

FDA SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Catheter, Coronary, Atherectomy
Device Trade Name:	DIAMONDBACK 360 Coronary Orbital Atherectomy System
Device Product Code:	MCX
Applicant's Name and Address:	Cardiovascular Systems, Inc. 651 Campus Drive St. Paul, MN 55112
Premarket Approval Application (PMA) Number:	P130005
Date of FDA Notice of Approval:	October 21, 2013

II. INDICATIONS FOR USE

The DIAMONDBACK 360 Coronary Orbital Atherectomy System is a percutaneous orbital atherectomy system indicated to facilitate stent delivery in patients with coronary artery disease (CAD) who are acceptable candidates for PTCA or stenting due to *de novo*, severely calcified coronary artery lesions.

III. CONTRAINDICATIONS

Use of the DIAMONDBACK 360 Coronary Orbital Atherectomy System (OAS) is contraindicated in the following situations:

- The guide wire cannot pass across the coronary lesion.
- The target lesion is within a bypass graft or stent.
- The patient is not an appropriate candidate for bypass surgery, angioplasty or atherectomy therapy.
- The patient has angiographic evidence of thrombus.
- The patient has only one open vessel.
- The patient has angiographic evidence of significant dissection at the treatment site.
- Women who are pregnant or children.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the DIAMONDBACK 360 Coronary Orbital Atherectomy System labeling.

V. DEVICE DESCRIPTION

The Cardiovascular Systems, Inc. (CSI) DIAMONDBACK 360 Coronary Orbital Atherectomy System (OAS) is a percutaneous, catheter-based orbital atherectomy system designed to facilitate stent deployment in patients with coronary artery lesions by using a rotating, diamond-coated crown. The DIAMONDBACK 360 Coronary OAS consists of the following components:

1. DIAMONDBACK 360 Coronary Orbital Atherectomy Device (OAD)
2. Saline Infusion Pump (SIP)
3. ViperWire Advance Coronary Guide Wire
4. ViperSlide Lubricant



The DIAMONDBACK 360 Coronary OAD is a hand-held device that includes a sheath-covered drive shaft and a diamond-coated crown. The diamond coating on the crown provides an abrasive surface which is designed to reduce occlusive tissue within coronary arteries. The coronary OAD crown is designed to track and rotate over the ViperWire Advance Coronary Guide Wire.

The SIP provides the saline pumping mechanism and power to the coronary OAD. The SIP is a small, reusable, portable pump that attaches to a standard five-wheel rolling intravenous (IV) pole. The SIP includes a built-in, audible 25 second spin time notification, system power and priming buttons, and status indicators.

The ViperWire Advance Coronary Guide Wire is a smooth, stainless steel wire, with a silicone coating, and a radiopaque distal spring tip. The guide wire allows for the positioning of the coronary OAD crown within coronary arteries and provides a center of rotation for the

coronary OAD driveshaft. A guide wire torquer is a plastic accessory, packaged with the guide wire, and provides a gripping surface for manipulating the guide wire.

The ViperSlide Lubricant is designed to reduce the friction between the CSI ViperWire Advance Coronary Guide Wire and the drive shaft of the CSI OAD.

Refer to the Operator's Manual for additional details.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Currently there are no percutaneous medical devices with specific indications for the treatment of severely calcified coronary lesions. There are several other alternatives for the treatment of calcified *de novo* coronary vessel disease including balloon angioplasty, cutting balloons, stenting, rotational atherectomy, and bypass 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 DIAMONDBACK 360 Coronary Orbital Atherectomy System has not been marketed in the United States or any foreign country.

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 system:

- Allergic reaction to medication/media/device components
- Aneurysm
- Angina (ischemic chest pain)
- Arrhythmias Arteriovenous fistula
- Bleeding
- Bruising/hematoma
- Cardiac/cardiopulmonary arrest
- Cardiac/pericardial tamponade
- Cerebrovascular accident (CVA)
- Death
- Embolization, distal (air, tissue, thrombus, device)
- Emergent coronary artery bypass graft surgery (CABG)
- Failure to deliver the system to the intended locations
- Fever
- Heart failure/dysfunction
- Hemorrhage, requiring transfusion
- Hypotension/hypertension
- Infection
- Myocardial infarction
- Pain

- Pericardial effusion
- Pseudoaneurysm
- Restenosis of treated segment leading to revascularization
- Renal insufficiency/failure
- Shock (cardiogenic, hypovolemic)
- Slow flow or no reflow phenomenon
- Stroke
- Thrombus
- Vessel closure, abrupt
- Vessel injury, requiring surgical repair
- Vessel dissection, perforation, rupture, or spasm
- Vessel occlusion

For the specific adverse events that occurred in the clinical studies, please see **Section X.D.1** below.

IX. SUMMARY OF PRECLINICAL STUDIES

CSI completed comprehensive *in vitro* bench and analytical testing, biocompatibility, animal studies and sterility, packaging and shelf-life testing on the DIAMONDBACK 360 Coronary Orbital Atherectomy System to support the safety and effectiveness of the device.

A. Laboratory Studies

1. Biocompatibility

Biocompatibility testing was conducted on the DIAMONDBACK 360 Coronary Orbital Atherectomy Device (OAD), ViperWire Advance Coronary Guide Wire, and ViperSlide Lubricant. Testing was conducted in accordance with applicable Good Laboratory Practices (21 CFR 58) and ISO 10993-1. The saline infusion pump (SIP) is non-patient contacting; therefore, testing was not required.

The contact time between the OAD and a subject during a procedure is expected to be less than 24 hours; therefore, the device is categorized as limited contact duration. Most device components do not contact circulating blood in the body and are classified as surface skin contact. The working end of the OAD is the driveshaft, crown, tip bushing, and sheath. These components are classified as external communicating components with circulating blood contact. The saline line and some of the handle components come into contact with the indirect blood path and are classified as external communicating devices with indirect blood path contact. The test results demonstrate that the materials and processes used to manufacture the DIAMONDBACK 360 Coronary OAD produce a finished device that is biocompatible. **Table 1** summarizes the biocompatibility testing completed on the DIAMONDBACK 360 Coronary OAD.

ViperSlide is classified as an external communicating device with circulating blood contact. This lubricant is a commercially-available lipid emulsion that is labeled as ViperSlide. Therefore, established testing supports its biocompatibility. However, further testing was performed to verify the biocompatibility of the ViperSlide lubricant after use

with an operating Coronary OAD. The test results demonstrate that the materials and processes used to manufacture the ViperSlide lubricant produce a finished product that is biocompatible. **Table 1** summarizes the biocompatibility testing completed on the ViperSlide lubricant.

The contact time between the ViperWire Advance Coronary Guide Wire and a subject during a procedure is expected to be less than 24 hours, and therefore the device is categorized as limited contact duration. The guide wire is classified as an external communicating component with circulating blood contact. The test results demonstrate that the materials and processes used to manufacture the ViperWire Advance Coronary Guide Wire produce a finished device that is biocompatible. **Table 1** summarizes the biocompatibility testing completed on the ViperWire Advance Coronary Guide Wire.

Table 1: Biocompatibility Testing Summary

Test Performed	Test Description	Purpose	OAD			Guide Wire	Viper Slide	Results
			Circulating Blood	Blood Path Indirect	Surface Skin			
Sensitization	ISO-10993-10	To evaluate the allergenic potential or sensitizing capacity of the test article in guinea pigs.	X	X		X		Pass
Irritation/ Intracutaneous Reactivity	ISO 10993-10	To evaluate local dermal irritation effects of leachables following intracutaneous injections into rabbits.	X	X	X	X		Pass
Acute Systemic Toxicity	ISO 10993-11	To evaluate acute systemic toxicity of leachables extracted from the test article following a single intravenous or intraperitoneal injection in mice.	X	X		X	X	Pass
Pyrogenicity	ISO 10993-11	To evaluate if a test extract induces a pyrogenic (fever) response following intravenous injection in rabbits.	X	X		X		Pass
Compliment Activation (SC5b-9 & C3a)	ISO 10993-4	To measure the compliment activating potential of the test article in human plasma.	X	X		X		Pass
Partial Thromboplastin Time	ISO 10993-4	To evaluate the effect of the test article on the clotting time of human plasma.	X	X		X		Pass
Platelet and Leukocyte Counts	ISO 10993-4	To determine if the test article will adversely affect the platelet and leukocyte ratios in human whole blood.	X	X		X		Pass
Cytotoxicity	ISO 10993-5	To qualitatively evaluate whether an extract of the test article could cause cytotoxicity using the L929 mouse fibroblast cell culture.	X	X	X	X	X	Pass
ASTM Hemolysis (Direct & Indirect)	ISO 10993-4	To determine the ability of a test article or its extract, to destroy red blood cells with the subsequent release of the hemoglobin.	X	X		X	X	Pass
Thrombogenicity	ISO 10993-4	To evaluate the potential of the test article to cause thrombus formation when placed in the vasculature of a dog.	Note ¹			X		Pass

Test Performed	Test Description	Purpose	OAD			Guide Wire	Viper Slide	Results
			Circulating Blood	Blood Path Indirect	Surface Skin			
<i>In-vitro</i> Hemocompatibility Assay	ISO 10993-4	To determine if the test article when exposed to human whole blood will adversely affect the make-up of various cellular and non-cellular components of the blood.					X	Pass

Evaluated as part of an *in vivo* study

Additional testing was performed on some surface contacting OAD components because they were associated with subassemblies that contained components which are classified as circulating blood and blood path. Thrombogenicity was evaluated as part of other *in vivo* studies conducted to evaluate the safety and effectiveness of the device. The test results demonstrate the DIAMONDBACK 360 Coronary OAS is biocompatible.

