

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Stent, Coronary

Device Trade Name: REBEL™ Platinum Chromium Coronary Stent System (Monorail® and Over-the-Wire) (REBEL Stent System)

Device Procode: MAF

Applicant's Name and Address: Boston Scientific Corporation
One Scimed Place
Maple Grove, MN 55311

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P130030

Date of FDA Notice of Approval: June 27, 2014

II. INDICATIONS FOR USE

The REBEL Platinum Chromium Coronary Stent System is indicated for improving coronary luminal diameter in patients with *de novo* lesions ≤ 28 mm in length in native coronary arteries with a reference vessel diameter (RVD) of ≥ 2.25 to ≤ 4.50 mm.

III. CONTRAINDICATIONS

Use of the REBEL Stent System is contraindicated in patients with the following:

- Known hypersensitivity to platinum, the platinum chromium alloy, or similar alloy types such as stainless steel.
- Known severe reaction to contrast agents that cannot be adequately premedicated prior to the REBEL Stent placement procedure.

Coronary artery stenting is contraindicated for use in the following:

- Patients who cannot receive recommended anti-platelet and/or anticoagulant therapy.
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or delivery device.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the REBEL Platinum Chromium Coronary Stent System labeling.

V. DEVICE DESCRIPTION

The REBEL Stent System is a single-use device comprised of a balloon-expandable, intracoronary REBEL stent pre-mounted on a rapid exchange, Monorail®, or Over-the-Wire delivery catheter. The REBEL stent is made from a platinum chromium alloy (PtCr). The stent is laser cut into a pattern which consists of serpentine rings connected by links and are polished to a uniform rounded surface.

The characteristics of the REBEL Stent System are described in **Table 1**.

Table 1: REBEL Platinum Chromium Coronary Stent System Product Description

	REBEL Monorail™ Stent Delivery System	REBEL Over-the-Wire Stent Delivery System
Stent		
Available Stent Lengths (mm)	8*, 12, 16, 20, 24, 28, 32*	
Available Stent Diameters (mm)	2.25*, 2.50*, 2.75, 3.00, 3.50, 4.00, 4.50*	
Stent Material	Platinum Chromium (PtCr) Alloy	
Stent Strut Thickness	0.0032 inches (0.081 mm) for diameters 2.25 mm to 3.50 mm 0.0034 inches (0.086 mm) for diameters 4.00 mm and 4.50 mm	
Delivery System		
Effective Length	144 cm	
Delivery System Ports	Single access port to inflation lumen. Guidewire exit port is located approximately 25 cm from tip. Designed for guidewire ≤0.014 inches (0.36 mm).	Y-Connector (Side arm for access to balloon inflation/deflation lumen. Straight arm is continuous with shaft inner lumen). Designed for guidewire ≤0.014 inches (0.36 mm).
Stent Delivery	A balloon, with two radiopaque balloon markers, nominally placed 0.4 mm (0.016 inches) beyond the stent at each end.	
Balloon Inflation Pressure	Nominal Inflation Pressure: 11 atm (1117 kPa)	
	Rated Burst Inflation Pressure: 18 atm (1827 kPa)	
Catheter Shaft Outer Diameter	2.1 F (.070 mm) proximal 2.7 F (0.95 mm) distal.	3.4F (≤1.20 mm) proximal for 2.25 to 4.50 mm sizes 2.4F (≤0.85 mm) distal for 2.25 to 2.75 mm sizes 2.7F (≤0.95 mm) distal for 3.00 to 4.50 mm sizes
Guide Catheter Minimum Inner Diameter Requirement	≥0.056 inches (1.42 mm) for 2.25 – 4.00 mm sizes ≥0.066 inches (1.68 mm) for 4.50 mm size	≥0.066 inches (1.68 mm)

* 32 mm length is not available in 2.25 mm and 2.50 mm diameter size. 8 mm length is not available in 4.50 mm diameter size.

