Long-term Clinical Outcomes of a Unique Sirolimus-eluting Stent with Fully Absorbable Polymer Coating

5-Year Results from DESSOLVE I and II Trials

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Relations of Interest Disclosure

Institutional Research Grants:
   Micell Technologies, MicroPort, St Jude-Abbott, Terumo
Advisory Board & honoraria:
   MicroPort
Shareholder & non-executive Board member:
   Argonauts, Genae
Crystalline Sirolimus with a Rapidly Absorbed Polymer Coating

**MiStent Crystalline Sirolimus**
- Unique to MiStent SES, micro-crystalline morphology
- Controlled and prolonged elution, as opposed to use of an amorphous, rapid-release form of the drug

**MiStent Rapidly Absorbable Polymer**
- Flows off the stent struts in 45 - 60 days
- Rapidly absorbed from tissue within 90 days
- Quickly eliminates source of inflammatory response

**MiStent Thin-Strut Stent**
- Cobalt-chromium
- Strut thickness 64 microns

No Drug Burst with Therapeutic Tissue Levels Up To 9 Months

Elimination of Polymer Within 90 Days

No Detectable Sirolimus Blood Levels

An initial uncontrolled burst of drug may delay re-endothelialization and coverage of the stent struts


MiStent SES
MiStent SES®
Highly Differentiated Drug-Eluting Stent

MiStent SES – Crystalline drug presence in the tissue after elimination of polymer

• Minimizes duration of inflammatory effect of polymer
• Retains anti-restenotic drug for 3X longer than polymer is present

Adapted from K. Dawkins, TCT 2014 & product websites
DESSOLVE I and II Investigational Sites

STUDY PRINCIPAL INVESTIGATORS
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Pacific Clinical Research Group (PCRG)

Core Labs
Angiography - Yale - Alexandra Lansky
IVUS - Stanford - Peter Fitzgerald
OCT - Case Western - Hiram Bezerra, Marco Costa

*DESSOLVE I sites
DESSOLVE I: Study Design

First-in-Human, 30 patients, 5 sites

- Mechanistic design to investigate quality of vessel healing
  - 4, 6, 8-month data - angiography, IVUS, OCT
  - 18-month data - angiography, IVUS, OCT

Ormiston et al. JACC CI 2013;6:1026-33
DESSOLVE I
Imaging Results

Healing demonstrated by OCT through 18 months

OCT Results
• Imaging with OCT demonstrated thin, homogeneous coverage with high rates of stent strut coverage at 6 - 8 months
• No evidence of definite neoatherosclerosis at 18 months

<table>
<thead>
<tr>
<th>Median</th>
<th>4-Month Group</th>
<th>6-Month Group</th>
<th>8-Month Group</th>
<th>18-Month Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Strut Coverage</td>
<td>93%</td>
<td>97%</td>
<td>96%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Ormiston, J., et al. JACC CI. 2013
DESSOLVE I Results

No Progression of In-stent Late Lumen Loss From 6/8 to 18 Months Follow Up

Results in low progression of target lesion revascularization (TLR) at 5 Years

Angiography In-Stent Late Lumen Loss

CD-TLR Over Time

Data represents matched cases for each time point with serial 3D analysis: 4M n=9, 6M n=9, 8M n=9, 18M n=27

N=148
DESSOLVE II
Study Design

2:1 RCT design for superiority of in-stent LLL at 9 months vs Endeavor
184 patients at 26 sites

<table>
<thead>
<tr>
<th>PROCEDURE</th>
<th>30D</th>
<th>6M</th>
<th>9M</th>
<th>12M</th>
<th>2Y</th>
<th>3Y</th>
<th>4Y</th>
<th>5Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>2:1 RCT 26 sites</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>MiStent SES n=123 Endeavor n=61</td>
<td></td>
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9M - MiStent SES
Angio, OCT, EFT, Clinical

12M
n=175
Clinical Follow-Up

2, 3, 4, 5Y
Long-term Clinical Follow-up

5-Year Completed

DESSOLVE II: Inclusion / Exclusion Criteria

Key Criteria

Patient
• stable or unstable angina pectoris (Class I, II, III or IV), documented ischemia, or documented silent ischemia
• no recent Q wave MI (<72 hrs) or no elevated cardiac biomarkers