2. Performance Studies

In-vitro performance testing to support the DIAMONDBACK 360 Coronary Orbital Atherectomy System (OAS) was developed based on design control requirements and potential risks. In February of 2012, CSI requested approval to introduce the 6F-compatible electric OAS into the ORBIT II study (the original system incorporated a pneumatic design). This request was approved in May of 2012. Performance testing indicated that the electric OAS remains safe and performs as intended. The sponsor was advised that a minimum of 100 patients would need to be treated with the electric OAS to support PMA approval.

A summary of the tests performed and associated results are provided in **Table 2** below.

Table 2: OAS Bench Testing Summary

OAS Component	Test	Test Summary	Acceptance Criteria	Summary of Results
OAS	Life Test	Verify the OAS is capable of functioning as intended without system failures while reaching and controlling rotational speed	Attribute test for ability to run full life test	Pass
OAD	Stall Test	Verify the survivability and continued functionality of the OAD when stalled in a lesion	Attribute test for ability to run full life test post 2 stalls	Pass
OAD	Dynamic Torque	Verify the maximum torque level by stalling device from high speed into torque sensor to read torque level delivered/available at crown/treatment site	Attribute test for maximum torque level	Pass
OAD	Tight Stenosis Crown Loading	Simulate treatment of a tight stenosis by crossing minimum pre-treatment diameter with acceptable speed loss	Attribute test for sufficient device torque and speed stability	Pass
OAD	Guide Catheter Compatibility	Verify that the OAD is capable of introduction and removal through standard 6F and 7F guide catheters	Attribute test for device functionality in 6F guide catheter in order to successfully perform life testing	Pass
OAD	Temperature Test	Verify the OAD does not generate heat by friction capable of blood or tissue damage	All devices must have an omega value of less than 0.50	Pass

OAS Component	Test	Test Summary	Acceptance Criteria	Summary of Results
OAD	Tensile Test	Verify multiple bonds meet a minimum tensile pull after operation of stall and life test	Attribute test for bond strength	Pass
OAD	Flexibility Test	Verify the robustness of the shaft while wrapped around a 0.5 inch radius	Attribute test for lack of damage to shaft	Pass
OAD	Track Test	Verify OAD's ability to reach, treat, and be removed from lesions in the coronary anatomy	Attribute test for maximum pushability and removal forces without kinking during simulation	Pass
OAD	Orbit Characterization	Verify orbit characteristics are similar to pneumatic device	No acceptance criteria; OAD must demonstrate similar orbit characteristics of pneumatic OAD at equivalent speeds	For characterization purposes only
OAD	Device User Interface Controls/ Switch and Logic Testing	Verify all functions of device can be manipulated and are repeatable for a total of 25 actuations/starts/ stops for each function/switch	Attribute test for switch functionality on 1 to 25 actuations	Pass
OAD	Guide Wire Brake Test	Verify guide wire brake functionally brakes/holds guide wire from any translation (tensile) or rotation (torque) during use	Variables test for guide wire movement during use	Pass
OAD	Flow Test	Verify saline delivery, leakage, and pressures are within previous device ranges	Attribute test for flow levels delivered	Pass
OAD	Motor Control Board	Verify all design requirements trace to test steps and conform to specifications	All samples must meet requirements	Pass
OAS	Electrical Safety	Testing completed per methods outlined in 60601-1	All samples must meet 60601-1 requirements	Pass
OAS	Electromagnetic Compatibility	Testing completed per methods outlined in 60601-1-2	All samples must meet 60601-1-2 requirements	Pass
OAD	Contrast Delivery	Verify contrast is delivered successfully and sheath remains undamaged and device operable after contrast delivery	Attribute test for lack of device damage	Pass

OAS Component	Test	Test Summary	Acceptance Criteria	Summary of Results
OAD	Particulate	Characterize the particles generated by the sanding crown	Variables test for similar particulate characteristics to the pneumatic OAD	For characterization purposes only
OAD	Miscellaneous	Verify conformance to various measurement requirements	Attribute test for conformance to measurements	Pass
SIP	SIP Functional Testing	Verify the expected flow rate, functionality of the low saline level sensor and audible notifications	Attribute test for pump functional specifications	Pass
SIP	SIP Physical Testing	Verify physical characteristics of the SIP design such as size, weight, and color	Attribute test for physical specifications	Pass
Guide Wire	Tensile Strength	Verify tensile strength using a load cell at a designated pull rate	All units must be able to withstand a 1.0 lb minimum tensile force	Pass
Guide Wire	Torque Strength	Determine the number of rotations the guide wire can withstand prior to guide wire fracture	Variable tests that all units withstand 10 full rotations within simulated coronary anatomy	Pass
Guide Wire	Tip Flexibility	Identify the maximum force required to deflect the distal tip of the guide wire when fixed at 5, 10, and 20 mm from the distal tip	Variable tests that all units must demonstrate maximum force to guide wire distal tip prolapse at the following lengths: <ul style="list-style-type: none"> • 5 mm \leq 6.34 g • 10 mm \leq 2.55 g • 20 mm \leq 1.09 g 	Pass
Guide Wire	Particulate	Characterization of particle size and volume of material released from guide wire when used with the OAD	No acceptance criteria; particle size and total volume of material removed from the guide wire during use were characterized	For characterization purposes only

OAS Component	Test	Test Summary	Acceptance Criteria	Summary of Results
Lubricant	Emulsion Admixture Stability	Testing was conducted to assess the stability of Intralipid 10% when mixed with normal saline and passed through a OAD while in operation at multiple time points	PFAT5 values are equal to or smaller than the currently approved material for each test interval	Pass

3. Sterilization Assurance

The DIAMONDBACK 360 Coronary Orbital Atherectomy Device (OAD) and ViperWire Advance Coronary Guide Wire are Ethylene Oxide sterilized and meet a sterility assurance level (SAL) of 10^{-6} . Validation and annual revalidation are completed based on the standards in ISO 11135-1:2007. The ViperSlide Lubricant is steam sterilized and meets an SAL of 10^{-6} .

4. Shelf Life and Packaging

The DIAMONDBACK 360 Coronary Orbital Atherectomy Device (OAD) was tested following accelerated aging to an equivalent of two (2) years per an approved shelf life protocol. Testing demonstrated the OAD met the established acceptance criteria. The OAD is packaged inside of a Polyethylene Terephthalate Glycol (PETG) tray and a snap-in-place retainer lid is used to hold the OAD and saline line in place. The OAD driveshaft is placed in a dispenser coil to protect it from kinking during shipment. The PETG tray is placed inside a header bag (sterile barrier), sealed, and placed into a shelf box. Testing demonstrated the OAD packaging system, including the sterile barrier remains intact through sterilization, aging, and distribution and is in compliance with ISO 11607-1/2:2006.

The Saline Infusion Pump (SIP) is a reusable pump that has an operating life of at least 875 hours. The SIP is provided non-sterile as it is used outside the sterile field during atherectomy procedures. It is placed in a plastic bag, and packed in a cardboard box surrounded by foam for shipment. Testing demonstrated the SIP packaging system remains intact through distribution and is in compliance with ISO 11607-1/2:2006.

The ViperWire Advance Coronary Guide Wire was tested following two (2) years of real time aging per an approved shelf life protocol. Testing demonstrated the guide wire met the established acceptance criteria. Each guide wire is inserted into a dispenser coil to prevent kinking during transit and placed in a Tyvek pouch that constitutes the sterile barrier. Five pouches are placed into each shelf carton. Testing demonstrated the guide wire packaging system, including the sterile barrier remains intact through sterilization, aging, and distribution and is in compliance with ISO 11607-1/2:2006.

The ViperSlide Lubricant has established stability data to support a two (2) year shelf life. ViperSlide is filled in 100 mL bag containers made from multilayered plastic film specifically designed for parenteral drugs. Ten (10) individual units are packaged in a corrugated shelf box and sealed. Testing demonstrated the ViperSlide packaging system, including the sterile barrier remains intact through sterilization, aging, and distribution.

B. Animal Studies

Three (3) *in vivo* studies were performed to demonstrate performance and safety of the DIAMONDBACK 360 Coronary Orbital Atherectomy System (OAS). All studies were conducted in accordance with Good Laboratory Practices (GLP) per 21 CFR 58. CSI utilized a native porcine vessel model for all coronary animal studies. **Table 3** provides a summary of the *in vivo* animal testing performed with the Coronary OAS.