The REBEL stent is available in four stent models across the range of reference vessel diameters indicated:

- Small Vessel (SV): 2.25 mm
- Small Workhorse (SWH): 2.50 mm and 2.75 mm
- Workhorse (WH): 3.00 mm and 3.50 mm
- Large Vessel (LV): 4.00 mm and 4.50 mm

The commercial matrix is shown in **Table 2** below:

Table 2: REBEL Stent System US Commercial Matrix

			Stent Length						
			8 mm	12 mm	16 mm	20 mm	24 mm	28 mm	32 mm
Balloon Diameter / Stent Model	SV	2.25 mm	X	X	X	X	X	X	
	SWH	2.50 mm	X	X	X	X	X	X	
		2.75 mm	X	X	X	X	X	X	X
	WH	3.00 mm	X	X	X	X	X	X	X
		3.50 mm	X	X	X	X	X	X	X
	LV	4.00 mm	X	X	X	X	X	X	X
		4.50 mm		X	X	X	X	X	X

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of coronary artery disease: exercise, diet, smoking cessation, drug therapy, percutaneous coronary interventions (such as angioplasty and placement of bare metal stents, coated stents, and other drug eluting stents), and coronary artery bypass graft surgery (CABG). 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 REBEL Stent System received CE Mark 05 February 2014. As of 31 May 2014, approximately 1,305 REBEL Stent Systems have been distributed outside the United States. **Table 3** contains a list of countries where the REBEL Stent System is currently available. No products have been withdrawn from the market in any country for any reason

The REBEL Stent System is a design iteration of the CE Marked OMEGA™ Platinum Chromium Coronary Stent System and contains many of the same design elements and materials. As of 31 October 2013, approximately 185,549 OMEGA Stent Systems have been distributed outside the United States. **Table 3** contains a list of countries where the OMEGA Stent System is currently available. No products have been withdrawn from the market in any country for any reason.

Table 3: Countries with REBEL (R) or OMEGA (O) Stent System Commercial Availability

Albania (R,O)	Algeria (R,O)	Andorra (R,O)	Antigua/Barbuda (R,O)
Argentina (O)	Armenia (R,O)	Aruba (R,O)	Australia (O)
Austria (R,O)	Azerbaijan (R,O)	Bahamas (R,O)	Bahrain (R,O)
Bangladesh (O)	Barbados (R,O)	Belgium (R,O)	Belize (R,O)
Belarus (O)	Bermuda (R,O)	Bolivia (O)	Bosnia (O)
Brazil (O)	Brunei (R,O)	Bulgaria (R,O)	Chile (R,O)
Colombia (O)	Costa Rica (O)	Croatia (R,O)	Cyprus (R,O)
Czech Republic (R,O)	Denmark (R,O)	Djibouti (R,O)	Dominican Republic (R,O)
Dutch Antilles (R,O)	Ecuador (O)	Egypt (O)	El Salvador (R,O)
Estonia (R,O)	Finland (R,O)	France (R,O)	Georgia (R,O)
Germany (R,O)	Great Britain (R,O)	Greece (R,O)	Guatemala (O)
Guyana (R,O)	Haiti (R,O)	Honduras (R,O)	Hong Kong (O)
Hungary (R,O)	Iceland (R,O)	India (O)	Indonesia (O)
Israel (O)	Iraq (R,O)	Ireland (R,O)	Italy (R,O)
Jamaica (R,O)	Jordan (O)	Kenya (R,O)	Korea (O)
Kuwait (R,O)	Latvia (R,O)	Lebanon (R,O)	Libya (R,O)
Liechtenstein (R,O)	Lithuania (R,O)	Luxembourg (R,O)	Macedonia (O)
Macau (O)	Malaysia (O)	Malta (R,O)	Martinique (R,O)
Moldavia (R,O)	Morocco (R,O)	Myanmar (R,O)	Nepal (R,O)
Netherlands (R,O)	New Zealand (O)	Nicaragua (R,O)	Norway (R,O)
Oman (R,O)	Pakistan (O)	Palestinian Territory (O)	Panama (O)
Paraguay (O)	Peru (O)	Philippines (O)	Poland (R,O)
Puerto Rico (O)	Portugal (R,O)	Qatar (R,O)	Romania (R,O)
Russia (O)	Saudi Arabia (O)	Serbia (O)	Singapore (O)
Slovakia (R,O)	Sri Lanka (O)	Slovenia (R,O)	South Africa (O)
Spain (R,O)	Surinam (R,O)	Sweden (R,O)	Switzerland (R,O)
Syria (O)	Taiwan (O)	Thailand (O)	Trinidad/Tobago (R,O)
Tunisia (R,O)	Turkey (O)	Ukraine (R,O)	United Arab Emirates (R,O)
Venezuela (O)	Vietnam (O)	Yemen (R,O)	-

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 REBEL Stent System.

