

# **SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)**

## **I. GENERAL INFORMATION**

Device Generic Name: Coronary Stent

Device Trade Name: TRYTON Side Branch Stent

Device Procode: MAF

Applicant's Name and Address: Tryton Medical, Inc.  
1000 Park 40 Plaza, Suite 325  
Durham, NC 27713

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P150039

Date of FDA Notice of Approval: February 21, 2017

## **II. INDICATIONS FOR USE**

The TRYTON Side Branch Stent is indicated for improving the side branch luminal diameter of de novo native coronary artery bifurcation lesions (Medina Classification 1.1.1; 0.1.1; 1.0.1) with a side branch diameter stenosis of  $\geq 50\%$  and a lesion length  $\leq 5.0\text{mm}$ , along with reference vessel diameters  $\geq 2.5\text{mm}$  to  $\leq 3.5\text{mm}$  in the side branch and  $\geq 2.5\text{mm}$  to  $\leq 4.0\text{mm}$  in the main branch.

The device is intended for use in conjunction with commercially available balloon expandable drug-eluting coronary stents in the main branch.

## **III. CONTRAINDICATIONS**

The TRYTON Side Branch Stent is contraindicated for use in patients with the following conditions or uses:

- Vessels that are totally occluded
- Vessels that have moderate to severe calcification
- Target lesions that have excessive tortuosity unsuitable for stent delivery and deployment
- Angiographic evidence of thrombus in the target vessel
- Lesions in which complete angioplasty balloon inflation cannot be achieved during pre-dilatation
- TRYTON Stent placement without angioplasty pre-dilatation of the main branch and side branch (i.e., direct stenting is contraindicated)
- TRYTON Stent placement alone, without implantation of a main branch stent

- An untreated significant (> 50%) stenosis proximal or distal to the main branch or side branch target lesion
- Impaired runoff in the treatment vessel with diffuse distal disease
- Ejection fraction  $\leq$  30%
- Impaired renal function (creatinine > 2.0 mg/dl or 150  $\mu$ mol/l)
- Platelet count <100,000 cells/mm<sup>3</sup> or > 700,000 cells/mm<sup>3</sup>, a WBC of < 3,000 cells/mm<sup>3</sup>, or documented or suspected liver disease (including laboratory evidence of hepatitis)
- Presence of a heart transplant
- Known allergy to cobalt chromium
- Hypersensitivity or contraindication to cobalt-chromium or structurally-related compounds, cobalt, chromium, nickel, or tungsten
- Anticipated use of rotational atherectomy
- Patients in whom the use of a drug eluting stent is contraindicated, e.g., who cannot receive the recommended dual anti-platelet (aspirin and an approved P<sub>2</sub>Y<sub>12</sub> Inhibitor) and/or anticoagulation therapy

#### IV. **WARNINGS AND PRECAUTIONS**

The warnings and precautions can be found in the TRYTON Side Branch Stent labeling.

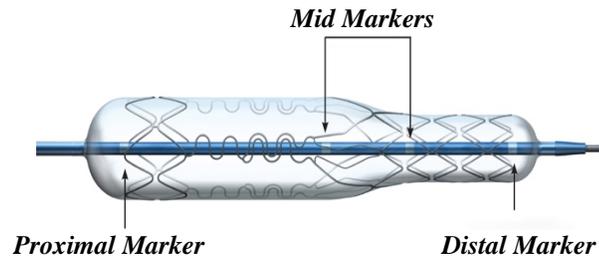
#### V. **DEVICE DESCRIPTION**

The TRYTON Side Branch Stent has been designed to treat coronary bifurcation lesions. It is intended to treat and maintain patency in the side branch/carina in conjunction with a currently approved balloon-expandable drug-eluting stent for treatment of the main vessel.

The TRYTON Side Branch Stent is a bare metal stent, composed entirely of L605 Cobalt Chromium (Co-Cr) Alloy. The TRYTON Side Branch Stent is available in three (3) sizes (internally referred to as D5, D5+, and D5+ Short) to address different vessel diameters and main vessel landing zones, and is placed on one (1) of seven (7) delivery systems to address a range of coronary dimensions. The TRYTON Side Branch Stent is composed of three (3) stent zones: a Side Branch Zone that is deployed within the side branch of a coronary artery; a Transition Zone that resides within the ostium of the side branch; and a Main Branch Zone, which is placed within the main vessel of a diseased bifurcated lesion. The TRYTON Side Branch Stent is pre-mounted on a rapid exchange delivery catheter provided in two configurations: standard-(straight) balloon and step-balloon delivery systems.

**Table 1** lists the catalog numbers and sizes of the TRYTON Side Branch Stent.

**Figure 1: Schematic of TRYTON Side Branch Stent mounted on Stepped Stent Delivery System**



**Table 1: TRYTON Side Branch Stent Matrix**

| Reference                  | Proximal Diameter (mm) | Distal Diameter (mm) | Stent Length (mm) | Balloon Configuration | Strut Wall Thickness / Width (µm) | Guide Catheter Compatibility |
|----------------------------|------------------------|----------------------|-------------------|-----------------------|-----------------------------------|------------------------------|
| T5-2525-191-US (D5)        | 2.5                    | 2.5                  | 19                | Straight              | 85 / 102                          | 5F                           |
| T5-2530-191-US (D5)        | 3.0                    | 2.5                  | 19                | Stepped               | 85 / 102                          | 5F                           |
| T5-2535-191-US (D5)        | 3.5                    | 2.5                  | 19                | Stepped               | 85 / 102                          | 5F                           |
| T5-3035-181-US (D5+)       | 3.5                    | 3.0                  | 18                | Stepped               | 85 / 102                          | 6F                           |
| T5-3540-181-US (D5+)       | 4.0                    | 3.5                  | 18                | Stepped               | 85 / 102                          | 6F                           |
| T5-3035-151-US (D5+ SHORT) | 3.5                    | 3.0                  | 15                | Stepped               | 85 / 102                          | 6F                           |
| T5-3540-151-US (D5+ SHORT) | 4.0                    | 3.5                  | 15                | Stepped               | 85 / 102                          | 6F                           |

The Side Branch Zone of the stent functions as a standard balloon expandable stent within the side branch. Once deployed, the Side Branch Zone part of the device is intended to provide radial strength, scaffolding, and coverage to the side branch. The length of this zone is approximately 6 mm. The Side Branch Zone of the stent is intended to function similarly to a standard balloon expandable stent deployed in the side branch.

The Transition Zone of the TRYTON Side Branch Stent spans the space between the Main Branch Zone and the Side Branch Zone. When deployed, the Transition Zone is located within the ostium of the side branch. When implanted using a “stepped” balloon configuration, the Transition Zone is initially expanded to a diameter larger than that of the Side Branch Zone of the device to achieve better apposition to the ostium and provide adequate scaffolding when a “step” in vessel size is seen in the target vessel.

The Main Branch Zone is intended to accommodate a standard main branch balloon expandable drug-eluting coronary stent within the TRYTON Side Branch Stent. The Main Branch Zone facilitates the positioning and passage of the standard main branch stent across

the bifurcation. Upon deployment of the main vessel drug-eluting stent, the fingers or fronds that extend from the Transition Zone into the Main Branch Zone become apposed to the main vessel stent to provide additional scaffolding within the origin of the ostium.

The TRYTON Side Branch Stent delivery system configurations combine a single-lumen proximal shaft with a dual-lumen mid-shaft and a coaxial lumen distal shaft to create a rapid exchange capability. The catheter employs four radiopaque balloon markers; proximal and distal markers indicate the proximal and distal segments of the stent as mounted on the balloon. In addition, two markers in the mid-section of the balloon indicate the boundaries of the Transition Zone. The radiopaque markers aid in positioning the stent and the delivery system during the implantation procedure.

## VI. **ALTERNATIVE PRACTICES AND PROCEDURES**

There are several other alternatives for the treatment of coronary bifurcation lesions. Provisional stenting (stenting the main branch with subsequent balloon angioplasty (POBA) of the side branch) is commonly used to treat bifurcation lesions. The side branch can also be stented if suboptimal results are seen post-POBA. A planned dual stent approach can also be used, employing different techniques such as culotte, crush, double-kiss crush, V-stenting, T-stenting, and simultaneous kissing stents. Other alternative procedures to treat coronary artery disease include medical therapy (e.g., antiplatelet agents, beta-blockers, lipid lowering agents), other transcatheter devices (e.g., conventional balloon angioplasty, plaque removal using cutting balloons or rotational atherectomy, lasers), and coronary artery bypass graft (CABG) surgery.

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

## VII. **MARKETING HISTORY**

The TRYTON Side Branch Stent has been marketed in Europe, Russia, South Africa, Israel, and parts of the Middle East. The TRYTON Side Branch Stent in its current design has not been withdrawn from the market for any reason relating to its safety or effectiveness.

## VIII. **POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device:

- Acute or subacute closure of the coronary artery
- Acute myocardial infarction
- Aneurysm
- Arrhythmia, including ventricular fibrillation
- Arteriovenous fistulas
- Coronary artery spasm
- Coronary vessel dissection, perforation, rupture or injury

- Death
- Drug reactions, allergic reactions to contrast medium
- Fever
- Hematoma or hemorrhage
- Hypotension or hypertension
- Hypersensitivity reactions
- Infection
- Myocardial ischemia
- Non-cardiac chest pain
- Pseudoaneurysm
- Restenosis of the dilated vessel
- Stent embolism or migration
- Stroke or cerebral vascular accident
- Total occlusion of the coronary artery or bypass graft
- Unstable or stable angina pectoris
- Vascular thrombosis or embolism

For the specific adverse events that occurred in the clinical studies, please see Section X.

## IX. **SUMMARY OF PRECLINICAL STUDIES**

A series of non-clinical laboratory studies were performed to evaluate the TRYTON Side Branch Stent. These evaluations included in vitro engineering testing, animal studies, biocompatibility studies, and sterilization.

### A. **In Vitro Engineering Testing**

Tryton Medical performed mechanical and functional testing to demonstrate that the TRYTON Side Branch Stent and Delivery System meets design input requirements and engineering specifications. Testing was conducted in accordance with FDA Guidance for Industry and Staff: *Non-Clinical Engineering Test and Recommended Labeling for Intravascular Stents and Associated Delivery Systems* (April 18, 2010). The results show that all design input requirements were met, thus supporting the safety and effectiveness of the TRYTON Side Branch Stent. These tests are summarized in **Table 2**.

Since the TRYTON Side Branch Stent is intended for coronary bifurcation lesions, the target deployment site was simulated with mock bifurcated vessels in the following tests: fretting corrosion, stress/strain analysis, fatigue analysis, accelerated durability testing, particulate evaluation, and delivery, deployment and retraction. Refer to each individual test in the table below.

**Table 2: Summary of TRYTON *In Vitro* Engineering Bench Testing**

| Test   | Purpose/Method   | Acceptance Criteria  | Results |
|--|--|--|---------|
| <b>Material Characterization</b>                     |  |  |         |
| Material Composition                                 | Material composition testing documents a baseline for evaluation of the effects of future changes in materials. The stent material (L605 Co-Cr alloy) was analyzed for chemical composition. Certification demonstrated that incoming raw materials conform to TRYTON specifications and L605 (ASTM F90/ISO 5832-5) material requirements.   | ASTM F90/ISO 5832-5  | Pass    |
| Corrosion Resistance – Fretting, Pitting and Crevice | Stent corrosion can cause or contribute to premature stent failure. In addition, corrosion byproducts may be toxic or cause other adverse biological and tissue responses. The stent was tested according to ASTM F2129-08 “Standard Test Method for Conducting Cyclic Potentiodynamic Measurements to Determine the Corrosion Susceptibility of Small Implant Devices.”                         | No evidence of localized corrosion (pitting, crevice, or fretting) after 400 million cycles (10 year equivalent) in a simulated bifurcation model.   | Pass    |
| Corrosion Resistance - Galvanic                      | Stent corrosion can cause or contribute to premature stent failure. In addition, corrosion byproducts may be toxic or cause other adverse biological and tissue responses. Galvanic corrosion characterization was evaluated with overlapped stents of dissimilar materials in accordance with ASTM G71 “Standard Guide for Conducting and Evaluating Galvanic Corrosion Tests in Electrolytes.” | No evidence of localized corrosion on the overlapping stents (TRYTON Side Branch Stent coupled with a stainless steel stent) in a PBS test solution. | Pass    |

| Test   | Purpose/Method  | Acceptance Criteria  | Results |
|--|---|--|---------|
| <b>Stent Dimensional and Functional Attributes</b> |   |  |         |
| Dimensional Verification                           | Accurate stent dimensions help the physician to achieve proper stent sizing and accurate placement in the body. Stent dimensions were measured, including distal and proximal crown heights, strut width, and strut wall thickness.   | Must pass visual inspection and 10x magnification. Dimensions must meet TRYTON Stent specifications.   | Pass    |
| Percent Surface Area                               | The area over which a stent contacts a vessel may affect the biologic response of the vessel. The amount of open, non-contact area may influence tissue prolapse or ingrowth. The percent surface area of the stent for the smallest and largest nominal expanded diameters was calculated.   | <i>D5+ and D5+ SHORT</i> : The surface area of the stent as a percent of the full cylindrical surface area of the vessel must be between 7 and 20% per ASTM F2081-06 (Section X1.6).<br><br><i>D5</i> : Must be between 10-20% | Pass    |
| Foreshortening                                     | Foreshortening (i.e., dimensional changes that may occur when deploying a stent), influences final stent length. Knowledge of the foreshortening characteristics aids in proper stent length selection and proper placement in the body. This test determined the percent change in length of the stent between when it is catheter-mounted and when it is expanded to nominal pressure and rated burst pressure (RBP). | Maximum foreshortening $\leq 15\%$   | Pass    |
| Recoil for Balloon Expandable Stents               | The recoil behavior of balloon expandable stents influences proper device selection, sizing, acute post-implant results, and long-term clinical outcomes. Recoil is a function of stent design and material selection; therefore, knowledge of stent recoil helps to characterize the behavior of a particular stent design. The change in diameter   | Maximum recoil $\leq 15\%$   | Pass    |

| Test                                 | Purpose/Method   | Acceptance Criteria   | Results |
|--------------------------------------|--|---|---------|
|                                      | <p>of the stent was measured between post-balloon expansion and after balloon deflation. Measurements were taken at nominal pressure and rated burst pressure (RBP) or greater.</p>  |   |         |
| Stent Integrity                      | <p>Stent defects, whether a result of manufacturing flaws or subsequent damage, can contribute to clinical complications. Laser cutting or other manufacturing processes may induce flaws that are not completely removed by polishing. Plastic deformation during loading or balloon expansion may cause cracks or other damage. Therefore, this test was performed to verify that the stent had no clinically significant defects or flaws after deployment, when over expanded.</p> | <p>No fractures or cracks of struts when examined under 10X-40X magnification. The ends and the midsection of the stent must expand uniformly (i.e., no distorted struts) and the space in between struts must be distributed evenly.</p> | Pass    |
| Radial Stiffness and Radial Strength | <p>These tests characterized the ability of the stent to resist collapse under short-term or long-term external loads. The radial strength test determines the pressure at which the stent experiences irrecoverable deformation. The radial stiffness calculation characterizes the change in stent diameter as a function of uniformly applied external radial pressure.</p>   | <p>Radial Strength: No more than 50% area loss at a pressure of 500 mmHg for D5 stent and 300 mmHg for D5+ and D5+ SHORT stents</p> <p>Radial Stiffness: Characterization only</p>  | Pass    |
| Mechanical Properties                | <p>Raw material properties determine incoming material quality and uniformity, and predict subsequent thermomechanical effects. Thermomechanical properties of the implanted stent affect clinical performance, as well as stress and fatigue behavior. The</p>  | TRYTON material specifications  | Pass    |

| Test                         | Purpose/Method  | Acceptance Criteria  | Results |
|------------------------------|---|--|---------|
|                              | mechanical properties of the stent raw material were evaluated; including ultimate tensile strength (UTS), yield strength (YS), and elongation.   |  |         |
| Stress/Strain Analysis (FEA) | Failure of a loaded stent may result in loss of radial support of the stented vessel or in perforation of the vessel by the stent struts. Stress/strain analysis, combined with fatigue analysis and accelerated durability testing, provides an indication of device durability. Using Finite Element Analysis (FEA), stress and strain analyses were performed on the stent to demonstrate that acceptable safety is maintained in stress loading environments. The analyses included simulation of manufacturing and clinical loading over the implant life. | Calculated static safety factors $\geq 1$  | Pass    |
| Fatigue Analysis             | Failure of a stent due to fatigue may result in loss of radial support of the stented vessel, thrombus formation or focal restenosis, or in perforation of the vessel by the stent struts. Fatigue analysis, combined with stress/strain analysis and accelerated durability testing, provides an indication of device durability. Fatigue analysis was conducted to determine the state of fatigue due to stress loading, including simulation of manufacturing and clinical loading over the implant life.  | Calculated static safety factors $\geq 1$  | Pass    |
| Accelerated Durability       | Accelerated durability testing validates fatigue analysis. It evaluates failure modes such as fretting, abrasion, wear, and fracture. Durability testing can  | All TRYTON and main vessel stents must be free of defects (scratches, cracks, fractures) when examined at up to 40X magnification in a | Pass    |

| Test  | Purpose/Method  | Acceptance Criteria   | Results |
|---|---|---|---------|
|   | help in the identification of device conditions, such as manufacturing anomalies, that were not modeled using analytical or computational methods. The accelerated durability of TRYTON Stents were evaluated when mated with main vessel stents after 400 million cycles (equivalent to 10 years) in a simulated bifurcation model.  | simulated bifurcation model.  |         |
| Particulate Evaluation                                    | The system was evaluated for particulates after simulated use through a tortuous track model. Measurement of the total quantity and size of particulates a device system may generate is an indication of embolic risk.   | Per USP <788>:<br>$\leq 6000$ particles/container for particle size $\geq 10 \mu\text{m}$<br>$\leq 600$ particles/container for particle size $\geq 25 \mu\text{m}$ | Pass    |
| Magnetic Resonance Imaging (MRI) Safety and Compatibility | <p><u>MRI Safety Information</u></p> <p>Non-clinical testing has demonstrated the TRYTON Side Branch Stent (19 mm stent alone and in combination with four 20 mm drug-eluting stainless steel stents, tested for a total stent length of 73 mm) is MR Conditional. A patient with this device can be safely scanned in an MR system meeting the following conditions:</p> <ul style="list-style-type: none"> <li>• Static magnetic field of 3-Tesla or 1.5-Tesla</li> <li>• Maximum spatial field gradient of 720 Gauss/cm (7.2 T/m)</li> <li>• Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2.0 W/kg (Normal Operating Mode)</li> </ul> | MR Conditional (poses no known hazards under specified conditions)  | Pass    |

| Test   | Purpose/Method   | Acceptance Criteria   | Results |
|--|--|---|---------|
|  | <p>Under the scan conditions defined above, the TRYTON Side Branch Stent is expected to produce a maximum temperature rise of less than 2.7°C after 15 minutes of continuous scanning.</p> <p>In non-clinical testing, the image artifact caused by the device extends a maximum of 11 mm from the TRYTON Side Branch Stent when imaged with a gradient echo pulse sequence and a 3T MRI system.</p> |   |         |
| Radiopacity  | Stent visibility using angiographic and/or radiographic imaging generally assures proper stent placement and allows follow-up and secondary treatment. Radiopacity evaluation was performed to confirm that the TRYTON stent is adequately visible using standard fluoroscopy equipment and that it demonstrates comparable visibility to the main vessel stents.                                    | Must be adequately visible using standard fluoroscopy equipment and demonstrate comparable visibility to the main vessel stents.                        | Pass    |
| <b>Delivery System Dimensional and Functional Attributes</b> |  |   |         |
| Dimensional Verification                                     | Stent delivery system dimensions influence the ability of the device to track to and across lesions. The crimped profile (distal, proximal), crimped stent length, overall working length, largest catheter ID and OD, and crossing profile were measured.   | Crimped profile (distal/proximal), crimped stent length, overall working length, catheter ID/OD, and crossing profile must meet product specifications. | Pass    |
| Delivery, Deployment, and Retraction                         | This test assessed the ability of the delivery system to deliver the stent to the intended location, deploy the stent, and retract under simulated use conditions.   | The balloon must pass through the following ID gauge size following deployment:<br>D5: 0.056" (5F)<br>D5+: 0.068" (6F)                                  | Pass    |

| Test   | Purpose/Method   | Acceptance Criteria   | Results |
|--|--|---|---------|
|  |  | <i>D5+ SHORT: 0.068" (6F)</i>   |         |
| Balloon Rated Burst Pressure                           | The rated burst pressure (RBP) is the pressure at which 99.9% of balloons can survive with 95% confidence. Failure of a balloon to survive at the RBP could result in device failure or vessel damage.   | No burst within working range (>14 atm). No radial failures.  | Pass    |
| Balloon Fatigue  | Balloons on stent delivery systems are often inflated multiple times during clinical use. Failure of the balloon to withstand multiple inflations could lead to device failure or vessel damage. Balloons were evaluated for the ability to withstand 10 repeated inflations to RBP without rupture.   | Each balloon must pass ten (10) cycles at 14 atm without balloon rupture.   | Pass    |
| Balloon Fatigue - Leakage                              | The purpose of this test was to demonstrate that there was no balloon leakage or burst following inflation/deflation 10 times from 0 to 14 atm with a dwell time at 14 atm of 30 seconds.  | No balloon leakage or burst following inflation cycles to RBP.  | Pass    |
| Stent Diameter vs. Balloon Pressure (Compliance Chart) | The diameter of a deployed balloon expandable stent varies with the balloon inflation pressure. A compliance chart in the labeling that relates stent diameter to balloon pressure guides selection of stent size to fit the target lesion. Incorrect selection of stent size may lead to device failure or vessel damage. This test determines how the diameter of the deployed stent varies with balloon inflation pressure. | Working range: All values must be within +/-10% of the compliance chart values between nominal and rated burst pressure.<br><br>Overexpansion: Compliance must not exceed 20% of the average overexpansion value. | Pass    |
| Balloon Inflation and Deflation Time                   | Balloons occlude the target vessel and obstruct blood flow while inflated. Inflation and deflation times affect occlusion  | <i>Inflation Time:</i><br><i>D5: &lt;15 seconds</i><br><i>D5+: &lt;15 seconds</i><br><i>D5+ SHORT: &lt;15 seconds</i>   | Pass    |