Table 3: Pre-Clinical Animal Study Summary

Study Design	Study Design and Objectives	Results															
Sub-Acute (5 days) Study in Native Porcine Coronary Arteries	To evaluate the sub-acute safety and performance of the Pneumatic OAS in native arteries when used at clinically relevant speeds in five (5) animals with three (3) arteries treated: LAD, RCA and LCX, as compared to a “plain old balloon angioplasty“ (POBA)-treated control artery per animal. Relevant parameters of the treatment and control vessels were evaluated as follows:	<ul style="list-style-type: none"> • The OAD and lubricant performed as expected. • The results of the angiographic and IVUS images, biomarker blood analysis and ECG results using the OAD and lubricant indicate no signs of MI injury. • Artery segments contained histologic changes of injury which were not consistent with that seen in POBA. • One device-related serious adverse event (SAE) occurred; due to an error in communication, an incorrect crown size was used resulting in a type F dissection. 															
	<table border="1"> <thead> <tr> <th data-bbox="410 793 769 835">Assessment</th> <th data-bbox="769 793 1097 835">Timing</th> </tr> </thead> <tbody> <tr> <td data-bbox="410 835 769 903">Angiographic assessment</td> <td data-bbox="769 835 1097 903">Pre, post-treatment, pre-sacrifice</td> </tr> <tr> <td data-bbox="410 903 769 936">IVUS assessment</td> <td data-bbox="769 903 1097 936">Pre, post-treatment</td> </tr> <tr> <td data-bbox="410 936 769 1037">Biomarkers total CK and CK-MB isoenzyme levels</td> <td data-bbox="769 936 1097 1037">Pre, post-treatment, 0, 8, 16, 24, 32, 40 and 48 hr</td> </tr> <tr> <td data-bbox="410 1037 769 1171">Histopathological evaluations of treated areas and myocardium perfused by treated arteries</td> <td data-bbox="769 1037 1097 1171">At sacrifice</td> </tr> <tr> <td data-bbox="410 1171 769 1239">ECG analysis</td> <td data-bbox="769 1171 1097 1239">Pre, post-treatment, pre sacrifice</td> </tr> <tr> <td data-bbox="410 1239 769 1306">Device and procedure-related adverse events</td> <td data-bbox="769 1239 1097 1306">During course of study</td> </tr> </tbody> </table>		Assessment	Timing	Angiographic assessment	Pre, post-treatment, pre-sacrifice	IVUS assessment	Pre, post-treatment	Biomarkers total CK and CK-MB isoenzyme levels	Pre, post-treatment, 0, 8, 16, 24, 32, 40 and 48 hr	Histopathological evaluations of treated areas and myocardium perfused by treated arteries	At sacrifice	ECG analysis	Pre, post-treatment, pre sacrifice	Device and procedure-related adverse events	During course of study	
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Study Design	Study Design and Objectives	Results				
<p>Chronic (5 and 14 days) Study in Native Porcine Coronary Arteries</p>	<p>To evaluate the acute safety and performance of the Electric OAS in native arteries when used at clinically relevant speeds. In a total of seven (7) animals, two of the three coronary arteries (LAD, RCA and LCX) in each animal were treated with the OAS and the remaining artery was treated with POBA control. Relevant parameters of the treatment and control vessels were evaluated as follows:</p>	<ul style="list-style-type: none"> • 1/7 animals had low speed simulations because of vascular resistance or mural injury causing the operator to cease high speed operation. • There were 4/7 episodes of non-lethal AV block or acute ischemia during TIMI in the OAS group. • Two animals experienced first degree anterior ventral blood islands (AVBI) after treatment of the 2nd vessel (11P0131) and 3rd vessel (11P0125). • Histopathological evaluations indicated all vessels were patent. After multiple treatments, 3/14 vessels in the OAS group revealed mural injury compared to none of the POBA vessels. 4/14 vessels treated with the OAS contained histological changes of injury including moderate or fragmented IEL. Smooth muscle hyperplasia and mural injury occurred in 3/14 vessels in the OAD group. • No device or procedure-related SAE requiring corrective invasive intervention or significant clinical abnormalities were observed during the study. 				
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¹ With the exception of one animal 11P0231, in which the ECG after the RCA, POBA treatment, was missed.

Study Design	Study Design and Objectives	Results													
Chronic(1 and 5 days) Study in Native Porcine Coronary Arteries	To evaluate the sub-acute safety and performance of the Electric OAS in native arteries when used at clinically relevant speeds. In a total of two (2) animals, two of the three coronary arteries (LAD, RCA and LCX) in each animal were treated with the OAS. Relevant parameters of the treatment and control vessels were evaluated as follows:	<ul style="list-style-type: none"> • The OAD sheath and lubricant performed as expected and met all performance criteria. • The results indicated that acute safety and performance criteria were met; OAS sheath deployment and introduction to the access site was successful in all animals; device reliability was sustained up to 450 psi and vessels were free from damage through deployment, introduction, device treatment and removal. • Histopathological evaluations indicated all vessels were patent. Most artery segments contained histologic changes of injury. • No device or procedure-related SAE requiring corrective invasive intervention or significant clinical abnormalities were observed during the study. 													
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X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant first performed a pilot clinical study (ORBIT I) at two sites in India. This was followed by a pivotal clinical study (ORBIT II) to establish a reasonable assurance of safety and effectiveness to facilitate stent delivery with the DIAMONDBACK 360 Coronary Orbital Atherectomy System for patients with *de novo*, severely calcified coronary artery lesions in the US under G090106. Data from this clinical study (ORBIT II) were the basis for the PMA approval decision. A summary of these clinical studies is provided in **Table 4** and discussed in detail below.

Table 4: Summary of Primary Clinical Studies

Clinical Study	Study Design	Objectives	Number of Sites	Number of Subjects
Pilot (ORBIT I)	Prospective, Single-Arm, Multi-Center Feasibility Study	1) Evaluate the safety of the OAS in treating subjects with <i>de novo</i> calcified coronary lesions. 2) Assess the performance and acute effectiveness of the OAS.	2 Sites in India	<ul style="list-style-type: none"> • 50 Enrolled <ul style="list-style-type: none"> ○ 49 treated ○ 1 not treated
Pivotal (ORBIT II)	Prospective, Single-Arm, Multi-Center Clinical Study	1) Demonstrate the OAS is safe in treating <i>de novo</i> , severely calcified coronary lesions 2) Demonstrate that the OAS successfully facilitates stent deployment in severely calcified coronary lesions.	49 Sites in US	<ul style="list-style-type: none"> • 443 Enrolled • 440 Treated <ul style="list-style-type: none"> ○ 437/440 evaluable at 30 days ○ 3/440 lost to follow-up

A. Study Design

Patients were treated between 25-May-2010 and 26-Nov-2013. The database for this PMA reflected data collected through 31-Jan-2013 and included 443 patients. Of the 443 patients, 343 were enrolled with the Pneumatic OAS and 100 with the Electric OAS. There were 49 investigational sites.

The ORBIT II study was a prospective, single arm, multi-center clinical study with the primary effectiveness endpoint evaluated at discharge and the primary safety endpoint evaluated at 30 days. Both primary safety and effectiveness endpoints were based on comparisons to pre-specified performance goals based on the literature from past trials (historical control). Kaplan-Meier analysis with a confidence interval based on Peto's method was used for the primary safety endpoint and an exact binomial confidence interval was used for procedural success. Descriptive statistics are provided for secondary endpoints.

Additional analyses included summaries of baseline data, examination of factors related to

primary endpoints (i.e., poolability analyses), analyses for alternate patient cohorts (i.e., a per protocol analysis), and sensitivity analyses to examine the impact of missing data on the primary endpoints.

MACE is a commonly used safety endpoint for interventional coronary trials and was used to assess the primary safety endpoint of the DIAMONDBACK 360 Coronary OAS. The OAS is designed to facilitate stent deployment in severely calcified lesions, therefore, the primary effectiveness endpoint was defined as success in facilitating stent delivery with a residual stenosis of <50% and without the occurrence of an in-hospital MACE in *de novo*, severely calcified lesions. Since the DIAMONDBACK 360 Coronary OAS is intended to facilitate stent deployment, potential safety concerns relevant to OAS treatment are likely to be observed during the index procedure or shortly thereafter. For this reason, the ORBIT II safety endpoint is based on 30-day follow-up and the effectiveness endpoint is based on in-hospital events.

Study endpoints were evaluated by three external groups:

- An independent Angiographic Core Laboratory assessed the occurrence of dissections and perforations and their severity, and final percent stenosis used to evaluate primary effectiveness endpoint.
- An independent Clinical Events Committee (CEC) reviewed all adverse events and provided adjudication of all study endpoint events with the exception of MI (that was based on CK-MB values).
- An independent Data Monitoring Committee (DMC) provided surveillance of subject safety according to the safety concerns specified in the study protocol as well as any unexpected adverse events.

After the site data were locked, final CEC review/adjudication of adverse events reported through the 31-Jan-2013 cutoff was performed and final Angiographic Core Laboratory data obtained for a database lock of 05-Mar-2013.

Study enrollment was completed in two parts as follows:

Part I: Safety Cohort

Enrollment and 30-day follow-up data of the first 50 subjects were required. As a result, the data from 54 subjects were collected and reported to the Food and Drug Administration (FDA) in an interim safety report. During the review of the interim report, enrollment continued with a cap of 100 total subjects until approval to proceed was obtained from FDA on 20-May-2011.

Part II: Full Cohort

Following FDA approval of the Part I results, the study received approval to enroll up to 429 subjects. However, following the introduction of the Electric OAS, the enrollment was expanded from a minimum of 429 subjects to a maximum of 479 subjects. This expansion was required to enroll and treat 100 subjects with the Electric OAS. The full cohort is inclusive of the safety cohort.

The trial was conducted in accordance with the study protocol and other applicable regulatory requirements (21 CFR §50, 54, 56, 812). The study was monitored by the applicant or its representatives through monitoring visits to the Investigational Sites with sufficient frequency to verify the following: subject enrollment, compliance with the protocol, the completeness and accuracy of data entered in the electronic data capture (EDC) database by verification against original source documents, device accountability, and recording of adverse events (AEs).