Target Lesion
• planned single, de novo, types A, B1 or B2 coronary lesions (according to the ACC/AHA classification) in the native coronary artery with >50% diameter stenosis
• vessel diameter 2.5 to 3.5 mm - maximum 30 mm long stent
• exclude if highly calcified, tortuous, thrombus present, proximal angulation
• exclude if located at side branch >2.5mm, ostial location, previously treated vessel

Non-Target Lesion
• may treat one critical non-target lesion in another vessel prior to target lesion
DESSOLVE II
9-Month Results

**Angiography**
*The MiStent SES was superior to Endeavor for the primary endpoint analysis of in-stent late lumen loss*

<table>
<thead>
<tr>
<th>Measure (Mean)</th>
<th>MiStent SES N=103</th>
<th>Endeavor ZES N=52</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late Lumen Loss</td>
<td>$0.27 \pm 0.46$</td>
<td>$0.58 \pm 0.41$</td>
<td>$&lt; 0.001$</td>
</tr>
</tbody>
</table>

**OCT**
*The proportion of uncovered struts and % strut malapposition was remarkably low in both groups*

<table>
<thead>
<tr>
<th>Measure (Median)</th>
<th>MiStent SES N=24</th>
<th>Endeavor ZES N=10</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Uncovered Struts</td>
<td>0.34</td>
<td>0.00</td>
</tr>
<tr>
<td>% Strut Malapposition</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

**Endothelial Function Testing**
*Dilation of the reference vessel segments after pacing indicating normal vasomotor function for both MiStent SES and Endeavor at 9 months*

<table>
<thead>
<tr>
<th>Measure (%)</th>
<th>MiStent SES N=19</th>
<th>Endeavor ZES N=10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responders</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Non-Responders</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Vasoconstrictors</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>
DESSOLVE II
5-Year Clinical Outcomes

Sustained clinical outcomes though 5 years for MiStent SES
• 3.4% TLR rate
• No Definite/Probable Stent Thrombosis for MiStent SES
DESSOLVE I and II
Conclusions

MiStent appears to provide outcomes indicative of optimized healing
• High rate of early strut coverage by OCT
• Maintenance of vasomotor function out to 9 months
• Absence of late “Catch-Up” in lumen loss out to 18 months
• Minimal progression of NIH out to 18 months
• No definite / probable Stent Thrombosis through 5 years
• Low MACE and TLR rates, stable up to 5 years

Pooled analysis of patients treated with MiStent SES, which has a unique bioabsorbable coating that provides continued drug delivery in the absence of polymer, suggests long term (5-years) safety and continued efficacy of this novel coronary stent
DESSOLVE Clinical Trials Program

DESSOLVE I
First-in-Human
N = 30 pts
Study Initiation: Q4 2010
Five-year follow-up completed: Q1 2016
-In-Stent LLL
Completed

DESSOLVE II
CE Mark Approval
N = 184 pts [vs. Endeavor DES]
Study Initiation: Q1 2011
Five-year follow-up completed: Q2 2016
-Superiority in-stent LLL at 9M
Completed

DESSOLVE III
Outcomes Trial
N = 1,400 pts [vs. Xience]
Study Initiation: Q1 2015
Enrollment completed: Q4 2015
-Non-inferiority of TLF at 12M
Results 2017

DESSOLVE III
OCT Sub-study
N = 60 pts [vs. Xience]
Study Initiation: Q1 2015
Enrollment completed: Q1 2016
-Superiority intimal hyperplasia progression

DESSOLVE CHINA
CFDA Approval
N = 428 pts [vs. Tivoli DES]
Study Initiation: Q2 2015
Enrollment to complete: Q1 2017
-Non-inferiority in-stent LLL at 9M

DESSOLVE CHINA
Angiographic Sub-study
N = 170 pts [vs. Tivoli DES]
Study Initiation: Q2 2015
Endpoint Report: Late 2019
-Superiority LLL progression at 3 years

Results 2017
DESSOLVE Clinical Trials Program

DESSOLVE JAPAN
PMDA Approval
N = 120 pt study supportive of the DESSOLVE III [vs. Xience]
- Initiated November 2016
- Prospective, balanced, randomized
- Five-year follow-up
- Non-inferiority of TLF at 12 months

CRYSTAL *
U.S. IDE
N = ~2000 pts [vs. Xience or Promus]
- Prospective, balanced, randomized
- Five-year follow-up
- Non-inferiority of TLF at 12 months

* Pending review with the FDA