ELUVIA™ Drug-Eluting Vascular Stent System

Delivering Durable Patient Outcomes and Economic Value with Eluvia
What is Peripheral Artery Disease (PAD) and Critical Limb Ischemia (CLI)?

**PAD** is a progressive arterial disease that limits blood flow to the legs and feet. PAD causes life-debilitating symptoms and can progress to critical limb ischemia, which often leads to amputations.

**Claudication** is pain and/or cramping in the lower leg due to inadequate blood flow to the muscles, typically felt while walking.

**CLI** is the most advanced stage of peripheral artery disease and manifests as ischemic rest pain, non-healing ulcers, and/or gangrene.

**5-Year Mortality for CLI patients is higher than Common Cancers and Heart Disease**\(^1\)
- 6x higher than Breast Cancer
- 3x higher than AMI

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## PAD & CLI are Massive Unmet Disease States

### Impact on prevalence

**Over 200 Million** people worldwide suffer from **PAD**\(^1\)

### Impact on quality of life

Only **50%** of **CLI patients** with an amputation undergo an angiogram\(^2\)

**Over Half** the patients who undergo an amputation **die within 5 years**\(^3\)

### Impact on healthcare

Total Medicare expenditures for PAD-related treatment are approximately **$4.4 billion**\(^4\)

After hospitalization for CLI, **1 out of 5 patients** (20%) will be readmitted within **30 days** versus AMI at 14.7%, PCI at 12.0%, and standard endovascular treatment at 8%\(^3\).

CMS states that **“readmissions correlates to reduced quality of care and patient satisfaction.”**

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Treatment Evolution to Drug Therapies To Increase Durability of Patient Outcomes

In the coronaries, Drug Therapies evolved into the gold standard for CAD treatment

1960s
Open Heart Surgery
CABG

1977-1990s
Balloon Angioplasty

Late 1980s
Bare Metal Stents

Early 2000s
Drug-Eluting Stents

1960s
Open Heart Surgery
CABG

1977-1990s
Balloon Angioplasty

Late 1980s
Bare Metal Stents

Early 2000s
Drug-Eluting Stents

This evolutionary shift is happening for PAD treatment today

Early 1980s
Balloon Angioplasty

Early 2000s
Bare-Metal Nitinol Stents

2012
Drug-coated Stent (ZilverPTX)

2014
Drug-coated Balloons (Lutonix)


ZilverPTX is a registered trademark of Cook Medical. Image sourced from Cook website. Lutonix is a registered trademark of CR Bard, Inc. Image sourced from Bard website.
Treating SFA Disease is Different Than Treating Coronary Artery Disease

**What?** Interventional treatment creates an injury and the artery responds with a healing process.  

**When?** Restenosis peaks in the SFA at around 12 months, versus 3-6 months in coronary arteries.  

**Why?** The SFA (located between the hip and knee) is exposed to mechanical forces like bending and twisting, therefore the healing process is much longer.

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**CLINICAL HISTORY OF RESTENOSIS**

ELUVIA is the only SFA therapy designed to sustain drug release beyond 1 year to match the disease process in the SFA

A New SFA Solution with Sustained Drug Release: Technology that allows you to achieve strong clinical outcomes and procedural economics that are highly favorable.

Enhance
Patient Experience

Strengthen
Quality Outcomes

Improve
Financial Health

Increase
Operational Efficiencies
The ELUVIA™ Drug-Eluting Stent is the first and only SFA treatment option that sustains drug release beyond 1 year to match the disease process in the SFA

- Eluvia addresses both the mechanical and biological challenges of the SFA
- Built on the Innova stent platform optimized for flexibility, strength and fracture resistance
- Utilizes Paclitaxel – current drug therapy used on all FDA approved antiproliferative devices for the SFA
- Proven polymer implanted in more than 20 million lesions\(^1\)
- Simple size matrix with only 10 UPNs
- Favorable reimbursement as compared to DCBs and Bypass

\(^1\) Data on file at Boston Scientific. Represents total global sales of the PROMUS (Boston Scientific) and XIENCE (Abbott) series of stents since 2007.
DES therapy keeps patients walking longer without pain

91% patients had no or minimal pain with walking at 2 years.

3.8% TLR rate means fewer visits to the hospital.