In addition, all primary safety and effectiveness endpoints data collected from the clinical sites were adjudicated by independent bodies such as the Angiographic Core Laboratory and the Clinical Events Committee (CEC). The overall safety of the clinical study was overseen by the independent Data Monitoring Committee (DMC).

Two OAS configurations were available during the ORBIT II study as described below:

- Pneumatic OAS - consists of:
 - A sterile single-use Orbital Atherectomy Device (OAD)
 - A sterile single-use Orbital Atherectomy guide wire
 - A re-useable Orbital Atherectomy Controller (OAC) console
 - Atherectomy lubricant solution (RotaGlide or ViperSlide)
- Electric OAS – consists of:
 - A sterile single-use Orbital Atherectomy Device (OAD)
 - A sterile single-use Orbital Atherectomy guide wire
 - A re-useable saline pump (SIP)
 - Atherectomy lubricant solution (ViperSlide)

1. Inclusion/Exclusion Criteria

Enrollment in the ORBIT II study was limited to patients who met the following inclusion criteria:

General Inclusion Criteria:

- 1) Subjects must be 18 or older.
- 2) Subjects must have a clinical indication for coronary intervention.
- 3) CK-MB must be less than or equal to the upper limit of lab normal value within 8 hours prior to the procedure.

Angiographic Inclusion Criteria:

- 4) The target lesion must be a de novo coronary lesion that has not been previously treated with any interventional procedure.
- 5) The target vessel must be a native coronary artery with:
 - a. A stenosis $\geq 70\%$ and $< 100\%$, or
 - b. A stenosis $\geq 50\% < 70\%$ with evidence of clinical ischemia via:
 - i. Positive stress test, or
 - ii. Fractional Flow Reserve (FFR) value ≤ 0.8 , or
 - iii. IVUS minimum lumen area (MLA) $\leq 4.0 \text{ mm}^2$
- 6) The target vessel reference diameter must be $\geq 2.5\text{mm}$ and $\leq 4.0\text{mm}$.
- 7) The target lesion must not exceed 40mm.
- 8) The target vessel must have a TIMI 3 flow at baseline.

- 9) The target lesion must have fluoroscopic or IVUS evidence of severe calcium deposit at the lesion site based on the protocol definition:
 - Presence of radio-opacities noted without cardiac motion prior to contrast injection involving both sides of the arterial wall in at least one location, total length of calcium (including segmented) must be at least 15mm and extend partially into the target lesion, or
 - Presence of $\geq 270^\circ$ of calcium at one cross section.
- 10) The lesion must be crossable with the study guide wire.

Patients were not permitted to enroll in the ORBIT II study if they met any of the following exclusion criteria:

General Exclusion Criteria:

- 1) Inability to understand the study or a history of non-compliance with medical advice.
- 2) Unwilling or unable to sign the ORBIT II Informed Consent Form (ICF).
- 3) History of any cognitive or mental health status that would interfere with study participation.
- 4) Currently enrolled in any other pre-approval investigational study (does not apply to long-term post-market studies unless these studies might clinically interfere with the current study endpoints (e.g., limit use of study-required medication, etc.)).
- 5) Female subjects who are pregnant or planning to become pregnant within the study period.
- 6) Known hypersensitivity or contraindication to aspirin, heparin, ticlopidine or clopidogrel without adequate alternative medications.
- 7) Known sensitivity to contrast media, which cannot be adequately pre-medicated.
- 8) Diagnosed with chronic renal failure unless under hemodialysis, or has a serum creatinine level >2.5 mg/dl.
- 9) Experienced acute MI (STEMI or non-STEMI: CK-MB greater than the upper limit of lab normal value) within 30 days prior to index procedure.
- 10) History of major cardiac intervention within 30 days, not including a PCI procedure for a staging purpose.
- 11) Evidence of current LVEF $\leq 25\%$ (where current is defined as the latest LVEF measurement completed within the last 6 months).
- 12) NYHA class III or IV heart failure.
- 13) History of a stroke or transient ischemic attack (TIA) within 6 months.
- 14) Active peptic ulcer or upper gastrointestinal (GI) bleeding within 6 months.
- 15) History of bleeding diathesis or coagulopathy or intention to refuse blood transfusion if one should become necessary.
- 16) Concurrent medical condition with a life expectancy of less than 12 months.
- 17) History of immune deficiency.
- 18) Uncontrolled insulin dependent diabetes.
- 19) Evidence of active infections on the day of the index procedure.
- 20) Subject has planned cardiovascular intervention within 60 days post index procedure.

- 21) Subject is not an acceptable candidate for emergent coronary artery bypass surgery.
- 22) Subject with known allergy to atherectomy lubricant components such as soybean oil, egg yolk phospholipids, glycerin and sodium hydroxide.
- 23) Subject with angiographically confirmed evidence of more than 1 lesion requiring intervention, unless the treatment of the lesions is staged.
- 24) Target lesion is located in a native vessel distal to anastomosis with a saphenous vein graft or LIMA/RIMA bypass.
- 25) Target vessel has other lesions with greater than 50% diameter stenosis based on visual estimate or on-line QCA.
- 26) Target vessel has angiographically visible or suspected thrombus.
- 27) Target vessel has a stent from previous PCI unless **1)** the stent was implanted greater than 30 days prior to the index procedure, and **2)** the stent has no higher than 30% in-stent stenosis, and **3)** the stent is on a different branch than the target lesion.
- 28) Target vessel is excessively tortuous.
- 29) Target lesion is an ostial location (within 5 mm of ostium) or an unprotected left main lesion.
- 30) Target lesion is a bifurcation.
- 31) Target lesion has a ≥ 1.5 mm side branch.
- 32) Angiographic evidence of a dissection prior to initiation of OAD.

2. Follow-up Schedule

All subjects were required to undergo percutaneous treatment with the coronary OAS followed by stent placement and were scheduled to return for follow-up examinations at 30 days post procedure with an office visit. In addition, subjects were required to complete an annual phone call or in-clinic follow-up at each anniversary until the study is closed or up to 5 years; whichever occurs first.

All preoperative evaluations performed in relation to the index procedure and postoperative assessments (the objective parameters measured during the study) are summarized in **Table 5**, at each stage of the study.

Adverse events and complications were recorded at all visits.

Table 5: Study Assessment Schedule and Requirements

Time Point	Compliance Window	Test and Procedure
Pre-procedure	≤ 14 days	Medical history Physical exam CCS Angina Class NYHA class 12-lead ECG CBC, serum creatinine Pregnancy test for female subjects of childbearing potential
	≤ 8 hours	CK and CK-MB Electrolyte panel

Time Point	Compliance Window	Test and Procedure
		Troponin
Procedure	During the procedure	ACT at the onset of the procedure Fluoroscopy and angiography/IVUS Monitor ECG changes
Post-procedure	As close to the procedure end as possible	12-lead ECG
	8±1 hour	CK and CK-MB Electrolyte panel Troponin Check for occurrences of adverse events
	17-1/+3 hours	CK and CK-MB Electrolyte panel Troponin Serum Creatinine Check for occurrences of adverse events
At discharge	Prior but as close to discharge time as possible	12-lead ECG Check for occurrences of adverse events
30-day follow-up visit	30 + 14 days	In clinic visit Check for occurrences of adverse events
Annual phone call or in clinic follow-up	Anniversary date ±60 days	General well-being Check for occurrences of adverse events
Any hospitalization	N/A	Check for occurrences of adverse events

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

3. Clinical Endpoints

Primary Safety Endpoint

The primary safety endpoint was to demonstrate that the OAS is safe when used to facilitate stent deployment in *de novo*, severely calcified coronary lesions. This was measured by a composite of major adverse cardiac events (MACE) at 30 days post-procedure. MACE is composed of:

- Cardiac death
- Myocardial infarction (MI) – defined as a CK-MB level > 3 times the upper limit of lab normal (ULN) value with or without new pathologic Q wave.
- Target vessel revascularization (TVR) – defined as revascularization at the target vessel (inclusive of the target lesion) after the completion of the index procedure.

A literature review was completed and the calculation of a performance goal of 83% freedom from MACE was determined to be clinically acceptable. The pre-specified hypothesis test for the primary safety endpoint was formulated as:

- $H_0: \pi_s \leq 83\%$
- $H_a: \pi_s > 83\%$

where: π_s = the probability of freedom from MACE within 30 days of the procedure of OAS device treatment.

Additional safety-related secondary endpoints evaluated in the ORBIT II study included:

- Severe Angiographic Complications defined as the rate of individual severe angiographic complication during the index procedure including severe dissections (Types C-F), perforation, persistent slow flow, persistent no reflow, and abrupt closure.
- 12-Month MACE

Primary Effectiveness Endpoint

The primary effectiveness endpoint was to demonstrate that the OAS is capable of successfully facilitating stent deployment in *de novo*, severely calcified coronary lesions. Procedural success was defined as success in facilitating stent delivery with a residual stenosis of < 50% (per Angiographic Core Laboratory) and without the occurrence of an in-hospital MACE.

The effectiveness endpoint rates in similar device trials suggest that a performance goal of 82% is clinically acceptable. The pre-specified hypothesis test for the primary effectiveness endpoint was formulated as:

- $H_0: \pi_e \leq 82\%$
- $H_a: \pi_e > 82\%$

where: π_e = the probability of the procedural success for OAS device measured by the success in facilitating stent delivery with < 50% residual stenosis and without in-hospital MACE.

