CYPHER (Polymer-based Sirolimus-eluting DES)

New Stent Platforms

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Cumulative Incidence of Myocardial Infarction

Cumulative Incidence of ARC Definite Stent Thrombosis

38 RCTs
18,000 pts

Cumulative Incidence of TLR

- **38 RCTs**
- **18,000 pts**

**Cumulative incidence of target lesion revascularisation (%)**

- **BMS**
- **PES**
- **SES**

**N of events/patients**
- BMS: 4763, 820/4746, 53/2795, 22/1871, 10/1543
- PES: 6328, 448/6280, 98/3950, 15/1999, 6/832
- SES: 6621, 356/6580, 68/3801, 16/2153, 14/999

**Years after initial procedure**

- SES vs BMS: HR 0.30 (95%-CI 0.24-0.37, p<0.0001)
- PES vs BMS: HR 0.42 (95%-CI 0.33-0.53, p<0.0001)
- SES vs PES: HR 0.70 (95%-CI 0.56-0.84, p=0.0021)

*TVR was used as a proxy for 3 studies*
The objective of this study is to show similar (non-inferior) safety and effectiveness between CYPHER® ELITE™ and the CYPHER® Sirolimus-Eluting Stent Systems in a prospective, multi-center, randomized clinical study for the treatment of de novo native coronary lesions.
CYPHER® ELITE™ Sirolimus-eluting Coronary Stent*

- CYPHER® ELITE™ Stent will feature a new stent design and advanced SDS
  - New SDS
  - Redesigned Platform
  - Stainless Steel
  - Sirolimus

*Investigational device. Not approved or available for sale in the U.S.
Study Design

- Approximately 1,770 patients to be enrolled in 12 months;
- Approximately 95 study sites;
- Randomized 2:1 (CYPHER® ELITE™ : CYPHER® BX™ VELOCITY);
- Subject randomization will be stratified by site, diabetes, and number of vessels treated (one or two);
- De novo atherosclerotic coronary artery lesions;
- 1 or 2 vessel disease;
- Lesion diameters ≤ 2.25mm to ≥ 4.0mm in diameter;
- Maximum lesion length of ≤ 30mm;
- Total implanted stent length ≤ 66mm;
- Angiographic (300 pts) and IVUS (120 pts) follow-up at 12-month post procedure;
- 5-Year Follow-up.
Endpoints

• Primary Endpoint:
  – Target lesion failure (TLF) 12-months post-procedure, defined as:
    • clinically-driven target lesion revascularization
    • target vessel myocardial infarction
    • cardiac death not clearly attributable to a vessel other than the target vessel.

Milestones and Timelines

• IDE Submission: July 31, 2007
• IDE Conditional Approval: August 31, 2007
• 95 Sites Selected
• IRB Approvals On-Going
Design Elements of Conor Sirolimus

Next Generation Stent and SDS
- Flexible and low profile CoCR Stent Platform

Conor RES Technology
- RES technology is designed to provide metered drug delivery protected from mechanical deformation

Polymers and Formulations
- Bioresorbable polymer designed to provide metered Sirolimus release without durable polymer

Note: Products under development and are not approved or available for sale or use in U.S.
Non-Deforming Reservoirs

• Reservoirs are macro-structures, representing about 1/3 of total stent volume

• Compared to surface coatings:
  – Their volumetric capacity is 4 - 10 times greater
  – Their depth is 8 - 20 times greater
  – They are designed to protect drug and polymer from mechanical damage during delivery and expansion
  – They allow complex drug dose and delivery profiles
Estimated Exposed Polymer Surface Area

Polymer Exposure

- Polymer Surface Area (Sq mm)
- Over Time =>

Surface Coated Stents

- Durable, Biostable Polymers
- Reservoir-Based, Bioresorbable Polymer Matrix
- No Residual Polymer or Drug

Conor Stent
Sirolimus Release In Vivo From Four Candidate Formulations

In Vivo Sirolimus Release

- CYCHER® Stent
- Formulation A
- Formulation B
- Formulation C
- Formulation D

Curve obtained from residual drug analysis on explanted stents in a porcine model. Drug levels obtained from HPLC method, N=3.
Sirolimus Levels in Arterial Tissues From Four Candidate Formulations

Curve obtained from drug analysis on tissues
Drug tissue levels obtained from LCMS method, N=3
Conor Bare Metal vs. Conor Sirolimus vs. CYPHER® Stent
Porcine Coronary 30 Day Histology

Conor Bare Metal*

Conor Sirolimus – Formulation 1*

Conor Sirolimus – Formulation 3*

CYPHER® Stent

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Proposed Conor Sirolimus Trial Design

Prospective, Randomized, Single-Blind, Non-Inferiority Trial

Single De Novo Native Coronary Artery Lesion <28 mm in a 2.5-3.5mm diameter vessel.

Conor Sirolimus-Eluting Stent

Approved DES

Primary Endpoint: 6-Month In-Stent Late Loss IVUS in a subset of patients

Clinical/MACE

Angiographic/IVUS

30 Day 3 Mo. 6 Mo. 9 Mo. 1 Yr. 2 Yr. 3 Yr. 4 Yr. 5 Yr.
Proposed Conor Sirolimus Trial
Design

**Primary Endpoint**
6-month in-stent late lumen loss

**Secondary Clinical Endpoints**
- Primary device, lesion and procedure success
- Clinically driven target lesion revascularization
- MACE/TLF at 1, 2, 3, 4 and 5 years

**Secondary Angio Endpoints**
- In-stent and in-segment binary restenosis and MLD
- In-segment LL at 6 months

**Secondary IVUS Endpoints**
- % volume obstruction
- Incidence of late acquired stent malapposition

**Secondary Analytical Subsets**
- Diabetes
- Overlapping stents
- Long lesions
- Small vessels
- Renal insufficiency
- Small vessels
Beyond Conor Sirolimus

• Future potential applications of RES Technology
  – Anti-thrombotic DES
  – DES for AMI
  – DES for diabetes
  – Peripheral DES
Future Cordis Corporation and Conor DES

1. CYPHER® ELITE™ Sirolimus-eluting Coronary Stent*

2. Conor Sirolimus

3. Combination Anti-thrombotic
   Combination AMI
   Combination Diabetic

4. Fully Bioresorbable DES

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