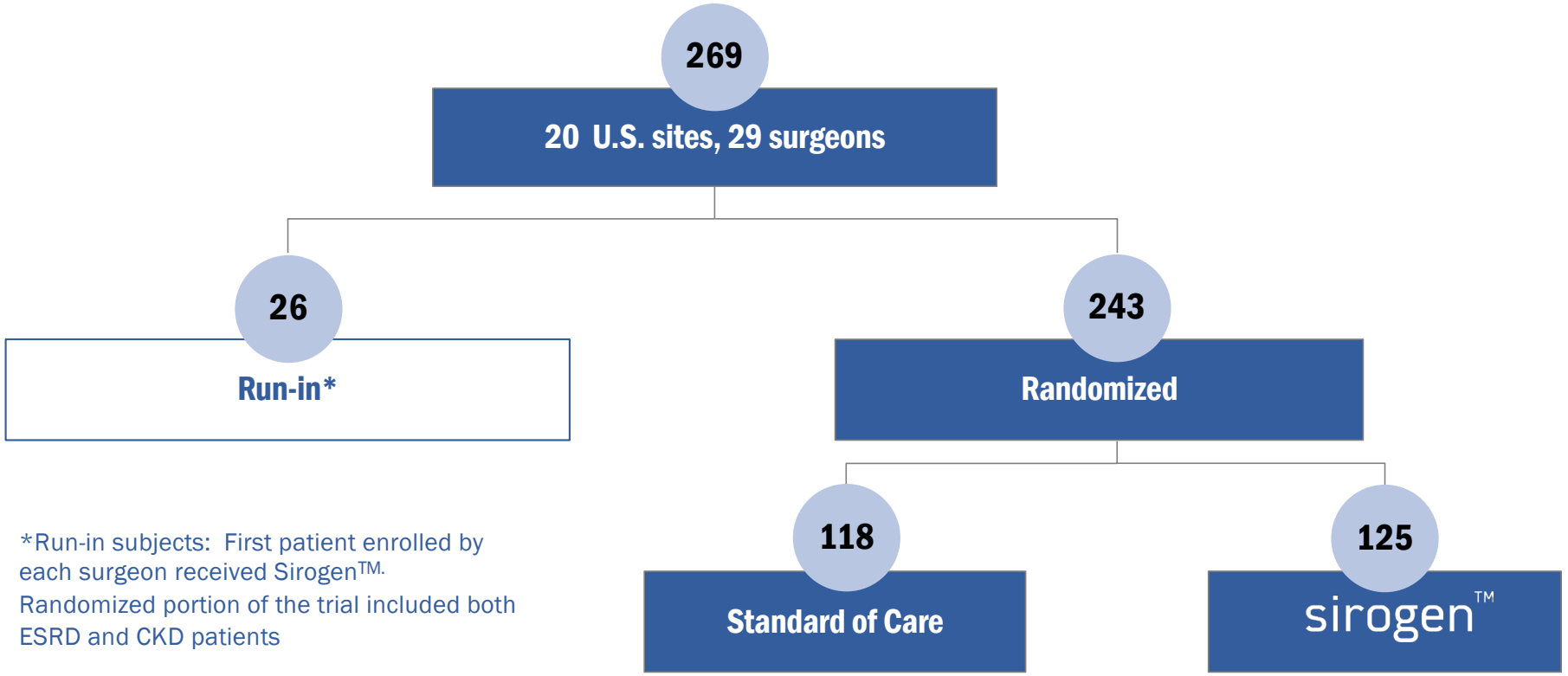
Easily applied during surgical AVF creation

- Drug delivery starts after implantation and is active for at least **8 weeks**
- Collagen is **bioresorbed after 12 weeks**
- **No long-term implant** or adjunctive procedures required
- **Patent protection through 2031 + 7 years of U.S. marketing exclusivity as an Orphan drug**



ACCESS 1 Trial – Phase 3 Clinical Study

Randomized, prospective, multi-center, single-blind



*Run-in subjects: First patient enrolled by each surgeon received Sirogen™.
Randomized portion of the trial included both ESRD and CKD patients