| Test  | Purpose/Method   | Acceptance Criteria   | Results |
|---|--|---|---------|
|   | time. Excessively slow inflation or deflation of a balloon could lead to prolonged ischemia and damage to the end organ. This testing was conducted to determine the amount of time required to inflate and deflate the delivery catheter balloon.   | <i>Deflation Time:</i><br><i>D5:</i> <15 seconds<br><i>D5+:</i> <30 seconds<br><i>D5+ SHORT:</i> <30 seconds        |         |
| Catheter Bond Strength and Tip Pull               | Failure delivery catheter bonds (including distal tip bonds) could lead to device failure or vessel damage. The tensile strength of all delivery system bonds was evaluated.   | <i>Tip Bond:</i> $\geq 1.5N$<br><i>Shaft to Balloon:</i> $\geq 3N$ or $\geq 5N$<br><i>Shaft to Luer:</i> $\geq 15N$ | Pass    |
| Flexibility and Kink Test                         | Stent delivery systems were evaluated to determine their ability to withstand flexural forces typical of clinical use. The catheter flexibility and kink resistance was evaluated by tracking samples through a tortuous model, designed in accordance with ASTM F2394 Figure X2.4, which included radii as small as 0.125" (3.2 mm).                        | No failures related to flexibility and kink in subsequent tests.  | Pass    |
| Flexibility and Kink Test – Bend Fixture Testing  | Stent delivery systems may be subjected to tight angulations in tortuous vasculature during use. Inability to withstand flexural forces that are typical of clinical use could lead to device failure or vessel damage. The distal part of the catheter (section between the balloon and transition site) was bent 180° over a mandrel with a radius of 4mm. | No kinking observed on the distal section of the catheter when bending over a radius of 4 mm.                       | Pass    |
| Flexibility and Kink Test – Tortuous Tracking 90° | Samples were tracked twice through a tortuous model and exited through a 90° branching artery with a 0.100" radius to simulate challenging anatomical conditions.  | No damage or kinks along the catheter.  | Pass    |

| Test                   | Purpose/Method  | Acceptance Criteria  | Results |
|------------------------|---|--|---------|
| Torque Strength        | Stent delivery systems may be subjected to torsional forces during use. Even non-fixed wire delivery systems could be subject to torsional forces if the tip is inadvertently caught on a previously deployed stent, calcified lesion, etc. Inability to withstand torsional forces that are typical of clinical use could lead to device failure or vessel damage. Stent delivery systems were evaluated to determine their ability to withstand torsional forces typical of clinical use.   | Catheter able to withstand a minimum of two rotations without failure. Failure defined as no inflation possible to nominal pressure, leakage of the catheter, or broken/damaged catheter and/or inner lumen. | Pass    |
| Coating Integrity      | Unintended delamination or degradation of a coating may lessen its benefit or otherwise negatively impact its clinical performance. This test examined the amount of coating removed from the shaft during handling in simulated clinical conditions.   | No patches of missing coating >0.2 mm <sup>2</sup> at a minimum of 10x magnification.  | Pass    |
| Particulate Evaluation | The system was evaluated for particulates after simulated use through a tortuous track model. Measurement of the total quantity and size of particulates a device system may generate is an indication of embolic risk. The test assessed the total number of particulates that could theoretically be released into the bloodstream during typical use of the stent system. Samples were preconditioned by advancing and retracting them twice through a tortuous track fixture per ASTM F2394 Fig x2.4. The TRYTON stent systems were then placed using standard accessories along with a DES main vessel stent into the same fixture and deployed. All stent inflations were | Per USP <788>:<br>≤6000 particles/container for particle size ≥10 μm<br>≤600 particles/container for particle size ≥25 μm  | Pass    |

| Test                                   | Purpose/Method  | Acceptance Criteria  | Results |
|--|---|--|---------|
|  | performed at a minimum of 16 atm. Total particulate was recorded.   |  |         |
| Stent Securement for Unsheathed Stents | Dislodgment of the stent prior to deployment can result in stent embolization. Stents without sheaths may dislodge if they catch on tortuous anatomy, guide catheters, or other devices. This test determined the force needed to remove the stent from the delivery system following passage through a tortuous track on advance (simulating tracking through a lesion) and retract (simulating retraction into a guiding catheter). | Individual D5 stents must pass the specification of $\geq 1.5$ N. Individual D5+ and D5+ SHORT stents must pass the specification of $\geq 2.0$ N. | Pass    |

### B. Animal Studies

The TRYTON Side Branch Stent was evaluated in three (3) animal studies in accordance with 21 CFR 58 Good Laboratory Practice (GLP) regulations in addition to some early product development animal studies. The acute performance characteristics of the D5+ stent were assessed in a porcine coronary artery model. In addition, a 30-day tissue response study was conducted using the D5 stent in a porcine model. These two (2) studies supplemented the safety data of the 180-day ovine study conducted on an earlier version TRYTON Side Branch Stent to assess short and long-term safety and biocompatibility. The results support the conclusion that the TRYTON Side Branch Stent is safe for commercial release. **Table 3** below provides an overview of the GLP animal study designs and results.

**Table 3: Summary of GLP Animal Studies**

| Study Number | Study Objective and Design  | Number and Type of Stents Evaluated                                      | Follow-Up Duration | Results  |
|--------------|---|--|--------------------|--|
| MEA00007     | <p><u>Objective:</u> To assess acute handling and performance characteristics of the TRYTON Stent.</p> <p><u>Design:</u> Three (3) swine were implanted with the TRYTON Side Branch Stent in a bifurcation of the</p> | 5 D5+ TRYTON Side Branch Stents in conjunction with TAXUS Liberte stents | Acute              | The handling and performance of the TRYTON Stent were considered acceptable in this porcine model. |

| Study Number | Study Objective and Design   | Number and Type of Stents Evaluated   | Follow-Up Duration  | Results  |
|--------------|--|---|---------------------|--|
|              | coronary bed, in conjunction with a TAXUS Liberte stent in the main vessel. One swine was implanted with two (2) TRYTON stents in separate straight coronary artery segments with no bifurcation/side branch stenting.   |   |                     |  |
| MEA00003     | <p><u>Objective:</u> To assess acute performance, safety and tissue response at 30 days.</p> <p><u>Design:</u> Four (4) treatment groups of six (6) implantations each in a total of 19 porcine models.</p> <p><u>Group 1 (Test Group):</u> TRYTON Stent deployed in bifurcations (overlapped with TAXUS Liberte)</p> <p><u>Group 2 (Control):</u> T-Stent with TAXUS/BMS Co-Cr Stent</p> <p><u>Group 3 (Control):</u> Provisional stenting with TAXUS/POBA</p> <p><u>Group 4 (Test Group):</u> TRYTON Stent deployed in straight segments (overlapped with TAXUS Liberte)</p> | <p>6 D5 TRYTON Side Branch Stents (in Groups 1 and 4)</p> <p>6 DES and BMS stents in each of the 4 treatment groups</p> | 30 Days             | The TRYTON Stent performed similarly to the controls in this porcine model. There were no side branch occlusions or device-related complications observed in the 19 animals implanted. |
| MEA00001     | <p><u>Objective:</u> To assess acute performance, safety and tissue response at 180 days.</p> <p><u>Design:</u> Twenty-five (25) ovine models were used with up to three (3) treated</p>   | <p>36 SD and LD TRYTON Stents</p> <p>10 main vessel, drug eluting stents</p>  | 5, 90, and 180 Days | There were a total of nine (9) early deaths in the study, associated with luminal thrombosis secondary to mural injury.  |

| Study Number | Study Objective and Design  | Number and Type of Stents Evaluated | Follow-Up Duration | Results  |
|--------------|---|-------------------------------------|--------------------|--|
|              | segments per animal.<br><br>Twenty-one (21) arterial segments, 10 using bifurcation deployment, six (6) using straight overlapping deployment, and five (5) provisional DES controls evaluated at each of the longer timepoints, 3 and 6 months; four (4) arterial segments using bifurcation deployment only were evaluated at 5 days. | (TAXUS Liberte vs. XIENCE V)        |                    | Device handling characteristics were scored as average.<br><br>No adverse effect on the tissue healing response of the stented artery after 180 days. The tissue response was comparable to the provisional control. |

**C. Biocompatibility Studies**

A series of Good Laboratory Practice (GLP) biocompatibility tests were conducted to demonstrate that the materials and components of the TRYTON Side Branch Stent are biocompatible. Testing was conducted separately on the stent implant and the stent delivery system. Tests were conducted on gamma irradiation-sterilized stents and stent delivery system. All biocompatibility testing was conducted in accordance with:

- International Standard ISO 10993-1 “Biological Evaluation of Medical Devices Part 1: Evaluation and Testing”
- Guidance for Industry and FDA Staff “Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems,” (April 18, 2010)
- Good Laboratory Practices Regulations (§21 CFR Part 58)

Tests were chosen based on duration of patient contact of the stent and the delivery system. The stent is an implanted product in contact with cardiovascular tissue and circulating blood, with a permanent (>30 days) duration of contact. The stent delivery system is an externally communicating device in contact with cardiovascular tissue and circulating blood, with a temporary (<24 hours) duration of contact.

All biocompatibility test results for both the stent and the delivery system indicated that the materials and processes used to manufacture the TRYTON Side Branch Stent are biocompatible and suitable for the intended use. **Tables 4** and **5** summarize the tests conducted and the results. Chronic toxicity and carcinogenicity testing were not

conducted on the TRYTON Side Branch Stent; an acceptable justification was given for the omission of these tests.

**Table 4: Summary of Stent Biocompatibility Testing**

| Test Name                 | Test Description   | Result                            |
|---------------------------|--|-----------------------------------|
| Cytotoxicity              | ISO 10993-5: In Vitro Cytotoxicity (MEM Elution)                   | PASS – Non-cytotoxic              |
| Sensitization             | ISO 10993-10: Sensitization (Guinea Pig Maximization)              | PASS – Non-sensitizing            |
| Intracutaneous Reactivity | ISO 10993-10: Irritation (Injection)                               | PASS – Non-irritant               |
| Systemic Toxicity         | ISO 10993-11: Systemic Toxicity (Acute)                            | PASS – Non-toxic                  |
| Pyrogenicity              | ISO 10993-11: Systemic Toxicity (Material-Mediated Rabbit Pyrogen) | PASS – Non-pyrogenic              |
| Subchronic Toxicity       | ISO 10993-6: Implantation (Rat)                                    | PASS – Non-toxic                  |
| Genotoxicity              | ISO 10993-3: Bacterial Reverse Mutation Assay (Ames Assay)         | PASS – Non-mutagenic              |
|                           | ISO 10993-3: In Vivo Mouse Micronucleus Test                       | PASS – Non-mutagenic              |
|                           | ISO 10993-3: Mouse Lymphoma  | PASS – Non-clastogenic            |
| Hemocompatibility         | ISO 10993-4: Direct Hemolysis                                      | PASS – Non-hemolytic              |
|                           | ISO 10993-4: Indirect Hemolysis (Extract)                          | PASS – Non-hemolytic              |
|                           | ISO 10993-4: <i>In vivo</i> Thrombogenicity (Canine)               | PASS – Non-significant thrombosis |
|                           | ISO 10993-4: Complement Activation C3a & SC5b-9 Assay              | PASS – No induction of complement |
| Implantation              | ISO 10993-6: Implantation (Rat) – 4 weeks                          | PASS – No different than control  |
|                           | ISO 10993-6: Implantation (Rat) – 13 weeks                         | PASS – No different than control  |
| Chronic Toxicity          | N/A  |                                   |
| Carcinogenicity           | N/A  |                                   |

**Table 5: Summary of Delivery System Biocompatibility Testing**

| Test Name                 | Test Description   | Result                 |
|---------------------------|--|------------------------|
| Cytotoxicity              | ISO 10993-5: In Vitro Cytotoxicity (MEM Elution)                   | PASS – Non-cytotoxic   |
| Sensitization             | ISO 10993-10: Sensitization (Guinea Pig Maximization)              | PASS – Non-sensitizing |
| Intracutaneous Reactivity | ISO 10993-10: Irritation (Injection)                               | PASS – Non-irritant    |
| Systemic Toxicity         | ISO 10993-11: Systemic Toxicity (Acute)                            | PASS – Non-toxic       |
| Pyrogenicity              | ISO 10993-11: Systemic Toxicity (Material-Mediated Rabbit Pyrogen) | PASS – Non-pyrogenic   |

| Test Name         | Test Description                                      | Result                            |
|-------------------|---|-----------------------------------|
| Hemocompatibility | ISO 10993-4: Direct Hemolysis                         | PASS – Non-hemolytic              |
|                   | ISO 10993-4: Indirect Hemolysis (Extract)             | PASS – Non-hemolytic              |
|                   | ISO 10993-4: <i>In vivo</i> Thrombogenicity (Canine)  | PASS – Non-significant thrombosis |
|                   | ISO 10993-4: Complement Activation C3a & SC5b-9 Assay | PASS – No induction of complement |

**D. Sterilization, Packaging, and Shelf-Life**

The TRYTON Side Branch Stent is sterilized using gamma irradiation in accordance with ISO 11137-1, *Sterilization Of Health Care Products – Radiation – Part 1: Requirements For Development, Validation, And Routine Control Of A Sterilization Process For Medical Devices*. Results obtained from the sterilization validation demonstrate that the TRYTON Side Branch Stent meets a Sterility Assurance Level (SAL) of  $10^{-6}$  when sterilized with a dose of 25 – 35 (-0/+10%) kGy.

Packaging verification testing was conducted to demonstrate that the design of the TRYTON Side Branch Stent packaging is robust and can maintain acceptable integrity and sterility throughout the product’s shelf life. Functional (bench) testing was conducted on aged product to validate that the device and packaging perform within product specifications for a labeled shelf life of two (2) years.

**X. SUMMARY OF PRIMARY CLINICAL STUDIES**

The applicant performed two clinical studies to establish a reasonable assurance of safety and effectiveness of the TRYTON Side Branch Stent for the treatment of native coronary artery bifurcation disease in the US and Europe under IDE # G090167. Data from these clinical studies were the basis for the PMA approval decision. A summary of each clinical study is presented below.

- **TRYTON Pivotal Randomized Controlled Trial (RCT)** - a prospective, multicenter, single blind controlled study. Subjects were randomized 1:1 to the TRYTON Side Branch Stent with main branch approved DES or side branch balloon angioplasty (POBA) and main branch approved DES for treatment of native coronary artery bifurcation disease.
- **TRYTON Extended Access (EA) Confirmatory Study** - a non-randomized, single arm extension of the TRYTON Pivotal RCT. Subjects were implanted with the TRYTON Side Branch Stent with main branch approved DES for treatment of native coronary artery bifurcation disease.

## 1. ***TRYTON PIVOTAL RANDOMIZED CONTROLLED TRIAL (RCT)***

### A. **TRYTON Pivotal RCT: Study Design**

Patients were treated between December 17, 2010 and November 20, 2012. The database for this PMA reflect data collected through January 30, 2015 and included 704 randomized patients in Europe, Israel, and the United States and 65 US roll-in (non-randomized) patients. There were 66 investigational sites.

The TRYTON Pivotal RCT was designed as a prospective, multicenter, randomized, single blind controlled study with subjects randomized in a 1:1 fashion to the TRYTON Side Branch Stent with main branch approved drug-eluting stent (DES) vs. side branch balloon angioplasty (POBA) and main branch approved DES for treatment of native coronary artery bifurcation disease. The first 187 subjects enrolled in each arm were to return for angiographic follow-up at 9 months. The first 64 subjects randomized to the TRYTON cohort and the first 32 subjects randomized to the Control cohort were to return for IVUS follow-up at 9 months at the same time as the angiographic follow-up at designated IVUS sites.

Sixty-five (65) roll-in subjects with use of the investigational device were allowed in the US for those sites that had not previously used the TRYTON Side Branch Stent (maximum 3 subjects per site and maximum of two (2) subjects per investigator). The purpose of these roll-in subjects was to address learning curve factors for sites with no prior experience with either the study device or equivalent devices. These subjects were not part of the angiographic or IVUS subgroup.

The primary objective of the Pivotal RCT was to demonstrate the safety and effectiveness of the TRYTON Side Branch Stent with main branch approved DES compared to side branch balloon angioplasty and main branch approved DES in the treatment of de novo native coronary artery bifurcation lesions with side branch diameter ranging from  $\geq 2.5$  mm to  $\leq 3.5$  mm and main branch diameter ranging from  $\geq 2.5$  mm to  $\leq 4.0$  mm.

#### **Statistical Analysis Plan Summary**

**Primary endpoint:** Target vessel failure [TVF, a composite of cardiac death, target vessel MI, and target vessel revascularization (TVR) involving the main branch or side branch] at 9 months

*Primary analysis population for the primary endpoint:* ITT, consisting of all randomized subjects, analyzed according to their randomly assigned group regardless of whether they received device or not; Lead-in subjects were not included

*Sample size calculation parameters:* The sample size of 704 subjects for the primary endpoint (non-inferiority) was determined as follows:

- 664 subjects randomized 1:1 to DES+TRYTON vs. DES+POBA
- Assumed TVF rate of 13% for DES+POBA and 11% for DES+TRYTON
- 81% power
- Non-inferiority margin (Delta)=5.5%
- 1-sided binomial test of proportions with a significance level of  $\alpha=0.025$ .
- Sample size increased to 704 subjects to account for an expected 6% loss to follow-up

*Hypotheses (non-inferiority test):*

$$H_0: p_{\text{TRY}} \geq p_{\text{POBA}} + \delta$$

$$H_1: p_{\text{TRY}} < p_{\text{POBA}} + \delta$$

Where,  $p_{\text{TRY}}$  and  $p_{\text{POBA}}$  are the 9-month TVF rates in the DES+TRYTON and DES+POBA arms, respectively, and  $\delta$  is the margin for non-inferiority (5.5%).

The primary analysis of the primary endpoint was performed on subjects with at least 270 days of follow-up or an adjudicated event. In addition, sensitivity analyses were performed to assess the impact of missing values from subjects lost to follow-up for the primary endpoint.

Powered secondary angiographic endpoint: Angiographic in-segment percent diameter stenosis (%DS) in the side branch at 9 months

*Sample size calculation parameters:* The sample size of 280 subjects for the angiographic endpoint was determined as follows:

- 318 subjects randomized 1:1 to DES+TRYTON vs. DES+POBA
- 90% power to show a reduction of 8%, from 31% in the DES+POBA arm to 22% in the DES+TRYTON, assuming a standard deviation of 22% in both arms
- Two-sided test with a significance level of  $\alpha=0.05$
- Sample size increased to 374 subjects (187 per arm) to account for an expected 12% loss to follow-up

*Hypotheses (superiority test):*

$$H_0: m_{\text{TRY}} = m_{\text{POBA}}$$

$$H_1: m_{\text{TRY}} \neq m_{\text{POBA}}$$

Where,  $m_{\text{TRY}}$  and  $m_{\text{POBA}}$  are the mean side-branch DS percentages in the DES+TRYTON and DES+POBA arms, respectively.

A Data Safety Monitoring Board (DSMB) reviewed data to ensure patient safety. An independent Clinical Events Committee (CEC) adjudicated endpoint events. There were independent angiographic, IVUS, and ECG core laboratories.

**Table 6: TRYTON Pivotal RCT Design Summary**

| <b>Study Type/Design</b>          | <ul style="list-style-type: none"> <li>• Multi-center study (66 centers), performed in the U.S., Europe and Israel</li> <li>• Prospective</li> <li>• Randomized two-arms</li> <li>• Patients treated with TRYTON Side Branch Stent with main branch approved DES or side branch balloon angioplasty (POBA) and main branch approved DES</li> </ul>   |  |  |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
|-----------------------------------|--|--|--|--|--|-----------|----|-----|-----|-----------|----|-----|-----|-----------|----|-----|-----|------------|----|-----|-----|------------|----|-----|-----|
| <b>Number of Patients</b>         | <p><b>N= 769</b></p> <ul style="list-style-type: none"> <li>• 704 Randomized (355 TRYTON, 349 POBA)</li> <li>• 65 Roll-in (TRYTON)</li> </ul>  |  |  |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>Lesion Criteria</b>            | <i>De novo</i> native coronary artery bifurcation lesions with side branch diameter ranging from $\geq 2.5$ mm to $\leq 3.5$ mm and main branch diameter ranging from $\geq 2.5$ mm to $\leq 4.0$ mm. Lesion length $\leq 28$ mm in the main branch (treatable with a single stent) and $\leq 5$ mm in the side branch.  |  |  |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>Stent Sizes Used in Study</b>  | <table border="1"> <thead> <tr> <th></th> <th><b>Stent Length (mm)</b></th> <th><b>Side Branch Nominal Diameter (mm)</b></th> <th><b>Main Branch Nominal Diameter (mm)</b></th> </tr> </thead> <tbody> <tr> <td><b>D5</b></td> <td>19</td> <td>2.5</td> <td>2.5</td> </tr> <tr> <td><b>D5</b></td> <td>19</td> <td>2.5</td> <td>3.0</td> </tr> <tr> <td><b>D5</b></td> <td>19</td> <td>2.5</td> <td>3.5</td> </tr> <tr> <td><b>D5+</b></td> <td>18</td> <td>3.0</td> <td>3.5</td> </tr> <tr> <td><b>D5+</b></td> <td>18</td> <td>3.5</td> <td>4.0</td> </tr> </tbody> </table> |  | <b>Stent Length (mm)</b>                 | <b>Side Branch Nominal Diameter (mm)</b> | <b>Main Branch Nominal Diameter (mm)</b> | <b>D5</b> | 19 | 2.5 | 2.5 | <b>D5</b> | 19 | 2.5 | 3.0 | <b>D5</b> | 19 | 2.5 | 3.5 | <b>D5+</b> | 18 | 3.0 | 3.5 | <b>D5+</b> | 18 | 3.5 | 4.0 |
|                                   | <b>Stent Length (mm)</b>   | <b>Side Branch Nominal Diameter (mm)</b> | <b>Main Branch Nominal Diameter (mm)</b> |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>D5</b>                         | 19   | 2.5                                      | 2.5                                      |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>D5</b>                         | 19   | 2.5                                      | 3.0                                      |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>D5</b>                         | 19   | 2.5                                      | 3.5                                      |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>D5+</b>                        | 18   | 3.0                                      | 3.5                                      |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>D5+</b>                        | 18   | 3.5                                      | 4.0                                      |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>Anti-Platelet Therapy</b>      | Aspirin indefinitely and clopidogrel, ticlopidine, prasugrel or ticagrelor for a minimum of 12-months post procedure   |  |  |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>Primary Endpoint</b>           | Target Vessel Failure at 9 months: A composite of cardiac death, target vessel MI and Target Vessel Revascularization (in the main or side branch) at 9-months   |  |  |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>Powered Secondary Endpoint</b> | In-segment percent diameter stenosis in the side branch evaluated at 9 months in the angiographic sub-study  |  |  |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>Follow-Up</b>                  | 30 days, 6 months, 9 months, 1 year, 2 years, and 3 years  |  |  |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the Pivotal RCT was limited to patients who met the following inclusion criteria:

Key General Inclusion Criteria:

1. The subject was  $\geq 18$  and  $\leq 90$  years of age;
2. Symptomatic ischemic heart disease (CCS class 1-4, Braunwald Class IB, IC, IIB, IIC, IIIB, IIIC, and/or objective evidence of MI);

3. The intent to treat the side branch of the target bifurcation based on angiographic evaluation;
4. Planned use of one of the following approved and commercially available DES for subject's index procedure: CYPHER, RESOLUTE Family of Stents, PROMUS, PROMUS ELEMENT Family of Stents, or XIENCE Family of Stents.