Patients treated with a DES versus Fempop Bypass had a significant reduction in procedure time and hospital stay:

- **DES**: Mean Procedure Time **59.6 minutes** and Mean Hospital Stay **2.5 days**
- **Bypass**: Mean Procedure Time **123 minutes** and Mean Hospital Stay **8 days**

Improved patient outcomes help you provide the highest quality patient care and enhance patient satisfaction.

Imperial US Pivotal IDE Trial: Study Objective & Design

Evaluate the safety and effectiveness of the Eluvia Drug-Eluting Vascular Stent System for treating Superficial Femoral Artery (SFA) and/or Proximal Popliteal Artery (PPA) lesions up to 140 mm in length.

Clinical Question: Does a drug-eluting stent with sustained drug release improve patency?

Trial Design

Global, multi-center trial consisting of:
- 465 subjects at 64 investigational sites worldwide
- A prospective, multicenter, 2:1 randomization against Cook’s Zilver™ PTX™ stent, controlled, single-blind, non-inferiority trial (RCT)
- Core lab adjudicated

Primary Endpoints

Safety:
- Major Adverse Events defined as all causes of death through 1 month, Target Limb Major Amputation through 12 months and/or Target Lesion Revascularization (TLR) through 12 months.

Efficacy:
- Assess primary vessel patency* at 12 months post-procedure.

*defined as a binary endpoint and will be determined to be a success when the duplex ultrasound (DUS) Peak Systolic Velocity Ratio (PSVR) is ≤ 2.4 at the 12-month follow-up visit, in the absence of clinically-driven TLR or bypass of the target lesion.
Eluvia demonstrated a statistically significant difference in primary patency compared to Zilver PTX at 12 months.

**12-Month Kaplan-Meier Estimate Primary Patency Rate**

![Graph showing Kaplan-Meier estimates for Eluvia and Zilver PTX at different time points. Eluvia has a higher cumulative event-free rate at 12 months (88.5%) compared to Zilver PTX (79.5%). The log-rank test statistic is p=0.0119.]

Kaplan Meier Estimate: Primary patency as determined by duplex ultrasound (DUS) Peak Systolic Velocity Ratio (PSVR) is ≤ 2.4 at the 12-month follow-up visit, in the absence of clinically-driven TLR or bypass of the target lesion.
Safety Results

95.1% of Eluvia patients were free of Major Adverse Events at 12 months

Eluvia demonstrated half the target lesion revascularization (TLR) rate of Zilver PTX at 12 months

<table>
<thead>
<tr>
<th>Clinically-Driven TLR Rate</th>
<th>Eluvia</th>
<th>Zilver PTX</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(12-month)</td>
<td>4.5%</td>
<td>9.0%</td>
<td>0.0975</td>
</tr>
<tr>
<td>12-month MAE</td>
<td>4.9%</td>
<td>9.0%</td>
<td></td>
</tr>
<tr>
<td>All Causes of Deaths at 1 Month</td>
<td>0.0%</td>
<td>0.0%</td>
<td>Undefined</td>
</tr>
<tr>
<td>Target Limb Major Amputation</td>
<td>0.3%</td>
<td>0.0%</td>
<td>1.0000</td>
</tr>
<tr>
<td>Clinically-driven TLR</td>
<td>4.5%</td>
<td>9.0%</td>
<td>0.0672</td>
</tr>
</tbody>
</table>

1Major Adverse Events (MAEs) defined as all causes of death through 1 month, target limb major amputation through 12 months and/or target lesion revascularization through 12 months.
Eluvia has demonstrated unprecedented outcomes in the SFA in all lesion and patient types

**MAJESTIC TRIAL**
Studied Claudicant Patients

**MUNSTER REGISTRY**
Studied CLI Patients

**36-MONTH FREEDOM FROM TLR**

83.5% Primary Patency at 2 years is the highest reported primary patency in similar SFA trials

Sustained durable patient outcomes
85.3% freedom from TLR rate at 3 years (K-M estimate)
- No target limb major amputation
- No stent fractures
- 91% patients walking without pain at 2 years

**12-MONTH PRIMARY PATENCY**

87% primary patency in patients who would typically qualify for femopop bypass

- 200mm mean lesion length
- Almost half of the patients had CLI
- 8 of 10 patients had CTOs
- No stent fractures

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Eluvia offers a simple matrix to minimize inventory management. Eluvia may simplify the procedure and reduce procedure time.

