First Report of the SELUTION Trial: 6-month Outcomes of a Novel Sirolimus Coated DCB Technology Evaluated in SFA

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On behalf of the SELUTION SFA Study Investigators
Thomas Zeller, MD

For the 12 months preceding this presentation, I disclose the following types of financial relationships:

- **Honoraria received from:** Abbott Vascular, Bard Peripheral Vascular, Veryan, Biotronik, Boston Scientific Corp., Cook Medical, Gore & Associates, Medtronic, Philips-Spectranetics, TriReme, Veryan, Shockwave, Biotronik
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- **Common stock:** Veryan, QT Medical
DCB Background

• Advantages of DCB are well understood
  – Leave nothing behind – preserves treatment options
  – Excellent mid-term patency & TLR
    • Emerging catch up out to four years
  – All peripheral experience with Paclitaxel to date

• Potential disadvantages have emerged with Paclitaxel DCB
  – No class effect
  – Performance in Ca++
  – Distal particulate embolization
  – Safety of Paclitaxel in sub-intimal PTA or DAART
Sirolimus vs Paclitaxel

- Mode of action is cytostatic vs cytotoxic
- Sirolimus is anti-inflammatory
- Sirolimus has a much wider therapeutic window/ higher safety margin
- Paclitaxel on balloons: easier to apply (tissue absorption is higher), but not better
SELUTION™ Sirolimus Coated Balloon

- Use of micro-reservoirs - biodegradable polymer intermixed with Sirolimus:
  - Controlled and sustained drug release mechanism
  - Maintains therapeutic effect over long period

- Proprietary Cell Adherent Technology – CAT™:
  - Transfer membrane that contains and protects micro-reservoirs during balloon insertion, lesion crossing and inflation
  - Transfer membrane releases from balloon surface and adheres to vessel lumen during short balloon inflation
  - Less drug loss during transit to lesion
  - Less drug loss during inflation
SELUTION™ vs. Competition

Drug Dispersion

<table>
<thead>
<tr>
<th></th>
<th>Med Alliance SELUTION</th>
<th>Bard LUTONIX</th>
<th>Medtronic IN.PACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost during procedure</td>
<td>36%</td>
<td>83%</td>
<td>83%</td>
</tr>
<tr>
<td>Retained on balloon</td>
<td>25%</td>
<td>12%</td>
<td>14%</td>
</tr>
<tr>
<td>Transferred to vessel (1 hr)</td>
<td>39%</td>
<td>5%</td>
<td>3%</td>
</tr>
</tbody>
</table>

SELUTION™ Sirolimus DCB

Therapeutic Effect $\geq 1\mu g/g$

Tissue Drug Concentration [μg/g]

Arterial Tissue Drug Concentration
Sirolimus (RAP) versus Paclitaxel (PAX)

Drug Dose per Balloon Size

Med Alliance SELUTION - RAP
Bard LUTONIX - PAX
Medtronic IN.PACT - PAX

Med Alliance – PK Study (2014-004)
Medtronic – Presentation R.J. Melder (LINC 2012)
SELUTION™ Sirolimus Coated Balloon

- Superior Coating Durability during transit and deployment
SELUTION FIM Trial
ClinicalTrials.gov ID: NCT02941224

Objective
To assess clinical safety and inhibition of restenosis of SELUTION™ DCB in treatment of Superficial Femoral (SFA) or Popliteal (PA) Artery lesions

Design
- Prospective, Controlled, Multi-Center, Open, Single Arm
- N=60

Primary Endpoint
- Angiographic Late Lumen Loss (LLL) by QVA
  - 6 months

Secondary Endpoints
- Major Adverse Events (Death, TLR, Amputation)
  - 6 months
- Primary Patency – Freedom from CD-TLR and Restenosis by DUS
  - 6, 12 and 24 months
- Angiographic Binary Restenosis (ABR) by QVA
  - 6 months
- Composite of Freedom from Amputation and Freedom from CD-TVR
  - 12 and 24 months
- Change of ABI, WIQ and QoL
  - 6, 12 and 24 months
SELUTION Trial Design