Key Angiographic Inclusion Criteria:

5. a) Single *de novo* lesion in a bifurcation involving both the main branch and the side branch  
b) The bifurcation: main branch and side branch with a visual diameter stenosis  $\geq 50\%$  (Medina classification 1.1.1; 0.1.1; 1.0.1) by visual assessment
6. Target lesion located in a native coronary artery
7. a) Bifurcation lesion main branch reference vessel diameter  $\geq 2.5$  mm and  $\leq 4.0$  mm, and  
b) Side branch reference vessel diameter  $\geq 2.5$  mm and  $\leq 3.5$  mm by visual estimate
8. a) Bifurcation lesion main branch lesion length  $\leq 28$  mm; and  
b) Side branch lesion length  $\leq 5.0$  mm (the ability to be treated with a single stent for both main and side branches)
9. Target lesion  $\geq 50\%$  and  $< 100\%$  stenosed by visual estimate in both the main branch and side branch
10. Subjects with multi-vessel coronary disease must have had successful treatment of no more than two distinct non-target lesions ( $< 30\%$  diameter stenosis by visual estimate without intra-procedural complication\*) with approved devices during the index procedure and prior to the target lesion treatment, provided non-target lesion(s):
  1. included no more than one lesion in the main branch target vessel distinct from and distal to the target lesion provided this non-index lesion was:
    - a)  $> 10$  mm from the margin of the index lesion;
    - b)  $\geq 2.25$  mm in diameter; and
    - c) met 2, 3, 4, and 5 below
  2. were not  $> 28$  mm (no overlapping stents);
  3. were not 100% occluded at baseline;
  4. were not highly calcified requiring rotoblator use; and
  5. were not bifurcations.

\*In addition to standard definitions of procedural success, the non-target lesion intervention should have been free of inter-procedural event(s) which were likely to lead to CKMB elevation (i.e., no-reflow, flow-limiting dissection, loss of side branch (<2.25 mm)).

11. Subjects with multi-vessel coronary disease were allowed to undergo successful treatment of no more than two distinct non-target lesions (<30% diameter stenosis by visual estimate without intra-procedural complication\*) with approved devices up to 60 days prior to target lesion treatment, provided non-target lesion(s):
  1. included no more than one lesion in the main branch target vessel distinct from and distal to the target lesion provided this non-index lesion was:
    - a) >10 mm from the margin of the index lesion;
    - b)  $\geq 2.25$  mm in diameter, and
    - c) met 2 and 3 below
  2. were not >28 mm (no overlapping stents); and
  3. were not bifurcations.

Randomization and inclusion in the ITT cohort occurred after repeat angiography documenting successful treatment of the non-target lesion(s) and baseline characteristics of the target lesion were assessed. If the non-target lesion intervention was performed fewer than 14 days prior to the index procedure intervention, normal baseline CKMB was to be documented.

Note: If CKMB analysis was not available on-site, subjects were allowed to be included if serial Troponins (6 hours apart) were obtained and demonstrated a downward trend. Baseline and follow-up blood samples were to be obtained for central lab CKMB analysis.

Patients were not permitted to enroll in the Pivotal RCT if they met any of the following exclusion criteria:

Key General Exclusion Criteria:

1. STEMI within 72 hours preceding the index procedure or >72 hours preceding the index procedure and CK and CKMB had not returned to within normal limits\* at the time of procedure
2. Non-STEMI within 7 days prior to index procedure with continued CKMB elevation\*
3. Non-target lesion PCI within 14 days prior to index procedure with continued CKMB elevation\*
4. Impaired renal function (serum creatinine >2.5 mg/dL or 221  $\mu$ mol/l) or on dialysis

5. Platelet count <100,000 cells/mm<sup>3</sup> or >700,000 cells/mm<sup>3</sup> or a WBC <3,000 cells/mm<sup>3</sup>
6. History of bleeding diathesis or coagulopathy or subjects in whom anti-platelet and/or anticoagulant therapy was contraindicated
7. Known hypersensitivity or contraindication to aspirin, heparin, bivalirudin, clopidogrel, ticlopidine, prasugrel, ticagrelor, stainless steel alloy, CoCr alloy, rapamycin, everolimus, zotarolimus, paclitaxel, and/or contrast sensitivity that could not be adequately pre-medicated
8. Cardiogenic shock or cardiac arrhythmias that created hemodynamic instability
9. Surgical or other procedure was planned within the following year which would have required discontinuation of dual antiplatelet therapy

Key Angiographic Exclusion Criteria:

10. Left main CAD (protected and unprotected)
11. Trifurcation lesion
12. Totally occluded target vessel (TIMI flow 0 or 1)
13. Severely calcified target lesion(s)
14. Highly calcified target lesion(s) requiring rotational atherectomy
15. Target lesion had excessive tortuosity unsuitable for stent delivery and deployment
16. Angiographic evidence of thrombus in the target lesion(s)
17. A significant (>50%) stenosis with an RVD of >2.0 mm proximal or distal to the target lesion in either the side branch or main branch that could not be covered by a single stent
18. Diffuse distal disease to target lesion with impaired runoff
19. LVEF ≤30%
20. Planned pre-treatment with devices other than balloon angioplasty. Cutting balloons, AngioSculpt balloons, atherectomy devices, or similar devices were not permitted
21. Lesions located with proximal edge of main branch <10 mm from a non-target large side branch (>2.0mm) causing TRYTON Stent to obstruct large side branch if implanted (for the purposes of this study, septal branches were not included)
22. Lesions with proximal edge of main branch <10 mm from the RCA, LCX or LAD origin causing TRYTON Stent to obstruct parent vessel if implanted.

2. Follow-up Schedule

The Pivotal RCT enrolled patients (randomized and roll-in patients) in both groups were required to receive dual antiplatelet therapy (DAPT) for 12 months and all patients were scheduled to return for clinical follow-up assessments at 30 days, 6 months, 9 months, 1 year, 2 years and 3 years post-index procedure.

Angiographic follow-up at 9 months was obtained in the first 374 randomized patients (N=195 TRYTON cohort, N=181 POBA cohort). Of those enrolled in the angiographic subgroup, the IVUS subgroup included 59 TRYTON patients and 35 POBA patients.

The following procedures and tests were performed prior to the index procedure and postoperatively, as indicated in **Table 7**. Adverse events and complications were recorded at all visits.

The key timepoints are shown below in the tables summarizing safety and effectiveness.

**Table 7: Schedule of Procedures and Tests**

| <b>PROCEDURE / TEST</b>  | <b>Baseline<br/>(within 7 days)</b> | <b>Pre-Procedure<br/>(within 24 hours)</b> | <b>Procedure</b> | <b>Post-Procedure</b> | <b>30 days (± 7 days)</b> | <b>6 months or 180-<br/>days (±30 days)</b> | <b>9 Months or 270-<br/>days (+ 30 days)<sup>8</sup></b> | <b>1 year (± 30 days)</b> | <b>2 year (± 30 days)</b> | <b>3 year (± 30 days)</b> | <b>Unscheduled visits</b> |
|--|-------------------------------------|--|------------------|-----------------------|---------------------------|---|--|---------------------------|---------------------------|---------------------------|---------------------------|
| Subject Medical/Clinical History (Age, Gender, Risk Factors, Angina Status, Cardiac History) | ✓                                   |  |                  |                       |                           |   |  |                           |                           |                           |                           |
| Angina Status  | ✓                                   | ✓  | ✓                | ✓                     | ✓                         | ✓   | ✓  | ✓                         | ✓                         | ✓                         | ✓                         |
| Subject Informed Consent   | ✓                                   |  |                  |                       |                           |   |  |                           |                           |                           |                           |
| General Eligibility Criteria   | ✓                                   |  |                  |                       |                           |   |  |                           |                           |                           |                           |
| Angiographic Eligibility Criteria  |                                     |  | ✓                |                       |                           |   |  |                           |                           |                           |                           |
| <b>Clinical Laboratory Test:</b>   |                                     |  |                  |                       |                           |   |  |                           |                           |                           |                           |
| Pregnancy Test (childbearing potential women only)   | ✓                                   |  |                  |                       |                           |   |  |                           |                           |                           |                           |
| CBC, Creatinine, BUN, blood chemistry  | ✓                                   |  |                  |                       |                           |   |  |                           |                           |                           |                           |
| Lipid profile  | ✓                                   |  |                  |                       |                           |   |  |                           |                           |                           |                           |
| CK, CK-MB, or Troponin*  |                                     | ✓ <sup>2</sup>                             |                  | ✓ <sup>3</sup>        |                           |   |  |                           |                           |                           | ✓ <sup>4</sup>            |

|                                 |  |                |                |                |                |                |                  |                |                |                |                |
|---------------------------------|--|----------------|----------------|----------------|----------------|----------------|------------------|----------------|----------------|----------------|----------------|
| 12-Lead ECG                     |  | ✓ <sup>2</sup> |                | ✓ <sup>1</sup> |                |                | ✓                |                |                |                | ✓ <sup>4</sup> |
| Coronary Angiogram (QCA)        |  |                | ✓              |                |                |                | ✓ <sup>8</sup>   |                |                |                |                |
| Intravascular Ultrasound (IVUS) |  |                |                | ✓ <sup>7</sup> |                |                | ✓ <sup>7,8</sup> |                |                |                |                |
| Left Ventriculography           |  |                | ✓ <sup>5</sup> |                |                |                |                  |                |                |                |                |
| Study Stent information         |  |                | ✓              |                |                |                |                  |                |                |                |                |
| Per Protocol Medications        |  | ✓              | ✓              | ✓ <sup>6</sup> | ✓ <sup>6</sup> | ✓ <sup>6</sup> | ✓ <sup>6</sup>   | ✓ <sup>6</sup> | ✓ <sup>6</sup> | ✓ <sup>6</sup> | ✓ <sup>6</sup> |
| Concomitant Cardiac Meds        |  |                | ✓              | ✓              | ✓              | ✓              | ✓                | ✓              | ✓              | ✓              | ✓              |
| Adverse Events Monitoring       |  |                | ✓              | ✓              | ✓              | ✓              | ✓                | ✓              | ✓              | ✓              | ✓              |

1. Between 12 hours post-procedure and discharge.
2. Within 48 hours pre-procedure will be acceptable except when there is evidence of acute or recent (<72 hours) myocardial infarction or unstable angina prior to the procedure, in which case pre-procedure draws/assessments must be within 24 hours.
3. If CK-MB is elevated  $\geq 2$  times upper limit of normal, serial measurements (minimum of two (2) samples 8 hours apart) of CK and CK-MB must be done until a decline is noted. \*If CK-MB analysis is not available on-site, patients may be included if serial Troponins are obtained and demonstrate a downward trend. Baseline and follow-up blood samples must be obtained for central lab CK-MB analysis
4. CK and CK-MB and ECG should be obtained for all suspected ischemic events. See note 3 regarding process if CK-MB is not available on-site.
5. LVEF at procedure if not documented within 6 months prior.
6. Clopidogrel, ticlopidine, prasugrel or ticagrelor (dose per manufacturer's directions for use) must be given for a minimum of 12 months as well as aspirin 75 to 162 mg daily (or dose per standard hospital practice) to be taken indefinitely.
7. IVUS procedures apply only to those subjects enrolled in the IVUS sub-study
8. For those patients in the angiographic and IVUS sub-groups, the clinical evaluation may be performed at the angiographic follow-up visit but **must occur prior** to angiographic/IVUS evaluation. The investigator must declare the presence of ischemic symptoms prior to the angiographic assessment.

### 3. Clinical Endpoints

The primary endpoint of the Pivotal RCT was Target Vessel Failure [TVF, a composite of cardiac death, target vessel MI, and clinically-indicated target vessel revascularization (in main or side branch)] at 9-month follow-up.

Powered secondary endpoint: Percent diameter stenosis in the side branch at 9 months in the angiographic sub study cohort.

Other secondary endpoints included a range of safety and effectiveness parameters including acute success, the individual components of TVF (cardiac death, target vessel MI, and TVR), all-cause mortality, rate of stent thrombosis and MACE (and the individual elements of MACE) evaluated at 30 days, 6 and 9 months and annually up to 3 years.

Acute success was classified according to the following definitions:

- **Device Success:** Device success was defined as achievement of a final in-stent residual diameter stenosis of <30% (by quantitative coronary angiography [QCA]), using the assigned device only and without a device malfunction.
- **Lesion Success:** Lesion success was defined as achievement of a final in-stent residual diameter stenosis of <50% (by QCA) using any percutaneous method.
- **Procedure Success:** Procedure success was defined as achievement of a final in-stent diameter stenosis of <50% (by QCA) using the assigned device and with any adjunctive devices, without the occurrence of cardiac death, Q-wave or non-Q-wave MI, or repeat revascularization of the target lesion during the hospital stay.

#### **B. TRYTON Pivotal RCT: Accountability of PMA Cohort**

At the time of database lock, of 704 patients enrolled in the PMA study, 92% (645/704) patients are available for analysis at the 2 year post-operative visit.

All 704 randomized subjects (355 TRYTON subjects and 349 POBA subjects) comprised the ITT population, which was the primary analysis set in this trial. Of the 355 subjects randomized to receive the TRYTON Side Branch Stent in conjunction with main branch approved DES, 14 subjects did not receive the TRYTON Stent for the following reasons: stent dislodgment from balloon before reaching the target lesion (n=6); failure of the coronary wire to cross the target lesion (n=2); failure of the stent to cross the target lesion (n=2); side branch not suitable for stenting (occlusive dissection with wire and side branch deemed too small for stenting) (n=2); and randomization error (n=2).

Of the 349 subjects randomized to receive side branch balloon angioplasty in conjunction with main branch approved DES, two (2) subjects (0.6%) received the TRYTON Stent and 34 received a non-study stent post POBA treatment in the side branch.

**Table 8** details all deaths, withdrawals and study exits of ITT subjects by treatment group and follow-up through 2 years.

**Table 8: ITT Subject Accountability at Each Follow-Up Through Two Years**

|   | 1 Month Follow-Up |      | 6 Months Follow-Up |      | 9 Months Follow-Up |      | 1 Year Follow-Up |      | 2 Years Follow-Up |      | TOTAL   |
|---|-------------------|------|--------------------|------|--------------------|------|------------------|------|-------------------|------|---------|
|   | TRYTON            | POBA | TRYTON             | POBA | TRYTON             | POBA | TRYTON           | POBA | TRYTON            | POBA | OVERALL |
| Completed Follow-Up Visit                       | 353               | 343  | 341                | 337  | 342                | 330  | 336              | 329  | 331               | 324  |         |
| Subjects Eligible for Follow-up                 | 355               | 347* | 350                | 342  | 349                | 340  | 343              | 335  | 338               | 332  |         |
| <b><i>Ineligible for Follow-up: Reasons</i></b> |                   |      |                    |      |                    |      |                  |      |                   |      |         |
| Death   | 4                 | 2    | 0                  | 2    | 2                  | 1    | 4                | 1    | 3                 | 2    | 21      |
| Withdrew Consent                                | 1                 | 3*   | 1                  | 0    | 2                  | 2    | 0                | 0    | 0                 | 0    | 11      |
| Exited for Other Reasons                        | 0                 | 0    | 0                  | 0    | 2                  | 2    | 1                | 2    | 0                 | 0    | 7       |

\*Two (2) withdrew consent prior to 30 days

**C. TRYTON Pivotal RCT: Study Population Demographics and Baseline Parameters**

The demographics of the study population were typical for a coronary stent study performed in the US (Table 9).

**Table 9: Baseline Patient Demographics and Clinical Characteristics (Intent-to-Treat)**

|                        | TRYTON<br>(N=355 Patients) | POBA<br>(N=349 Patients) |
|------------------------|----------------------------|--------------------------|
| <b>Age</b>             |                            |                          |
| Mean±SD (N)            | 64.50±10.61 (355)          | 64.58±9.40 (349)         |
| <b>Number of Men</b>   | 71.8% (255/355)            | 73.4% (256/349)          |
| <b>Ethnicity</b>       |                            |                          |
| Hispanic or Latino     | 4.9% (17/347)              | 6.5% (22/341)            |
| Not Hispanic or Latino | 95.1% (330/347)            | 93.5% (319/341)          |

|   | <b>TRYTON<br/>(N=355 Patients)</b> | <b>POBA<br/>(N=349 Patients)</b> |
|---|------------------------------------|----------------------------------|
| <b>Race</b>   |                                    |                                  |
| American Indian or Alaska Native                      | 0.0% (0/355)                       | 0.3% (1/349)                     |
| Asian   | 1.1% (4/355)                       | 1.7% (6/349)                     |
| Black or African American                             | 1.7% (6/355)                       | 4.3% (15/349)                    |
| Native Hawaiian or Other Pacific Islander             | 0.0% (0/355)                       | 0.6% (2/349)                     |
| White   | 95.8% (340/355)                    | 89.1% (311/349)                  |
| Other   | 1.4% (5/355)                       | 4.0% (14/349)                    |
| <b>Risk Factors</b>                                   |                                    |                                  |
| MI  | 30.0% (105/350)                    | 37.8% (131/347)                  |
| PCI   | 38.0% (135/355)                    | 41.8% (146/349)                  |
| CABG  | 2.5% (9/353)                       | 2.0% (7/349)                     |
| TIA   | 2.8% (10/351)                      | 2.3% (8/346)                     |
| CVA   | 2.3% (8/350)                       | 3.8% (13/343)                    |
| CHF   | 1.7% (6/355)                       | 0.9% (3/349)                     |
| Diabetes Mellitus                                     | 23.9% (85/355)                     | 28.1% (98/349)                   |
| Hypertension  | 73.2% (260/355)                    | 73.6% (256/348)                  |
| Hypercholesterolemia                                  | 74.1% (260/351)                    | 77.3% (266/344)                  |
| Renal Insufficiency/failure or on dialysis            | 0.0% (0/355)                       | 0.3% (1/348)                     |
| Premature CAD in a first degree relative              | 36.9% (114/309)                    | 32.5% (101/311)                  |
| <b>Smoking Status</b>                                 |                                    |                                  |
| Current   | 17.5% (62/355)                     | 15.2% (53/348)                   |
| Former  | 34.6% (123/355)                    | 35.9% (125/348)                  |
| <b>Atrial Fibrillation</b>                            | 10.7% (38/354)                     | 6.9% (24/348)                    |
| <b>Assessment of Anginal Status</b>                   |                                    |                                  |
| <b>Intervention prompted by myocardial infarction</b> | 10.7% (38/355)                     | 9.7% (34/349)                    |
| <b>Angina Type</b>                                    |                                    |                                  |
| Stable  | 73.8% (262/355)                    | 74.8% (261/349)                  |
| Unstable  | 20.0% (71/355)                     | 19.8% (69/349)                   |
| Silent Ischemia                                       | 5.6% (20/355)                      | 5.2% (18/349)                    |
| No Angina   | 0.6% (2/355)                       | 0.3% (1/349)                     |
| <b>Canadian Cardiovascular Society Class</b>          |                                    |                                  |
| I   | 13.6% (34/250)                     | 16.7% (41/245)                   |
| II  | 57.6% (144/250)                    | 55.1% (135/245)                  |
| III   | 25.2% (63/250)                     | 22.9% (56/245)                   |
| IV  | 3.6% (9/250)                       | 5.3% (13/245)                    |

|   | <b>TRYTON<br/>(N=355 Patients)</b> | <b>POBA<br/>(N=349 Patients)</b> |
|---|------------------------------------|----------------------------------|
| <b>Positive functional test of ischemia</b> | 62.7% (126/201)                    | 63.2% (117/185)                  |
| <b>LVEF (%)</b>                             |                                    |                                  |
| Mean±SD (N)                                 | 57.66±9.61 (334)                   | 57.48±9.87 (330)                 |
| Range (min,max)                             | (32.00,86.00)                      | (31.00,87.00)                    |
| Median                                      | 60.00                              | 60.00                            |

When assessed by the angiographic core laboratory, true bifurcation lesions (Medina Classification 1.1.1; 0.1.1; or 1.0.1) were present at randomization in 89.8% (318/354) of the lesions in the TRYTON group and 86.2% (301/349) of the lesions in the POBA group (Table 10).

**Table 10: Medina Classification**

| <b>Medina Classification</b>                     | <b>Site Reported</b> |                    | <b>Core Lab</b>    |                    |
|--|----------------------|--------------------|--------------------|--------------------|
|  | <b>POBA</b>          | <b>TRYTON</b>      | <b>POBA</b>        | <b>TRYTON</b>      |
| 1,1,1  | 68.7%<br>(239/348)   | 73.2%<br>(260/355) | 42.1%<br>(147/349) | 49.2%<br>(174/354) |
| 1,1,0*   | 0.0%<br>(0/348)      | 0.0%<br>(0/355)    | 4.9%<br>(17/349)   | 2.3%<br>(8/354)    |
| 1,0,1  | 12.4%<br>(43/348)    | 11.5%<br>(41/355)  | 16.0%<br>(56/349)  | 15.8%<br>(56/354)  |
| 0,1,1  | 18.7%<br>(65/348)    | 14.6%<br>(52/355)  | 28.1%<br>(98/349)  | 24.9%<br>(88/354)  |
| 1,0,0*   | 0.0%<br>(0/348)      | 0.3%<br>(1/355)    | 2.6%<br>(9/349)    | 1.4%<br>(5/354)    |
| 0,1,0*   | 0.0%<br>(0/348)      | 0.0%<br>(0/355)    | 4.0%<br>(14/349)   | 2.8%<br>(10/354)   |
| 0,0,1*   | 0.3%<br>(1/348)      | 0.3%<br>(1/355)    | 2.3%<br>(8/349)    | 3.4%<br>(12/354)   |
| 0,0,0*   | 0.0%<br>(0/348)      | 0.0%<br>(0/355)    | 0.0%<br>(0/349)    | 0.3%<br>(1/354)    |
| 1,1,0 OR 1,0,0 OR<br>0,1,0 OR 0,0,1 OR<br>0,0,0* | 0.0%<br>(0/348)      | 0.0%<br>(0/355)    | 0.0%<br>(0/349)    | 0.0%<br>(0/354)    |

\*Protocol deviation

**Table 11** details the baseline lesion characteristics of ITT patients.

**Table 11: Baseline Lesion Characteristics**

|   | <b>Tryton<br/>(N = 355)</b>  | <b>POBA<br/>(N = 349)</b>    | <b>P-value</b> |
|---|------------------------------|------------------------------|----------------|
| Mean Main Branch Lesion Length $\pm$ SD<br>(mm) (N) | 16.8 ( $\pm$ 7.3)<br>(354)   | 16.0 ( $\pm$ 6.8)<br>(348)   | 0.109          |
| Mean Side Branch RVD $\pm$ SD<br>(mm) (N)           | 2.25 ( $\pm$ 0.30)<br>(354)  | 2.21 ( $\pm$ 0.33)<br>(348)  | 0.093          |
| Mean Side Branch Lesion Length $\pm$ SD<br>(mm) (N) | 4.84 ( $\pm$ 1.56)<br>(354)  | 4.43 ( $\pm$ 1.12)<br>(348)  | <.001          |
| Mean Minimum Lesion Diameter $\pm$ SD<br>(mm) (N)   | 0.95 ( $\pm$ 0.34)<br>(354)  | 1.02 ( $\pm$ 0.34)<br>(347)  | 0.009          |
| Mean Percent Diameter Stenosis $\pm$ SD<br>(mm) (N) | 58.0% ( $\pm$ 14.3)<br>(354) | 54.0% ( $\pm$ 14.5)<br>(347) | <.001          |

**D. TRYTON Pivotal RCT: Safety and Effectiveness Results**

The analysis of safety and effectiveness was based on the intent-to-treat cohort of 704 patients available for the 9-month and 2-year evaluations and the Intended Population cohort (QCA-assessed side branch diameter of  $\geq$ 2.25 mm) post hoc analysis of 289 patients for the 9-month and 2-year evaluations. The key safety and effectiveness outcomes for this study are presented below in **Tables 12 to 27** and **Figures 2 to 4**. Serious adverse events are reported in **Table 28**.