ACCESS 1 Trial – Prespecified Endpoints

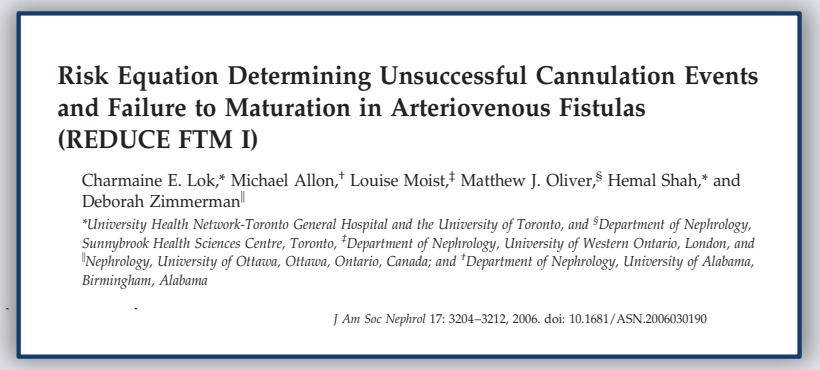
Excellent safety results – but no statistical difference between Sirogen and controls in the efficacy endpoints

Endpoints		Sirogen	Controls	p
Primary P < 0.01	Fistula Suitability for Dialysis at 6 Months (FSD6)	63.2%	68.5%	0.2942
Secondary P <0.05	Fistula Suitability for Dialysis at 12 Months (FSD12)	73.4%	71.8%	0.9224
	Fistula Maturation by Day 90	54.1%	59.5%	0.2116
	Secondary Patency (12 mo)	81.0%	81.9%	0.8072
	Re-intervention Rate (per patient)	1.0	1.0	0.3186

Results led to a post-hoc evaluation of hazard ratios/risks: Age, Race and Gender

Age is an Important Risk Factor for Fistula Maturation

Validated Risk Equation for Fistula Maturation



Risk Equation Determining Unsuccessful Cannulation Events and Failure to Maturation in Arteriovenous Fistulas (REDUCE FTM I)

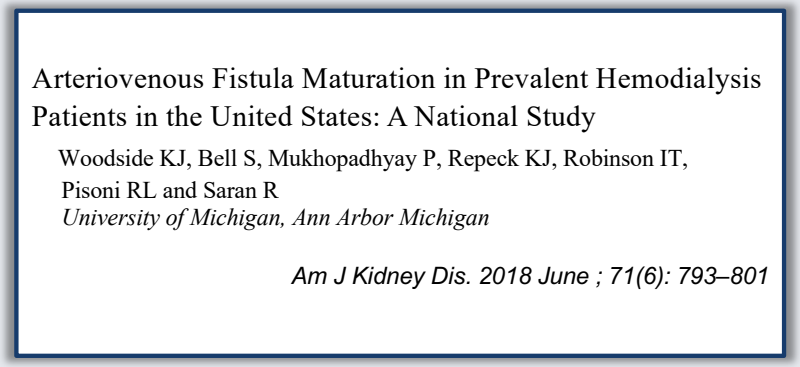
Charmaine E. Lok,* Michael Allon,† Louise Moist,‡ Matthew J. Oliver,§ Hemal Shah,* and Deborah Zimmerman‖

*University Health Network-Toronto General Hospital and the University of Toronto, and §Department of Nephrology, Sunnybrook Health Sciences Centre, Toronto, ‡Department of Nephrology, University of Western Ontario, London, and ‖Nephrology, University of Ottawa, Ottawa, Ontario, Canada; and †Department of Nephrology, University of Alabama, Birmingham, Alabama

J Am Soc Nephrol 17: 3204–3212, 2006. doi: 10.1681/ASN.2006030190

Age ≥65y, Race, CAD, PAD

Predictors of AVF Maturation 39,820 Patients (USRDS Data)



Arteriovenous Fistula Maturation in Prevalent Hemodialysis Patients in the United States: A National Study

Woodside KJ, Bell S, Mukhopadhyay P, Repeck KJ, Robinson IT, Pisoni RL and Saran R