Enrollment: Oct 26th 2016 – May 23rd 2017

**Pre-screening**
- Non-Clinical Inclusion / Exclusion Criteria
- Clinical and Anatomic Inclusion / Exclusion Criteria

**Screening**
- Successful Pre-Dilatation?
  - NO

**Treatment**
- SELUTION DCB
  - Screening Failure (Treat per std practice)

**Analysis**
- Bailout Stenting?
  - NO
  - Secondary Analysis (ITT Stented)
  - Primary Analysis (ITT)
  - Secondary Analysis (ITT Non-Stented)
Key Inclusion Criteria
- SFA & Popliteal Artery (PA)
- Male or non-pregnant female ≥ 18 years of age
- De-novo or restenotic lesion(s) with composite length ≤ 15 cm
- Target vessel reference diameter ≥ 3.0 mm and ≤ 7.0 mm
- Multiple target lesions can be treated with maximum of 2 overlapping DCBs
- Rutherford class 2-3-4

Key Exclusion Criteria
- Known hypersensitivity or contra-indication to aspirin, heparin or other anticoagulant / anti-platelet therapies
- Prior vascular surgery of target lesion
- Known inadequate distal outflow / significant inflow disease
- Remaining acute or sub-acute thrombus in target vessel
- Use of adjunctive treatment therapies (i.e. laser, atherectomy, cryoplasty, scoring/cutting balloon, etc.)
Trial Centers
Herzzentrum Bad Krozingen
Franziskus Krankenhaus, Berlin
Vivantes Klinikum Neukoelln, Berlin
Hubertus Krankenhaus, Berlin

Independent CEC committee
P. Gaines, M. Lichtenberg, G. Tepe

CRO
Corelab
Sponsor

T. Zeller (PI)
K. Brechtel
T. Albrecht
D. Meyer
Enrollment: Oct 26th 2016 – May 23rd 2017

Non-Clinical Inclusion / Exclusion Criteria
Screened N = 88

Successful Pre-Dilatation?

30 D FU Completed N=48
Missed Visit N=1

6M FU Completed N=43
Missed Visit N=2
DUS Completed N = 43
Angio FU Completed N = 34

Not Eligible
N=35

Screening Failure (Treat per std practice)
N=3

Bailout Stenting
N=4

SELUTION™ DCB
N=50

Withdrew N=1

Withdrew N=4
### Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Y ± SD</td>
<td>69.6 ± 10.4</td>
</tr>
<tr>
<td>Male, % (n)</td>
<td>58 % (29)</td>
</tr>
<tr>
<td>Previous Intervention, % (n)</td>
<td>30 % (13)</td>
</tr>
<tr>
<td>Myocardial Infarction, % (n)</td>
<td>6 % (3)</td>
</tr>
<tr>
<td>Renal Insufficiency, % (n)</td>
<td>22 % (11)</td>
</tr>
<tr>
<td>Hypertension, % (n)</td>
<td>80 % (40)</td>
</tr>
<tr>
<td>Hyperlipidemia, % (n)</td>
<td>90 % (45)</td>
</tr>
<tr>
<td>Diabetes (Type 2), % (n)</td>
<td>28 % (14)</td>
</tr>
<tr>
<td>Smoking History, % (n)</td>
<td>58 % (29)</td>
</tr>
<tr>
<td>Anticoagulation Therapy</td>
<td>22 % (11)</td>
</tr>
<tr>
<td>Angina Pectoris</td>
<td>14 % (7)</td>
</tr>
</tbody>
</table>

### Lesion Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=50</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Novo</td>
<td>96 % (48)</td>
</tr>
<tr>
<td>Lesion Length, mm ± SD</td>
<td>64.30 ± 42.8</td>
</tr>
<tr>
<td>RVD, mm ± SD</td>
<td>5.1 ± 0.8</td>
</tr>
<tr>
<td>% Diameter Stenosis, % ± SD</td>
<td>90 ± 8.0</td>
</tr>
<tr>
<td>Occlusion</td>
<td>30% (15)</td>
</tr>
<tr>
<td>Calcification</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>12 % (6)</td>
</tr>
<tr>
<td>Mild</td>
<td>44 % (22)</td>
</tr>
<tr>
<td>Moderate</td>
<td>10 % (5)</td>
</tr>
<tr>
<td>Moderately severe</td>
<td>26 % (13)</td>
</tr>
<tr>
<td>Severe</td>
<td>8 % (4)</td>
</tr>
<tr>
<td>Target Lesion Location, % (n)</td>
<td></td>
</tr>
<tr>
<td>SFA prox</td>
<td>12 % (6)</td>
</tr>
<tr>
<td>SFA mid</td>
<td>34 % (17)</td>
</tr>
<tr>
<td>SFA dist</td>
<td>54 % (27)</td>
</tr>
<tr>
<td>POP 1</td>
<td>24 % (12)</td>
</tr>
<tr>
<td>POP 2/ POP 3/ TPT</td>
<td>16 % (8)</td>
</tr>
</tbody>
</table>
SELUTION Primary Endpoint
LLL at 6 Months