- Abrupt closure
- Allergic reaction (including to medications, contrast, stent materials)
- Aneurysm (coronary)
- Angina
- Arrhythmias, including ventricular fibrillation and ventricular tachycardia
- Arteriovenous fistula
- Bleeding
- Cardiac tamponade
- Cardiogenic shock
- Cardiomyopathy
- Death
- Emboli (including air, tissue, thrombus, plaque, or device materials)
- Heart failure
- Hematoma
- Hemorrhage
- Hypotension/hypertension
- Infection, local and/or systemic
- Ischemia, myocardial
- Myocardial infarction
- Pain
- Pericardial effusion
- Pseudoaneurysm, femoral
- Pulmonary edema
- Renal insufficiency or failure
- Respiratory failure
- Restenosis of stented segment
- Shock
- Stent embolization
- Stent fracture
- Stent migration
- Stent thrombosis and/or vessel occlusion
- Stroke/cerebrovascular accident/transient ischemic attack
- Total occlusion of coronary artery
- Vessel spasm
- Vessel injury (including dissection, perforation, rupture or trauma)

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

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Testing

1. Biocompatibility Studies

A series of biocompatibility tests were conducted to demonstrate that the components of the REBEL Stent System are biocompatible. Testing was conducted separately for the stent implant and the stent delivery system. Tests were conducted on ethylene oxide-sterilized bare metal, platinum chromium alloy (PtCr) stents and balloon catheters. These test articles were processed in a manner similar to the finished REBEL Stent System product. There were some manufacturing differences that were determined not to impact the biocompatibility of the final device.

All biocompatibility testing was conducted in accordance with:

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

The tests summarized in **Table 4** have been conducted in support of the REBEL stent component as recommended for a permanent implantable device contacting circulating blood for > 30 days.

Table 4: Biological Evaluation Tests Performed on Stent

Test Performed / Applicable ISO 10993 Part Number	Test Purpose	Acceptance Criteria	Results
Cytotoxicity MEM Elution / Part 5	To determine the potential for cytotoxicity	The test article meets test requirements if none of the cultures treated with the test article show greater than Mild reactivity (Grade 2).	Pass Non-Cytotoxic
Sensitization Guinea Pig Max / Part 10	To evaluate the allergenic potential or sensitizing capacity of a test article.	Skin reaction scores received by the test group must be equal or less than the scores received by the negative control group.	Pass Non-Sensitizer
Irritation Intracutaneous Reactivity / Part 10	To screen test article extracts for potential irritation effects.	The requirements of the test are met if the difference between the test article and the control mean score is 1.0 or less (negligible or slight).	Pass Non-Irritant
Acute Systemic Toxicity / Part 11	To screen test article extracts for potential systemic toxic effects.	Test is considered negative if none of the animals injected with the test article show a significantly greater biological reaction than the animals treated with the vehicle control.	Pass Negative, Non-toxic
Material-Mediated Rabbit Pyrogenicity / Part 11	To determine the presence of chemical pyrogens in extracts of a test article causing a febrile response in rabbits.	If no rabbit shows an individual rise in temperature of 0.5°C or more above baseline, the test article meets the requirements of the test.	Pass Non-Pyrogenic
Hemolysis Direct Contact / Part 4	To assess the hemolytic activity of the test article when in direct contact with blood.	Results are considered “pass” if the hemolytic index of test article is 5% or less.	Pass Non-Hemolytic

Test Performed / Applicable ISO 10993 Part Number	Test Purpose	Acceptance Criteria	Results
Hemolysis Indirect Contact / Part 4	To assess the hemolytic activity of a test article extract in contact with blood.	Results are considered “pass” if the hemolytic index of test article extract is 5% or less.	Pass Non-Hemolytic
Complement Activation / Part 4	Measurement of complement activation indicates whether a test article is capable of inducing a complement-induced inflammatory immune response in humans.	The concentration of C3a and SC5b-9 in serum exposed to the positive control should be significantly greater than those in the corresponding untreated serum. The test article will be considered positive or negative based upon a statistical comparison to the positive control.	Pass Negative for C3a and SC5b-9 assays
In Vitro Hemocompatibility Assay / Part 4	To determine if the test article would adversely affect the various cellular and non-cellular components of the blood.	Test article results should be comparable to the results of the negative blood control or the reference material controls.	Pass Results comparable to negative control
Partial Thromboplastin Time / Part 4	To determine the time citrated plasma exposed to a test material takes to form a clot when exposed to a suspension of phospholipid particles and calcium chloride.	Results are considered “pass” if the average clotting time of the test article is at least 50% compared to that of the negative control.	Pass Results comparable to negative control
Genotoxicity Ames Assay / Part 3	To evaluate the mutagenic potential of leachables from the test article.	The test article is considered negative if it does not cause increase in 2-fold the mean revertant in all test strains of bacteria.	Pass Non-Mutagenic
Genotoxicity Mouse Lymphoma / Part 3	To evaluate mutagenicity of the test agents.	The test article is considered negative if the test article-dosed cultures have a mutation frequency (MF) of less than 1.8 fold higher than that of the concurrent negative control plates.	Pass Non-Mutagenic
Sub-chronic Toxicity, Implantation/ Part 6 & 11	To evaluate the potential for local and systemic toxicity of a test article implanted subcutaneously in rats for 13 weeks.	Test is considered negative if the test article did not induce a significantly greater biological reaction than the control article.	Pass No systemic toxicity, Non-Irritant
Implantation - In Vivo Thrombogenicity / Part 4 & 6	This test is to confirm there is no abnormal thrombosis related to the stent.	No significant differences in vascular response between test article and control stents in stent-related mortality or luminal thrombus.	Pass No stent-related mortality. No luminal thrombus.