Additional effectiveness-related secondary endpoints evaluated in the ORBIT II study included:

- Angiographic Success defined as success in facilitating stent delivery with < 50% residual stenosis and without severe angiographic complications. Severe angiographic complications include severe dissections (Types C-F), perforation, persistent slow flow, persistent no reflow, and abrupt closure.

Secondary Endpoints

Procedural Parameters including the following:

- Number of crown(s) used per lesion
- Percent of each size OAD used
- Percent of lesions where balloon dilation was done prior to stenting
- Percent of lesions where post-stent placement dilation was necessary
- Procedure time – defined as the time from when the first guide catheter was placed in the access site to the time the last guide catheter was removed from the access site
- OAS treatment time – defined as total device rotation time per patient
- Fluoroscopy time
- Amount of contrast agent used during the procedure

4. Statistical Methodology

Patient demographics, medical history, risk factors, pre- and post- procedure lesion characteristics, procedure characteristics, and outcome variables were summarized using descriptive statistics for continuous variables and frequency tables or proportions for discrete variables. For the primary safety endpoint, Kaplan-Meier method and Peto's method were used to obtain the estimate and the corresponding 95% confidence interval (CI), respectively. The pre-specified hypothesis test for the primary safety endpoint was conducted based on the 95% CI. For the primary effectiveness endpoint, Clopper-Pearson Exact method was used to calculate the 95% CI and perform the pre-specified hypothesis test. The point estimates of the secondary endpoints are also reported.

The potential impact of missing data of the primary safety and effectiveness endpoints on the study conclusions were assessed in sensitivity analyses.

5. Subject Sample Size

The overall sample size was based on the safety endpoint. Assuming the true 30-day MACE free rate of 88%, an evaluable sample size of 408 subjects was required to achieve approximate 80% power to reject the null hypothesis for the primary safety endpoint that the true 30-day MACE free rate is at most 83% at a one-sided α -level of 0.025.

Adjusting for a 5% rate of attrition and missing data at 30 days post-procedure, enrollment of 429 subjects was determined to be required. As described earlier, the overall study sample size was increased up to 479 subjects to ensure the inclusion of 100 subjects treated with the Electric OAS.

B. Accountability of PMA Cohort

There were a total of 443 subjects who provided informed consent to participate in the ORBIT II study and in whom the study guide wire crossed the lesion. Of the 443 subjects enrolled, three (3) subjects were immediately withdrawn from the study as the OAD was never inserted (but the guide wire crossed the lesion and therefore, the subjects were considered enrolled in the study).

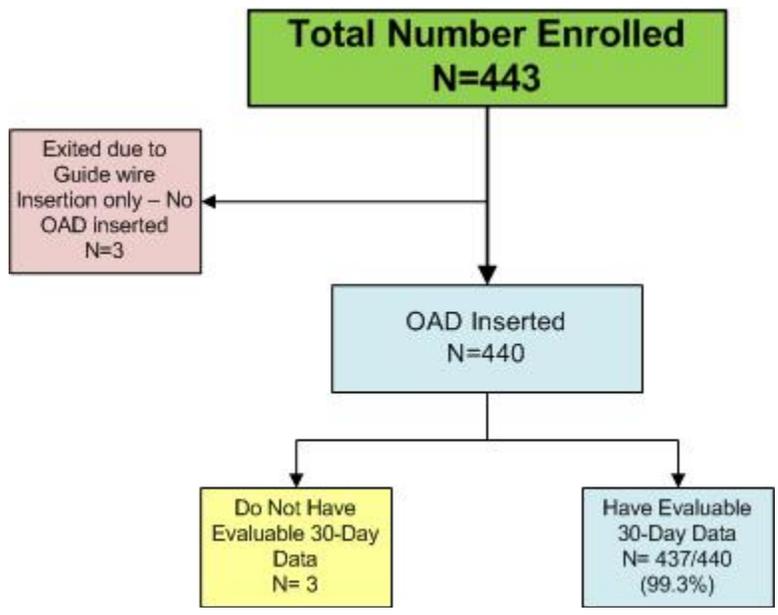
The safety endpoint was evaluated based on the intent-to-treat cohort defined as enrolled subjects (N=443). The effectiveness analysis was based on all evaluable subjects where the guide wire crossed the lesion and the OAD was inserted (N=440). Additional statistical analyses of the primary endpoints were also performed for a “per protocol” subject population defined as subjects treated with OAS and with no or minimal protocol deviations. At the time of database lock, of 443 patients enrolled in PMA study, 99.3% (437/440) patients were available for analysis at the completion of the study, the 30-day post-operative visit.

Of the 440 subjects where the OAD was inserted:

- 437/440 had evaluable 30-day data
- 3/440 had no post 30-day data collected (subjects refused to return for the 30-day visit and were classified as lost to follow-up after the 30-day window).

Therefore, at the time of the database lock, 48.5% (215/443) subjects completed 1-year follow-up, 3.8% (17/443) expired, 0.7% (3/443) were lost to follow-up and 0.2% (1/443) voluntarily withdrew from the study.

Figure 1: Subject Disposition Flow Chart



C. Study Population Demographics and Baseline Parameters

An analysis of previous trials reported in the literature with similar indications that included calcified lesions showed a range of male enrollment as 63.0-86.3%. The ORBIT II trial, which included enrollment of 64.6% males, had comparable gender ratios to the other previously published studies. The patient population enrolled in this study was older and had higher eGFR compared to past trials; however, this was not unexpected as ORBIT II is a study that evaluated patients with severely calcified lesions which are difficult to treat, have higher comorbidities and, therefore, often excluded from clinical trials.

Table 6 summarizes demographics by OAS treatment group. Subject demographics were similar between Pneumatic and Electric OAS groups. The majority of the subjects were Caucasian (87.8%) males (64.6%). Of the three (3) subjects with ethnicity reported as “other,” one (1) subject was reported as “West Indian” and the other two (2) subjects were reported as unknown.

Table 6: Demographics for ORBIT II Subjects

Demographic	Pneumatic OAS	Electric OAS	Overall
Number of Subjects Enrolled	N=343	N=100	N=443
Gender			
Male	221/343 (64.4%)	65/100 (65.0%)	286/443 (64.6%)
Female	122/343 (35.6%)	35/100 (35.0%)	157/443 (35.4%)
Ethnicity			
Caucasian	305/343 (88.9%)	84/100 (84.0%)	389/443 (87.8%)
Black or African American	22/343 (6.4%)	3/100 (3.0%)	25/443 (5.6%)
Asian	7/343 (2.0%)	2/100 (2.0%)	9/443 (2.0%)
Hispanic or Latino	6/343 (1.7%)	10/100 (10.0%)	16/443 (3.6%)
Native American	0/343 (0.0%)	1/100 (1.0%)	1/443 (0.2%)
Other	3/343 (0.9%)	0/100 (0.0%)	3/443 (0.7%)
Age (years)			
N	343	100	443
Mean ± SE	71.4 ± 0.5	71.5 ± 1.0	71.4 ± 0.5
Min – Max	37.4 - 92.2	39.8 - 91.4	37.4 - 92.2
BMI			
N	343	100	443
Mean ± SE	29.5 ± 0.3	29.2 ± 0.6	29.4 ± 0.3
Min – Max	15.2 - 60.7	16.1 - 51.4	15.2 - 60.7
eGFR			
N	341	100	441
Mean ± SE	76.0 ± 1.4	74.9 ± 2.4	75.8 ± 1.2
Min – Max	4.6 - 191.7	7.4 - 181.0	4.6 - 191.7

Table 7 summarizes clinical history for the subjects enrolled in the study. More than 90% of ORBIT II subjects have hypertension and dyslipidemia, more than 75% have a history of angina (most are considered stable angina), approximately 66% are smokers or previously smoked, over 35% have diabetes, and more than 22% have previously had a MI. “Other” treated vessels were reported most commonly as obtuse marginal, diagonal, or posterior descending artery (PDA).

Table 7: Clinical History of ORBIT II Subjects

Clinical History	Pneumatic OAS	Electric OAS	Overall
Number of Subjects Enrolled	N=343	N=100	N=443
History of Diabetes mellitus			
No	220/343 (64.1%)	63/100 (63.0%)	283/443 (63.9%)
Yes, Type I	6/343 (1.7%)	4/100 (4.0%)	10/443 (2.3%)
Yes, Type II	117/343 (34.1%)	33/100 (33.0%)	150/443 (33.9%)
Smoking			
No, Never smoked	105/343 (30.6%)	45/100 (45.0%)	150/443 (33.9%)
Yes, Current smoker	62/343 (18.1%)	13/100 (13.0%)	75/443 (16.9%)
Yes, Former smoker	176/343 (51.3%)	42/100 (42.0%)	218/443 (49.2%)
History of dyslipidemia			
No	23/343 (6.7%)	12/100 (12.0%)	35/443 (7.9%)
Unknown	1/343 (0.3%)	0/100 (0.0%)	1/443 (0.2%)
Yes	319/343 (93.0%)	88/100 (88.0%)	407/443 (91.9%)
History of hypertension			
No	30/343 (8.7%)	7/100 (7.0%)	37/443 (8.4%)
Yes	313/343 (91.3%)	93/100 (93.0%)	406/443 (91.6%)
History of stroke/TIA			
No	313/343 (91.3%)	90/100 (90.0%)	403/443 (91.0%)
Unknown	1/343 (0.3%)	0/100 (0.0%)	1/443 (0.2%)
Yes	29/343 (8.5%)	10/100 (10.0%)	39/443 (8.8%)
History of MI			
No	261/343 (76.1%)	78/100 (78.0%)	339/443 (76.5%)
Unknown	5/343 (1.5%)	0/100 (0.0%)	5/443 (1.1%)
Yes	77/343 (22.4%)	22/100 (22.0%)	99/443 (22.3%)
History of Angina			