University of Michigan, Ann Arbor Michigan

Am J Kidney Dis. 2018 June ; 71(6): 793–801

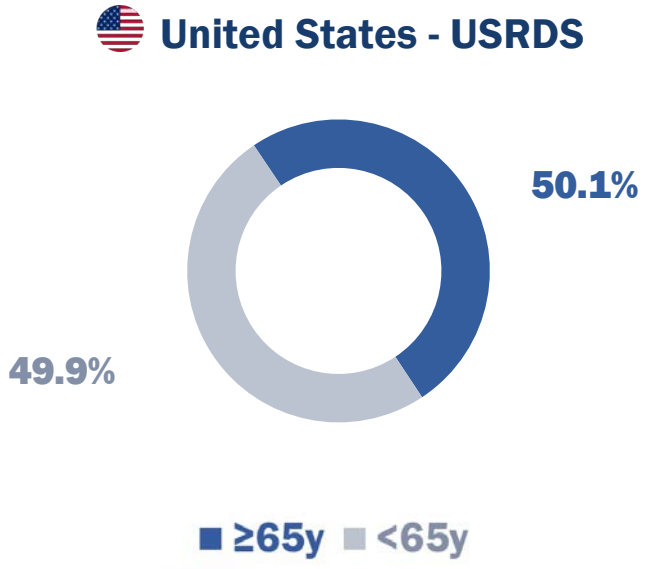
Age ≥65y, Gender, Race, Comorbidities, Geographic Location, Dialysis Vintage

The ACCESS 1 Trial

Control arm had a significantly higher proportion of younger (<65y) low-risk patients

ESRD Patient Enrollment

Age	Patients	Sirogen (N=92)	Controls (N=82)
≥ 65y Higher Risk	58/174 (33%)	37 (40.2%)	21 (25.6%)
< 65y Lower Risk	116/174 (67%)	55 (59.8%)	61 (74.4%)



Randomization Did Not Balance Risk as Expected

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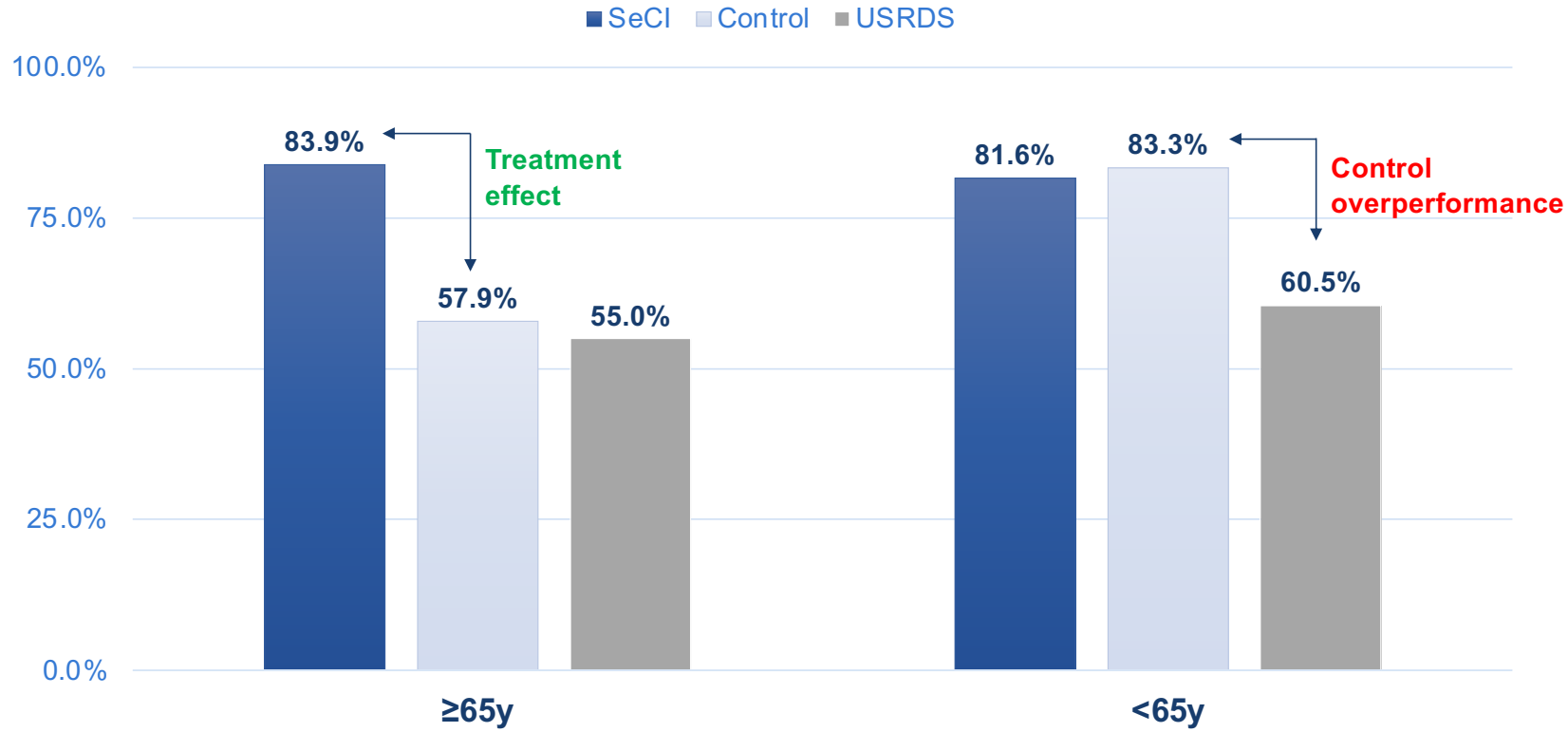
ACCESS 1 Trial – ESRD Patients

