Final 6-Month Results of the DIRECT (Direct-on-a-Wire Implantation of Rapamycin-Eluting Stent with Bioabsorbable Carrier Technology) First-In-Human Study

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Potential Conflict(s) of Interest

Speaker's name: Mark Webster

I have the following potential conflicts of interest to report:

X Research contract
Svelte Medical Systems

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

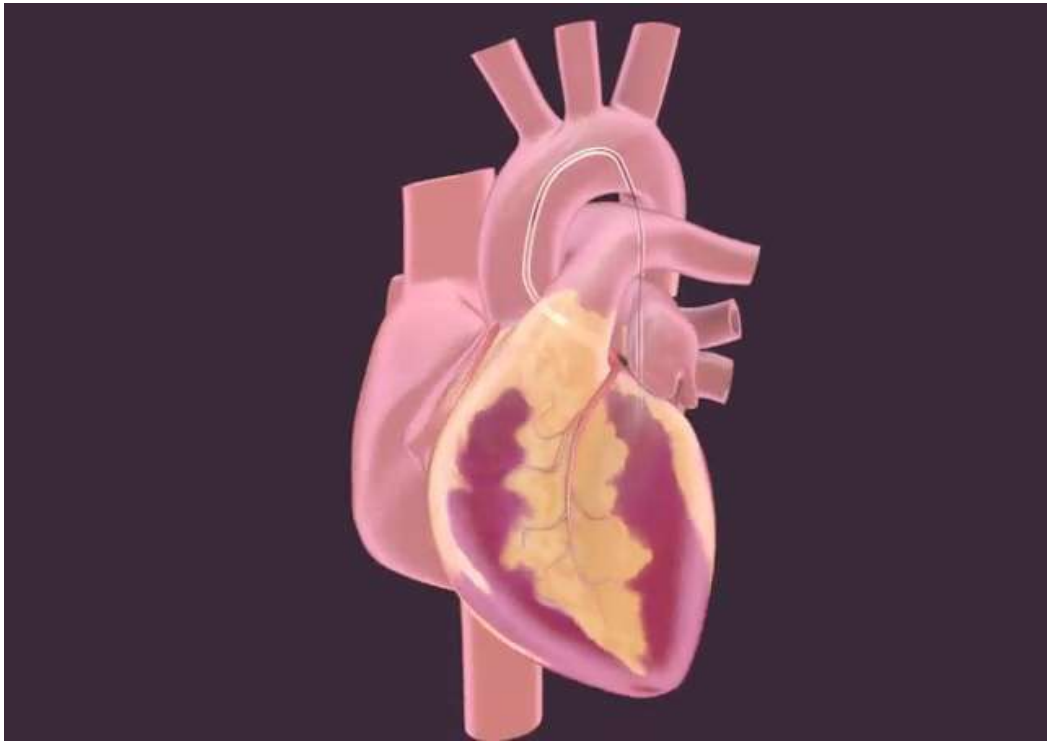
Svelte IDS Balloon Technology Designed for Direct Stenting

Elastic Balloon Control Bands (BCBs) located on the proximal and distal balloon shoulders are designed to

- Provide a smooth leading edge during delivery
- Focus pressure under stent for controlled deployment
- Minimize longitudinal balloon growth and contact with vessel wall