**Simple matrix – only 10 SKU’s**

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>Length (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>40 60 80 100 120</td>
</tr>
<tr>
<td>7</td>
<td>40 60 80 100 120</td>
</tr>
</tbody>
</table>

**Treatment Options Today**

- **DCBs**
  - + 20-40% Bailout Stent¹

- **Bypass Grafts**
  - Mean Procedure Time **123 minutes**
  - Mean Hospital Stay **8 days²**

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### Economic Impact

#### Cases with One Eluvia Stent

<table>
<thead>
<tr>
<th></th>
<th>Fem/Pop Stent CPT® 37226</th>
<th>Fem/Pop Stent + Atherectomy CPT® 37227</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reimbursement</strong></td>
<td>$9,669</td>
<td>$15,355</td>
</tr>
<tr>
<td><strong>Device Cost</strong></td>
<td>$2,595</td>
<td>$5,795</td>
</tr>
<tr>
<td>(1 Eluvia Stent)</td>
<td></td>
<td>(1 Eluvia Stent + Jetstream)</td>
</tr>
<tr>
<td><strong>Economic Impact</strong></td>
<td><strong>$7,074</strong></td>
<td><strong>$9,560</strong></td>
</tr>
</tbody>
</table>

#### Cases with Two Eluvia Stents

<table>
<thead>
<tr>
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<th>Fem/Pop Stent CPT® 37226</th>
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<tr>
<td><strong>Reimbursement</strong></td>
<td>$9,669</td>
<td>$15,355</td>
</tr>
<tr>
<td><strong>Device Cost</strong></td>
<td>$5,190</td>
<td>$8,390</td>
</tr>
<tr>
<td>(2 Eluvia Stents)</td>
<td></td>
<td>(2 Eluvia Stents + Jetstream)</td>
</tr>
<tr>
<td><strong>Economic Impact</strong></td>
<td><strong>$4,479</strong></td>
<td><strong>$6,965</strong></td>
</tr>
</tbody>
</table>

Reimbursement shown is Medicare hospital outpatient National Average. Device cost does not account for other needed devices such as sheath, wires, balloons, etc. CPT is a registered trademark of the American Medical Association.
## Economic Impact

### Cases with One DCB

<table>
<thead>
<tr>
<th>Fem/Pop PTA/DCB CPT® 37224</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Reimbursement</td>
<td>$4,679</td>
</tr>
<tr>
<td>Device Cost (1 DCB)</td>
<td>$1,500</td>
</tr>
<tr>
<td><strong>Economic Impact</strong></td>
<td><strong>$3,179</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fem/Pop PTA/DCB + Atherectomy CPT® 37225</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Reimbursement</td>
<td>$9,669</td>
</tr>
<tr>
<td>Device Cost (1 DCB + Jetstream)</td>
<td>$4,700</td>
</tr>
<tr>
<td><strong>Economic Impact</strong></td>
<td><strong>$4,969</strong></td>
</tr>
</tbody>
</table>

### Cases with Two DCBs

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<th>Fem/Pop PTA/DCB CPT® 37224</th>
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<td>Device Cost (2 DCBs)</td>
<td>$3,000</td>
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<td><strong>Economic Impact</strong></td>
<td><strong>$1,679</strong></td>
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<tr>
<td>Reimbursement</td>
<td>$9,669</td>
</tr>
<tr>
<td>Device Cost (2 DCBs + Jetstream)</td>
<td>$6,200</td>
</tr>
<tr>
<td><strong>Economic Impact</strong></td>
<td><strong>$3,469</strong></td>
</tr>
</tbody>
</table>
## Summary

<table>
<thead>
<tr>
<th>Enhance Patient Experience</th>
<th>91% of patients had <strong>minimal or no pain</strong> with walking at 2 years</th>
</tr>
</thead>
</table>
| Strengthen Quality Outcomes | **Lowest TLR rates of any PVD therapy** reduces the need for reintervention  
Half the TLR rate versus ZilverPTX |
| Increase Operational Efficiencies | **Simple matrix**  
May simplify the procedure and reduce procedure/fluoro time |
| Improve Financial Health | **Highly Favorable reimbursement** as compared to DCBs and Bypass |
Backup Slides
Primary Patency Rates from SFA Trials
In Perspective to Bare Metal Stent Studies