FSD12 Outcomes evaluated by risk

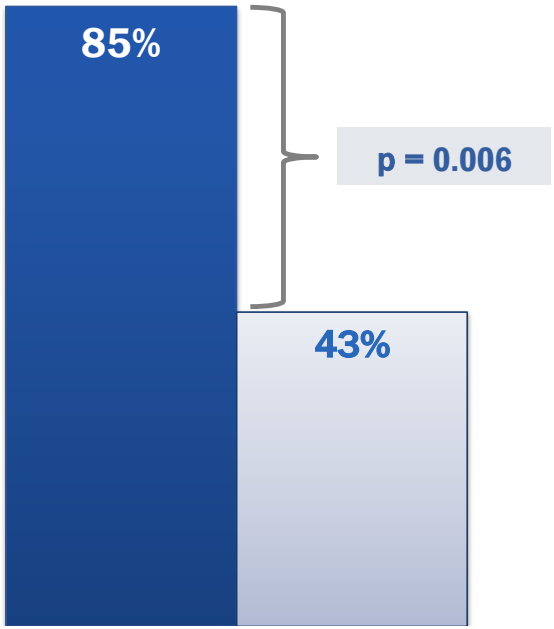


The positive treatment effect in the ≥ 65y patients was masked by control overperformance in the low risk <65y age group (67% of enrolled patients)

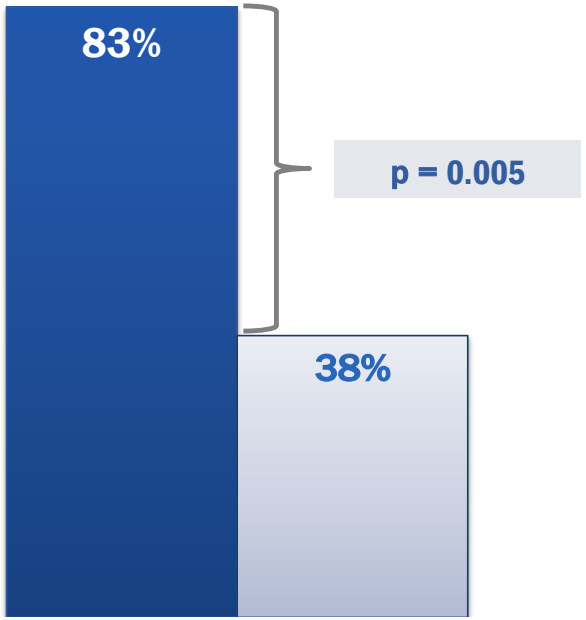
vascular therapies

AVF Clinical Outcomes from ACCESS 1

Phase 3 randomized multi-center clinical trial
Radiocephalic fistulas (RCF) in ESRD patients ≥ 65y