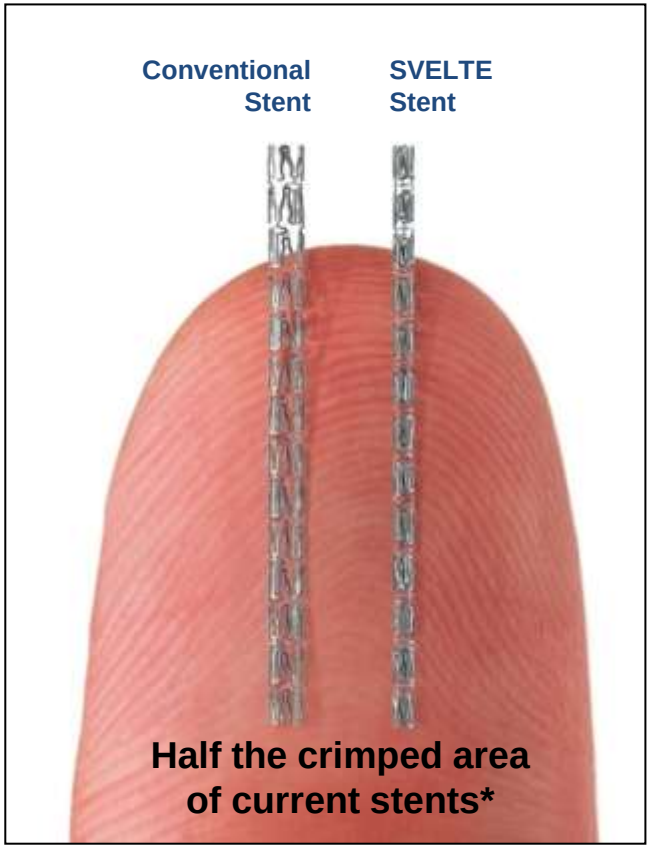
Lower Compliance Balloon Material allows higher pressure inflations in order to optimize luminal gain

- Flatter compliance curve: **¼ size above RBP**, **high MBP (26 ATM)**; more consistent with NC than SDS balloon
- Nominal 10-12 ATM; RBP 18 ATM
- **Designed for multiple inflations**



Svelte DES Platform Overview

- Thinner-strut (81µ) L 605 CoCr stent
  - Same as Xience
- Hybrid design to maximize flexibility and radial strength, provide uniform drug elution
- Low profile optimizes the radial approach
- Study sizes
  - 2.5, 3.0 & 3.5 mm diameters, 18 & 23 mm lengths

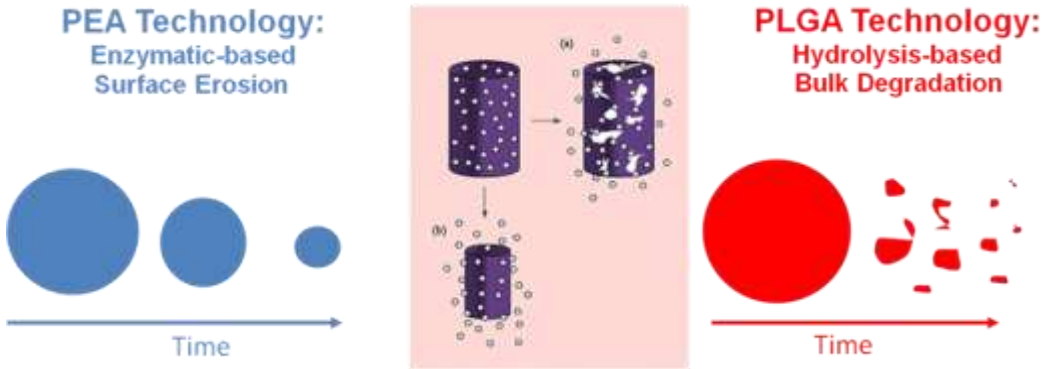


* Profile defined as the crimped stent cross-sectional area.

Svelte DES Bioabsorbable Drug Carrier

- **Amino acid-based coating**
  - Occurs naturally in the human body
  - Non-thrombogenic, non-inflammatory, high mechanical integrity
  - Fully biodegradable via enzymatic surface erosion with no pH change or activation of the complement cycle

- **Mixed with sirolimus, applied to stent in single application**
  - Coating thickness ~ 6 µm
  - Drug loading ~ 220 µg/cm^2 (3.0 x 18mm drug dose: ~130 µg)
  - Elution profile, tissue levels similar to Cypher, Xience