Test Performed / Applicable ISO 10993 Part Number	Test Purpose	Acceptance Criteria	Results
Implantation / Part 6	To evaluate the potential for a local irritant or toxic response to material(s) implanted in direct contact with subcutaneous tissue of the rabbit.	Test is considered negative if the test article did not induce a significantly greater biological reaction than the control article.	Pass Non-Irritant
USP Physicochemical Test for Plastics / Part 18	To determine the physical and chemical properties of an extract of a test material.	Non-volatile residue <15mg, residue on ignition <5mg (only performed when Non-volatile residue is > 15 mg), heavy metals <1ppm and buffering capacity <10ml.	Pass

The tests summarized in Table 5 have been performed in support of the REBEL delivery system catheter as recommended for externally communicating device contacting the circulating blood with limited exposure of < 24 hours.

Table 5: Biological Evaluation Tests Performed on Delivery System Catheter

Test Performed / Applicable EN ISO 10993 Part Number	Test Purpose	Acceptance Criteria	Results
Cytotoxicity MEM Elution / Part 5	To determine the potential for cytotoxicity	The test article meets test requirements if none of the cultures treated with the test article show greater than Mild reactivity (Grade 2).	Pass Non-Toxic
Sensitization Guinea Pig Maximization / Part 10	To evaluate the allergenic potential or sensitizing capacity of a test article.	Skin reaction scores received by the test group must be equal or less than the scores received by the negative control group.	Pass Non-Sensitizer
Irritation Intracutaneous Reactivity / Part 10	To screen test article extracts for potential irritation effects.	The requirements of the test are met if the difference between the test article and the control mean score is 1.0 or less (negligible or slight).	Pass Non-Irritant
Acute Systemic Toxicity / Part 11	To screen test article extracts for potential systemic toxic effects.	Test is considered negative if none of the animals injected with the test article show a significantly greater biological reaction than the animals treated with the vehicle control.	Pass Non-Toxic
Material-Mediated Rabbit Pyrogenicity / Part 11	To determine the presence of chemical pyrogens in extracts of a test article causing a febrile response in rabbits.	If no rabbit shows an individual rise in temperature of 0.5°C or more above baseline, the test article meets the requirements of the test.	Pass Non-Pyrogenic

Test Performed / Applicable EN ISO 10993 Part Number	Test Purpose	Acceptance Criteria	Results
Hemolysis Direct Contact / Part 4	To assess the hemolytic activity of the test article when in direct contact with blood.	Results are considered “pass” if the hemolytic index of test article is 5% or less.	Pass Non-Hemolytic
Hemolysis Indirect Contact / Part 4	To assess the hemolytic activity of a test article extract in contact with blood.	Results are considered “pass” if the hemolytic index of test article extract is 5% or less.	Pass Non-Hemolytic
Complement Activation / Part 4	Measurement of complement activation indicates whether a test article is capable of inducing a complement-induced inflammatory immune response in humans.	The concentration of C3a and SC5b-9 in serum exposed to the positive control should be significantly greater than those in the corresponding untreated serum. The test article will be considered positive or negative based upon a statistical comparison to the positive control.	Pass Negative for C3a and SC5b-9 assays
In Vitro Hemocompatibility Assay / Part 4	To determine if the test article would adversely affect the various cellular and non-cellular components of the blood.	Test article results should be comparable to the results of the negative blood control or the reference material controls.	Pass Results comparable to negative control
Partial Thromboplastin Time / Part 4	To determine the time citrated plasma exposed to a test material takes to form a clot when exposed to a suspension of phospholipid particles and calcium chloride.	Results are considered “pass” if the average clotting time of the test article is at least 50% compared to that of the negative control.	Pass Results comparable to negative control
USP Physicochemical Test for Plastics <661> / Part 18	To determine the physical and chemical properties of an extract of a test material.	Non-volatile residue <15mg, residue on ignition <5mg (only performed when Non-volatile residue is > 15 mg), heavy metals <1ppm and buffering capacity <10ml.	Pass