**Graph:**

- **IMPERIAL**
  - Eluvia: 88.5%
  - Zilver PTX: 79.5%

- **RESILIENT** (LifeStent)
  - 81.3%

- **STROLL** (S.M.A.R.T.)
  - 79.5%

- **DURABILITY II** (EverFlex)
  - 77.2%

**Table: Average lesion length and severity**

<table>
<thead>
<tr>
<th></th>
<th>IMPERIAL</th>
<th>RESILIENT</th>
<th>STROLL</th>
<th>DURABILITY II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Average lesion length</strong></td>
<td>8.7 cm</td>
<td>7.1 cm</td>
<td>7.7 cm</td>
<td>8.9 cm</td>
</tr>
<tr>
<td>Severe calcification</td>
<td>40%</td>
<td>25%</td>
<td>19%</td>
<td>43%</td>
</tr>
<tr>
<td>Distal SFA</td>
<td>66%</td>
<td>50%</td>
<td>20%</td>
<td>70%</td>
</tr>
<tr>
<td>Proximal popliteal</td>
<td>18%</td>
<td>5%</td>
<td>16%</td>
<td>2%</td>
</tr>
<tr>
<td>Total occlusions</td>
<td>31%</td>
<td>17%</td>
<td>24%</td>
<td>48%</td>
</tr>
<tr>
<td>Rutherford ≥ 3</td>
<td>67%</td>
<td>56%</td>
<td>54%</td>
<td>61%</td>
</tr>
</tbody>
</table>


Results from different clinical investigations are not directly comparable. Information provided for educational purposes only.

PI-571301-AC APR 2019
Primary Patency Rates from SFA Trials
In Perspective to DCB Studies


Average lesion length 8.7 cm 8.2 cm 8.9 cm 8.0 cm 7.0 cm
Severely calcified 40% 32% 8% 44% 10%
Distal SFA 66% 65% Not reported 34% 30%
Proximal popliteal 18% 13% Not reported 4% 10%
Total occlusions 31% 30% 26% 19% 21%
Rutherford ≥ 3 67% 72% 62% 69% 70%

Results from different clinical investigations are not directly comparable. Information provided for educational purposes only.
Eluvia™ DES clinical program

The Eluvia clinical trials are expected to study more than **2,000** patients across more than **100** centers

<table>
<thead>
<tr>
<th>Study</th>
<th>Enrollment Status</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAJESTIC</td>
<td>n=57</td>
<td>Prospective, multicenter single-arm, open label</td>
</tr>
<tr>
<td>IMPERIAL RCT</td>
<td>n=528</td>
<td>Prospective, multicenter, 2:1 randomization vs. ZILVER PTX</td>
</tr>
<tr>
<td>EMINENT RCT</td>
<td>n=750</td>
<td>Prospective, multicenter, superioty 2:1 randomization vs. BMS</td>
</tr>
<tr>
<td>REGAL Registry</td>
<td>n=500</td>
<td>All-comers, multicenter registry</td>
</tr>
<tr>
<td>SPORTS RCT</td>
<td>n=222</td>
<td>Prospective, multicenter, randomized Eluvia vs. DCB and BMS</td>
</tr>
</tbody>
</table>

**FROM PROMISE TO PROVEN**

- CE Mark for Eluvia Stent: 3-year data available
- FDA approval for Eluvia Stent: Enrollment complete
- Efficacy and economic data: Currently enrolling
- Efficacy and new label indications: Currently enrolling
- Efficacy in long lesions: Currently enrolling
Operational Efficiencies by requiring less inventory management

A simple size matrix with only 10 UPNs

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</table>

- **Working length**: 130 cm
- **Sheath compatibility**: 6F (2 mm) (across all sizes)
- **0.035” (0.89 mm) guidewire compatible**
Review of 1-Year TLRs in Contemporary Trials

Patients treated with ELUVIA™ have demonstrated the lowest reintervention rate compared to other PVD technologies.