DIRECT First-In-Human Study

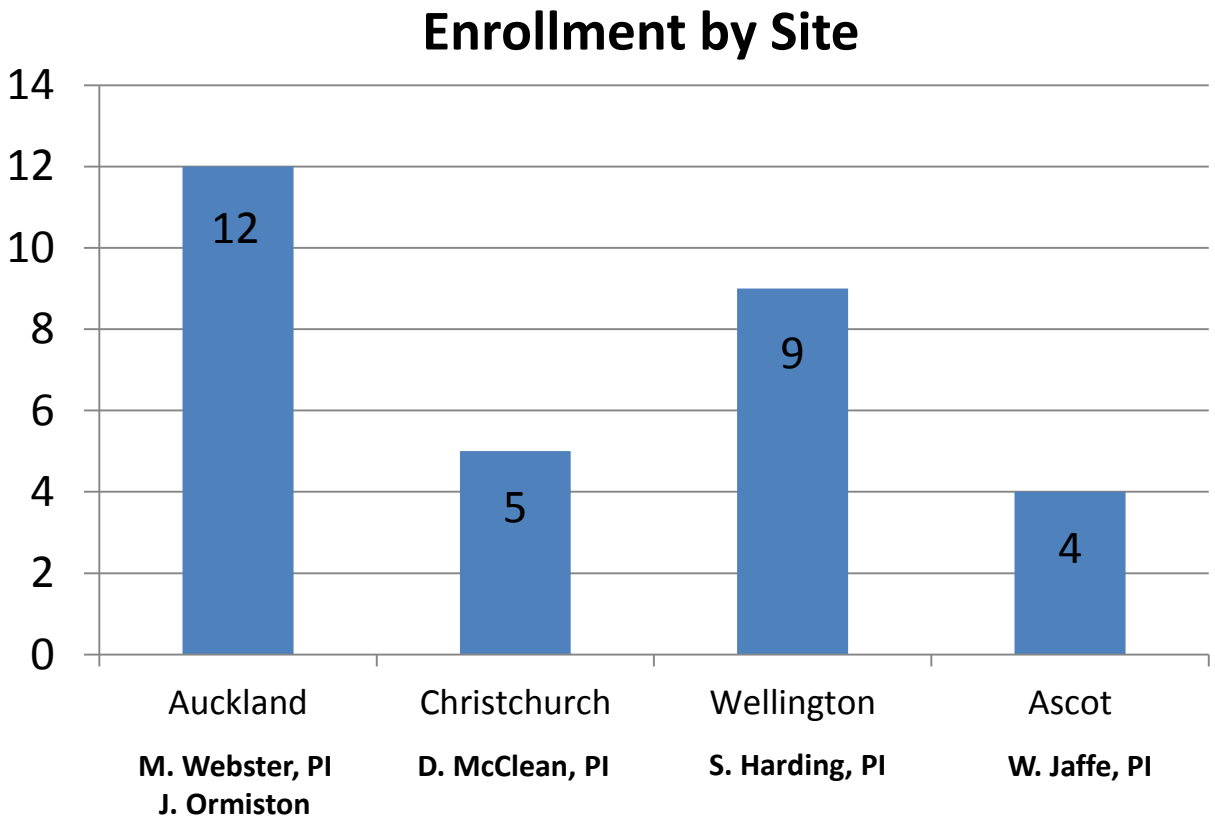
- Feasibility study evaluating the safety and performance of the Svelte DES Integrated Delivery System
  - Prospective, non-randomized clinical trial
  - 30 patients at 4 New Zealand centers
  - Clinical, angiographic, IVUS and OCT follow-up at 6 months
    - **Primary safety endpoint: angiographic TVF**
    - **Primary efficacy endpoint: angiographic in-stent late lumen loss**
    - Additional clinical follow-up at 1 and 6 mos.; annually up to 5 yrs.
  - Safety continuously monitored by independent DSMB
  - QCA, IVUS, OCT data reviewed by independent core lab (Cardialysis)

DIRECT = **D**irect **I**mplantation of **R**apamycin-eluting stent with bio-**E**roding **C**arrier **T**echnology