Acute Success

As presented in **Table 12**, device, lesion and procedure success were achieved more frequently in the TRYTON arm compared to the POBA arm:

Device success: Attainment of <30% residual stenosis within the side branch using the assigned device only and without a device malfunction, was achieved in 90.8% (316/348) of the lesions in the TRYTON group compared to 39.0% (135/346) of the lesions in the POBA group.

Lesion success: Attainment of <50% residual stenosis using any percutaneous method, was achieved in all (100%; 337/337) of the lesions in the TRYTON group compared to 88.1% (304/345) of the lesions in the POBA group.

Procedure success: Lesion success without the occurrence of in-hospital MACE, was achieved in 80.3% (281/350) of the subjects in the TRYTON group compared to 70.5% (102/346) of the subjects in the POBA group.

**Table 12: Acute Success – Intent-to-Treat Analysis Set**

|  | <b>TRYTON</b> | <b>POBA</b> |
|--|---------------|-------------|
| Lesions evaluable for Lesion Success     | 337           | 345         |
| Lesions evaluable for Device Success     | 348           | 346         |
| Patients evaluable for Procedure Success | 350           | 346         |

|                              | <b>TRYTON</b>    | <b>POBA</b>     |
|------------------------------|------------------|-----------------|
| <b>Lesion<sup>1</sup></b>    |                  |                 |
| Success                      | 337              | 304             |
| % Success                    | 100.0% (337/337) | 88.1% (304/345) |
| Failure                      | 0                | 41              |
| % Failure                    | 0.0% (0/337)     | 11.9% (41/345)  |
| <b>Device<sup>2</sup></b>    |                  |                 |
| Success                      | 316              | 135             |
| % Success                    | 90.8% (316/348)  | 39.0% (135/346) |
| Failure                      | 32               | 211             |
| % Failure                    | 9.2% (32/348)    | 61.0% (211/346) |
| <b>Procedure<sup>3</sup></b> |                  |                 |
| Success                      | 281              | 244             |
| % Success                    | 80.3% (281/350)  | 70.5% (244/346) |
| Failure                      | 69               | 102             |
| % Failure                    | 19.7% (69/350)   | 29.5% (102/346) |

<sup>1</sup>Lesion success and failure are presented per lesion.

<sup>2</sup>Device success and failure are presented per lesion.

<sup>3</sup>Procedure success and failure are presented per patient.

#### Primary Endpoint: ITT Subjects

The primary endpoint (TVF at 9-months) was performed on all ITT subjects who had at least 270 days of follow-up or who experienced a primary endpoint event within 270 days (i.e., available cases). The 9-month TVF rate was 16.7% (58/348) in the TRYTON group compared to 12.6% (43/341) in the POBA group. The difference in 9-month TVF rates between the groups was 4.1% with two-sided 95% CI of [-1.5%, 9.6%]. Since the upper bound of this CI is higher than 5.5% (the delta for non-inferiority), the null hypothesis is not rejected and the TRYTON Stent is not considered non-inferior to POBA (non-inferiority not met) with regards to 9-month TVF (**Table 13**).

**Table 13: Primary Endpoint at 9 Months**

|                         | <b>TRYTON<br/>(N=355<br/>Patients)</b> | <b>POBA<br/>(N=349<br/>Patients)</b> | <b>Difference<br/>[95% CI]</b>     | <b>Delta</b> |
|-------------------------|--|--------------------------------------|------------------------------------|--------------|
| <b>TVF to 270 Days</b>  |  |                                      |                                    |              |
| Intent-to-Treat         |  |                                      |                                    |              |
| <b>Available Cases*</b> | <b>16.7% (58/348)</b>                  | <b>12.6% (43/341)</b>                | <b>4.1%</b><br><b>[-1.5%,9.6%]</b> | <b>5.50%</b> |
| Worst Case              | 18.3% (65/355)                         | 12.3% (43/349)                       | 6.0%<br>[0.4%,11.6%]               |              |
| Multiple Imputation     | 17.1%                                  | 13.1%                                | 4.0%<br>[-2.0%,10.0%]              |              |
| Kaplan-Meier Estimates  | 16.4%                                  | 12.4%                                | 4.0%<br>[-1.2%,9.2%]               |              |
| Per-Protocol            |  |                                      |                                    |              |
| <b>Available Cases*</b> | <b>16.0% (53/332)</b>                  | <b>12.4% (40/323)</b>                | <b>3.6%</b><br><b>[-2.1%,9.2%]</b> | <b>5.50%</b> |
| Worse Case              | 17.7% (60/339)                         | 12.1% (40/330)                       | 5.6%<br>[-0.1%,11.3%]              |              |
| Multiple Imputation     | 16.8%                                  | 13.4%                                | 3.4%<br>[-2.7%,9.5%]               |              |
| Kaplan-Meier Estimates  | 15.7%                                  | 12.2%                                | 3.5%<br>[-1.7%,8.8%]               |              |

\*Available cases include subjects with at least 270 days of follow-up or subjects who experienced the primary endpoint within 270 days.

Secondary Safety and Effectiveness Endpoints: ITT Subjects

**Tables 14 and 15** show the secondary safety and effectiveness endpoints among ITT subjects evaluated in the trial. Data are presented at two time points: 9 months (**Table 14**) and 2 years (the latest endpoint that all patients had reached at time of data lock, **Table 15**).

**Table 14: Secondary Safety and Effectiveness Endpoints to 270 days (9 Months) – Intent-to-Treat Analysis Set**

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=355<br/>Patients)</b> | <b>POBA<br/>(N=349<br/>Patients)</b> |
|--|--|--------------------------------------|
| <b>Target Lesion Failure</b> (TLF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Lesion Revascularization) | 16.4% (57/348)                         | 12.0% (41/341)                       |
| <b>Stent Thrombosis</b> (ARC Definite, Probable)   | 0.6% (2/347)                           | 0.3% (1/340)                         |

| <b>Event<sup>1</sup></b>  | <b>TRYTON<br/>(N=355<br/>Patients)</b> | <b>POBA<br/>(N=349<br/>Patients)</b> |
|---|--|--------------------------------------|
| Main Vessel   | 0.6% (2/347)                           | 0.3% (1/340)                         |
| Side Branch   | 0.6% (2/347)                           | 0.0% (0/339)                         |
| <b>MACE</b> (Death, MI, Emergent CABG, Ischemia Driven or Clinically Indicated Target Lesion Revascularization) | 17.9% (63/352)                         | 13.1% (45/344)                       |
| <b>Death</b>  | 1.1% (4/351)                           | 1.2% (4/343)                         |
| Cardiac   | 0.0% (0/347)                           | 0.0% (0/339)                         |
| Vascular  | 0.3% (1/348)                           | 0.0% (0/339)                         |
| Non-Cardiovascular  | 0.9% (3/350)                           | 1.2% (4/343)                         |
| Non-Cardiac   | 1.1% (4/351)                           | 1.2% (4/343)                         |
| <b>Modified ARC MI<sup>2</sup></b>  | 14.9% (52/348)                         | 11.1% (38/342)                       |
| Peri-Procedural PCI   | 12.9% (45/348)                         | 10.0% (34/340)                       |
| Peri-CABG   | 0.3% (1/347)                           | 0.0% (0/339)                         |
| Spontaneous   | 2.0% (7/347)                           | 1.5% (5/341)                         |
| Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)                                      | 0.6% (2/347)                           | 0.3% (1/339)                         |
| Non-Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)                                  | 14.4% (50/348)                         | 10.5% (36/342)                       |
| <b>Target Vessel MI<sup>2</sup></b>   | 14.4% (50/348)                         | 10.6% (36/341)                       |
| Q-wave MI   | 0.6% (2/347)                           | 0.3% (1/339)                         |
| Non-Q-wave MI   | 13.8% (48/348)                         | 10.0% (34/341)                       |
| <b>Non-Target Vessel MI<sup>2</sup></b>   | 0.6% (2/347)                           | 0.6% (2/340)                         |
| Q-wave MI   | 0.0% (0/347)                           | 0.0% (0/339)                         |
| Non-Q-wave MI   | 0.6% (2/347)                           | 0.6% (2/340)                         |
| Emergent CABG   | 0.0% (0/347)                           | 0.3% (1/339)                         |
| <b>Target Lesion Revascularization (TLR)</b>  | 4.9% (17/347)                          | 3.2% (11/340)                        |
| <b>Ischemia Driven or Clinically Indicated Target Lesion Revascularization (TLR)<sup>3</sup></b>                | 4.0% (14/347)                          | 2.9% (10/340)                        |
| Main Vessel   | 3.5% (12/347)                          | 2.4% (8/340)                         |
| Side Branch   | 2.6% (9/347)                           | 1.5% (5/340)                         |
| CABG  | 0.3% (1/347)                           | 0.3% (1/339)                         |
| Main Vessel   | 0.3% (1/347)                           | 0.3% (1/339)                         |
| Side Branch   | 0.3% (1/347)                           | 0.3% (1/339)                         |
| PCI   | 3.7% (13/347)                          | 2.6% (9/340)                         |
| Main Vessel   | 3.2% (11/347)                          | 2.1% (7/340)                         |
| Side Branch   | 2.3% (8/347)                           | 1.2% (4/340)                         |

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=355<br/>Patients)</b> | <b>POBA<br/>(N=349<br/>Patients)</b> |
|--|--|--------------------------------------|
| Non-Ischemia Driven TLR  | 0.9% (3/347)                           | 0.6% (2/339)                         |
| <b>Target Vessel Revascularization (TVR)</b>   | 5.2% (18/347)                          | 3.8% (13/340)                        |
| Ischemia Driven or Clinically Indicated Target Vessel Revascularization (TVR) <sup>3</sup> | 4.3% (15/347)                          | 3.5% (12/340)                        |
| Main Vessel  | 3.7% (13/347)                          | 2.9% (10/340)                        |
| Side Branch  | 2.6% (9/347)                           | 1.5% (5/340)                         |
| CABG   | 0.3% (1/347)                           | 0.6% (2/339)                         |
| Main Vessel  | 0.3% (1/347)                           | 0.6% (2/339)                         |
| Side Branch  | 0.3% (1/347)                           | 0.3% (1/339)                         |
| PCI  | 4.0% (14/347)                          | 2.9% (10/340)                        |
| Main Vessel  | 3.5% (12/347)                          | 2.4% (8/340)                         |
| Side Branch  | 2.3% (8/347)                           | 1.2% (4/340)                         |
| Non-Ischemia Driven Target Vessel Revascularization (TVR)                                  | 1.2% (4/347)                           | 0.6% (2/339)                         |
| Non-Target Vessel Revascularization  | 4.0% (14/347)                          | 3.5% (12/339)                        |

<sup>1</sup>Events in this table have been adjudicated by the CEC.

Denominators reflect the number of patients with an adjudicated event of follow-up through 270 days.

<sup>2</sup>If the relationship to the target vessel could not be determined, the MI was considered a target vessel MI. ECGs were not available in every MI subject to determine whether a Q-wave or non-Q-wave MI occurred.

Myocardial infarction was defined using a modified version of the Joint ESC/ACC/AHA/WHF Task Force for the Redefinition of Myocardial Infarction and Academic Research Consortium criteria.

<sup>3</sup>Ischemia-Driven Target Lesion Revascularization (ID-TLR) and Ischemia-Driven Target Vessel Revascularization (ID-TVR) are defined as revascularization at the target lesion/vessel associated with any of the following: (1) Positive functional ischemia study; (2) Ischemic symptoms and angiographic MLD stenosis  $\geq 50\%$  by core laboratory QCA; (3) Revascularization of a target lesion with diameter stenosis  $\geq 70\%$  by core laboratory.

Clinically-Indicated Revascularization (TLR/TVR) is defined as a revascularization of the target lesion/vessel when angiography at follow-up shows a percent diameter stenosis  $\geq 50\%$  (Angiographic Core Laboratory QCA assessment) and if one of the following occurs: (1) A positive history of recurrent angina pectoris, presumably related to the target vessel; (2) Objective signs of ischemia at rest (ECG changes) or during exercise test (or equivalent), presumably related to the target vessel; (3) Abnormal results of any invasive functional diagnostic test; (4) A TLR or TVR with a diameter stenosis  $\geq 70\%$  even in the absence of the above-mentioned ischemic signs or symptoms.

<sup>4</sup>MI: Myocardial Infarction; ARC: Academic Research Consortium; MACE: Major Adverse Cardiac Event; CABG: Coronary Artery Bypass Graft; PCI: Percutaneous Coronary Intervention; TLR: Target Lesion Revascularization; TVR: Target Vessel Revascularization; ESC/ACC/AHA/WHF: European Society of Cardiology/ American College of Cardiology/American Heart Association/World Heart Federation.

**Table 15: Secondary Safety and Effectiveness Endpoints to 730 days (2 years) – Intent-to-Treat Analysis Set**

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=355<br/>Patients)</b> | <b>POBA<br/>(N=349<br/>Patients)</b> |
|--|--|--------------------------------------|
| <b>Target Vessel Failure</b> (TVF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Vessel Revascularization) | 21.1% (71/337)                         | 16.9% (56/331)                       |
| <b>Target Lesion Failure</b> (TLF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Lesion Revascularization) | 19.6% (66/336)                         | 15.1% (50/331)                       |
| <b>Stent Thrombosis</b> (ARC Definite, Probable)   | 0.6% (2/333)                           | 0.6% (2/327)                         |
| Main Vessel  | 0.6% (2/333)                           | 0.6% (2/327)                         |
| Side Branch  | 0.6% (2/333)                           | 0.0% (0/325)                         |
| <b>MACE</b> (Death, MI, Emergent CABG, Ischemia Driven or Clinically Indicated Target Lesion Revascularization)  | 22.9% (79/345)                         | 17.1% (57/334)                       |
| <b>Death</b>   | 2.9% (10/343)                          | 1.8% (6/330)                         |
| Cardiac  | 0.3% (1/334)                           | 0.3% (1/326)                         |
| Vascular   | 0.9% (3/336)                           | 0.0% (0/325)                         |
| Non-Cardiovascular   | 1.8% (6/339)                           | 1.5% (5/329)                         |
| Non-Cardiac  | 2.6% (9/342)                           | 1.5% (5/329)                         |
| <b>Modified ARC MI<sup>2</sup></b>   | 17.6% (59/336)                         | 12.7% (42/331)                       |
| Peri-Procedural PCI  | 13.8% (46/334)                         | 10.4% (34/328)                       |
| Peri-CABG  | 0.6% (2/334)                           | 0.0% (0/325)                         |
| Spontaneous  | 3.9% (13/334)                          | 3.4% (11/328)                        |
| Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)   | 0.9% (3/334)                           | 0.9% (3/326)                         |
| Non-Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)   | 16.4% (55/335)                         | 11.5% (38/330)                       |
| <b>Target Vessel MI<sup>2</sup></b>  | 15.5% (52/336)                         | 11.5% (38/330)                       |
| Q-wave MI  | 0.9% (3/334)                           | 0.9% (3/326)                         |
| Non-Q-wave MI  | 14.6% (49/335)                         | 10.3% (34/329)                       |
| Non-Target Vessel MI <sup>2</sup>  | 2.1% (7/333)                           | 1.5% (5/326)                         |

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=355<br/>Patients)</b> | <b>POBA<br/>(N=349<br/>Patients)</b> |
|--|--|--------------------------------------|
| Q-wave MI  | 0.0% (0/333)                           | 0.0% (0/325)                         |
| Non-Q-wave MI  | 1.8% (6/333)                           | 1.5% (5/326)                         |
| Emergent CABG  | 0.0% (0/333)                           | 0.3% (1/326)                         |
| <b>Target Lesion Revascularization (TLR)</b>   | 8.7% (29/335)                          | 6.4% (21/329)                        |
| <b>Ischemia Driven or Clinically Indicated<br/>Target Lesion Revascularization (TLR)<sup>3</sup></b> | 6.9% (23/334)                          | 5.2% (17/328)                        |
| Main Vessel  | 5.1% (17/334)                          | 4.3% (14/328)                        |
| Side Branch  | 4.8% (16/334)                          | 2.1% (7/327)                         |
| CABG   | 0.9% (3/334)                           | 0.6% (2/326)                         |
| Main Vessel  | 0.9% (3/334)                           | 0.6% (2/326)                         |
| Side Branch  | 0.6% (2/334)                           | 0.6% (2/326)                         |
| PCI  | 6.3% (21/333)                          | 4.9% (16/327)                        |
| Main Vessel  | 4.5% (15/333)                          | 4.0% (13/327)                        |
| Side Branch  | 4.2% (14/333)                          | 1.5% (5/326)                         |
| Non-Ischemia Driven TLR  | 2.4% (8/334)                           | 1.5% (5/326)                         |
| <b>Target Vessel Revascularization (TVR)</b>   | 10.4% (35/337)                         | 8.5% (28/329)                        |
| <b>Ischemia Driven or Clinically Indicated Target<br/>Vessel Revascularization (TVR)<sup>3</sup></b> | 8.6% (29/336)                          | 7.3% (24/328)                        |
| Main Vessel  | 6.8% (23/336)                          | 6.4% (21/328)                        |
| Side Branch  | 4.8% (16/334)                          | 2.1% (7/327)                         |
| CABG   | 1.2% (4/334)                           | 0.9% (3/326)                         |
| Main Vessel  | 1.2% (4/334)                           | 0.9% (3/326)                         |
| Side Branch  | 0.6% (2/334)                           | 0.6% (2/326)                         |
| PCI  | 7.8% (26/335)                          | 6.7% (22/327)                        |
| Main Vessel  | 6.0% (20/335)                          | 5.8% (19/327)                        |
| Side Branch  | 4.2% (14/333)                          | 1.5% (5/326)                         |
| Non-Ischemia Driven Target Vessel<br>Revascularization (TVR)   | 3.0% (10/334)                          | 1.5% (5/326)                         |
| Non-Target Vessel Revascularization  | 10.4% (35/335)                         | 8.0% (26/325)                        |

<sup>1</sup>Events in this table have been adjudicated by the CEC.

Denominators reflect the number of patients with an adjudicated event or follow-up through 730 days.

<sup>2</sup>If the relationship to the target vessel could not be determined, the MI was considered a target vessel MI. ECGs were not available in every MI subject to determine whether a Q-wave or non-Q-wave MI occurred.

Myocardial infarction was defined using a modified version of the Joint ESC/ACC/AHA/WHF Task Force for the Redefinition of Myocardial Infarction and Academic Research Consortium criteria.

<sup>3</sup>Refer to Footnote 3 in Table 14

**Powered Secondary Endpoint: ITT Subjects**

The powered secondary angiographic endpoint (side branch in-segment %DS as determined by QCA at 9 months) was analyzed in the angiographic cohort using available data from qualified angiograms. The side branch in-segment %DS at 9 months was significantly lower in the TRYTON group compared to POBA: 31.57% ±22.91 vs. 38.63% ±16.16, P=0.002 (**Table 16**). The secondary superiority endpoint was met.

**Table 16: Powered Secondary Angiographic Endpoint at 9 Months**

|  | <b>TRYTON<br/>(N=158 Patients)</b> | <b>POBA<br/>(N=168 Patients)</b> | <b>Difference<br/>[95% CI]</b> | <b>P-<br/>value</b> |
|--|------------------------------------|----------------------------------|--------------------------------|---------------------|
| <b>In-Segment Side-Branch Percent Diameter Stenosis at 9 months*</b> |                                    |                                  |                                |                     |
| Intent-to-Treat  |                                    |                                  |                                |                     |
| Mean±SD (N)  | 31.57±22.91 (155)                  | 38.63±16.16 (168)                | -7.06<br>[-11.42,-2.71]        | 0.002               |
| Range (min, max)   | (2.30,100.00)                      | (4.59,76.84)                     |                                |                     |
| Median   | 28.90                              | 39.95                            |                                |                     |
| Per-Protocol   |                                    |                                  |                                |                     |
| Mean±SD (N)  | 31.75±22.96 (153)                  | 38.36±16.05 (163)                | -6.61<br>[-11.00,-2.22]        | 0.003               |
| Range (min, max)   | (2.30,100.00)                      | (4.59,76.84)                     |                                |                     |
| Median   | 28.90                              | 39.81                            |                                |                     |

\*Analysis of the powered secondary angiographic endpoint is based on subjects with a qualified 9 month angiogram (Angiographic Analysis Set). In calculating the %DS, distal normal was used for the calculation of RVD in the side branch.

The in-segment binary restenosis rates at 9 months are shown in **Table 17**.

**Table 17: In-Segment Binary Restenosis Rate at 9 Months**

|  | <b>Intent-to-Treat Patients</b> |                         |
|--|---------------------------------|-------------------------|
|  | <b>TRYTON<br/>(N=158)</b>       | <b>POBA<br/>(N=168)</b> |
| <b>In-Segment Binary Restenosis Rate</b> | 22.6% (35/155)                  | 26.8% (45/168)          |

**Primary Endpoint: Intended Population (Side Branch RVD ≥2.25 mm) Post Hoc Analysis**

Analysis of the patient population enrolled in the study revealed that only 41% of the study population (146 TRYTON subjects and 143 POBA subjects) had side branch diameters meeting the expected size for treatment with the TRYTON Stent per the angiographic inclusion criteria (i.e., side branch diameter ≥2.25 mm per QCA, equivalent to ~≥2.5 mm per visual estimate). When the primary endpoint was analyzed among ITT subjects with side branch RVD ≥2.25 mm by QCA (the Intended Population), the 9-

month TVF rate was 10.5% (15/143) in the TRYTON group compared to 14.8% (21/142) in the POBA group. The difference in 9-month TVF rates between the groups was -4.3% with two-sided 95% CI of [-12.7%, 4.1%] (**Table 18**). The upper bound of the CI is lower than 5.5% (the delta for non-inferiority), indicating TRYTON is non-inferior to POBA with regards to the primary endpoint of 9-month TVF in the side branch RVD  $\geq 2.25$  mm subgroup. However, given the post-hoc nature of this analysis, a formal conclusion of non-inferiority cannot be made for this subgroup.