Fistula Maturation @ 6-months
ACCESS 2 Primary Endpoint



Suitability for Dialysis @ 12-months

Sirogen Controls

vascular therapies

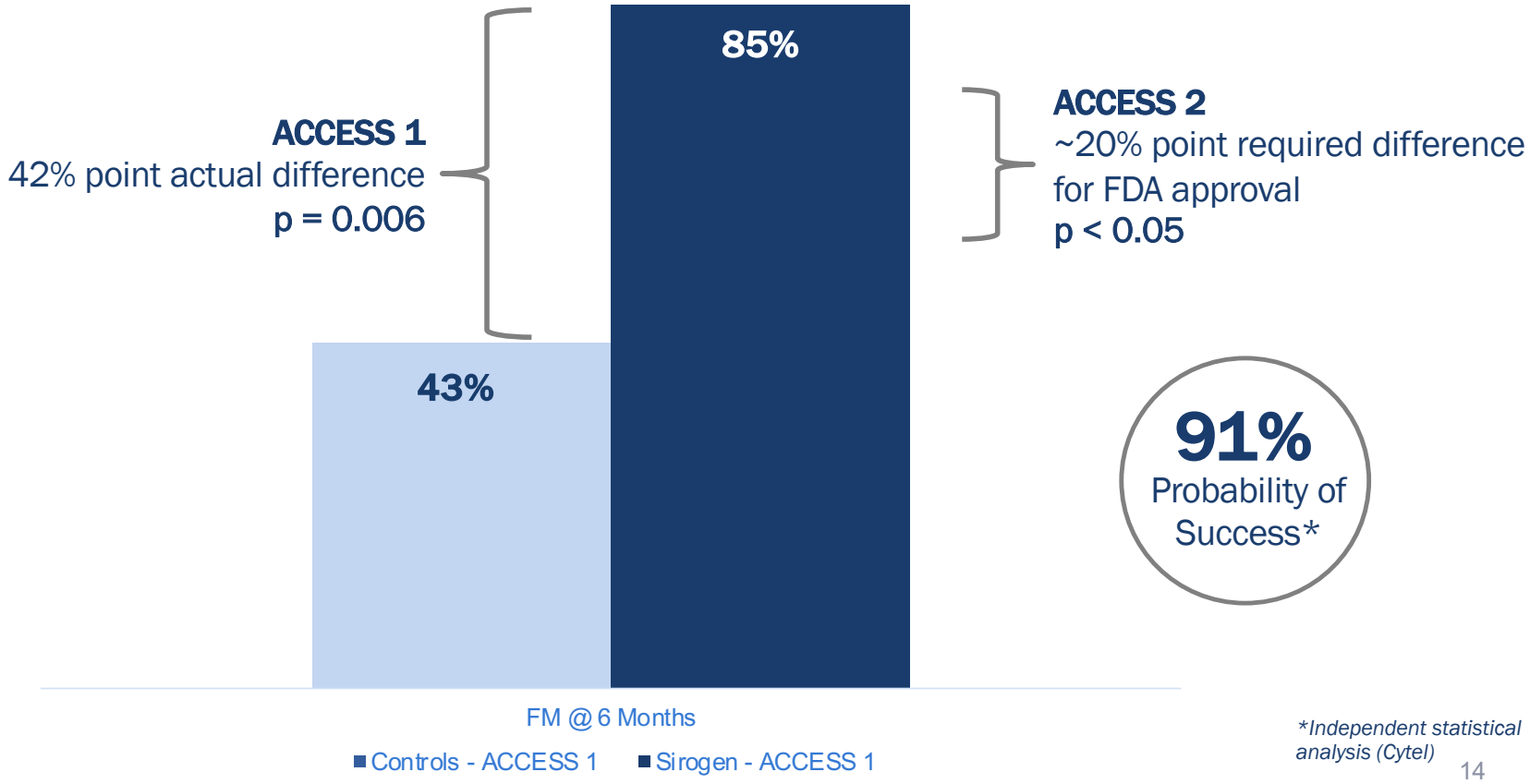
Comparing ACCESS 1 and ACCESS 2

Prospective, multicenter, randomized, controlled AV Fistula Trials

	ACCESS 1 (Protocol VT-304)	**ACCESS 2** (Protocol VT-305)
Number of randomized patients	243	120
Patient Characteristics	All ages, both genders	≥65y years, at least 30% females
Fistula Location	80% RCF, 20% BCF	Only RCF
Primary Endpoint	Fistula Suitability for Dialysis – 6 months	Fistula Maturation (FM) – 6 months
p value	≤ 0.01	≤ 0.05
Secondary Endpoint	FSD12 (12 months)	FSD12 (12 months)
	Secondary Patency (12 months)	Secondary Patency (12 months)
Principal Investigators	Nephrologists	Surgeons and Nephrologists

ACCESS 2 - Results Required for FDA Approval

ACCESS 1 outcomes were 2X+ more than what is required for success in ACCESS 2



**Independent statistical analysis (Cytel)*

vascular therapies

Sirogen™ Regulatory Pathway

ACCESS 2 randomized trial for AVF
IND amendment Sept 2021 - plan to start enrollment in Q2 2022