DIRECT Study
Main Eligibility Criteria

- Clinical evidence of ischemic heart disease, stable or unstable angina, silent ischemia, and/or positive functional study
- Single target lesion, or two lesions (target and non-target) located in separate coronary arteries (non-target must be successfully treated first)
- RVD ≥ 2.5 mm and ≤ 3.5 mm
  - No stent deployment in target vessel within prior 6-months
- Target lesion ≤ 20 mm with stenosis ≥ 50% and < 100%
  - Treatment with device other than PTCA prior to stent placement not permitted
  - Ostial lesions (within 5mm of vessel origin) excluded
- MI within 72-hours of the index procedure excluded, with the following exceptions:
  - Patients with STEMI and PCI to culprit lesion may be included if a suitable lesion in another vessel exists patient is clinically and hemodynamically stable for 72-hours
  - Patients with non-STEMI may be included if troponin normal 24-hours pre-procedure

DIRECT Study Enrollment



Enrollment completed May 2012

euro PCR 2013

DIRECT Study
Baseline Characteristics

Baseline Patient / Lesion Characteristics	Patients (n=30)
Age (years ± SD)	61 ± 11
Male	24/30 (80%)
Diabetes	**5/30 (17%)**
Hypertension	18/30 (60%)
Hyperlipidemia	22/30 (73%)
Prior MI	17/30 (57%)
Prior PCI / CABG	8/30 (27%)
Target Vessel	
LAD	14/30 (47%)
LCX	8/30 (27%)
RCA	8/30 (27%)
Lesion Type, ACC/AHA	
A	2/30 (7%)
B1	13/30 (43%)
B2/C	**15/30 (50%)**
Reference Vessel Diameter (mm ± SD)	**2.69 ± 0.48**
Lesion Length (mm ± SD)	**11.72 ± 3.99**

Direct Study
Procedural, 6-Month Clinical Outcomes

Procedural Outcomes	Patients (n=30)
Device Success	29/30 (97%)*
Procedure Success	30/30 (100%)
6-Month Clinical Outcomes	**Patients (n=29)**
Cardiac Death	0/29 (0%)
Myocardial Infarction	0/29 (0%)
TLR, Clinically-Driven	**0/29 (0%)**
TVR (non-TLR) Clinically-Driven	0/29 (0%)
TLR, Angiographically-Driven	1/29 (3.4%)
TVR, non-TLR, Angiographically-Driven	1/29 (3.4%)
TVF	2/29 (6.9%)
Total MACE	2/29 (6.9%)
Stent Thrombosis	**0/29 (0%)**

Clinical outcomes unchanged through 12 Months

*** All investigators were first-time operators with the IDS. Clinical data per ARC definitions.**

Direct Study 6-Month Quantitative Coronary Angiography

Post-Procedure, 6-Month QCA	Patients (n=29)
RVD Pre-Procedure	2.69 ± 0.48
Post-Procedure	
RVD (mm ± SD)	2.76 ± 0.45
In-Stent MLD (mm ± SD)	**2.47 ± 0.46**
In-Segment* MLD (mm ± SD)	2.20 ± 0.45
In-Stent % DS (% ± SD)	10.9 ± 6.37
In-Segment* % DS (% ± SD)	18.5 ± 7.28
6-Month Follow-Up	
RVD (mm ± SD)	2.70 ± 0.46
In-Stent MLD (mm ± SD)	2.24 ± 0.53
In-Segment* MLD (mm ± SD)	2.05 ± 0.50
In-Stent % DS (% ± SD)	17.6 ± 9.61
In-Segment* % DS (% ± SD)	23.0 ± 10.7
Late Loss (in-stent)	**0.22 ± 0.27 mm**
Late Loss (in-segment*)	**0.14 ± 0.27 mm**
Binary Restenosis (in-stent), n (%)	**1 (3.4%)**
Binary Restenosis (in-segment*), n (%)	**1 (3.4%)**

Independently reviewed core lab data (Cardialysis)
*** In-segment defined as +5 mm proximal, distal to stent**