**Table 18: Primary Endpoint at 9 Months –Side Branch RVD  $\geq 2.25$  mm**

|                         | <b>TRYTON<br/>(N=146<br/>Patients)</b> | <b>POBA<br/>(N=143<br/>Patients)</b> | <b>Difference<br/>[95% CI]</b> | <b>Delta</b> |
|-------------------------|--|--------------------------------------|--------------------------------|--------------|
| <b>TVF to 270 Days</b>  |  |                                      |                                |              |
| Intent-to-Treat         |  |                                      |                                |              |
| <b>Available Cases*</b> | <b>10.5% (15/143)</b>                  | <b>14.8% (21/142)</b>                | <b>-4.3%<br/>[-12.7%,4.1%]</b> | <b>5.50%</b> |
| Worst Case              | 12.3% (18/146)                         | 14.7% (21/143)                       | -2.4%<br>[-10.9%,6.2%]         |              |
| Multiple Imputation     | 10.3%                                  | 14.8%                                | -4.6%<br>[-12.2%,3.1%]         |              |
| Kaplan-Meier Estimates  | 10.3%                                  | 14.7%                                | -4.4%<br>[-12.0%,3.2%]         |              |
| Per-Protocol            |  |                                      |                                |              |
| Available Cases*        | 9.5% (13/137)                          | 14.7% (20/136)                       | -5.2%<br>[-13.7%,3.2%]         | 5.50%        |
| Worse Case              | 11.4% (16/140)                         | 14.6% (20/137)                       | -3.2%<br>[-11.8%,5.5%]         |              |
| Multiple Imputation     | 9.3%                                   | 14.7%                                | -5.5%<br>[-13.1%,2.2%]         |              |
| Kaplan-Meier Estimates  | 9.3%                                   | 14.6%                                | -5.3%<br>[-12.9%,2.3%]         |              |

\*Available cases include subjects with at least 270 days of follow-up or subjects who experienced the primary endpoint within 270 days.

Secondary Safety and Effectiveness Endpoints: Intended Population (Side Branch RVD  $\geq 2.25$  mm) Post Hoc Analysis

**Tables 19** and **20** show the secondary safety and effectiveness endpoints among ITT subjects with side branch RVD  $\geq 2.25$  mm by QCA. This was a post-hoc analysis. Data are presented at 9 months (**Table 23**) and 2 years (**Table 24**).

**Table 19: Secondary Safety and Effectiveness Endpoints to 270 days (9 Months) – Intent-to-Treat Analysis Set - Side Branch RVD  $\geq$ 2.25 mm**

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=146<br/>Patients)</b> | <b>POBA<br/>(N=143<br/>Patients)</b> |
|--|--|--------------------------------------|
| <b>Target Lesion Failure</b> (TLF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Lesion Revascularization) | 10.5% (15/143)                         | 13.4% (19/142)                       |
| <b>Stent Thrombosis</b> (ARC Definite, Probable)   | 0.7% (1/143)                           | 0.0% (0/142)                         |
| Main Vessel  | 0.7% (1/143)                           | 0.0% (0/142)                         |
| Side Branch  | 0.7% (1/143)                           | 0.0% (0/142)                         |
| <b>MACE</b> (Death, MI, Emergent CABG, Ischemia Driven or Clinically Indicated Target Lesion Revascularization)  | 11.7% (17/145)                         | 14.7% (21/143)                       |
| <b>Death</b>   | 1.4% (2/145)                           | 0.7% (1/143)                         |
| Cardiac  | 0.0% (0/143)                           | 0.0% (0/142)                         |
| Vascular   | 0.7% (1/144)                           | 0.0% (0/142)                         |
| Non-Cardiovascular   | 0.7% (1/144)                           | 0.7% (1/143)                         |
| Non-Cardiac  | 1.4% (2/145)                           | 0.7% (1/143)                         |
| <b>Modified ARC MI<sup>2</sup></b>   | 8.4% (12/143)                          | 12.0% (17/142)                       |
| Peri-Procedural PCI  | 7.7% (11/143)                          | 11.3% (16/142)                       |
| Peri-CABG  | 0.7% (1/143)                           | 0.0% (0/142)                         |
| Spontaneous  | 0.0% (0/143)                           | 0.7% (1/142)                         |
| Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)   | 0.7% (1/143)                           | 0.0% (0/142)                         |
| Non-Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)   | 7.7% (11/143)                          | 12.0% (17/142)                       |
| <b>Target Vessel MI<sup>2</sup></b>  | 8.4% (12/143)                          | 11.3% (16/142)                       |
| Q-wave MI  | 0.7% (1/143)                           | 0.0% (0/142)                         |
| Non-Q-wave MI  | 7.7% (11/143)                          | 11.3% (16/142)                       |
| <b>Non-Target Vessel MI<sup>2</sup></b>  | 0.0% (0/143)                           | 0.7% (1/142)                         |
| Q-wave MI  | 0.0% (0/143)                           | 0.0% (0/142)                         |
| Non-Q-wave MI  | 0.0% (0/143)                           | 0.7% (1/142)                         |
| Emergent CABG  | 0.0% (0/143)                           | 0.0% (0/142)                         |
| <b>Target Lesion Revascularization (TLR)</b>   | 3.5% (5/143)                           | 2.8% (4/142)                         |
| <b>Ischemia Driven or Clinically Indicated Target Lesion Revascularization (TLR)<sup>3</sup></b>   | 3.5% (5/143)                           | 2.8% (4/142)                         |
| Main Vessel  | 2.8% (4/143)                           | 2.1% (3/142)                         |
| Side Branch  | 2.8% (4/143)                           | 1.4% (2/142)                         |
| CABG   | 0.7% (1/143)                           | 0.0% (0/142)                         |

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=146<br/>Patients)</b> | <b>POBA<br/>(N=143<br/>Patients)</b> |
|--|--|--------------------------------------|
| Main Vessel  | 0.7% (1/143)                           | 0.0% (0/142)                         |
| Side Branch  | 0.7% (1/143)                           | 0.0% (0/142)                         |
| PCI  | 2.8% (4/143)                           | 2.8% (4/142)                         |
| Main Vessel  | 2.1% (3/143)                           | 2.1% (3/142)                         |
| Side Branch  | 2.1% (3/143)                           | 1.4% (2/142)                         |
| Non-Ischemia Driven TLR  | 0.0% (0/143)                           | 0.0% (0/142)                         |
| <b>Target Vessel Revascularization (TVR)</b>   | 3.5% (5/143)                           | 4.2% (6/142)                         |
| Ischemia Driven or Clinically Indicated Target Vessel Revascularization (TVR) <sup>3</sup> | 3.5% (5/143)                           | 4.2% (6/142)                         |
| Main Vessel  | 2.8% (4/143)                           | 3.5% (5/142)                         |
| Side Branch  | 2.8% (4/143)                           | 1.4% (2/142)                         |
| CABG   | 0.7% (1/143)                           | 0.7% (1/142)                         |
| Main Vessel  | 0.7% (1/143)                           | 0.7% (1/142)                         |
| Side Branch  | 0.7% (1/143)                           | 0.0% (0/142)                         |
| PCI  | 2.8% (4/143)                           | 3.5% (5/142)                         |
| Main Vessel  | 2.1% (3/143)                           | 2.8% (4/142)                         |
| Side Branch  | 2.1% (3/143)                           | 1.4% (2/142)                         |
| Non-Ischemia Driven Target Vessel Revascularization (TVR)                                  | 0.0% (0/143)                           | 0.0% (0/142)                         |
| Non-Target Vessel Revascularization  | 2.8% (4/143)                           | 2.1% (3/142)                         |

<sup>1</sup>Events in this table have been adjudicated by the CEC.

Denominators reflect the number of patients with an adjudicated event or follow-up through 270 days.

<sup>2</sup>If the relationship to the target vessel could not be determined, the MI was considered a target vessel MI.

Myocardial infarction was defined using a modified version of the Joint ESC/ACC/AHA/WHF Task Force for the Redefinition of Myocardial Infarction and Academic Research Consortium criteria.

<sup>3</sup>Refer to Footnote 3 in Table 14

**Table 20: Secondary Safety and Effectiveness Endpoints to 730 days (2 Years) – Intent-to-Treat Analysis Set - Side Branch RVD  $\geq$ 2.25 mm**

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=146<br/>Patients)</b> | <b>POBA<br/>(N=143<br/>Patients)</b> |
|--|--|--------------------------------------|
| <b>Target Vessel Failure</b> (TVF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Vessel Revascularization) | 14.4% (20/139)                         | 18.7% (26/139)                       |

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=146<br/>Patients)</b> | <b>POBA<br/>(N=143<br/>Patients)</b> |
|--|--|--------------------------------------|
| <b>Target Lesion Failure</b> (TLF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Lesion Revascularization) | 12.9% (18/139)                         | 15.8% (22/139)                       |
| <b>Stent Thrombosis</b> (ARC Definite, Probable)   | 0.7% (1/137)                           | 0.0% (0/139)                         |
| Main Vessel  | 0.7% (1/137)                           | 0.0% (0/139)                         |
| Side Branch  | 0.7% (1/137)                           | 0.0% (0/139)                         |
| <b>MACE</b> (Death, MI, Emergent CABG, Ischemia Driven or Clinically Indicated Target Lesion Revascularization)  | 16.8% (24/143)                         | 18.6% (26/140)                       |
| <b>Death</b>   | 3.5% (5/142)                           | 1.4% (2/140)                         |
| Cardiac  | 0.7% (1/138)                           | 0.0% (0/139)                         |
| Vascular   | 0.7% (1/138)                           | 0.0% (0/139)                         |
| Non-Cardiovascular   | 2.1% (3/140)                           | 1.4% (2/140)                         |
| Non-Cardiac  | 2.8% (4/141)                           | 1.4% (2/140)                         |
| <b>Modified ARC MI<sup>2</sup></b>   | 11.5% (16/139)                         | 12.9% (18/139)                       |
| Peri-Procedural PCI  | 8.0% (11/137)                          | 11.5% (16/139)                       |
| Peri-CABG  | 1.4% (2/138)                           | 0.0% (0/139)                         |
| Spontaneous  | 2.2% (3/138)                           | 1.4% (2/139)                         |
| Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)   | 1.4% (2/138)                           | 0.0% (0/139)                         |
| Non-Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)   | 9.4% (13/138)                          | 12.9% (18/139)                       |
| <b>Target Vessel MI<sup>2</sup></b>  | 9.4% (13/139)                          | 11.5% (16/139)                       |
| Q-wave MI  | 1.4% (2/138)                           | 0.0% (0/139)                         |
| Non-Q-wave MI  | 8.0% (11/138)                          | 11.5% (16/139)                       |
| Non-Target Vessel MI <sup>2</sup>  | 2.2% (3/137)                           | 1.4% (2/139)                         |
| Q-wave MI  | 0.0% (0/137)                           | 0.0% (0/139)                         |
| Non-Q-wave MI  | 1.5% (2/137)                           | 1.4% (2/139)                         |
| Emergent CABG  | 0.0% (0/137)                           | 0.0% (0/139)                         |
| <b>Target Lesion Revascularization (TLR)</b>   | 5.8% (8/138)                           | 5.8% (8/139)                         |
| <b>Ischemia Driven or Clinically Indicated Target Lesion Revascularization (TLR)<sup>3</sup></b>   | 5.1% (7/138)                           | 5.0% (7/139)                         |
| Main Vessel  | 2.9% (4/138)                           | 3.6% (5/139)                         |
| Side Branch  | 4.3% (6/138)                           | 2.2% (3/139)                         |
| CABG   | 0.7% (1/138)                           | 0.0% (0/139)                         |
| Main Vessel  | 0.7% (1/138)                           | 0.0% (0/139)                         |
| Side Branch  | 0.7% (1/138)                           | 0.0% (0/139)                         |

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=146<br/>Patients)</b> | <b>POBA<br/>(N=143<br/>Patients)</b> |
|--|--|--------------------------------------|
| PCI  | 4.4% (6/137)                           | 5.0% (7/139)                         |
| Main Vessel  | 2.2% (3/137)                           | 3.6% (5/139)                         |
| Side Branch  | 3.6% (5/137)                           | 2.2% (3/139)                         |
| Non-Ischemia Driven TLR  | 1.5% (2/137)                           | 0.7% (1/139)                         |
| <b>Target Vessel Revascularization (TVR)</b>   | <b>7.9% (11/139)</b>                   | <b>8.6% (12/139)</b>                 |
| Ischemia Driven or Clinically Indicated Target Vessel Revascularization (TVR) <sup>3</sup> | 7.2% (10/139)                          | 7.9% (11/139)                        |
| Main Vessel  | 5.0% (7/139)                           | 6.5% (9/139)                         |
| Side Branch  | 4.3% (6/138)                           | 2.2% (3/139)                         |
| CABG   | 1.4% (2/138)                           | 0.7% (1/139)                         |
| Main Vessel  | 1.4% (2/138)                           | 0.7% (1/139)                         |
| Side Branch  | 0.7% (1/138)                           | 0.0% (0/139)                         |
| PCI  | 5.8% (8/138)                           | 7.2% (10/139)                        |
| Main Vessel  | 3.6% (5/138)                           | 5.8% (8/139)                         |
| Side Branch  | 3.6% (5/137)                           | 2.2% (3/139)                         |
| Non-Ischemia Driven Target Vessel Revascularization (TVR)                                  | 2.2% (3/137)                           | 0.7% (1/139)                         |
| Non-Target Vessel Revascularization  | 10.1% (14/138)                         | 5.8% (8/139)                         |

<sup>1</sup>Events in this table have been adjudicated by the CEC.

Denominators reflect the number of patients with an adjudicated event or follow-up through 730 days.

<sup>2</sup>If the relationship to the target vessel could not be determined, the MI was considered a target vessel MI. ECGs were not available in every MI subject to determine whether a Q-wave or non-Q-wave MI occurred.

Myocardial infarction was defined using a modified version of the Joint ESC/ACC/AHA/WHF Task Force for the Redefinition of Myocardial Infarction and Academic Research Consortium criteria.

<sup>3</sup>Refer to Footnote 3 in Table 14

**Powered Secondary Endpoint: Intended Population (Side Branch RVD  $\geq$ 2.25 mm) Post Hoc Analysis**

Among ITT subjects with side branch RVD  $\geq$ 2.25 mm by QCA and qualified 9-month angiograms, the side branch in-segment %DS at 9 months was significantly lower in the TRYTON group compared to the POBA group: 30.43%  $\pm$ 22.53 vs. 40.61%  $\pm$ 17.20, P = 0.004 (**Table 21**). This was a post-hoc analysis.

**Table 21: Powered Secondary Angiographic Endpoint at 9 Months – Side Branch RVD  $\geq$  2.25 mm**

|  | <b>TRYTON<br/>(N=64 Patients)</b> | <b>POBA<br/>(N=81 Patients)</b> | <b>Difference<br/>[95% CI]</b> | <b>P-<br/>value</b> |
|--|-----------------------------------|---------------------------------|--------------------------------|---------------------|
| <b>In-Segment Side-Branch Percent Diameter Stenosis at 9 months*</b> |                                   |                                 |                                |                     |
| Intent-to-Treat  |                                   |                                 |                                |                     |
| Mean $\pm$ SD (N)  | 30.43 $\pm$ 22.53 (63)            | 40.61 $\pm$ 17.20 (81)          | -10.18<br>[-16.89,-3.47]       | 0.004               |
| Per-Protocol   |                                   |                                 |                                |                     |
| Mean $\pm$ SD (N)  | 30.85 $\pm$ 22.67 (61)            | 40.40 $\pm$ 17.21 (80)          | -9.56<br>[-16.38,-2.73]        | 0.007               |

\*Analysis of the powered secondary angiographic endpoint is based on subjects with a qualified 9 month angiogram (Angiographic Analysis Set). In calculating the %DS, distal normal was used for the calculation of RVD in the side branch.

The in-segment binary restenosis rates at 9 months for ITT subjects with side branch RVD  $\geq$ 2.25 mm by QCA are shown in **Table 22**.

**Table 22: In-Segment Binary Restenosis Rate at 9 Months – Side Branch RVD  $\geq$  2.25 mm**

|  | <b>Intended Population<br/>Side Branch RVD <math>\geq</math>2.25 mm</b> |                        |
|--|---|------------------------|
|  | <b>TRYTON<br/>(N=64)</b>  | <b>POBA<br/>(N=81)</b> |
| <b>In-Segment Binary Restenosis Rate</b> | 22.2% (14/63)   | 32.1% (26/81)          |

Primary Endpoint: Unintended Population (Side Branch RVD  $<$ 2.25 mm) Post Hoc Analysis

When the primary endpoint was analyzed among ITT subjects with side branch RVD  $<$ 2.25 mm by QCA, the 9-month TVF rate was 21.1% (43/204) in the TRYTON group compared to 10.6% (21/198) in the POBA group. The difference in 9-month TVF rates between the groups was 10.5% with two-sided 95% CI of [2.9%, 18.0%] (**Table 23**).

**Table 23: Primary Endpoint at 9 Months – Side Branch RVD  $<$  2.25 mm**

|                         | <b>TRYTON<br/>(N=208<br/>Patients)</b> | <b>POBA<br/>(N=205<br/>Patients)</b> | <b>Difference<br/>[95% CI]</b> | <b>Delta</b> |
|-------------------------|--|--------------------------------------|--------------------------------|--------------|
| <b>TVF to 270 Days</b>  |  |                                      |                                |              |
| Intent-to-Treat         |  |                                      |                                |              |
| <b>Available Cases*</b> | <b>21.1% (43/204)</b>                  | <b>10.6% (21/198)</b>                | <b>10.5%<br/>[2.9%,18.0%]</b>  | <b>5.50%</b> |
| Worst Case              | 22.6% (47/208)                         | 10.2% (21/205)                       | 12.4%<br>[4.8%,19.9%]          |              |

|                        | <b>TRYTON<br/>(N=208<br/>Patients)</b> | <b>POBA<br/>(N=205<br/>Patients)</b> | <b>Difference<br/>[95% CI]</b> | <b>Delta</b> |
|------------------------|--|--------------------------------------|--------------------------------|--------------|
| Multiple Imputation    | 21.5%                                  | 11.5%                                | 10.0%<br>[2.1%,17.9%]          |              |
| Kaplan-Meier Estimates | 20.7%                                  | 10.3%                                | 10.5%<br>[3.5%,17.4%]          |              |
| <b>Per-Protocol</b>    |  |                                      |                                |              |
| Available Cases*       | 20.5% (40/195)                         | 10.7% (20/187)                       | 9.8%<br>[2.1%,17.5%]           | 5.50%        |
| Worse Case             | 22.1% (44/199)                         | 10.4% (20/193)                       | 11.7%<br>[4.0%,19.5%]          |              |
| Multiple Imputation    | 20.8%                                  | 11.4%                                | 9.4%<br>[1.5%,17.3%]           |              |
| Kaplan-Meier Estimates | 20.2%                                  | 10.4%                                | 9.8%<br>[2.7%,16.8%]           |              |

\*Available cases include subjects with at least 270 days of follow-up or an adjudicated event within 270 days.

Secondary Safety and Effectiveness Endpoints: Unintended Population (Side Branch RVD <2.25 mm) Post Hoc Analysis

**Tables 24** and **25** show the secondary safety and effectiveness endpoints among ITT subjects with side branch RVD <2.25 mm by QCA. Data are presented at 9 months (**Table 23**) and 2 years (**Table 24**).

**Table 24: Secondary Safety and Effectiveness Endpoints to 270 days (9 Months) – Intent-to-Treat Analysis Set – Side Branch RVD < 2.25 mm**

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=208<br/>Patients)</b> | <b>POBA<br/>(N=205<br/>Patients)</b> |
|--|--|--------------------------------------|
| <b>Target Lesion Failure</b> (TLF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Lesion Revascularization) | 20.6% (42/204)                         | 10.6% (21/198)                       |
| <b>Stent Thrombosis</b> (ARC Definite, Probable)   | 0.5% (1/203)                           | 0.5% (1/198)                         |
| Main Vessel  | 0.5% (1/203)                           | 0.5% (1/198)                         |
| Side Branch  | 0.5% (1/203)                           | 0.0% (0/197)                         |
| <b>MACE</b> (Death, MI, Emergent CABG, Ischemia Driven or Clinically Indicated Target Lesion Revascularization)  | 22.3% (46/206)                         | 11.5% (23/200)                       |
| <b>Death</b>   | 1.0% (2/205)                           | 1.5% (3/200)                         |
| Cardiac  | 0.0% (0/203)                           | 0.0% (0/197)                         |
| Vascular   | 0.0% (0/203)                           | 0.0% (0/197)                         |

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=208<br/>Patients)</b> | <b>POBA<br/>(N=205<br/>Patients)</b> |
|--|--|--------------------------------------|
| Non-Cardiovascular   | 1.0% (2/205)                           | 1.5% (3/200)                         |
| Non-Cardiac  | 1.0% (2/205)                           | 1.5% (3/200)                         |
| <b>Modified ARC MI<sup>2</sup></b>   | 19.6% (40/204)                         | 10.1% (20/199)                       |
| Peri-Procedural PCI  | 16.7% (34/204)                         | 8.6% (17/197)                        |
| Peri-CABG  | 0.0% (0/203)                           | 0.0% (0/197)                         |
| Spontaneous  | 3.4% (7/203)                           | 2.0% (4/199)                         |
| Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)                       | 0.5% (1/203)                           | 0.5% (1/197)                         |
| Non-Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)                   | 19.1% (39/204)                         | 9.0% (18/199)                        |
| <b>Target Vessel MI<sup>2</sup></b>  | 18.6% (38/204)                         | 9.6% (19/198)                        |
| Q-wave MI  | 0.5% (1/203)                           | 0.5% (1/197)                         |
| Non-Q-wave MI  | 18.1% (37/204)                         | 8.6% (17/198)                        |
| Non-Target Vessel MI <sup>2</sup>  | 1.0% (2/203)                           | 0.5% (1/198)                         |
| Q-wave MI  | 0.0% (0/203)                           | 0.0% (0/197)                         |
| Non-Q-wave MI  | 1.0% (2/203)                           | 0.5% (1/198)                         |
| Emergent CABG  | 0.0% (0/203)                           | 0.5% (1/197)                         |
| <b>Target Lesion Revascularization (TLR)</b>   | 5.9% (12/203)                          | 3.5% (7/198)                         |
| <b>Ischemia Driven or Clinically Indicated Target Lesion Revascularization (TLR)<sup>3</sup></b> | 4.4% (9/203)                           | 3.0% (6/198)                         |
| Main Vessel  | 3.9% (8/203)                           | 2.5% (5/198)                         |
| Side Branch  | 2.5% (5/203)                           | 1.5% (3/198)                         |
| CABG   | 0.0% (0/203)                           | 0.5% (1/197)                         |
| Main Vessel  | 0.0% (0/203)                           | 0.5% (1/197)                         |
| Side Branch  | 0.0% (0/203)                           | 0.5% (1/197)                         |
| PCI  | 4.4% (9/203)                           | 2.5% (5/198)                         |
| Main Vessel  | 3.9% (8/203)                           | 2.0% (4/198)                         |
| Side Branch  | 2.5% (5/203)                           | 1.0% (2/198)                         |
| Non-Ischemia Driven TLR  | 1.5% (3/203)                           | 1.0% (2/197)                         |
| <b>Target Vessel Revascularization (TVR)</b>   | 6.4% (13/203)                          | 3.5% (7/198)                         |
| <b>Ischemia Driven or Clinically Indicated Target Vessel Revascularization (TVR)<sup>3</sup></b> | 4.9% (10/203)                          | 3.0% (6/198)                         |
| Main Vessel  | 4.4% (9/203)                           | 2.5% (5/198)                         |
| Side Branch  | 2.5% (5/203)                           | 1.5% (3/198)                         |
| CABG   | 0.0% (0/203)                           | 0.5% (1/197)                         |
| Main Vessel  | 0.0% (0/203)                           | 0.5% (1/197)                         |
| Side Branch  | 0.0% (0/203)                           | 0.5% (1/197)                         |

| <b>Event<sup>1</sup></b>                                     | <b>TRYTON<br/>(N=208<br/>Patients)</b> | <b>POBA<br/>(N=205<br/>Patients)</b> |
|--|--|--------------------------------------|
| PCI  | 4.9% (10/203)                          | 2.5% (5/198)                         |
| Main Vessel  | 4.4% (9/203)                           | 2.0% (4/198)                         |
| Side Branch  | 2.5% (5/203)                           | 1.0% (2/198)                         |
| Non-Ischemia Driven Target Vessel<br>Revascularization (TVR) | 2.0% (4/203)                           | 1.0% (2/197)                         |
| Non-Target Vessel Revascularization                          | 4.9% (10/203)                          | 4.6% (9/197)                         |

<sup>1</sup>Events in this table have been adjudicated by the CEC.