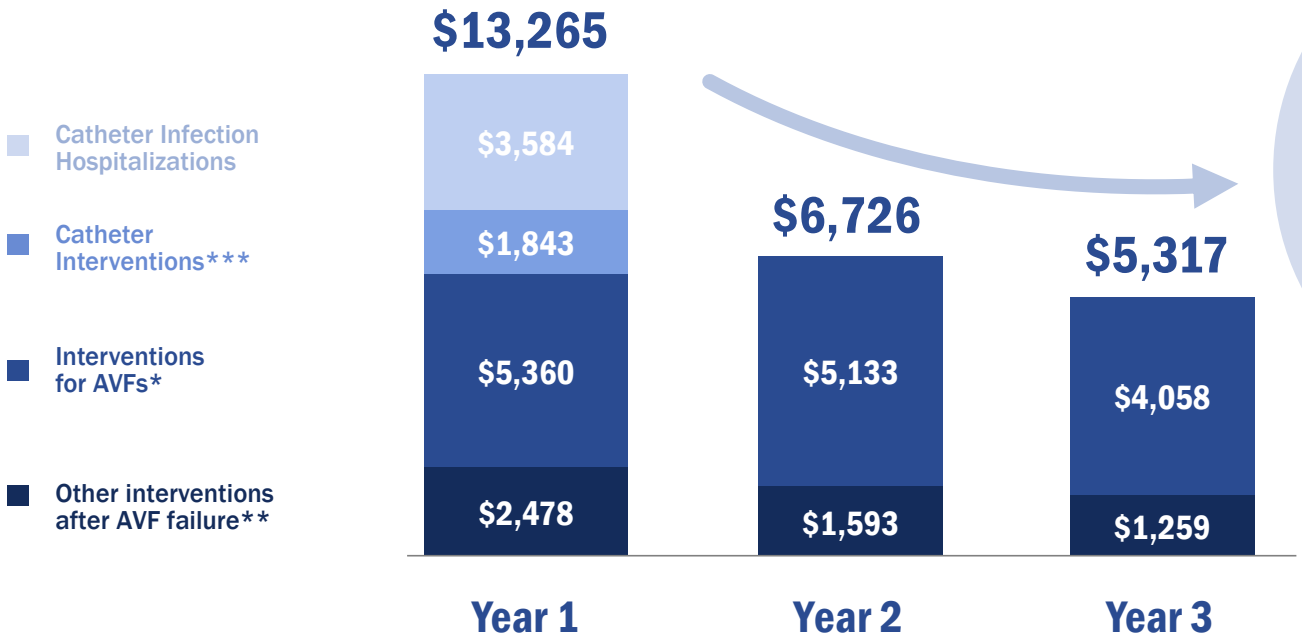
AVF NDA filing expected in early 2024
Estimated FDA approval in early 2025

ACCESS 3 randomized trial for AVG
IND planned for 2023 – start enrollment in 2024

Fast Track Status and Orphan Drug designation in the U.S. and E.U. 7/10 years marketing exclusivity

Cost Savings Compared to Current AVF Standard of Care

Total savings per patient with Sirogen™ from ACCESS 1 compared to medicare costs for literature-based controls



$25K

Total 3-year savings per patient with Sirogen™

Boston Healthcare Associates Analysis
March 2021

Vascular Therapies

*Interventions for AVFs include procedures performed before fistula needs to be replaced, such as: administration of antibiotics, thrombolytics, and angioplasty
**Other interventions after AVF failure include receiving a new catheter, a new AVF, or a graft
***Catheter interventions include incremental removals, replacements, repositioning and thrombolytics for patients not receiving Sirogen

Sirogen™ Reimbursement

Covered under the

Medicare Outpatient Prospective Payment System (OPPS)

- Manufacturer sets price
- Not included in “access bundle”
- Reimbursement at FDA approval (C9399)
- Apply for both C code and J code
- Pass-through status for ~3 years
- ASP + 6%

Post pass-through payment based upon clinical efficacy, adoption, cost savings and patient access