LLL
N= 34

Median
0.19 mm
(-1.16; 3.07)
# SELUTION Trial

## Angio & Clinical Results at 6 Months

The table below summarizes the clinical outcomes for the SELUTION Trial at 6 months:

<table>
<thead>
<tr>
<th>Primary Endpoint</th>
<th>ITT</th>
<th>SELUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underwent 6M Clinical FU – N (%)</td>
<td>43 (86%)</td>
<td></td>
</tr>
<tr>
<td>Underwent 6M QCA</td>
<td>34 (68%)</td>
<td></td>
</tr>
<tr>
<td>LLL (mm)</td>
<td>0.19 (-1.16;3.07)</td>
<td></td>
</tr>
<tr>
<td>cd TLR %</td>
<td>2.3 % (1)</td>
<td></td>
</tr>
</tbody>
</table>

### Cumulative Clinical Events
- Death: 0%
- Major or Minor Amputation: 0%

### Change in Rutherford Class
- Improvement: 73%
- None: 27%
- Worsening: 0%
**SELUTION Trial Rutherford, WIQ & ABI**

**Baseline & 6 Months**

### Rutherford Change

<table>
<thead>
<tr>
<th>Category</th>
<th>Baseline (%)</th>
<th>6 Months (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(4) Ischemic Rest Pain</td>
<td>83,0%</td>
<td>14,3%</td>
</tr>
<tr>
<td>(3) Severe Claudication</td>
<td>21,4%</td>
<td>26,2%</td>
</tr>
<tr>
<td>(2) Moderate Claudication</td>
<td>17,0%</td>
<td>38,1%</td>
</tr>
<tr>
<td>(1) Mild Claudication</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>(0) Asymptomatic</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

### WIQ - Distance Score

- Baseline: 20
- 6 Months: 69

### Ankle-Brachial Index (ABI)

- Baseline: 0.81
- Post Procedure: 0.91
- 6 Months: 0.96
**SELUTION Results in Context**

**Late Lumen Loss**

**6-month TLR**

Results from different trials are not directly comparable. Information provided for educational purposes.

<table>
<thead>
<tr>
<th>Trial</th>
<th>RANGER SFA</th>
<th>PACIFIER</th>
<th>Tepe et al</th>
<th>LEVANT I</th>
<th>FemPac</th>
<th>BIOLUX-PI</th>
<th>ILLUMENATE</th>
<th>SELUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Therapy</strong></td>
<td>Ranger</td>
<td>IN.PACT</td>
<td>DCB not specified</td>
<td>Lutonix</td>
<td>Ptx coated</td>
<td>Passeo-18</td>
<td>Stellarex</td>
<td>SELUTION</td>
</tr>
<tr>
<td><strong>Mean Lesion Length (mm)</strong></td>
<td>6.8</td>
<td>7.0</td>
<td>5.7</td>
<td>8.1</td>
<td>5.7</td>
<td>6.1</td>
<td>7.2</td>
<td>6.4</td>
</tr>
<tr>
<td><strong>Bailout Stenting (%)</strong></td>
<td>21%</td>
<td>21%</td>
<td>11%</td>
<td>3%</td>
<td>9%</td>
<td>N/A</td>
<td>5%</td>
<td>8%</td>
</tr>
</tbody>
</table>

SELUTION – Zeller, T. LINC 2018
SELUTION Conclusions

- First demonstration of Sirolimus safety and efficacy in peripheral intervention in human
- Met the primary endpoint of LLL (median 0.19mm) at 6 Month
- SELUTION Sirolimus DCB is safe and effective
- 6 Months clinical outcomes are non-inferior to other FIH studies using paclitaxel balloons
- Low 6-month CD TLR 2.3%
- Excellent outcomes despite 34% Ca++
- Further studies are required to confirm these findings in larger patient populations
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