Denominators reflect the number of patients with an adjudicated event or follow-up through 270 days.

<sup>2</sup>If the relationship to the target vessel could not be determined, the MI was considered a target vessel MI. ECGs were not available in every MI subject to determine whether a Q-wave or non-Q-wave MI occurred.

Myocardial infarction was defined using a modified version of the Joint ESC/ACC/AHA/WHF Task Force for the Redefinition of Myocardial Infarction and Academic Research Consortium criteria.

<sup>3</sup>Refer to Footnote 3 in Table 14

**Table 25: Secondary Safety and Effectiveness Endpoints to 730 days (2 years) – Intent-to-Treat Analysis Set – Side Branch RVD < 2.25 mm**

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=208<br/>Patients)</b> | <b>POBA<br/>(N=205<br/>Patients)</b> |
|--|--|--------------------------------------|
| <b>Target Vessel Failure</b> (TVF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Vessel Revascularization) | 25.8% (51/198)                         | 15.2% (29/191)                       |
| <b>Target Lesion Failure</b> (TLF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Lesion Revascularization) | 24.4% (48/197)                         | 14.1% (27/191)                       |
| <b>Stent Thrombosis</b> (ARC Definite, Probable)   | 0.5% (1/196)                           | 1.1% (2/188)                         |
| Main Vessel  | 0.5% (1/196)                           | 1.1% (2/188)                         |
| Side Branch  | 0.5% (1/196)                           | 0.0% (0/186)                         |
| <b>MACE</b> (Death, MI, Emergent CABG, Ischemia Driven or Clinically Indicated Target Lesion Revascularization)  | 27.2% (55/202)                         | 15.5% (30/193)                       |
| <b>Death</b>   | 2.5% (5/201)                           | 2.1% (4/190)                         |
| Cardiac  | 0.0% (0/196)                           | 0.5% (1/187)                         |
| Vascular   | 1.0% (2/198)                           | 0.0% (0/186)                         |
| Non-Cardiovascular   | 1.5% (3/199)                           | 1.6% (3/189)                         |

| <b>Event<sup>1</sup></b>   | <b>TRYTON<br/>(N=208<br/>Patients)</b> | <b>POBA<br/>(N=205<br/>Patients)</b> |
|--|--|--------------------------------------|
| Non-Cardiac  | 2.5% (5/201)                           | 1.6% (3/189)                         |
| <b>Modified ARC MI<sup>2</sup></b>   | 21.8% (43/197)                         | 12.0% (23/191)                       |
| Peri-Procedural PCI  | 17.8% (35/197)                         | 9.0% (17/188)                        |
| Peri-CABG  | 0.0% (0/196)                           | 0.0% (0/186)                         |
| Spontaneous  | 5.1% (10/196)                          | 4.8% (9/189)                         |
| Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)                       | 0.5% (1/196)                           | 1.6% (3/187)                         |
| Non-Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)                   | 21.3% (42/197)                         | 10.0% (19/190)                       |
| <b>Target Vessel MI<sup>2</sup></b>  | 19.8% (39/197)                         | 11.1% (21/190)                       |
| Q-wave MI  | 0.5% (1/196)                           | 1.6% (3/187)                         |
| Non-Q-wave MI  | 19.3% (38/197)                         | 9.0% (17/189)                        |
| <b>Non-Target Vessel MI<sup>2</sup></b>  | 2.0% (4/196)                           | 1.6% (3/187)                         |
| Q-wave MI  | 0.0% (0/196)                           | 0.0% (0/186)                         |
| Non-Q-wave MI  | 2.0% (4/196)                           | 1.6% (3/187)                         |
| Emergent CABG  | 0.0% (0/196)                           | 0.5% (1/187)                         |
| <b>Target Lesion Revascularization (TLR)</b>   | 10.7% (21/197)                         | 6.8% (13/190)                        |
| <b>Ischemia Driven or Clinically Indicated Target Lesion Revascularization (TLR)<sup>3</sup></b> | 8.2% (16/196)                          | 5.3% (10/189)                        |
| Main Vessel  | 6.6% (13/196)                          | 4.8% (9/189)                         |
| Side Branch  | 5.1% (10/196)                          | 2.1% (4/188)                         |
| CABG   | 1.0% (2/196)                           | 1.1% (2/187)                         |
| Main Vessel  | 1.0% (2/196)                           | 1.1% (2/187)                         |
| Side Branch  | 0.5% (1/196)                           | 1.1% (2/187)                         |
| PCI  | 7.7% (15/196)                          | 4.8% (9/188)                         |
| Main Vessel  | 6.1% (12/196)                          | 4.3% (8/188)                         |
| Side Branch  | 4.6% (9/196)                           | 1.1% (2/187)                         |
| Non-Ischemia Driven TLR  | 3.0% (6/197)                           | 2.1% (4/187)                         |
| <b>Target Vessel Revascularization (TVR)</b>   | 12.1% (24/198)                         | 8.4% (16/190)                        |
| <b>Ischemia Driven or Clinically Indicated Target Vessel Revascularization (TVR)<sup>3</sup></b> | 9.6% (19/197)                          | 6.9% (13/189)                        |
| Main Vessel  | 8.1% (16/197)                          | 6.3% (12/189)                        |
| Side Branch  | 5.1% (10/196)                          | 2.1% (4/188)                         |
| CABG   | 1.0% (2/196)                           | 1.1% (2/187)                         |
| Main Vessel  | 1.0% (2/196)                           | 1.1% (2/187)                         |
| Side Branch  | 0.5% (1/196)                           | 1.1% (2/187)                         |
| PCI  | 9.1% (18/197)                          | 6.4% (12/188)                        |

| <b>Event<sup>1</sup></b>                                     | <b>TRYTON<br/>(N=208<br/>Patients)</b> | <b>POBA<br/>(N=205<br/>Patients)</b> |
|--|--|--------------------------------------|
| Main Vessel  | 7.6% (15/197)                          | 5.9% (11/188)                        |
| Side Branch  | 4.6% (9/196)                           | 1.1% (2/187)                         |
| Non-Ischemia Driven Target Vessel<br>Revascularization (TVR) | 3.6% (7/197)                           | 2.1% (4/187)                         |
| Non-Target Vessel Revascularization                          | 10.7% (21/197)                         | 9.7% (18/186)                        |

<sup>1</sup>Events in this table have been adjudicated by the CEC.

Denominators reflect the number of patients with an adjudicated event or follow-up through 730 days.

<sup>2</sup>If the relationship to the target vessel could not be determined, the MI was considered a target vessel MI. ECGs were not available in every MI subject to determine whether a Q-wave or non-Q-wave MI occurred.

Myocardial infarction was defined using a modified version of the Joint ESC/ACC/AHA/WHF Task Force for the Redefinition of Myocardial Infarction and Academic Research Consortium criteria.

<sup>3</sup>Refer to Footnote 3 in Table 14

Powered Secondary Endpoint: Unintended Population (Side Branch RVD <2.25 mm)  
Post Hoc Analysis

Among ITT subjects with side branch RVD <2.25 mm by QCA and qualified 9-month angiograms, the side branch in-segment %DS at 9 months in the TRYTON group compared to the POBA group was: 32.35% ±23.26 vs. 36.79%±14.99, P = 0.129 (**Table 26**).

**Table 26: Powered Secondary Angiographic Endpoint at 9 Months –  
Side Branch RVD < 2.25 mm**

|  | <b>TRYTON<br/>(N=94 Patients)</b> | <b>POBA<br/>(N=87 Patients)</b> | <b>Difference<br/>[95% CI]</b> | <b>P-<br/>value</b> |
|--|-----------------------------------|---------------------------------|--------------------------------|---------------------|
| <b>In-Segment Side-Branch Percent Diameter Stenosis at 9 months*</b> |                                   |                                 |                                |                     |
| Intent-to-Treat  |                                   |                                 |                                |                     |
| Mean±SD (N)  | 32.35±23.26 (92)                  | 36.79±14.99 (87)                | -4.44<br>[-10.15,1.26]         | 0.129               |
| Per-Protocol   |                                   |                                 |                                |                     |
| Mean±SD (N)  | 32.35±23.26 (92)                  | 36.39±14.68 (83)                | -4.04<br>[-9.75,1.66]          | 0.167               |

\*Analysis of the powered secondary angiographic endpoint is based on subjects with a qualified 9 month angiogram (Angiographic Analysis Set). In calculating the %DS, distal normal was used for the calculation of RVD in the side branch.

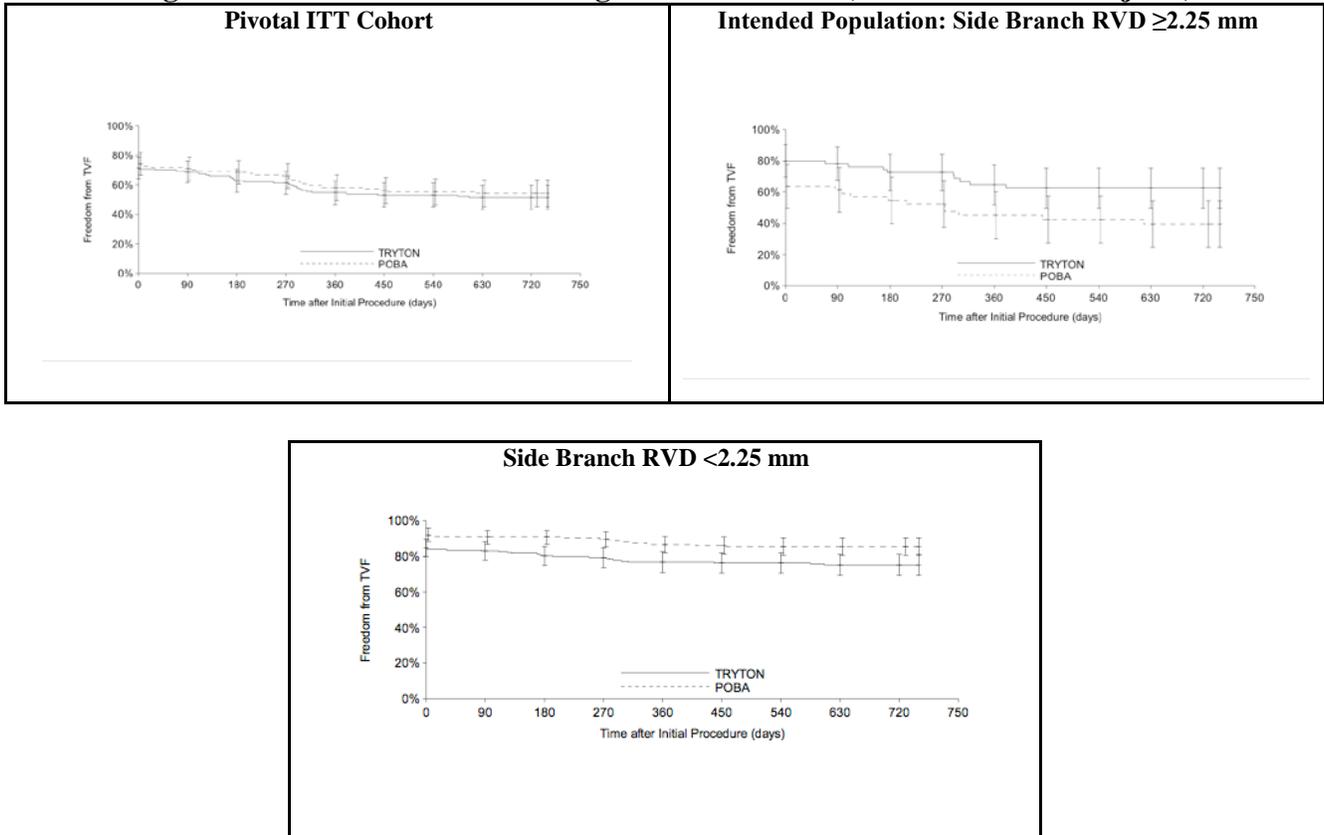
The in-segment binary restenosis rates at 9 months for ITT subjects with side branch RVD <2.25 mm by QCA are shown in **Table 27**.

**Table 27: In-Segment Binary Restenosis Rate at 9 Months – Side Branch RVD < 2.25 mm**

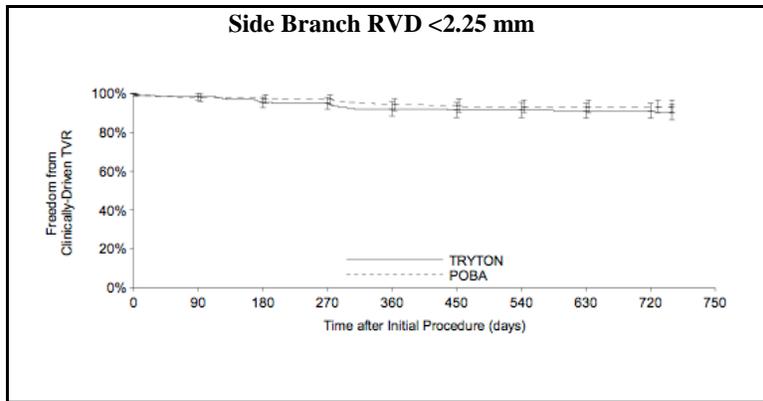
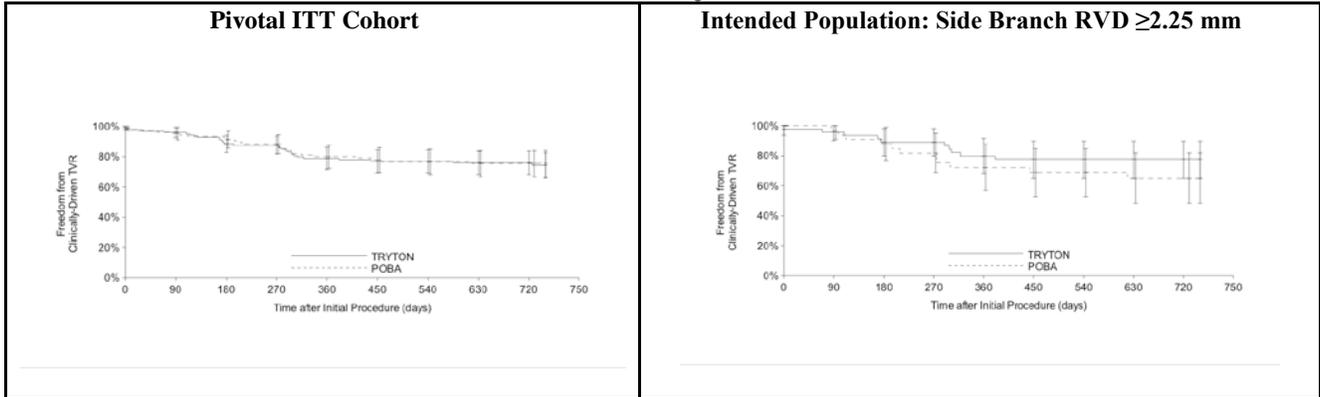
|  | Side Branch RVD <2.25 mm |                |
|--|--------------------------|----------------|
|  | TRYTON<br>(N=94)         | POBA<br>(N=87) |
| <b>In-Segment Binary Restenosis Rate</b> | 22.8% (22/92)            | 21.8% (19/87)  |

Kaplan-Meier survival curves for up to two years are shown in **Figures 2** through **4** for ITT subjects, ITT subjects with QCA-assessed side branch RVD  $\geq 2.25$  mm, and ITT subjects with QCA-assessed side branch RVD < 2.25 mm.

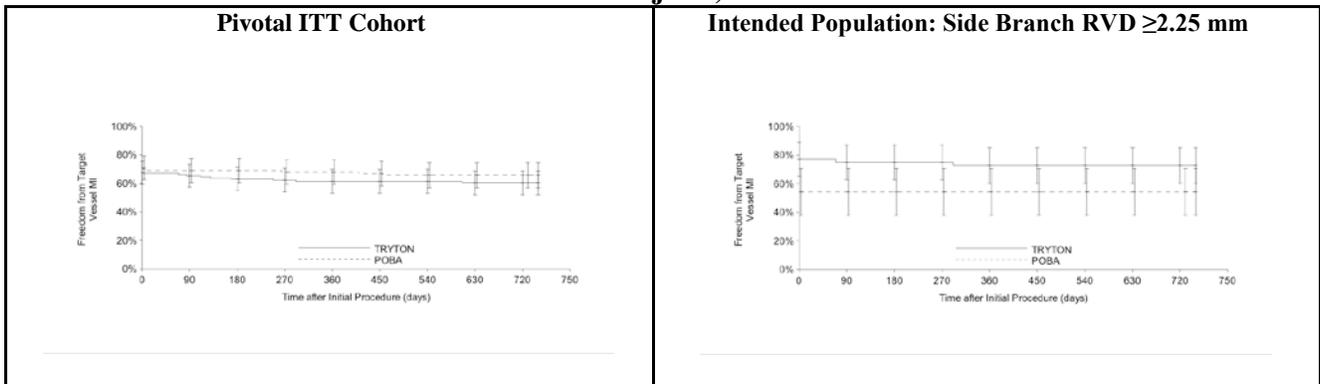
**Figure 2: Survival Free From Target Vessel Failure (Intent-to-Treat Subjects)**

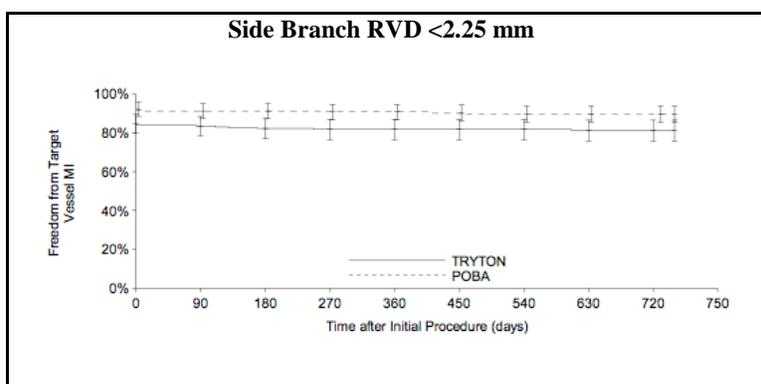


**Figure 3: Survival Free From Clinically Driven Target Vessel Revascularization (Intent-to-Treat Subjects)**



**Figure 4: Survival Free From Target Vessel Myocardial Infarction (Intent-to-Treat Subjects)**





### Serious Adverse Events in the TRYTON Pivotal RCT

The following serious adverse events (SAEs) were observed with incidence rate and number noted in **Table 28**.

All SAEs were adjudicated by the CEC. Event categories with a >5% incidence are shown with events with an incidence of >1% (more than one patient/event) are listed. Event categories with <5% incidence are not shown.

**Table 28: Serious Adverse Events to 730 Days – Intent-to-Treat Analysis Set**

|   | <b>TRYTON<br/>(N=355 Patients)</b> | <b>POBA<br/>(N=349 Patients)</b> |
|---|------------------------------------|----------------------------------|
| <b>Any SAE</b>  | 46.76% (166/355)                   | 38.11% (133/349)                 |
| <b>Cardiac disorders</b>                                    | 26.20% (93/355)                    | 22.06% (77/349)                  |
| Acute myocardial infarction                                 | 1.97% (7/355)                      | 2.87% (10/349)                   |
| Angina pectoris   | 10.42% (37/355)                    | 8.88% (31/349)                   |
| Angina unstable   | 2.82% (10/355)                     | 2.58% (9/349)                    |
| Cardiac failure   | 1.13% (4/355)                      | 1.15% (4/349)                    |
| Coronary artery dissection                                  | 1.13% (4/355)                      | 1.43% (5/349)                    |
| Coronary artery stenosis                                    | 0.56% (2/355)                      | 1.15% (4/349)                    |
| Myocardial infarction                                       | 5.92% (21/355)                     | 3.72% (13/349)                   |
| <b>General disorders and administration site conditions</b> | 6.76% (24/355)                     | 7.16% (25/349)                   |
| Non-cardiac chest pain                                      | 3.94% (14/355)                     | 4.01% (14/349)                   |
| <b>Infections and infestations</b>                          | 5.07% (18/355)                     | 2.87% (10/349)                   |
| Pneumonia   | 1.13% (4/355)                      | 1.72% (6/349)                    |
| <b>Injury, poisoning and procedural complications</b>       | 5.92% (21/355)                     | 2.87% (10/349)                   |
| <b>Respiratory, thoracic and mediastinal disorders</b>      | 5.07% (18/355)                     | 3.72% (13/349)                   |
| Chronic obstructive pulmonary disease                       | 0.28% (1/355)                      | 1.15% (4/349)                    |
| Dyspnea   | 2.25% (8/355)                      | 1.43% (5/349)                    |

### 3. Subgroup Analyses

The effects of gender on the primary endpoint of 9-month TVF and the secondary powered angiographic endpoint of side branch in-segment %DS were assessed, and the results are presented in **Table 29**. Among ITT subjects, no significant interactions were detected in regard to 9-month TVF or 9-month side branch in-segment %DS and whether the subject was male or female.