Clinical History	Pneumatic OAS	Electric OAS	Overall
No	77/343 (22.4%)	18/100 (18.0%)	95/443 (21.4%)
Yes	266/343 (77.6%)	82/100 (82.0%)	348/443 (78.6%)
For subjects with history of angina, type			
Stable	167/266 (62.8%)	56/82 (68.3%)	223/348 (64.1%)
Unstable	99/266 (37.2%)	26/82 (31.7%)	125/348 (35.9%)
LVEF (%)			
N	338	99	437
Mean ± SE	56.7 ± 0.5	56.4 ± 1.0	56.6 ± 0.5
Min - Max	26.0 - 78.0	30.0 - 80.0	26.0 - 80.0
NYHA classification of Heart Failure			
No History of Heart Failure	10/340 (2.9%)	18/100 (18.0%)	28/440 (6.4%)
Class I	217/340 (63.8%)	32/100 (32.0%)	249/440 (56.6%)
Class II	111/340 (32.6%)	50/100 (50.0%)	161/440 (36.6%)
Class III	2/340 (0.6%)	0/100 (0.0%)	2/440 (0.5%)
Class IV	0/340 (0.0%)	0/100 (0.0%)	0/440 (0.0%)

The ORBIT II protocol allowed treatment of severely calcified *de novo* coronary lesions in any native coronary artery, including the Left Main artery. Target vessel and lesion characteristics, including determination of pre-procedure percent stenosis (as determined by Investigator) are reported in **Table 8**.

Table 8: Vessel & Lesion Characteristics

Characteristic	Pneumatic OAS	Electric OAS	Overall
Subjects with OAD inserted	N=340	N=100	N=440
Target Lesion Vessel			
LAD	169/340 (49.7%)	58/100 (58.0%)	227/440 (51.6%)
LCX	44/340 (12.9%)	20/100 (20.0%)	64/440 (14.5%)
Left Main	9/340 (2.6%)	1/100 (1.0%)	10/440 (2.3%)
RCA	112/340 (32.9%)	20/100 (20.0%)	132/440 (30.0%)
Ramus	6/340 (1.8%)	1/100 (1.0%)	7/440 (1.6%)
Pre-Procedure Target Lesion Length (mm)			

Characteristic	Pneumatic OAS	Electric OAS	Overall
N	340	100	440
Mean ± SE	18.4 ± 0.5	20.6 ± 1.0	18.9 ± 0.4
Min - Max	3.0 - 40.0	5.0 - 40.0	3.0 - 40.0
Pre-Procedure Average RVD (mm)			
N	340	100	440
Mean ± SE	3.1 ± 0.0	3.1 ± 0.0	3.1 ± 0.0
Min - Max	2.5 - 4.0	2.5 - 4.0	2.5 - 4.0
ACC/AHA lesion classification			
A	0/340 (0.0%)	0/100 (0.0%)	0/440 (0.0%)
B1	86/340 (25.3%)	28/100 (28.0%)	114/440 (25.9%)
B2	148/340 (43.5%)	49/100 (49.0%)	197/440 (44.8%)
C	106/340 (31.2%)	23/100 (23.0%)	129/440 (29.3%)
Pre-Procedure MLD (mm)			
N	340	100	440
Mean ± SE	0.5 ± 0.0	0.5 ± 0.0	0.5 ± 0.0
Min - Max	0.0 - 1.4	0.0 - 1.2	0.0 - 1.4
Pre-Procedure percent stenosis			
N	340	100	440
Mean ± SE	84.3 ± 0.5	84.5 ± 0.9	84.4 ± 0.4
Min - Max	60.0 - 99.0	60.0 - 99.0	60.0 - 99.0

Vessel calcification (as determined by the Investigator) is reported in **Table 9**.

Angiographically, severe calcification was defined as a total length of calcium (including segmented) > 15mm with calcium visible on both sides of the vessel in at least one location. Revision 08 and 09 of the protocol also permitted calcification severity to be determined via IVUS defined as ≥ 270° of calcium seen at one cross-section. However, the majority of subjects (92% overall) had angiography to determine the calcification of the target vessel. The overall mean length of calcium treated was 28.6 ± 0.8 mm, ranging from 9.0 -100 mm.

Table 9: Vessel Calcification

Characteristic	Pneumatic OAS	Electric OAS	Overall
Subjects with calcification determined by angiography only	316/340 (92.9%)	89/100 (89.0%)	405/440 (92.0%)
Total length of calcium (including segmented) (mm)			
N	316	89	405
Mean ± SE	28.4 ± 0.9	29.0 ± 1.6	28.6 ± 0.8
Min - Max	9.0 - 100.0	15.0 - 100.0	9.0 - 100.0
Subjects with calcium visible on both sides of the vessel	316/316 (100.0%)	89/89 (100.0%)	405/405 (100.0%)
Subjects with calcification determined by IVUS	24/340 (7.1%)	11/100 (11.0%)	35/440 (8.0%)
Maximum degree of calcium via IVUS (°)			
N	24	11	35
Mean ± SE	296.7 ± 7.6	291.4 ± 10.7	295.0 ± 6.1
Min - Max	270.0 - 360.0	270.0 - 360.0	270.0 - 360.0

D. Safety and Effectiveness Results**1. Safety Results**

The analysis of safety was based on the intent-to-treat cohort of 443 enrolled subjects, of which 46 subjects experienced 30-day post-procedural MACE events, 5 subjects were censored for 30-day post-procedural MACE event data, and 392 subjects were free from 30-day post-procedural MACE. The key safety outcome for this study is presented below in **Table 10**. Adverse effects are reported in **Table 11** and **Table 12**.

The safety of the OAS was measured by a primary safety endpoint consisting of a composite of freedom from MACE at 30 days post-procedure. The null hypothesis that the true 30-day post-procedure MACE-free rate is at most 83% was to be rejected in favor of the alternative if the lower bound of the 2-sided 95% confidence interval (CI) for the 30-day MACE-free rate was greater than the pre-specified performance goal of 83%. All 443 enrolled subjects have been included in the primary safety endpoint analysis.

At 30 days post index procedure, MACE occurred in 46 subjects. The observed rate of freedom from MACE was 89.6% with 95% CI of (86.7%, 92.5%). The lower bound of the 95% CI, 86.7%, was greater than the pre-defined performance goal of 83%. The null hypothesis that the true 30-day post-procedure MACE-free rate is at most 83% was

rejected and the performance goal of the primary safety endpoint was met successfully (Table 10).

Table 10: Primary Safety Endpoint (30 days MACE)

Primary Safety Endpoint	% [95% CI] ¹	Hypothesis	Decision	Conclusion
Freedom from MACE within 30 days post-procedure ²	89.6% [86.7%-92.5%]	H ₀ : $\pi_s \leq 83\%$ H _a : $\pi_s > 83\%$	Reject H ₀	Performance Goal Met
¹ Kaplan-Meier method used to obtain estimate of freedom from MACE. Peto's method used to obtain the 95% confidence interval for the estimate.				
² The Freedom from MACE within 30 days post-procedure includes all subjects where the guidewire crossed the lesion.				

At the time of the data lock, 64 of 443 subjects (14.4%) had a MACE event. The freedom from MACE through 12 months of follow-up was estimated as 82.1% via a Kaplan-Meier analysis. All subjects where the guide wire crossed the lesion have been included in the analysis of the 12-month MACE rate.

Adverse effects that occurred in the PMA clinical study:

Table 11 outlines the rate and number of all device-related (definite, probably, or possibly related to the OAS) serious adverse events (SAE), all procedure-related (definite, probably, or possibly related) SAE, and SAE up to 30 days post-procedure, as adjudicated by the CEC. **Table 12** outlines the rate and number of all device-related non-serious AEs (non-SAEs), all procedure-related non-SAEs and all non-SAEs up to 30 days post-procedure. All events listed are in descending order of clinical importance, as determined by their severity and/or incidence.