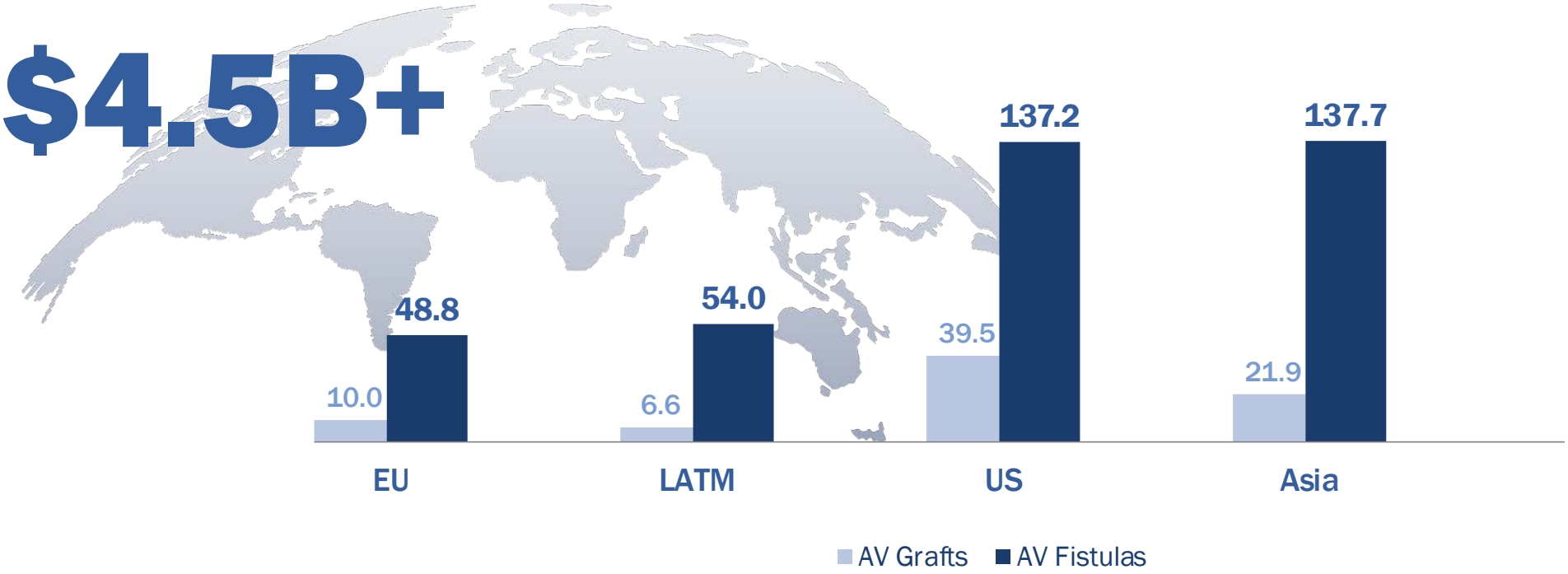
- Significant unmet need
- HECON demonstrates cost savings
- KDOQI Clinical Guidelines = AVF
- Apply for permanent HCPCS code
- Advocacy: DPC, AAKP, SVS, VASA, etc

~85% of AVF surgeries performed in an out-patient setting

AV Access Total Available Market

AVF and AVG Annual Procedures (000's)

