A Novel Sustained Limus Release Eluting Balloon: 2-Year Data from the SELUTION SFA Trial

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

- **Honoraria received from:** Abbott Vascular, B. Braun, Biotronik, Boston Scientific Corp., Cook Medical, Gore & Associates, Medtronic, Philips-Spectranetics, TriReme, Veryan, Shockwave

- **Consulted for:** Boston Scientific Corp., Cook Medical, Gore & Associates, Medtronic, Spectranetics, Veryan, Intact Vascular, MedAlliance, Vesper Medical

- **Common stock:** QT Medical
Drug Coated Balloon Clinical Need

- Novel angioplasty balloon **coated** with an **anti-restenotic drug**
- Overcoming **unmet clinical need**:
  - Homogenous delivery of anti-restenotic drug **reduces amount of restenosis**
  - Due to absence of any stent **no stent fracture or vessel injury**
  - Allows original anatomy to remain intact **Positive remodeling**
  - “Leaving nothing behind” **allowing fast ‘normalization’** of vascular function
    - True normalization of vasomotor function,
    - Restoration of physiological responses to stress
    - NO long-term consequences related to inflammation, accelerated atherosclerosis and thrombosis
    - No need for long term DAPT
# Ptx On Balloons: Easier, Not Better

## Mode of action
- **LIMUS**: Cytostatic
- **PACLITAXEL**: Cytotoxic

## Margin of safety
- **LIMUS**: 10,000 fold
- **PACLITAXEL**: 100 fold

## Anti-restenosis
- **LIMUS**: Optimal
- **PACLITAXEL**: Good

## Tissue absorption and elution
- **LIMUS**: More difficult
- **PACLITAXEL**: Easier

## Level of competition
- **LIMUS**: Low
- **PACLITAXEL**: Very high

## Physician perception
- **LIMUS**: Positive
- **PACLITAXEL**: Controversial

Source: Oral presentation TCT 2016, P. Stella.
Sirolimus-Eluting Balloon with Sustained Release

Proprietary MicroReservoir Technology
- MicroReservoirs combining sirolimus & biodegradable polymer
- Sirolimus - a proven safe & effective cytostatic drug
- Offering a wider therapeutic range

MicroReservoirs: Miniature Drug-Delivery Systems
- Optimal size micro-reservoirs achieve elution kinetics similar to best in class DES
- Controlled and sustained release of sirolimus
- Providing therapeutic effect for over 60 days

Cell Adherent Technology (CAT™)
- Proprietary amphipatic lipid technology binds MicroReservoirs to balloon surface
- Contains and protects micro-reservoirs during insertion and inflation
- Facilitates higher drug transfer efficiency allowing for low drug dose on balloon surface
- Maximises drug bioavailability

*Device not approved and available for sale in the US
Coating Durability during handling and deployment

NO FLAKING
# SELUTION SFA FIM TRIAL

ClinicalTrials.gov ID: NCT02941224

<table>
<thead>
<tr>
<th><strong>OBJECTIVES</strong></th>
<th>To assess the safety and efficacy of the SELUTION SLR DEB in treatment of de-novo occluded/stenotic or re-occluded/restenotic lesions of SFA and/or PA, assessed at multiple time points clinical, angiographic and/or ultrasound assessment</th>
</tr>
</thead>
</table>
| **DESIGN**     | - Prospective, controlled, multi-center, open, single-arm clinical investigation  
- 50 patients |
| **PRIMARY ENDPOINTS** | - Angiographic Late Lumen Loss (LLL) by QVA – 6M |
| **SECONDARY ENDPOINTS** | - **Major adverse Events** (Death, Thrombosis, Amputation, CD-TLR) 6M  
- **Primary Patency** – Freedom from CD-TLR and absence of Restenosis by DUS - 6, 12 and 24M  
- **Angiographic Binary Restenosis** (ABR) by QVA – 6M  
- **Composite of Freedom from Amputation and Freedom from CD-TVR** – 12 and 24M  
- Change of ABI, WIQ and Qol - 6, 12 and 24M |
SELUTION SFA Trial Design

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.)
SELUTION SFA Trial Management

TRIAL CENTERS

Herzzentrum Bad Krozingen
T. Zeller (PI)
Franziskus Krankenhaus, Berlin
K. Brechtel
Vivantes Klinikum Neukoelln, Berlin
T. Albrecht
Hubertus Krankenhaus, Berlin
D. Meyer

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

CRO
MD-CLINICALS

CORELAB
coreLab

SPONSOR
MedAlliance
Enrollment: Oct 26th 2016 – May 23rd 2017

**SCREENING**

- Non-Clinical Inclusion / Exclusion Criteria
  - Screened N=88
  - Not Eligible N=35
  - Withdrew Consent Prior to Procedure N=1
  - Withdrawn by Site N=2

**PROCEDURE**

- **SELUTION™ DCB**
  - N=50
  - Completed N=43 (86%)
  - DUS Completed N=43
  - Angio FU Completed N=34 (68%)
  - Bailout Stenting N=4
    - Withdrew N=2
  - Missed Visit N=5

**6 M FOLLOW-UP**

- Completed N=42* (84%)
  - DUS completed N=38 (76%)

**12 M FOLLOW-UP**

- Completed N=47* (94%)
  - DUS completed N=37 (74%)

**24 M FOLLOW-UP**

- Completed N=42* (84%)
  - DUS completed N=38 (76%)

Notes:
- *10 Patient telephone contact only: TLR & Vital status
- *4 Patient telephone contact only: TLR & Vital status
## Clinical Characteristics