Table 11: Summary of Serious Adverse Events

	All Device Related SAEs N=443		All Procedure Related SAEs N=443		SAEs through 30 days N=443	
	Subjects n (%)	Events, N	Subjects n (%)	Events N	Subjects n (%)	Events N
Death (No disorder specified)	4 (0.9%)	4	4 (0.9%)	4	2 (0.5%)	2
Cardiac death	3 (0.7%)	3	3 (0.7%)	3	1 (0.2%)	1
Non-cardiac death	1 (0.2%)	1	1 (0.2%)	1	1 (0.2%)	1
Cardiovascular Disorders	33 (7.4%)	37	51 (11.5%)	56	60 (13.5%)	68
Ventricular fibrillation	1 (0.2%)	1	2 (0.5%)	2	2 (0.5%)	2
PEA arrest	1 (0.2%)	1	1 (0.2%)	1	1 (0.2%)	1
Ventricular tachycardia	0 (0.0%)	0	1 (0.2%)	1	1 (0.2%)	1

	All Device Related SAEs N=443		All Procedure Related SAEs N=443		SAEs through 30 days N=443	
	Subjects n (%)	Events, N	Subjects n (%)	Events N	Subjects n (%)	Events N
Ventricular tachycardia/ventricular fibrillation	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Cardiogenic shock	2 (0.5%)	2	2 (0.5%)	2	2 (0.5%)	2
Shock (Acute RV dysfunction and acute blood loss hypovolemic)	1 (0.2%)	1	1 (0.2%)	1	1 (0.2%)	1
Acute MI, Q-wave	1 (0.2%)	1	3 (0.7%)	3	4 (0.9%)	4
Acute MI, non-Q wave	28 (6.3%)	28	39 (8.8%)	39	39 (8.8%)	39
Cardiac/pericardial tamponade	2 (0.5%)	2	4 (0.9%)	4	4 (0.9%)	4
Endocarditis	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Non-target vessel revascularization	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Angina pectoris	1 (0.2%)	1	2 (0.5%)	2	4 (0.9%)	4
Atrial fibrillation	0 (0.0%)	0	0 (0.0%)	0	2 (0.5%)	2
Atrioventricular block, II degree	0 (0.0%)	0	1 (0.2%)	1	1 (0.2%)	1
Sick sinus syndrome	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Pericarditis	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Chest pain	0 (0.0%)	0	0 (0.0%)	0	2 (0.5%)	2
Neurologic/Psychiatric Disorders	0 (0.0%)	0	4 (0.9%)	4	4 (0.9%)	4
Cerebrovascular accident (CVA)	0 (0.0%)	0	3 (0.7%)	3	3 (0.7%)	3
Sundowning/ICU "psychosis"	0 (0.0%)	0	1 (0.2%)	1	1 (0.2%)	1
Respiratory/Thoracic Disorders	0 (0.0%)	0	2 (0.5%)	4	7 (1.6%)	9
Respiratory failure, requiring intubation	0 (0.0%)	0	1 (0.2%)	1	1 (0.2%)	1
Respiratory failure	0 (0.0%)	0	1 (0.2%)	1	1 (0.2%)	1
Aspiration	0 (0.0%)	0	1 (0.2%)	1	1 (0.2%)	1
Anoxia due to aspiration	0 (0.0%)	0	1 (0.2%)	1	1 (0.2%)	1
Pneumonia	0 (0.0%)	0	0 (0.0%)	0	2 (0.5%)	2
COPD	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1

	All Device Related SAEs N=443		All Procedure Related SAEs N=443		SAEs through 30 days N=443	
	Subjects n (%)	Events, N	Subjects n (%)	Events N	Subjects n (%)	Events N
Bronchitis	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Dyspnea/Shortness of breath	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Angiographic Complications	3 (0.7%)	3	7 (1.6%)	7	7 (1.6%)	7
Thrombosis formation at site of treated lesion	1 (0.2%)	1	1 (0.2%)	1	1 (0.2%)	1
Coronary artery embolism of air, plaque, thrombosis, or debris	1 (0.2%)	1	3 (0.7%)	3	3 (0.7%)	3
Slow flow or no reflow phenomena	1 (0.2%)	1	3 (0.7%)	3	3 (0.7%)	3
Vascular Disorders	1 (0.2%)	1	10 (2.3%)	10	11 (2.5%)	11
Hypotension	1 (0.2%)	1	2 (0.5%)	2	2 (0.5%)	2
Hemorrhage, major, requiring transfusion	0 (0.0%)	0	3 (0.7%)	3	3 (0.7%)	3
Pulmonary embolism	0 (0.0%)	0	1 (0.2%)	1	1 (0.2%)	1
Peripheral artery pseudoaneurysm	0 (0.0%)	0	3 (0.7%)	3	3 (0.7%)	3
Hematoma at access site, requiring intervention	0 (0.0%)	0	1 (0.2%)	1	1 (0.2%)	1
Peripheral artery/vascular disease	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Renal/Genitourinary Disorders	0 (0.0%)	0	1 (0.2%)	1	2 (0.5%)	2
Renal insufficiency	0 (0.0%)	0	1 (0.2%)	1	1 (0.2%)	1
Urinary tract infection (UTI)	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Other Disorders	0 (0.0%)	0	1 (0.2%)	1	5 (1.1%)	5
Infection at access site	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Left arm AV graft infection	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Fever	0 (0.0%)	0	1 (0.2%)	1	1 (0.2%)	1
Bone fracture	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Lower extremity pain	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Digestive Disorders	0 (0.0%)	0	1 (0.2%)	1	6 (1.4%)	6
Gastrointestinal bleeding	0 (0.0%)	0	0 (0.0%)	0	3 (0.7%)	3
Colitis	0 (0.0%)	0	1 (0.2%)	1	1 (0.2%)	1

	All Device Related SAEs N=443		All Procedure Related SAEs N=443		SAEs through 30 days N=443	
	Subjects n (%)	Events, N	Subjects n (%)	Events N	Subjects n (%)	Events N
Esophageal spasm	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Nausea and/or vomiting	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Any Adverse Event	35 (7.9%)	45	72 (16.3%)	88	91 (20.5%)	114

Table 12: Summary of Non-Serious Adverse Events

	All Device Related Non-Serious AEs N=443		All Procedure Related Non-Serious AEs N=443		Non-Serious AEs to 30-Day follow-up N=443	
	Subjects n (%)	Events N	Subjects n (%)	Events N	Subjects n (%)	Events N
Angiographic Complications	1 (0.2%)	1	1 (0.2%)	1	1 (0.2%)	1
Slow flow or no reflow phenomena	1 (0.2%)	1	1 (0.2%)	1	1 (0.2%)	1
Cardiovascular Disorders	0 (0.0%)	0	2 (0.5%)	2	5 (1.1%)	5
Chest pain	0 (0.0%)	0	0 (0.0%)	0	2 (0.5%)	2
Atrial fibrillation	0 (0.0%)	0	2 (0.5%)	2	2 (0.5%)	2
Diaphragmatic stimulation by pacemaker	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Neurologic/Psychiatric Disorders	0 (0.0%)	0	0 (0.0%)	0	9 (2.0%)	9
Respiratory/Thoracic Disorders	0 (0.0%)	0	0 (0.0%)	0	10 (2.3%)	10
Vascular Disorders	0 (0.0%)	0	2 (0.5%)	2	11 (2.5%)	12
Renal/Genitourinary Disorders	0 (0.0%)	0	1 (0.2%)	1	7 (1.6%)	7
Digestive Disorders	0 (0.0%)	0	1 (0.2%)	1	16 (3.6%)	20
Abnormal Tests/Lab Finding	0 (0.0%)	0	0 (0.0%)	0	1 (0.2%)	1
Other Disorders	0 (0.0%)	0	1 (0.2%)	1	22 (5.0%)	27
Any Adverse Event	1 (0.2%)	1	8 (1.8%)	8	69 (15.6%)	92

Table 13 and **Table 14**, respectively, summarize the presence and types of dissections and perforations as assessed by the Angiographic Core Laboratory.

Table 13: Summary of Dissections at Index Procedure

Dissection	Subjects N=443
Coronary vessel dissection present on subjects treated with OAD	52/443 (11.7%)
Type: A	9/52 (17.3%)
Type: B	22/52 (42.3%)
Type: C	8/52 (15.4%)
Type: D	4/52 (7.7%)
Type: E	1/52 (1.9%)
Type: F	1/52 (1.9%)
Type: Not Analyzable	7/443 (1.6%)
Coronary vessel dissection present on subjects not treated with OAD	1/443 (0.2%)
Non-coronary, Aortic Root dissection present on subjects treated with OAD	2/443 (0.5%)
Non-coronary, possible Aortic Cusp dissection present on subjects treated with OAD	1/443 (0.2%)

Table 14: Summary of Perforations at Index Procedure

Perforation	Subjects N=443
Coronary vessel perforation present on subjects treated with OAD	8/443 (1.8%)
Type: I (fully contained)	0/8 (0.0%)
Type: II (limited extravasation)	2/8 (25.0%)
Type: III (brisk extravasation)	5/8 (62.5%)
Type: cavity spilling	0/8 (0.0%)
Type: Not Analyzable	1/8 (12.5%)
Non-coronary right ventricle vessel perforation present on subjects treated with OAD	1/443 (0.2%)

Table 15 summarizes the first observed occurrence of the dissection or perforation as assessed by the Angiographic Core Laboratory. Perforations and dissections occurred both prior to, and following, OAS use.

Table 15: Summary of Dissections and Perforations by Occurrence

Dissection First Identified	Subjects N=52
Prior to OAS	8/52 (15.4%)
Pre-OAS/post-balloon	0/52 (0.0%)
Post-OAS	24/52 (46.2%)
Post-OAS #1/post-balloon/pre-OAS #2	1/52 (1.9%)
Post-OAS/pre-stent/post-balloon	7/52 (13.5%)
Post-stent	11/52 (21.2%)
Post-stent/post-balloon	0/52 (0.0%)
Not Analyzable	1/52 (1.9%)
Perforation First Identified	Subjects N=8
Prior to OAS	0/8 (0.0%)
Pre-OAS/post-balloon	0/8 (0.0%)
Post-OAS	4/8 (50.0%)
Post-OAS/pre-stent/post-balloon	0/8 (0.0%)
Post-stent	4/8 (50.0%)
Post-stent/post-balloon	0/8 (0.0%)
Not Analyzable	0/8 (0.0%)

2. Effectiveness Results

The analysis of effectiveness was based on the 440 evaluable subjects at the 30-day time point. The key effectiveness outcome is presented in **Table 16**.