**Table 29: Gender Analysis of the Primary and Powered Secondary Endpoints**

| Endpoint  | Male                 |                      |                         | Female              |                     |                        |
|---|----------------------|----------------------|-------------------------|---------------------|---------------------|------------------------|
|   | TRYTON<br>(N=255)    | POBA<br>(N=256)      | Difference<br>[95% CI]  | TRYTON<br>(N=100)   | POBA<br>(N=93)      | Difference<br>[95% CI] |
| <b>TVF<sup>1</sup></b>  |                      |                      |                         |                     |                     |                        |
| Intent-to-Treat   | 15.9%<br>(40/251)    | 13.1%<br>(33/251)    | 2.8%<br>[-3.4%,9.0%]    | 18.6%<br>(18/97)    | 11.1%<br>(10/90)    | 7.4%<br>[-2.7%,17.5%]  |
| Per-Protocol  | 15.2%<br>(37/243)    | 13.5%<br>(32/237)    | 1.7%<br>[-4.5%,8.0%]    | 18.0%<br>(16/89)    | 9.3%<br>(8/86)      | 8.7%<br>[-1.4%,18.7%]  |
| <b>In-Segment Side-Branch Percent Diameter Stenosis at 9 months<sup>2</sup></b> |                      |                      |                         |                     |                     |                        |
| Intent-to-Treat   |                      |                      |                         |                     |                     |                        |
| Mean±SD (N)   | 31.15±22.31<br>(116) | 38.45±16.42<br>(123) | -7.29<br>[-12.28,-2.30] | 32.81±24.88<br>(39) | 39.14±15.60<br>(45) | -6.33<br>[-15.37,2.71] |
| Per-Protocol  |                      |                      |                         |                     |                     |                        |
| Mean±SD (N)   | 31.16±22.41<br>(115) | 38.06±16.27<br>(118) | -6.90<br>[-11.94,-1.86] | 33.53±24.80<br>(38) | 39.14±15.60<br>(45) | -5.61<br>[-14.72,3.50] |

<sup>1</sup>Events presented in this table have been adjudicated by the CEC.

Denominators are the number of patients with follow-up of at least 270 days or a TVF event within 270 days.

<sup>2</sup>Angiographic data presented in this table were provided by the Angiographic Core Laboratory.

### 4. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

## **E. TRYTON Pivotal RCT: Financial Disclosure**

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 410 total investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

## 2. ***TRYTON EXTENDED ACCESS (EA) CONFIRMATORY STUDY***

### A. **TRYTON EA Confirmatory Study: Study Design**

Patients were treated in the TRYTON Extended Access (EA Confirmatory) Study between July 28, 2014 and July 29, 2015. The database for this PMA reflected data collected through September 29, 2015 and included 133 patients. There were 28 investigational sites in the US and Europe.

The EA Confirmatory Study is a single arm study of 133 subjects treated with the TRYTON Side Branch Stent with main branch approved DES for treatment of native coronary artery bifurcation disease. The EA Confirmatory Study enrollment criteria mirrored the TRYTON Pivotal RCT study protocol but with a periprocedural MI (PPMI) as the primary endpoint, and there was an emphasis on proper side branch selection, targeting patients in particular with side branch RVD  $\geq 2.5$  mm by visual estimate, which corresponds to an angiographic core lab QCA assessed RVD of  $\geq 2.25$  mm.

The primary objective of the EA Study was to assure the continued safety and effectiveness of the TRYTON Side Branch Stent with main branch approved DES in the treatment of *de novo* native coronary artery bifurcation lesions with side branch diameter ranging from  $\geq 2.5$  mm to  $\leq 3.5$  mm and main branch diameter ranging from  $\geq 2.5$  mm to  $\leq 4.0$  mm.

There were three (3) primary goals of the study: (1) to confirm the ability of physicians to enroll appropriate patients, with an appropriately-sized side branch diameter to accommodate the TRYTON Stent; (2) to confirm the acute safety profile of the TRYTON Stent as seen in the post hoc analysis in the Pivotal RCT, specifically confirming an acceptable periprocedural MI rate; and (3) to confirm the results seen in the intended population of the Pivotal RCT (patients with side branch reference vessel diameter  $\geq 2.25$ mm).

The study used a pre-specified PPMI (defined as  $>3X$  URL CK-MB within the first 48 hours post-procedure) performance goal derived from the PPMI rates observed in the Pivotal RCT.

Expected true PPMI rate: 8.9%

- PPMI performance goal (PG): 17.9%, derived as follows:
  - In the subset of subjects with side branch  $\geq 2.25$  mm in the TRYTON IDE trial, the observed endpoint rates were 11.9% for DES+POBA (control) and 8.2% for DES+TRYTON.
  - The PG was adjusted from the control rate of 11.9% by adding 6.0% to account for sample variability
- Analysis used a 1-sided exact binomial proportion confidence interval with  $\alpha=0.05$ .

Sample size calculation and hypothesis: 127 subjects yields 90% power to reject the following null hypothesis in favor of the corresponding alternative hypothesis:

H<sub>0</sub>: p<sub>TRY</sub> ≥ 0.179 (or 17.9%)

H<sub>1</sub>: p<sub>TRY</sub> < 0.179 (or 17.9%)

Where p<sub>TRY</sub> is the primary endpoint rate in the DES+TRYTON. Six additional subjects to be enrolled to account for an expected 4% loss to follow-up before the primary endpoint was measured, so the total enrolled sample size was planned to be 133.

Enrolling 127 subjects affords 90% power to compare the primary endpoint rate from the EA Study to a performance goal of 17.9%, assuming a true endpoint rate of 8.9% for DES+TRYTON.

A Data Safety Monitoring board (DSMB) reviewed data to ensure patient safety. An independent CEC assessed all endpoint events. There were independent angiographic and ECG core laboratories.

**Table 30: TRYTON Extended Access (EA Confirmatory) Study Design**

| <b>Study Type/Design</b>         | <ul style="list-style-type: none"> <li>• Multi-center study (28 centers enrolled), performed in the U.S., Europe and Israel</li> <li>• Prospective</li> <li>• Single arm</li> <li>• Patients treated with TRYTON Side Branch Stent with main branch approved DES</li> </ul>  |  |  |  |                          |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
|----------------------------------|--|--|--|--|--------------------------|--|--|-----------|----|-----|-----|-----------|----|-----|-----|-----------|----|-----|-----|------------|----|-----|-----|------------|----|-----|-----|
| <b>Number of Patients</b>        | N= 133   |  |  |  |                          |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>Lesion Criteria</b>           | <i>de novo</i> native coronary artery bifurcation lesions with side branch diameter ranging from ≥2.5 mm to ≤3.5 mm and main branch diameter ranging from ≥2.5 mm to ≤4.0 mm.  |  |  |  |                          |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>Stent Sizes Used in Study</b> | <table border="1"> <thead> <tr> <th></th> <th><b>Stent Length (mm)</b></th> <th><b>Side Branch Nominal Diameter (mm)</b></th> <th><b>Main Branch Nominal Diameter (mm)</b></th> </tr> </thead> <tbody> <tr> <td><b>D5</b></td> <td>19</td> <td>2.5</td> <td>2.5</td> </tr> <tr> <td><b>D5</b></td> <td>19</td> <td>2.5</td> <td>3.0</td> </tr> <tr> <td><b>D5</b></td> <td>19</td> <td>2.5</td> <td>3.5</td> </tr> <tr> <td><b>D5+</b></td> <td>18</td> <td>3.0</td> <td>3.5</td> </tr> <tr> <td><b>D5+</b></td> <td>18</td> <td>3.5</td> <td>4.0</td> </tr> </tbody> </table> |  |  |  | <b>Stent Length (mm)</b> | <b>Side Branch Nominal Diameter (mm)</b> | <b>Main Branch Nominal Diameter (mm)</b> | <b>D5</b> | 19 | 2.5 | 2.5 | <b>D5</b> | 19 | 2.5 | 3.0 | <b>D5</b> | 19 | 2.5 | 3.5 | <b>D5+</b> | 18 | 3.0 | 3.5 | <b>D5+</b> | 18 | 3.5 | 4.0 |
|                                  | <b>Stent Length (mm)</b>   | <b>Side Branch Nominal Diameter (mm)</b> | <b>Main Branch Nominal Diameter (mm)</b> |  |                          |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>D5</b>                        | 19   | 2.5                                      | 2.5                                      |  |                          |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>D5</b>                        | 19   | 2.5                                      | 3.0                                      |  |                          |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>D5</b>                        | 19   | 2.5                                      | 3.5                                      |  |                          |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>D5+</b>                       | 18   | 3.0                                      | 3.5                                      |  |                          |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>D5+</b>                       | 18   | 3.5                                      | 4.0                                      |  |                          |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>Anti-Platelet Therapy</b>     | Aspirin indefinitely and clopidogrel, ticlopidine, prasugrel or ticagrelor for a minimum of 12 months post procedure   |  |  |  |                          |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>Primary Endpoint</b>          | Peri-procedural MI (PPMI) > 3x URL CK-MB at 48 hours after PCI (per modified ARC definition)   |  |  |  |                          |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |
| <b>Follow-Up</b>                 | 30 days and 1 year   |  |  |  |                          |  |  |           |    |     |     |           |    |     |     |           |    |     |     |            |    |     |     |            |    |     |     |

1. Clinical Inclusion and Exclusion Criteria

The inclusion and exclusion criteria for the EA Confirmatory Study are same as those for the Pivotal RCT Study, as listed in Section 1.

2. Follow-up Schedule

All EA Confirmatory study enrolled patients were required to receive DAPT for 12 months and clinical follow-up assessments were scheduled at 30 days and 12 months post-procedure. Adverse events and complications were recorded at all visits.

The key timepoints are shown below in the tables summarizing safety and effectiveness.

**Table 31: Schedule of Procedures and Tests**

| <b>PROCEDURE / TEST</b>  | <b>Baseline<br/>(Within 7 days)</b> | <b>Pre-Procedure<br/>(Within 24 hours)</b> | <b>Procedure</b> | <b>12 hrs. Post-<br/>Procedure and<br/>Discharge</b> | <b>30 days (± 7 days)</b> | <b>1 year (± 30 days)</b> | <b>Unscheduled visits</b> |
|--|-------------------------------------|--|------------------|--|---------------------------|---------------------------|---------------------------|
| Subject Medical/Clinical History (Age, Gender, Risk Factors, Angina Status, Cardiac History) | ✓                                   |  |                  |  |                           |                           |                           |
| Angina Status  | ✓                                   | ✓  | ✓                | ✓  | ✓                         | ✓                         | ✓                         |
| Subject Informed Consent   | ✓                                   |  |                  |  |                           |                           |                           |
| General Eligibility Criteria   | ✓                                   |  |                  |  |                           |                           |                           |
| Angiographic Eligibility Criteria  |                                     |  | ✓                |  |                           |                           |                           |
| <b>Clinical Laboratory Test:</b>   |                                     |  |                  |  |                           |                           |                           |
| Pregnancy Test (childbearing potential women only)   | ✓                                   |  |                  |  |                           |                           |                           |
| CBC, Creatinine, BUN, blood chemistry  | ✓                                   |  |                  |  |                           |                           |                           |
| Lipid profile  | ✓                                   |  |                  |  |                           |                           |                           |
| CK-MB  |                                     | ✓ <sup>2</sup>                             |                  | ✓ <sup>3</sup>                                       |                           |                           | ✓ <sup>4</sup>            |
| 12-Lead ECG  |                                     | ✓ <sup>2</sup>                             |                  | ✓ <sup>1</sup>                                       |                           |                           | ✓ <sup>4</sup>            |
| Left Ventriculography  |                                     |  | ✓ <sup>5</sup>   |  |                           |                           |                           |
| Study Stent information  |                                     |  | ✓                |  |                           |                           |                           |
| Per Protocol Medications   |                                     | ✓  | ✓                | ✓ <sup>6</sup>                                       | ✓ <sup>6</sup>            | ✓ <sup>6</sup>            | ✓ <sup>6</sup>            |

| <b>PROCEDURE / TEST</b>         | <b>Baseline<br/>(Within 7 days)</b> | <b>Pre-Procedure<br/>(Within 24 hours)</b> | <b>Procedure</b> | <b>12 hrs. Post-<br/>Procedure and<br/>Discharge</b> | <b>30 days (± 7 days)</b> | <b>1 year (± 30 days)</b> | <b>Unscheduled visits</b> |
|---------------------------------|-------------------------------------|--|------------------|--|---------------------------|---------------------------|---------------------------|
| Concomitant Cardiac Medications |                                     |  | ✓                | ✓  | ✓                         | ✓                         | ✓                         |
| Adverse Events Monitoring       |                                     |  | ✓                | ✓  | ✓                         | ✓                         | ✓                         |

1. Between 12 hours post-procedure and discharge.
2. Within 48 hours pre-procedure acceptable except when there is evidence of acute or recent (<72 hours) myocardial infarction (MI) or unstable angina prior to the procedure, in which case pre-procedure draws/assessments must be within 24 hours.
3. If CK-MB is elevated  $\geq 2$  times upper limit of normal, serial measurements (minimum of two samples 8 hours apart) of CK-MB must be done until a decline is noted.
4. CK-MB and ECG should be obtained for all suspected ischemic events. See note 3 regarding process if CK-MB is not available on-site.
5. LVEF at procedure if not documented within 6 months prior.
6. Clopidogrel, ticlopidine, prasugrel or ticagrelor (dose per manufacturer's directions for use) must be given for a minimum of 12 months as well as aspirin 75 to 162 mg daily (or dose per standard hospital practice) to be taken indefinitely.

3. Clinical Endpoints

The primary endpoint: Periprocedural MI defined as PCI CK-MB elevation with value >3 times the upper range limit within the first 48 hours after PCI.

Key secondary endpoints included all-cause mortality, Major Adverse Cardiac Events (MACE), and rates of stent thrombosis using the ARC definition.

Acute success was classified according to the following definitions:

- **Device Success:** Device success was defined as achievement of a final in-stent residual diameter stenosis of <30% (by quantitative coronary angiography [QCA]), using the assigned device only and without a device malfunction.
- **Lesion Success:** Lesion success was defined as achievement of a final in-stent residual diameter stenosis of <50% (by QCA) using any percutaneous method.
- **Procedure Success:** Procedure success was defined as achievement of a final in-stent diameter stenosis of <50% (by QCA) using the assigned device and with any adjunctive devices, without the occurrence of cardiac death, MI, or repeat revascularization of the target lesion during the hospital stay.

## **B. TRYTON EA Confirmatory Study: Accountability of PMA Cohort**

At the time of database lock, of 133 patients enrolled in the TRYTON EA Confirmatory Study, 98% (131) patients were available for analysis at the 1-month post-operative visit.

All 133 subjects comprised the ITT population, which was the primary analysis set. All subjects were treated with the TRYTON Side Branch Stent in conjunction with main branch approved DES.

Of the 133 subjects treated in the EA Confirmatory Study, 132 (99.2%) received the study stent in the side branch. Stent dislodgement occurred in one patient; therefore, the stent was not delivered to the side branch.

**Table 32** details all deaths, withdrawals and study exits of ITT subjects at 1-month follow-up.

**Table 32: Intent to Treat (ITT) Subject Accountability at 1 Month Follow-Up**

|  | <b>1 Month Follow-Up</b> |
|--|--------------------------|
| Completed Follow-Up Visit <sup>1</sup>   | 131 <sup>2</sup>         |
| Subjects Eligible for Follow-up          | 133                      |
| <b>Ineligible for Follow-up: Reasons</b> |                          |
| Death                                    | 0                        |
| Withdrew Consent                         | 0                        |
| Exited for Other Reasons                 | 0                        |

<sup>1</sup>Denominator for 30-day contact includes only patients who had the visit or who had at least 37 days of follow-up by the time of data export (24Aug2015), and did not die or exit within 30 days post-procedure.

Updated data used from Appendix II Table 4 EA Confirmatory Report run (1Oct2015)

<sup>2</sup>Two patients received 30 day follow-up on day 22, outside 30 day window

## **C. TRYTON EA Confirmatory Study: Study Population Demographics and Baseline Parameters**

The demographics and baseline clinical characteristics of ITT patients were typical for a coronary stent study performed in the US (**Table 33**).

**Table 33: Baseline Patient Demographics and Clinical Characteristics – Intent to Treat (ITT) Extended Access Analysis Set**

|  | <b>ITT EA<br/>(N=133 Patients)</b> |
|--|------------------------------------|
| <b>Age</b>                                 |                                    |
| Mean±SD (N)                                | 65.57±9.54 (133)                   |
| <b>Number of Men</b>                       | 69.9% (93/133)                     |
| <b>Ethnicity</b>                           |                                    |
| Hispanic or Latino                         | 3.8% (5/131)                       |
| Not Hispanic or Latino                     | 96.2% (126/131)                    |
| <b>Race</b>                                |                                    |
| American Indian or Alaska Native           | 0.0% (0/133)                       |
| Asian                                      | 0.8% (1/133)                       |
| Black or African American                  | 2.3% (3/133)                       |
| Native Hawaiian or Other Pacific Islander  | 0.0% (0/133)                       |
| White                                      | 97.0% (129/133)                    |
| Other                                      | 0.0% (0/133)                       |
| <b>Risk Factors</b>                        |                                    |
| MI   | 32.3% (43/133)                     |
| PCI  | 39.8% (53/133)                     |
| CABG                                       | 2.3% (3/133)                       |
| TIA  | 4.5% (6/133)                       |
| CVA  | 3.8% (5/132)                       |
| CHF  | 6.0% (8/133)                       |
| Diabetes Mellitus                          | 25.8% (34/132)                     |
| Hypertension                               | 82.0% (109/133)                    |
| Hypercholesterolemia                       | 71.2% (94/132)                     |
| Renal Insufficiency/failure or on dialysis | 0.0% (0/133)                       |
| Premature CAD in a first degree relative   | 32.3% (31/96)                      |
| <b>Smoking Status</b>                      |                                    |
| Current                                    | 21.1% (28/133)                     |
| Former                                     | 27.8% (37/133)                     |
| Atrial Fibrillation                        | 7.5% (10/133)                      |
| History of peripheral vascular disease     | 6.7% (8/120)                       |
| <b>Assessment of Anginal Status</b>        |                                    |
| <b>Angina Type</b>                         |                                    |
| Stable                                     | 73.7% (98/133)                     |
| Unstable                                   | 18.0% (24/133)                     |
| Silent Ischemia                            | 6.0% (8/133)                       |

|  |                                    |
|--|------------------------------------|
|  | <b>ITT EA<br/>(N=133 Patients)</b> |
| No Angina                                    | 2.3% (3/133)                       |
| <b>Canadian Cardiovascular Society Class</b> |                                    |
| I  | 15.3% (15/98)                      |
| II   | 55.1% (54/98)                      |
| III  | 27.6% (27/98)                      |
| IV   | 2.0% (2/98)                        |
| Positive functional test of ischemia         | 64.2% (34/53)                      |
| Positive Stress Test                         | 97.1% (33/34)                      |
| <b>LVEF (%)</b>                              |                                    |
| Mean±SD (N)                                  | 56.27±9.51 (123)                   |
| <b>Killip Class</b>                          |                                    |
| I  | 96.9% (62/64)                      |
| II   | 3.1% (2/64)                        |
| III  | 0.0% (0/64)                        |
| IV   | 0.0% (0/64)                        |

As assessed by the angiographic core laboratory, true bifurcation lesions (Medina Classification 1.1.1; 0.1.1; 1.0.1) at enrollment were present in 100% (133/133) of the subjects (**Table 34**). The mean ( $\pm$ SD) main branch lesion length was 17.23 ( $\pm$ 7.89) mm, and side branch lesions had a mean length at baseline of 5.94 ( $\pm$ 2.53) mm. The mean ( $\pm$ SD) QCA-assessed side branch RVD was 2.49 $\pm$ 0.20 mm. Operators were able to select bifurcation lesion side branches  $\geq$ 2.25 mm in diameter by QCA in 99.2% (132/133) of subjects.

**Table 34: Medina Classification**

| <b>Medina Classification</b>                  | <b>Site Reported</b> | <b>Core Lab</b> |
|---|----------------------|-----------------|
| 1,1,1   | 71.4% (95/133)       | 50.4% (67/133)  |
| 1,1,0*  | 0.0% (0/133)         | 0.0% (0/133)    |
| 1,0,1   | 11.3% (15/133)       | 15.0% (20/133)  |
| 0,1,1   | 17.3% (23/133)       | 34.6% (46/133)  |
| 1,0,0*  | 0.0% (0/133)         | 0.0% (0/133)    |
| 0,1,0*  | 0.0% (0/133)         | 0.0% (0/133)    |
| 0,0,1*  | 0.0% (0/133)         | 0.0% (0/133)    |
| 0,0,0*  | 0.0% (0/133)         | 0.0% (0/133)    |
| 1,1,0 OR 1,0,0 OR 0,1,0<br>OR 0,0,1 OR 0,0,0* | 0.0% (0/133)         | 0.0% (0/133)    |

\*Protocol deviation

#### **D. TRYTON EA Confirmatory Study: Safety and Effectiveness Results**

The analysis of safety and effectiveness was based on the intent-to-treat cohort of 133 patients available for the peri-procedural evaluation and 131 patients available with safety and effectiveness data at 1 month. The key safety and effectiveness outcomes for this study are presented below in **Tables 35 to 38**. Serious adverse events are reported in **Table 39**.

##### Acute Success

As presented in **Table 35**, device, lesion and procedure success were achieved in the TRYTON ITT group:

Device success: Attainment of <30% residual stenosis within the side branch using the assigned device only and without a device malfunction, was achieved in 93.8% (122/130) of the lesions treated with the TRYTON Side Branch Stent.

Lesion success: Attainment of <50% residual stenosis using any percutaneous method, was achieved in all (100%; 130/130) of the lesions treated with the TRYTON Side Branch Stent.

Procedure success: Lesion success without the occurrence of in-hospital MACE, was achieved in 89.3% (117/131) of the subjects treated with the TRYTON Side Branch Stent.

**Table 35: Acute Success – Intent to Treat Extended Access Analysis Set**

|                   | <b>ITT EA<br/>(N=133 Patients)</b> |
|-------------------|------------------------------------|
| Lesion Success    | 100.0% (130/130 <sup>1</sup> )     |
| Device Success    | 93.8% (122/130)                    |
| Procedure Success | 89.3% (117/131)                    |

<sup>1</sup>Core lab assessment unavailable

##### Primary Endpoint

The upper bound of the 95% CI for the PPMI rate in TRYTON treated subjects was less than the pre-specified performance goal of 17.9%. The observed PPMI rate was 10.5% (14/133), 1-sided 95% upper confidence bound 16.0%, p=0.014 (**Table 35**). Thus, the PPMI primary endpoint was met for the ITT population.

Sensitivity analyses were performed to assess the impact of missing values on the primary endpoint using a tipping point analysis. When the primary endpoint was analyzed among all EA subjects using an initial sensitivity analysis (i.e., the 3 subjects with missing CKMB information were excluded from the analysis), the periprocedural MI rate was 10.8% (14/130) with a 1-sided confidence interval of 16.3% compared to performance goal of 17.9% (**Table 36**), thus meeting the primary endpoint.