Direct Study 6-Month IVUS

Post-Procedure, 6-Month IVUS	Patients N=25 post-procedure n=28 at 6-Months
Vessel Volume (mm^3 ± SD)	
Post-Procedure	292.3 ± 104.1
6-Months	288.4 ± 92.9
Stent Volume (mm^3 ± SD)	
Post-Procedure	148.6 ± 48.2
6-Months	141.3 ± 45.6
Luminal Volume (mm^3 ± SD)	
Post-Procedure	148.1 ± 47.6
6-Months	138.4 ± 46.8
6-Month In-Stent Neointimal Volume (mm^3 ± SD)	**3.28 ± 4.39**
6-Month In-Stent Volume Obstruction (% ± SD)	**2.70 ± 4.54**

Independently reviewed core lab data (Cardialysis)

Direct Study 6-Month OCT

Post-Procedure, 6-Month OCT	Patients N=14 post-procedure n=15 at 6-Months
Stent Volume (mm^3 ± SD)	
Post-Procedure	148.9 ± 36.0
6-Months	150.2 ± 35.4
Luminal Volume (mm^3 ± SD)	
Post-Procedure	142.8 ± 36.5
6-Months	132.5 ± 38.0
Incomplete Stent Apposition (% ± SD)	
Post-Procedure	9.16 ± 7.18
6-Months	0.44 ± 0.99
6-Month Covered Struts (% ± SD)	**97.9 ± 3.58**
6-Month Mean Strut Coverage (mm^3 ± SD)	**0.12 ± 0.06**

Independently reviewed core lab data (Cardialysis)

DIRECT Study Outcomes

	Svelte DES FIM (DIRECT Study)	Xience DES FIM (SPIRIT FIRST Study)
Reference Vessel Diameter	2.69 mm	2.61 mm
Lesion Length	11.7 mm	10.1 mm
Diabetics	17%	11%
Clinically-Driven TLR	0%	3.8%
Clinically-Driven TVF	0%	7.7%
MACE*	0%	7.7%
Neointimal Volume	3 mm^3	9 mm^3
In-Stent Volume Obstruction	3%	7%
In-Stent Late Loss	0.22 mm	0.12 mm
Diameter Stenosis	18%	17%

6-Month Follow-Up

DIRECT study outcomes in-line with current-generation DES despite more challenging patient population and first-time operators

* MACE as defined for both studies as death, MI or clinically-driven TLR.

Next Steps: DIRECT II RCT

- Non-inferiority evaluation of the safety and performance of the Svelte DES Integrated Delivery System (IDS)
  - Prospective, active-control, randomized, multi-center clinical trial
  - 159 subjects (2:1 randomization Svelte IDS : Resolute Integrity™)
  - Clinical, angiographic follow-up at 6-months
    - Primary safety endpoint: angiographic TVF
    - Primary efficacy endpoint: angiographic in-stent late lumen loss
    - Additional clinical follow-up at 1 and 6-months; annually up to 5-years
  - OCT sub-study with follow-up at 6-months (4 clinical sites, n=30)
  - Independent DSMB, core lab review
  - PI Europe: Stefan Verheye, MD, PhD
  - PI Brazil: Alexandre Abizaid, MD, PhD
  - First patient Enrolled Q1 2013

Conclusions

- **Svelte DES with Integrated Delivery System (IDS) is an attractive and novel approach to direct stenting PCI**
  - Low profile, BCBs optimized for direct stenting, use with the radial approach
  - IDS offers potential for procedural time, cost savings
  - Bioabsorbable drug carrier mixed with sirolimus demonstrates excellent suppression of hyperplastic response
- **DIRECT First-In-Human 6-month results impressive, with clinical results sustained through 12-months**
  - No clinically-driven TLR, TVR
  - 2.7% in-stent volume obstruction
  - No stent thrombosis
- **DIRECT II RCT underway**
  - Non-inferiority vs conventional DES
  - 6-month outcomes expected Q1 2014