Procedural success was measured by success in facilitating stent delivery with < 50% residual stenosis and without in-hospital MACE for the treated subject. The null hypothesis that the true procedural success rate is at most 82% was to be rejected in favor of the alternative if the lower bound of the 2-sided 95% confidence interval (CI) for the primary effectiveness endpoint was greater than the pre-specified performance goal of 82%. Only subjects treated by the OAD (the guide wire crossed the lesion and OAD was inserted, N=440) have been included in the primary effectiveness endpoint analysis. The final percent stenosis of the treated lesion was obtained from the Angiographic Core Laboratory data.

Procedural success occurred in 391 of 440 evaluable subjects. The observed rate of procedural success was 88.9% with 95% CI of (85.5%, 91.6%). The lower bound of the 95% CI, 85.5%, was greater than the pre-defined performance goal of 82%. The null hypothesis that the true procedural success rate is at most 82% was rejected and the performance goal of the primary effectiveness endpoint was met successfully (**Table 16**).

Sensitivity analyses were conducted to evaluate the potential impact of the missing data on the conclusion of the hypothesis test for the primary effectiveness endpoint. At the worst case scenario where all subjects with missing primary effectiveness endpoint or without post-procedural CK-MB and troponin data were assumed with procedural failures, the primary effectiveness endpoint was still successfully met.

Table 16: Primary Effectiveness Endpoint

Primary Effectiveness Endpoint	n/N ¹	% [95% CI] ²	Hypothesis	Decision	Conclusion
Procedural Success	391/440	88.9% [85.5%-91.6%]	H ₀ : $\pi_e \leq 82\%$ H _a : $\pi_e > 82\%$	Reject H ₀	Performance Goal Met
¹ n/N is the number of subjects meeting the primary effectiveness endpoint over the number of subjects with study guide wire crossing the lesion. Of the three subjects, one had an in-hospital TVR (non-TLR) and MI (non-Q-Wave). ² Clopper-Pearson Exact two-sided 95% confidence interval.					

Angiographic success (defined as success in facilitating stent delivery with <50% residual stenosis and without severe angiographic complications) was achieved in 91.4% (405/443) of subjects. Results were similar for the Pneumatic OAS and Electric OAS versions of the device, with rates of 91.0% (312/343) and 93.0% (93/100) respectively. Additional information on the primary effectiveness endpoint components is provided in **Table 17**.

Table 17: Primary Effectiveness Endpoint Components

Criteria	Subjects
Subjects with study guide wire crossing lesion and OAD inserted	N=440
Procedural Success	391/440 (88.9%)
Stent delivered	
Yes	430/440 (97.7%)
No	10/440 (2.3%)
Residual stenosis (%)	
< 50% Residual Stenosis	434/440 (98.6%)
≥ 50% Residual Stenosis	6/440 (1.4%)
In hospital MACE	
Yes	43/440 (9.8%)
No	397/440 (90.2%)

Cardiac Death	
No	439/440 (99.8%)
Yes	1/440 (0.2%)
MI	
No	399/440 (90.7%)
Yes	41/440 (9.3%)
Target Vessel Revascularization ¹	
No	437/440 (99.3%)
Yes	3/440 (0.7%)
¹ Includes Target Lesion Revascularizations	

Severe angiographic (defined as perforation, dissection type C-F, abrupt closure, persistent slow flow or no reflow), complications occurred at a rate of 7.2% (32/443 subjects). Results were similar for the Pneumatic OAS and Electric OAS devices with a nominally lower rate for the Electric OAS (5.0% versus 7.9% for Pneumatic OAS).

Procedural parameters identified as secondary endpoints are provided in **Table 18**.

Table 18: Procedural Parameters

Parameter	Pneumatic	Electric	Overall
Parameters per subject	Avg ± SE (N)	Avg ± SE (N)	Avg ± SE (N)
Mean OAD devices used per subject	1.1 ± 0.0 (334)	1.0 ± 0.0 (98)	1.1 ± 0.0 (432)
Post-OAD/Pre-stent balloon dilation performed	43.2% (147/340)	34.0% (34/100)	41.1% (181/440)
Post-stent placement balloon dilation performed	52.9% (180/340)	47.0% (47/100)	51.6% (227/440)
Mean total procedure time (minutes)	53.0 ± 1.7 (339)	50.5 ± 2.7 (100)	52.5 ± 1.4 (439)
Mean total OAD Run Time (seconds)	69.7 ± 2.7 (333)	56.9 ± 2.7 (98)	66.8 ± 2.2 (431)
Mean total fluoroscopy time (minutes)	18.4 ± 0.7 (336)	17.3 ± 1.1 (100)	18.2 ± 0.6 (436)
Mean total volume of contrast used (ml)	179.7 ± 4.9 (338)	154.6 ± 6.7 (100)	173.9 ± 4.1 (438)
OAD Devices Used	m/n ¹ (%)	m/n ¹ (%)	m/n ¹ (%)
DB-C12-125	320/357 (89.6%)	N/A	320/457 (70.0%)
DB-C12-150	33/357 (9.2%)	N/A	33/457 (7.2%)
DB-C12-175	2/357 (0.6%)	N/A	2/457 (0.4%)
DB-C12-200	2/357 (0.6%)	N/A	2/457 (0.4%)
DB-EC-125	N/A	98/100 (98.0%)	98/457 (21.4%)
DB-EC-150	N/A	2/100 (2.0%)	2/457 (0.4%)

¹ “m” = number of specific device model number used in the study “n” = overall number of devices in the study.

3. Subgroup Analyses

The preoperative characteristic of gender was evaluated for potential association with outcomes. Thirty-day post-procedure MACE occurred in 31 out of 286 enrolled male subjects and 15 out of 157 enrolled female subjects. The 30-day freedom from MACE

rate for males was 89.2%; and for females was 90.4%. No significant difference in 30-day post-procedural MACE rates between males and females was detected (p = 0.6613 based on the univariate Cox proportional hazards regression analysis).

The procedural success rate for males was 88.4% (251/284) and for females was 89.7% (140/156). No significant difference in the procedural success rate between males and females was detected (p = 0.6639 based on the univariate logistic regression analysis).

E. 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 274 investigators of which none were full-time or part-time employees of the sponsor and 9 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: none
- Significant payment of other sorts: 6
- Proprietary interest in the product tested held by the investigator: none
- Significant equity interest held by investigator in sponsor of covered study: 3

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. 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)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System 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

The pre-specified performance goal of 82% for the primary effectiveness endpoint was met with 88.9% (95% CI of 85.5% - 91.6%) of the subjects having a stent successfully delivered with < 50% residual stenosis without an in-hospital MACE event. The primary effectiveness endpoint was still met under the worst-case scenario where all subjects with missing primary effectiveness endpoint data or without post-procedural CK-MB and troponin data were assumed as having procedural failures.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in a clinical study conducted to support PMA approval as described above. The pre-specified performance goal of 83% for the primary safety endpoint was met with 89.6% (95% CI of 86.7% – 92.5%) of the subjects free from MACE within 30 days post index procedure. The primary safety endpoint was still met under the worst-case scenario where all subjects with missing primary safety endpoint data or without post-procedural CK-MB and troponin data were assumed as having 30-day MACE events. The risk of the occurrence of a dissection and/or perforation was within an expected range for the specific patient population that was studied in the ORBIT II clinical study.

C. Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The primary safety endpoint was 89.6% freedom from 30-day major adverse cardiac events (MACE), compared to its performance goal of 83%. The primary effectiveness endpoint (successful stent delivery with residual stenosis < 50% post-stent without in-hospital MACE) was 88.9%, compared to the performance goal of 82%. Stent delivery occurred successfully in 97.7% and < 50% stenosis occurred in 98.6% of subjects. Using the OAS as a lesion preparation tool prior to stent deployment may offer patients with severely calcified coronary lesions an alternative treatment option for the treatment of severely calcified coronary lesions.

In conclusion, given the available information above, the data support that for facilitating stent delivery in patients with coronary artery disease who are acceptable candidates for PTCA or stenting due to de novo, severely calcified coronary artery lesions, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The combination of preclinical and clinical experience with the DIAMONDBACK 360 Coronary Orbital Atherectomy System (OAS) supports the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

Preclinical bench testing was performed on the OAS in accordance with applicable guidance documents and national and international standards. The testing confirmed that the OAS met performance and design specifications.

Biocompatibility testing was performed on all applicable materials of the OAS in accordance with the applicable international standards. All testing met the requirements as specified in the applicable standard, ensuring the finished device is biocompatible.

Sterilization, packaging, and shelf life testing were performed on the OAS as applicable. The testing demonstrated that the orbital atherectomy device (OAD) and guide wire maintain a Sterility Assurance Level of 10^{-6} . The results of shelf life testing confirmed that the OAD, guide wire, and ViperSlide maintain functionality and packaging integrity.

throughout a 2 year shelf life. The Saline Infusion Pump is reusable and has an operating life of at least 875 hours.

The performance goals for both the primary safety and effectiveness endpoints were met, demonstrating the safety and effectiveness of the DIAMONDBACK 360 Coronary OAS in treating severely calcified coronary lesions, lesions that are difficult to treat and typically excluded from clinical studies. The primary results were confirmed by additional supportive and sensitivity analyses and results were clinically acceptable in the patient population studied. Therefore, the data in the PMA application provide reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

XIII. CDRH DECISION

CDRH issued an approval order on October 21, 2013.

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.