**Table 36: Tipping Point Analysis of Primary Endpoint – Intent to Treat Extended Access Population**

| <b>Primary Endpoint</b>  | <b>ITT EA<br/>(N=133<br/>Patients)</b> | <b>1-sided<br/>Upper<br/>95% CI</b> | <b>Performance<br/>Goal</b> | <b>P-value</b> |
|--|--|-------------------------------------|-----------------------------|----------------|
| <b>Peri-procedural MI within 48 hours</b>                        |  |                                     |                             |                |
| ITT Available (Assumes 0 of 3 patients with missing CKMB failed) | 10.5%<br>(14/133)                      | 16.0%                               | 17.9%                       | 0.014          |
| <b>ITT Tipping Point</b>   |  |                                     |                             |                |
| Assumes 1 of 3 patient with missing CKMB failed                  | 11.3%<br>(15/133)                      | 16.8%                               | 17.9%                       | 0.025          |
| Assumes 2 of 3 patient with missing CKMB failed                  | 12.0%<br>(16/133)                      | 17.7%                               | 17.9%                       | 0.044          |
| Assumes 3 of 3 patient with missing CKMB failed                  | 12.8%<br>(17/133)                      | 18.6%                               | 17.9%                       | 0.073          |
| ITT Sensitivity (excludes 3 patients with missing CKMB)          | 10.8%<br>(14/130)                      | 16.3%                               | 17.9%                       | 0.018          |

Secondary Safety and Effectiveness Endpoints

**Tables 37** and **38** show safety and effectiveness endpoints in-hospital (**Table 37**) and at 30 days (**Table 38**).

**Table 37: Secondary Safety and Effectiveness Endpoints In-Hospital – Intent to Treat Extended Access Analysis Set**

| <b>Event<sup>1</sup></b>   | <b>ITT EA<br/>(N=133<br/>Patients)</b> |
|--|--|
| <b>Target Vessel Failure</b> (TVF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Vessel Revascularization) | 10.5% (14/133)                         |
| <b>Target Lesion Failure</b> (TLF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Lesion Revascularization) | 10.5% (14/133)                         |
| <b>Stent Thrombosis</b> (ARC Definite, Probable)   | 1.5% (2/133)                           |
| Main Vessel  | 1.5% (2/133)                           |
| Side Branch  | 1.5% (2/133)                           |
| <b>MACE</b> (Death, MI, Emergent CABG, Ischemia Driven or Clinically Indicated Target Lesion Revascularization)  | 10.5% (14/133)                         |
| <b>Death</b>   | 0.0% (0/133)                           |
| <b>Modified ARC MI<sup>2</sup></b>   | 10.5% (14/133)                         |
| Peri-Procedural PCI  | 10.5% (14/133)                         |
| Peri-CABG  | 0.0% (0/133)                           |

| <b>Event<sup>1</sup></b>   | <b>ITT EA<br/>(N=133<br/>Patients)</b> |
|--|--|
| Spontaneous  | 0.0% (0/133)                           |
| Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel) <sup>3</sup>          | 1.5% (2/133)                           |
| Non-Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel) <sup>3</sup>      | 6.8% (9/133)                           |
| <b>Target Vessel MI<sup>2</sup></b>  | 10.5% (14/133)                         |
| Q-wave MI <sup>3</sup>   | 1.5% (2/133)                           |
| Non-Q-wave MI <sup>3</sup>   | 6.8% (9/133)                           |
| Non-Target Vessel MI   | 0.0% (0/133)                           |
| Emergent CABG  | 0.8% (1/133)                           |
| <b>Target Lesion Revascularization (TLR)</b>   | 1.5% (2/133)                           |
| <b>Ischemia Driven or Clinically Indicated Target Lesion Revascularization (TLR)<sup>4</sup></b> | 1.5% (2/133)                           |
| Main Vessel  | 0.8% (1/133)                           |
| Side Branch  | 1.5% (2/133)                           |
| CABG   | 0.0% (0/133)                           |
| PCI  | 1.5% (2/133)                           |
| Main Vessel  | 0.8% (1/133)                           |
| Side Branch  | 1.5% (2/133)                           |
| Non-Ischemia Driven TLR  | 0.8% (1/133)                           |
| <b>Target Vessel Revascularization (TVR)</b>   | 1.5% (2/133)                           |
| <b>Ischemia Driven or Clinically Indicated Target Vessel Revascularization (TVR)<sup>4</sup></b> | 1.5% (2/133)                           |
| Main Vessel  | 0.8% (1/133)                           |
| Side Branch  | 1.5% (2/133)                           |
| CABG   | 0.0% (0/133)                           |
| Main Vessel  | 0.0% (0/133)                           |
| Side Branch  | 0.0% (0/133)                           |
| PCI  | 1.5% (2/133)                           |
| Main Vessel  | 0.8% (1/133)                           |
| Side Branch  | 1.5% (2/133)                           |
| Non-Ischemia Driven Target Vessel Revascularization (TVR)  | 0.8% (1/133)                           |
| Non-Target Vessel Revascularization  | 0.8% (1/133)                           |

<sup>1</sup>Events in this table have been adjudicated by the CEC.

<sup>2</sup>If the relationship to the target vessel could not be determined, the MI was considered a target vessel MI.

Myocardial infarction was defined using a modified version of the Joint ESC/ACC/AHA/WHF Task Force for the Redefinition of Myocardial Infarction and Academic Research Consortium criteria.

<sup>3</sup>Three target vessel MIs were not yet adjudicated for the type of MI (Q wave/non-Q wave).

<sup>4</sup>Ischemia-Driven Target Lesion Revascularization (ID-TLR) and Ischemia-Driven Target Vessel Revascularization (ID-TVR) are defined as revascularization at the target lesion/vessel associated with any of the following: (1) Positive functional ischemia study; (2) Ischemic symptoms and angiographic MLD stenosis  $\geq 50\%$  by core laboratory QCA; (3) Revascularization of a target lesion with diameter stenosis  $\geq 70\%$  by core laboratory.

Clinically-Indicated Revascularization (TLR/TVR) is defined as a revascularization of the target lesion/vessel when angiography at follow-up shows a percent diameter stenosis  $\geq 50\%$  (Angiographic Core Laboratory QCA assessment) and if one of the following occurs: (1) A positive history of recurrent angina pectoris, presumably related to the target vessel; (2) Objective signs of ischemia at rest (ECG changes) or during exercise test (or equivalent), presumably related to the target vessel; (3) Abnormal results of any invasive functional diagnostic test; (4) A TLR or TVR with a diameter stenosis  $\geq 70\%$  even in the absence of the above-mentioned ischemic signs or symptoms.

**Table 38: Secondary Safety and Effectiveness Endpoints to 30 days (1 month) – Intent-to-Treat Extended Access Analysis Set**

| <b>Event<sup>1</sup></b>   | <b>EA ITT<br/>(N = 133<br/>Patients)</b> |
|--|--|
| <b>Target Vessel Failure</b> (TVF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Vessel Revascularization) | 10.7% (14/131)                           |
| <b>Target Lesion Failure</b> (TLF – Cardiac Death, Target Vessel MI (Modified ARC Definition) and Ischemia Driven or Clinically Indicated Target Lesion Revascularization) | 10.7% (14/131)                           |
| <b>Stent Thrombosis</b> (ARC Definite, Probable)   | 1.5% (2/131)                             |
| Main Vessel  | 1.5% (2/131)                             |
| Side Branch  | 1.5% (2/131)                             |
| <b>MACE</b> (Death, MI, Emergent CABG, Ischemia Driven or Clinically Indicated Target Lesion Revascularization)  | 10.7% (14/131)                           |
| <b>Death</b>   | 0.0% (0/131)                             |
| <b>Modified ARC MI<sup>2</sup></b>   | 10.7% (14/131)                           |
| Peri-Procedural PCI  | 10.7% (14/131)                           |
| Peri-CABG  | 0.0% (0/131)                             |
| Spontaneous  | 0.0% (0/131)                             |
| Re-Infarction  | 0.8% (1/131)                             |
| Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)   | 2.3% (3/131)                             |

| <b>Event<sup>1</sup></b>   | <b>EA ITT<br/>(N = 133<br/>Patients)</b> |
|--|--|
| Non-Q-wave MI (Cumulative of Target Vessel, Non-Target Vessel, Unknown Vessel)                   | 6.9% (9/131)                             |
| <b>Target Vessel MI<sup>2</sup></b>  | 10.7% (14/131)                           |
| Q-wave MI  | 2.3% (3/131)                             |
| Non-Q-wave MI  | 6.9% (9/131)                             |
| Non-Target Vessel MI <sup>2</sup>  | 0.0% (0/131)                             |
| Emergent CABG  | 0.8% (1/131)                             |
| <b>Target Lesion Revascularization (TLR)</b>   | 2.3% (3/131)                             |
| <b>Ischemia Driven or Clinically Indicated Target Lesion Revascularization (TLR)<sup>3</sup></b> | 2.3% (3/131)                             |
| Main Vessel  | 1.5% (2/131)                             |
| Side Branch  | 1.5% (2/131)                             |
| CABG   | 0.0% (0/131)                             |
| Main Vessel  | 0.0% (0/131)                             |
| Side Branch  | 0.0% (0/131)                             |
| PCI  | 2.3% (3/131)                             |
| Main Vessel  | 1.5% (2/131)                             |
| Side Branch  | 1.5% (2/131)                             |
| Non-Ischemia Driven TLR  | 0.8% (1/131)                             |
| <b>Target Vessel Revascularization (TVR)</b>   | 2.3% (3/131)                             |
| <b>Ischemia Driven or Clinically Indicated Target Vessel Revascularization (TVR)<sup>3</sup></b> | 2.3% (3/131)                             |
| Main Vessel  | 1.5% (2/131)                             |
| Side Branch  | 1.5% (2/131)                             |
| CABG   | 0.0% (0/131)                             |
| Main Vessel  | 0.0% (0/131)                             |
| Side Branch  | 0.0% (0/131)                             |
| PCI  | 2.3% (3/131)                             |
| Main Vessel  | 1.5% (2/131)                             |
| Side Branch  | 1.5% (2/131)                             |
| Non-Ischemia Driven Target Vessel Revascularization (TVR)  | 0.8% (1/131)                             |
| Non-Target Vessel Revascularization  | 0.8% (1/131)                             |

<sup>1</sup>Events in this table have either final or preliminary adjudication by the CEC.

Denominators reflect the number of patients with an adjudicated event through 30 days or follow-up through 23 days.

<sup>2</sup>If the relationship to target vessel could not be determined, MI was considered a target vessel MI.

Myocardial infarction was defined using a modified version of the Joint ESC/ACC/AHA/WHF Task Force for the Redefinition of Myocardial Infarction and Academic Research Consortium criteria.

<sup>3</sup>Refer to Footnote 4 in Table 37

Serious Adverse Events that Occurred in the PMA EA Confirmatory Study

The following Serious Adverse Events (SAEs) were observed during the EA Confirmatory Study, with incidence rate and number noted in **Table 39**.

All SAEs were adjudicated by the CEC. Event categories with a >5% incidence are shown with events with an incidence of >1% (more than one patient/event) listed. Event categories with <5% incidence are not shown.

**Table 39: Serious Adverse Events to 30 Days – Intent-to-Treat Analysis Set EA Confirmatory Study**

|                             | <b>ITT EA<br/>(N=133 Patients)</b> |
|-----------------------------|------------------------------------|
| <b>Any SAE</b>              | 11.28% (15/133)                    |
| <b>Cardiac disorders</b>    | 8.27% (11/133)                     |
| Acute myocardial infarction | 2.26% (3/133)                      |
| Coronary artery dissection  | 2.26% (3/133)                      |
| Myocardial infarction       | 3.01% (4/133)                      |

**E. TRYTON EA Confirmatory Study: Financial Disclosure**

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants, who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The EA Confirmatory study included 152 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

**XI. PANEL MEETING RECOMMENDATION AND FDA’S POST-PANEL ACTION**

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory Systems Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

## XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

### A. Effectiveness Conclusions

#### Clinical Studies

The TRYTON Pivotal RCT evaluated the effectiveness of the TRYTON Side Branch Stent with main branch approved DES compared to side branch balloon angioplasty and main branch approved DES in the treatment of de novo native coronary artery bifurcation lesions (Medina Classification 1.1.1; 0.1.1; 1.0.1) with a side branch diameter stenosis of  $\geq 50\%$  and a lesion length  $\leq 5.0$  mm, along with reference vessel diameters  $\geq 2.5$  mm to  $\leq 3.5$  mm in the side branch and  $\geq 2.5$  mm to  $\leq 4.0$  mm in the main branch. The results can be summarized as follows:

- Clinically-driven TVR (a component of the primary endpoint, TVF), was slightly higher in the TRYTON arm than POBA in the ITT analysis.
- Treatment with the TRYTON Side Branch Stent reduced stenosis of the side branch compared to POBA as demonstrated by significantly lower %DS at the 9-month angiographic follow-up.

A post hoc analysis of the primary and secondary endpoints among ITT subjects with side branch RVD  $\geq 2.25$  mm by QCA ( $>2.5$  mm by visual assessment) demonstrated the following:

- Clinically-driven TVR (a component of the primary endpoint, TVF), was comparable in the TRYTON arm to POBA in intended population of side branch RVD  $\geq 2.25$  mm by QCA ( $>2.5$  mm by visual assessment).
- Treatment with the TRYTON Side Branch Stent was associated with significantly lower %DS of the side branch at the 9-month angiographic follow-up compared with POBA.

### B. Safety Conclusions

#### Preclinical Studies

The engineering testing conducted on the stent and delivery systems demonstrated that the performance characteristics met product specifications or were acceptable.

Packaging testing demonstrated that the design of the TRYTON Side Branch Stent packaging is robust and can maintain acceptable integrity and sterility throughout the product's shelf life.

The results from the sterilization validation testing demonstrated that the product can be adequately sterilized and is acceptable for clinical use.

The shelf life testing has established acceptable performance for a labeled shelf life up to 2 years for the TRYTON Side Branch Stent.

The biocompatibility and animal studies demonstrated that the acute and chronic in vivo performance characteristics of the TRYTON Side Branch Stent provide reasonable assurance of safety and acceptability for clinical use.

#### Clinical Studies

The TRYTON Pivotal RCT evaluated the safety of the TRYTON Side Branch Stent with main branch approved DES compared to side branch balloon angioplasty and main branch approved DES in the treatment of de novo native coronary artery bifurcation lesions (Medina Classification 1.1.1; 0.1.1; 1.0.1) with a side branch diameter stenosis of  $\geq 50\%$  and a lesion length  $\leq 5.0$  mm, along with reference vessel diameters  $\geq 2.5$  mm to  $\leq 3.5$  mm in the side branch and  $\geq 2.5$  mm to  $\leq 4.0$  mm in the main branch. The results can be summarized as follows:

- In the ITT population, treatment with the TRYTON Side Branch Stent did not meet the non-inferiority primary clinical endpoint of 9-month TVF when compared with POBA, principally due to periprocedural MI defined by CKMB elevations that were not associated with clinical sequelae.
- Implantation of the TRYTON Stent was associated with low rates of stent thrombosis, clinically significant MIs, cardiac deaths and clinically driven revascularizations through 2 years post-procedure.

In post hoc analyses of the primary and secondary endpoints among ITT subjects with side branch RVD  $\geq 2.25$  mm by QCA ( $> 2.5$  mm by visual assessment) the following results were demonstrated:

- Treatment with the TRYTON Side Branch Stent was comparable to POBA in regards to the primary clinical endpoint of 9-month TVF; however, although these results were observed in the intended study population, given the post-hoc nature of this analysis, a formal conclusion of non-inferiority cannot be made for this subgroup.
- Long term safety endpoints show no safety signals.

The EA Confirmatory Study provided additional procedural safety data on the TRYTON Side Branch Stent. There were three (3) primary goals of the study: (1) to confirm the ability of physicians to enroll appropriate patients with an appropriately-sized side branch diameter to accommodate the TRYTON Stent; (2) to confirm the acute safety profile of the TRYTON Stent as seen in the post hoc analysis in the Pivotal RCT, specifically confirming an acceptable periprocedural MI rate; and (3) to confirm the results seen in the intended population of the Pivotal RCT (patients with QCA assessed side branch RVD  $\geq 2.25$ mm). The results can be summarized as follows:

- Treatment with TRYTON Side Branch Stent met its primary endpoint with an observed PPMI rate of 10.5%, supporting the acute safety profile of the TRYTON Stent as seen in the TRYTON Pivotal RCT post hoc analysis of subjects with a QCA assessed side branch RVD  $\geq 2.25$  mm.
- Physicians were able to select side branches with RVD  $> 2.5$  mm ( $\geq 2.25$  mm by QCA), the intended population, in 99.2% (132/133) of subjects.

### C. **Benefit-Risk Determination**

The probable benefits of the device are based on data collected in the clinical studies conducted to support PMA approval. The TRYTON Side Branch Stent with main branch approved DES has been shown to be comparable to POBA for the treatment of de novo native coronary artery bifurcation lesions (Medina Classification 1.1.1; 0.1.1; 1.0.1) with a side branch diameter stenosis of  $\geq 50\%$  and a lesion length  $\leq 5.0$  mm, along with reference vessel diameters  $\geq 2.5$  mm to  $\leq 3.5$  mm in the side branch and  $\geq 2.5$  mm to  $\leq 4.0$  mm in the main branch. The TRYTON Stent provides improved angiographic outcome vs. POBA, increasing the likelihood of side branch patency while maintaining main vessel results.

Additional factors that were considered in concluding a favorable benefit-risk profile of the TRYTON Side Branch Stent included:

- Higher procedural success rate, improved acute angiographic results, and higher rate of side branch patency at 9-month follow-up compared to POBA.
- Safety similar to POBA with low rates of stent thrombosis, clinically significant MI, cardiac death, and clinically-driven revascularization through 2 years post procedure.
- No unexpected adverse events associated with the TRYTON Side Branch Stent observed.
- Alternative treatments are available, such as provisional stenting, as described in Section V. Patient and lesion characteristics should be considered in the treatment decision.

#### 1. Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that for improving the side branch luminal diameter of de novo native coronary artery bifurcation lesions (Medina Classification 1.1.1; 0.1.1; 1.0.1) with a side branch diameter stenosis of  $\geq 50\%$  and a lesion length  $\leq 5.0$  mm, along with reference vessel diameters  $\geq 2.5$  mm to  $\leq 3.5$  mm in the side branch and  $\geq 2.5$  mm to  $\leq 4.0$  mm in the main branch (using the device in conjunction with commercially available balloon expandable drug-eluting coronary stents in the main branch), the probable benefits outweigh the probable risks.

#### **D. Overall Conclusions**

The data in this application support the reasonable assurance of safety and effectiveness of the TRYTON Side Branch Stent when used in accordance with the indications for use. Specifically, data from the Pivotal RCT and EA Confirmatory Study support the safety and effectiveness of the TRYTON Side Branch Stent for the treatment of de novo bifurcation lesions when used according to the Instructions for Use.

#### **XIII. CDRH DECISION**

CDRH issued an approval order on February 21, 2017. The final conditions of approval cited in the approval order are described below.

1. ODE Lead PMA Post-Approval Study – TRYTON Side Branch Stent PIVOTAL Randomized Controlled Trial (RCT): The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. The TRYTON Side Branch Stent PIVOTAL Randomized Controlled Trial (RCT) is a prospective, multi-center, single blind controlled trial which enrolled 704 subjects randomized 1:1 to implantation of the TRYTON Side Branch Stent and a main branch approved drug-eluting stent (DES) (N=355) in the investigational device arm vs. side branch balloon angioplasty (POBA) and main branch implantation of an approved DES (N=349) in the control arm (Provisional cohort). The primary endpoint of the PIVOTAL RCT was clinically-indicated target vessel failure [TVF: defined as a composite of cardiac death, target vessel myocardial infarction (TV MI), and clinically-indicated target vessel revascularization (TVR)] of the TRYTON Side Branch Stent with main branch DES at 9 months.

The applicant must collect and report to the Agency clinical outcomes through 3 years post-procedure on subjects enrolled in the PIVOTAL RCT. When appropriate or requested by FDA, the applicant should submit PMA supplements requesting approval to update your Instructions for Use (IFU) to include follow-up data from this trial.

2. ODE Lead PMA Post-Approval Study – TRYTON Side Branch Stent Extended Access (EA) Confirmatory Study: The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. The TRYTON Side Branch Stent EA Confirmatory Study is a single-arm study, which enrolled 133 subjects treated with the TRYTON Side Branch Stent plus implantation of an approved DES in the main branch for treatment of native coronary artery bifurcation disease. The EA Confirmatory study mirrored the TRYTON Pivotal RCT study protocol enrollment criteria supplemented with an emphasis on proper side branch size selection, targeting patients with a side branch RVD  $\geq 2.5$ mm by visual estimate and  $\geq 2.25$ mm by QCA as assessed by the angiographic core laboratory. The primary endpoint of the EA Confirmatory Study was peri-procedural MI (PPMI) after

percutaneous coronary intervention (PCI) defined as a CK-MB elevation >3 times the upper range limit within the first 48 hours after PCI.

The applicant must collect and report to the Agency clinical outcomes through 1 year post-procedure on subjects enrolled in the EA Confirmatory Study. When appropriate or requested by FDA, the applicant should submit PMA supplements requesting approval to update your Instructions for Use (IFU) to include follow-up data from this trial.

3. OSB Lead PMA Post-Approval Study – TRYTON Side Branch Stent New Enrollment Study: The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval. The TRYTON Side Branch Stent New Enrollment Study is a prospective, open label, multi-center evaluation of the PMA-approved, commercially-distributed TRYTON Side Branch Stent.

The applicant must conduct a prospective, open label, multi-center evaluation of the TRYTON Side Branch Stent consisting of at least 300 US patients that receive the device post-approval. The effort should assess the rate of target vessel failure (TVF) within one year of index procedure, according to the clinical follow-up schedule in patients treated with the TRYTON Side Branch Stent according to its labeled indications for use. TVF is defined as the composite endpoint of cardiac death, myocardial infarction (Q Wave and Non-Q wave MI), and clinically-indicated target vessel revascularization. The evaluation should also assess the following endpoints: device success (i.e., attainment of <30% residual stenosis within the side branch using the TRYTON Stent without device malfunction), lesion success (attainment of <30% residual stenosis using any percutaneous method), and procedure success (lesion success without the occurrence of in-hospital MACE). Patients should be evaluated through 3 years post-procedure according to the clinical follow-up schedule.

The applicant must provide an operator training program that includes an assessment plan to evaluate the effectiveness of training on the recommended procedure for TRYTON Side Branch Stent implantation. Within the post-approval effort as part of this training program, the applicant must conduct an angiographic sub-analysis of at least 150 patients consecutively implanted by inexperienced operators to evaluate compliance with side branch reference vessel diameter criteria for TRYTON Side Branch Stent implantation. For this angiographic sub-analysis, the applicant should provide quarterly interim progress reports to FDA.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. **APPROVAL SPECIFICATIONS**

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.