$4.5B+

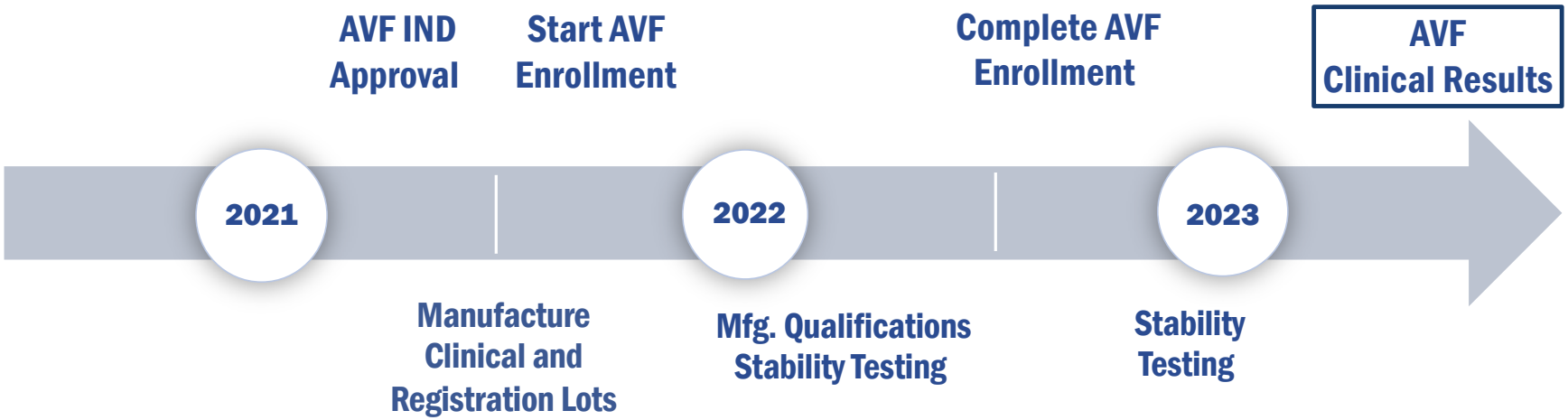


Total AVF and AVG annual procedures = 377,700 and 78,000 respectively (455,700 total). Does not include Canada, Middle East, China or India. ASP is $10,000 per procedure. Data from 2018 USRDS, ERA-EDTA Registry, JSDT Renal Data Registry, DOPPS and Meichelboeck, W (2017) Global Trends in ESRD

vascular therapies

Sirogen™ Clinical/Operations Timeline

Valuation catalyst with ACCESS 2 clinical results – estimated end of 2023



Estimated NDA filing in 2024 and anticipated FDA approval in early 2025

Leadership Team

John McDermott
Chief Executive Officer

30+ years of executive leadership in private and public vascular medical technology companies

IMPRA BARD Endologix

Sriram Iyer, MD, FACC, FSCAI
Founder,
Chief Scientific Officer

Interventional cardiologist and vascular medicine specialist with over 30 years of patient care and clinical trial experience. Former Associate Chairman of the Department of Cardiology and the Director of Peripheral Vascular and Carotid Interventions at Lenox Hill Hospital NYC

Lenox Hill Hospital Northwell Health

Paul Barkofsky
Vice President,
R&D

20-year career in the medical device, drug delivery, and specialty chemicals fields specializing in new product and process development

Cordis

Ronald Eggan, Jr.
Sr. Director,
Manufacturing

25 years of leadership experience in medical device manufacturing and engineering operations. Black belt certified in process and lean manufacturing.

Cordis Edwards INTEGRA

Maureen Harrison
Vice President,
Quality Assurance

30-year career in the life sciences industry with leadership roles in global pharmaceutical and biopharmaceutical research companies.

Wyeth Pfizer Agouron Pharmaceuticals, Inc.

Priya Jambhekar
Regulatory Consultant

30 years of worldwide regulatory, quality and clinical experience. Multiple NDA submissions and approvals

Accellient Partners

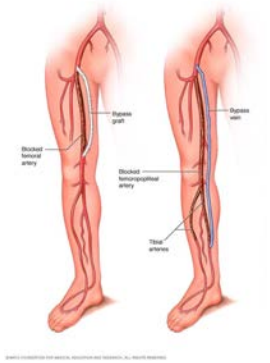
gsk GlaxoSmithKline

Johnson & Johnson

Vascular Therapies

Sirogen™ - Future Potential Indications

Peripheral Bypass

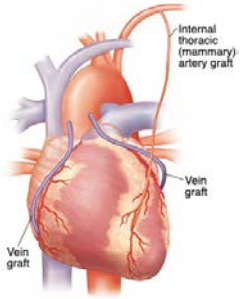


200,000
GLOBAL
Annual
Procedures

Phase 2 Complete
Positive
efficacy signal

$2B TAM

Coronary Bypass



800,000
GLOBAL
Annual
Procedures

$8B TAM

TAM = Total Addressable Market = Procedures X $10,000 ASP
Procedure estimates based upon MRG 2018 and company estimates

Financing – Use of Proceeds

Creating value by advancing clinical program and manufacturing

ACCESS 2 Clinical Program

- AVF IND amendment in 2021
- Complete AVF enrollment and primary endpoint clinical results in 2023
- AVG IND submission planned in 2023

Manufacturing

- Clinical and stability builds in 2022
- 1-year stability testing in 2023
- Manufacturing Process Qualification in 2023

Vascular Therapies – Summary

$4.5B AV Access Market Opportunity

- No therapeutic competition
- Patent protection + orphan drug exclusivity
- Attractive new growth market for vascular and renal companies
- Favorable health care economics

Clear Pathway for Regulatory Approval

- Alignment with FDA
- ACCESS 2 clinical trial has a high probability of success

Attractive Financial Profile

- Significant growth potential
- Expected high gross margins (~90%)
- Ability to leverage existing commercial infrastructure for vascular companies
- Opportunity to expand indications into PV and Cardiovascular

vascular therapies

For Additional Information:

John McDermott
Chief Executive Officer
jmcdermott@vasculartx.com
602-684-7309

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