1-year TLR (reintervention rate) after index procedure

<table>
<thead>
<tr>
<th>Procedure</th>
<th>1-Year TLR Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELUVIA</td>
<td>3.8%</td>
</tr>
<tr>
<td>DES: Zilver PTX</td>
<td>9.5%</td>
</tr>
<tr>
<td>BMS</td>
<td>14.3%</td>
</tr>
<tr>
<td>Angioplasty</td>
<td>21.7%</td>
</tr>
<tr>
<td>DCB</td>
<td>7.4%</td>
</tr>
<tr>
<td>DCB with BMS</td>
<td>17.0%</td>
</tr>
<tr>
<td>Bypass</td>
<td>9.0%</td>
</tr>
</tbody>
</table>

References
- Majestic trial 2015
- Dake et al. 2015
- Micari et al. 2015
- Micari et al. 2015
- Pietzsh et al. 2014
- Liistro et al. 2013
- Tsai et al. 2015
**CAUTION:** Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete “Directions for Use” for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator’s Instructions.

**INTENDED USE/INDICATIONS FOR USE:** The ELUVIA Drug-Eluting Vascular Stent System is intended to improve luminal diameter in the treatment of symptomatic de-novo or restenotic lesions in the native superficial femoral artery (SFA) and/or proximal popliteal artery with reference vessel diameters (RVD) ranging from 4.0-6.0 mm and total lesion lengths up to 190 mm.

**CONTRAINDICATIONS:** Women who are pregnant, breastfeeding, or plan to become pregnant in the next 5 years should not receive an ELUVIA Drug-Eluting Stent. It is unknown whether paclitaxel will be excreted in human milk, and there is a potential for adverse reaction in nursing infants from paclitaxel exposure. Patients who cannot receive recommended anti-platelet and/or anti-coagulant therapy.

**WARNINGS:** The delivery system is not designed for use with power injection systems. Only advance the stent delivery system over a guidewire. The stent delivery system is not intended for arterial blood monitoring. In the event of complications such as infection, pseudoaneurysm or fistula formation, surgical removal of the stent may be required. Do not remove the thumbwheel lock prior to deployment. Premature removal of the thumbwheel lock may result in an unintended deployment of the stent. It is strongly advised that the treating physician follow the Inter-Society Consensus (TASC II) Guidelines recommendations (or other applicable country guidelines) for antiplatelet therapy pre-procedure to reduce the risk of thrombosis. Post-procedure dual antiplatelet therapy is required for a minimum of 60 days.

**PRECAUTIONS:** Stenting across a bifurcation or side branch could compromise future diagnostic or therapeutic procedures. The stent is not designed for repositioning. Once the stent is partially deployed, it cannot be “recaptured” or “reconstrained” using the stent delivery system. The stent may cause embolization from the site of the implant down the arterial lumen. This product should not be used in patients with uncorrected bleeding disorders or patients who cannot receive anticoagulation or antiplatelet aggregation therapy. Persons with a known hypersensitivity to paclitaxel (or structurally-related compounds), to the polymer or its individual components (see details in Primer Polymer and Drug Matrix Copolymer Carrier section), nickel, or titanium may suffer an allergic response to this implant. Persons with poor kidney function may not be good candidates for stenting procedures.

**PROBABLE ADVERSE EVENTS** - Probable adverse events which may be associated with the use of a peripheral stent include but are not limited to: Allergic reaction (to drug/polymer, contrast, device or other); Amputation; Arterial aneurysm; Arteriovenous fistula; Death; Embolization (air, plaque, thrombus, device, tissue, or other); Hematoma; Hemorrhage (bleeding); Infection/Sepsis; Ischemia; Need for urgent intervention or surgery; Pseudoaneurysm formation; Renal insufficiency or failure; Restenosis of stented artery; Thrombosis/thrombus; Transient hemodynamic instability (hypotensive/hypertensive episodes); Vasospasm; Vessel injury, including perforation, trauma, rupture and dissection; Vessel occlusion.

Probable adverse events not captured above that may be unique to the paclitaxel drug coating: Allergic/immunologic reaction to drug (paclitaxel or structurally-related compounds) or the polymer stent coating (or its individual components); Alopecia; Anemia; Gastrointestinal symptoms; Hematologic dyscrasias (including leukopenia, neutropenia, thrombocytopenia); Hepatic enzyme changes; Histologic changes in vessel wall, including inflammation, cellular damage or necrosis; Myalgia/Arthralgia; Peripheral neuropathy.

There may be other potential adverse events that are unforeseen at this time.

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