<table>
<thead>
<tr>
<th>Clinical Characteristics</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>Lesion Characteristics</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 SFA Primary Endpoint

LLL at 6M (N=34)

- Calcified Target Lesion (CoreLab assessed by 360 score)

*Late Lumen Loss presented as median value
SELUTION SFA Minimal Lumen Diameter

Cumulative density function

MLD (mm)

Pre 0.80 ± 0.73
FU 3.24 ± 1.02
Post 3.62 ± 0.71
SELUTION SFA Results In Context

- 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>Therapy</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>Mean Lesion Length (mm)</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>Bailout Stenting (%)</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>


*LLL Solution presented as median value
## SELUTION SFA TRIAL ANALYSIS

### Clinical Results at 6M, 12M and 24M

<table>
<thead>
<tr>
<th>Cumulative Clinical Events</th>
<th>6M</th>
<th>12M</th>
<th>24M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Minor and Major Amputation</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Primary Patency (ITT)</td>
<td>88.4%</td>
<td>75.7%</td>
<td>81.6%</td>
</tr>
<tr>
<td>Primary Patency (PP)</td>
<td>95.2%</td>
<td>88.9%</td>
<td>94.4%</td>
</tr>
<tr>
<td>Freedom from Index Limb Amputation and CD TVR</td>
<td>97.7%</td>
<td>87.6%</td>
<td>85.4%</td>
</tr>
<tr>
<td>TLR (ITT)</td>
<td>1 (2.3%)</td>
<td>6 (12.5%)</td>
<td>6 (12.5%)</td>
</tr>
<tr>
<td>TLR (PP Lesion Prep)¹</td>
<td>1 (2.3%)</td>
<td>2 (4.3%)</td>
<td>2 (4.3%)</td>
</tr>
<tr>
<td>TLR (Ca++)²</td>
<td>0 (0%)</td>
<td>1 (6.6%)</td>
<td>1 (7.7%)</td>
</tr>
</tbody>
</table>

1. Inadequate Lesion Prep: Residual Stenosis >35% by CoreLab Assessment
2. Moderately Severe/ Severe Calcification = Calcification score 3 or 4 by 360Score = outside of Protocol

ITT: all patients enrolled in the trial, whether or not they were treated the Investigational Device
PP: all patients enrolled and treated with the Investigational Device and had no bailout. Includes only patients who had a post-procedure angio residual stenosis ≤ 30%
SELUTION SFA Freedom from TLR
Kaplan Meier Estimates

Freedom from TLR (%)

Days post-procedure

87.5 %
Mortality Rates from Trials of SFA Therapy

All-Cause Death at 2 Years

P Schneider, LINC 2019, Oral Presentation
Mortality Rates from Trials of SFA Therapy

DCB: All-Cause Death at 2 Years

Adapted from P Schneider, LINC 2019, Oral Presentation
SELUTION SFA Trial Rutherford
Baseline, 6M, 12 M and 24M

Improvement from Baseline to 24M
> 2 categories in 67% of patients
>1 category in 84% of patients
SELUTION SFA Trial ABI & WIQ

Baseline, 6M, 12 M and 24M

Change from Baseline to 24M: p = 0.0242
Change from Baseline to 12M: p < 0.0001
Change from 6M to 12M: p = 0.0125
SELUTION SFA Trial Conclusions

- First demonstration of Sirolimus safety and efficacy in peripheral intervention
- Met the primary endpoint (Median LLL 0.19mm at 6M)
- Low 6 M CD TLR maintained through 24 M
- No primary TLR event after Month 11
- Clinical improvements in Rutherford classification, ABI and Walking Impairment @ 6M and was further improved to 12M and maintained to 24M
- **SELUTION Sirolimus DEB is safe and effective**
- Based on these data, TLR with SELUTION SLR™ DEB is not impacted by Ca++
- CD TLR were associated with high residual stenosis post procedure
- Further studies are required to confirm these findings in larger patient populations
- These results support CE Mark submission of the SELUTION SLR™ 018 PTA
FDA Granted Breakthrough Designation for BTK

September 20, 2019

MedAlliance, LLC
% Wenda Carlyle, PhD
Principal Consultant
CardioMed Device Consultants, LLC
1783 Forest Drive, Suite 254
Annapolis, Maryland 21401

Re: Q191832
Trade/Device Name: **SELUTION Sirolimus Coated PTA Balloon Catheter**
Received: September 6, 2019

Dear Dr. Carlyle:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has received the above submission requesting designation as a Breakthrough Device. The proposed indications for use includes "The SELUTION Sirolimus Coated PTA Balloon Catheter is indicated for percutaneous transluminal angioplasty, after pre-dilatation, of de novo or restenotic lesions up to 150 mm in length in native arteries below the knee with reference vessel diameters of 1.5-4.5 mm." We are pleased to inform you that your combination product and proposed indication for use meet the criteria and have been granted designation as a Breakthrough Device. Please refer to the FDA guidance document entitled "Breakthrough Devices Program", for more information regarding the program, available at [https://www.fda.gov/media/108135/download](https://www.fda.gov/media/108135/download).

We recommend you review the FDA guidance document for the Breakthrough Devices Program referenced above for the available mechanisms for obtaining feedback from the Agency on device development for designated breakthrough devices. When submitting any new requests, please reference Q191832. Any new submission should include two copies (one hardcopy and a valid ecopy), the FDA reference number for this submission, and should be submitted to the following address:
• THANKYOU!
A Novel Sustained Limus Release Eluting Balloon:
2-Year Data from the SELUTION SFA Trial

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