LimFlow PROMISE I Study Results: First Prospective Multi-center Trial On DVA

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I have the following potential conflicts of interest to report:

- Consulting: Philips, Medtronic, Boston Scientific, Intact, PQ Bypass, Limflow, Cagent, Silk Road Medical, Surmodics, Profusa, CSI
Permanently Bypass Unreconstructible Arteries
LimFlow Procedure Overview

1. Venous Catheter
2. Crossing is done.
3. Valvulotome renders valves incompetent.
4. Limflow Self-Expanding Covered Extension Stents
5. Tapered Covered Crossing Stent
6. Forward flow is achieved.
## LimFlow Trials Overview

<table>
<thead>
<tr>
<th></th>
<th>Pilot</th>
<th>Pre and Post CE Mark</th>
<th>U.S. Feasibility (EFS)</th>
<th>OUS Post-Market</th>
<th>U.S. Pivotal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong># Patients</strong></td>
<td>7</td>
<td>36</td>
<td>10 → 25</td>
<td>50</td>
<td>60 – 120</td>
</tr>
<tr>
<td><strong># Centers</strong></td>
<td>1</td>
<td>9</td>
<td>3 → 6</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td><strong>Protocol</strong></td>
<td>Single-center, prospective, open label</td>
<td>Multi-center, prospective, open label</td>
<td>Multi-center, prospective, single-arm</td>
<td>Multi-center, prospective, single-arm</td>
<td>Multi-center, prospective, efficacy and safety study</td>
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<tr>
<td><strong>Countries</strong></td>
<td>Singapore</td>
<td>France, Germany, Italy, Netherlands, Singapore</td>
<td>U.S.</td>
<td>EU, Singapore</td>
<td>U.S., TBD</td>
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</tbody>
</table>

The LimFlow System is approved for sale in markets regulated by the CE Mark. Caution: Investigational device in the United States. Limited by U.S. federal law to investigational use only in the U.S.
PROMISE I Study Purpose

• PROMISE I is an Early Feasibility Study (EFS)*, launched mid-2017
• The clinical study was conducted to:
  – Establish clinical safety to move into a pivotal study
  – Identify and address operator challenges
  – Determine patient characteristics that impact performance
  – Identify therapeutic parameters that impact performance
• EFS experience allows us to:
  – Optimize operator technique
  – Develop subsequent protocols and refine:
    • Patient screening
    • Wound analysis
    • Patient follow-up

*FDA Guidance, issued October 1, 2013. Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies
PROMISE I Study Design

Key Endpoints

Primary safety endpoint
- Amputation Free Survival (AFS) at 30d

Secondary endpoints
- AFS at 6M
- Procedure & Technical Success
- Wound Healing
- Patency

Key Inclusion/Exclusion Criteria

Inclusion:
- Rutherford 5/6
- No-Option CLTI
- Approval by independent review committee

Exclusion:
- Life expectancy <12 months
- Dialysis
- Severe heart failure

Follow-Up Schedule

<table>
<thead>
<tr>
<th></th>
<th>BL</th>
<th>1M</th>
<th>3M</th>
<th>6M</th>
<th>9M</th>
<th>1Y</th>
<th>2Y</th>
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<tbody>
<tr>
<td>Wound Assessment</td>
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<td>✓</td>
<td>✓</td>
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<tr>
<td>TcPO2</td>
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<td>Doppler</td>
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<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
Target Vessels (n=32)

Comorbidities (n=32)
- Diabetes: 69%
- Type I: 13%
- Type II: 56%
- Hypertension: 88%
- Renal insufficiency: 34%

Baseline Characteristics (n=32)
- Age (Avg, years): 71 (42-94)
- Gender (% Male): 66%

Procedural Characteristics (n=32)
- Success Rate: 97%
Promise I Primary Endpoint
Amputation Free Survival (N=32)

6M AFS = 74%
Promise I
Survival, Limb Salvage, Amputation Free Survival (N=32)

AFS Kaplan–Meier, Breakout

6M AFS = 74%

Days Post LimFlow Index Procedure

# at risk 32 28 22 22 18 17 13 10 9 8
Promise I

Wound Evaluation

Two patients experienced TMA of their treated foot between 3 and 6 months.

Data on File, LimFlow

<table>
<thead>
<tr>
<th>Time</th>
<th>Wound Area cm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (N=28)</td>
<td>10.01</td>
</tr>
<tr>
<td>1M (N=25)</td>
<td>16.19</td>
</tr>
<tr>
<td>3M (N=18)</td>
<td>3.96</td>
</tr>
<tr>
<td>6M (N=19)</td>
<td>6.86*</td>
</tr>
<tr>
<td>9M (N=13)</td>
<td>2.12</td>
</tr>
</tbody>
</table>

Core lab adjudicated

Data on File, LimFlow
Promise I

Wound Evaluation: Healing Status

Wound Status Over Time

- **Healed + Healing**
  - 0% (1 Month, N=26)
  - 31% (3 Month, N=20)
  - 75% (6 Months, N=21)
  - 100% (9 Month, N=13)

- **Healed**
  - 0% (1 Month, N=26)
  - 15% (3 Month, N=20)
  - 29% (6 Months, N=21)
  - 62% (9 Month, N=13)

Data on File, LimFlow
Promise I: Case Example

- 65 y/o, BL Wtfl 213
- Hx of type II diabetes, CKD, smoking, and hyperlipidemia
- Multiple failed prior interventions
- Nonhealing wound at location of 5th toe amputation

Data on File, LimFlow
Promise I: Case Example, Wound Progression

Wound Healing Over Time

Follow-up Timepoint

BL 1M 3M 6M 9M

No images captured; Site reported wound healed

EFS Patient: 65 y/o M, Rutherford 5, Type II Diabetes, WiFi 231
Nonhealing wound (lateral aspect), absence of adequate target artery, no vessel visualized in the foot

CAUTION: Investigational device. Limited by Federal (or United States) law to investigational use.
Wound Evolution post pDVA

Baseline
Area: 17.8 cm²
Volume: 1.5 cm³

1 Month
Area: 7.7 cm²
Volume: 0.8 cm³

3 Month
Area: 6.1 cm²
Volume: 0.5 cm³

CAUTION: Investigational device. Limited by Federal (or United States) law to investigational use.
Lessons Learned

• Patient selection
  – Not appropriate for all limbs, requires salvageable tissue

• Wound care
  – Multidisciplinary collaboration
  – Minor amputation management, debridement, timing

• Fistula maturation
  – Close monitoring

• Reinterventions may be required
Dialysis Population: Unmet Need
Conclusions

• The LimFlow System is a **novel, safe, and reproduceable** approach for treating patients with no-option CLTI

• It may improve wound healing rates and reduce amputation rates in a population for whom amputation would otherwise be considered inevitable

• Initial findings from this early feasibility trial are very promising

• The US Pivotal Trial (**PROMISE II**) is currently underway and enrolling patients
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