2. In Vitro Engineering Testing

In vitro engineering testing on the REBEL Stent System was conducted, as applicable, in accordance with:

- *FDA Guidance for Industry and Staff: Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*, 18 April 2010
- *FDA Guidance for Industry and Staff: Establishing Safety and Compatibility of Passive Implants in the Magnetic Resonance (MR) Environment*, August 2008

The in vitro engineering studies are summarized in **Table 5**. “Pass” denotes that the test results met product specifications and/or the recommendation in the above-referenced guidance documents.

Table 5: Stent and Delivery Catheter Engineering Testing

In Vitro Test	Summary of Results	Results
Material Characterization Testing		
Material Composition	Chemical analysis was conducted on the platinum chromium alloy (PtCr) and is provided by the material supplier to confirm both chemical analysis and inclusion/impurity content as provided by ASTM F138-00 “Standard Specification for Wrought 18 Chromium-14 Nickel-2.5 Molybdenum Stainless Steel Bar and Wire for Surgical Implants (UNS S31673:”	Pass. This is a characterization test.
Stent Corrosion Resistance	<p>Uncoated Element stents were tested to determine the corrosion susceptibility using cyclic potentiodynamic polarization per ASTM F2129-06, "Conducting Cyclic Potentiodynamic Polarization Measurements."</p> <p>Galvanic Corrosion characterization was performed when the Uncoated Element stent was overlapped with a stent of different metal/metal alloy per ASTM G7 1-81, "Conducting and Evaluation Galvanic Corrosion Tests in Electrolytes."</p> <p>Fretting Corrosion and Crevice Corrosion was assessed on uncoated Element stents after pulsatile fatigue cycling. The corrosion series testing indicated that the corrosion resistance characteristics of the REBEL stent met product specification.</p>	Pass. The results showed little to no fretting or crevice corrosion.
Dimensional Verification	The purpose of this evaluation is to measure and inspect the stent to document that the stent dimensional specifications meet the product design requirements, including un-expanded stent dimensions, expanded diameter, and length (see also Stent Delivery System Dimensional and Functional Attributes testing). Results indicated that the product specifications were met for dimensional verification.	Pass. Products were shown to meet their labeled dimensions within specifications.
Percent Surface Area	Stent surface coverage as a function of stent diameter was quantified for the stent. The percent surface area is determined by dividing the measured total contact surface area of the stent by the surface area of the artery based on deployed stent measurements at the nominal stent diameter.	Pass. The percent surface area is identical to the approved PROMUS PREMIER

In Vitro Test	Summary of Results	Results
Foreshortening	The foreshortening test determined the change in length of the stent between the catheter-mounted condition and the condition in which the stent was expanded (deployed) to the nominal diameter. Results indicated that the product specifications were met for foreshortening.	<p>Pass. Testing showed that the length change after expansion must be less than or equal to 20% of the crimped length or less than or equal to:</p> <p>2.0mm for diameters of 2.25 through 2.75mm,</p> <p>2.5mm for diameters of 3.0 and 3.5mm,</p> <p>3.0mm for 4.0mm diameter, or</p> <p>4.0mm for 4.5mm diameter; whichever imposes a tighter requirement.</p>
Recoil for Balloon Expandable Stents	The stent was evaluated for the amount of elastic recoil. Results indicated that the product specifications were met for recoil of the stent.	Pass. The recoil was less than 5% for stents 3.0mm diameter and larger. The recoil was less than 7% for those stents 2.75mm and shorter.
Stent Integrity (Stent Over Expansion)	The purpose of this testing is to verify the stent integrity post-stent deployment when expanded above unconstrained diameter. The stents were examined and exhibited no structural damage after over expansion.	Pass. The stent integrity was shown to be acceptable at over expansion

In Vitro Test	Summary of Results	Results
Radial Stiffness and Radial Strength (Compression Resistance)	The stent was evaluated for the ability to resist collapse when subject to a radial loads.	Pass. The stent was able to resist all clinically relevant loads
Mechanical Properties	Ultimate tensile strength, yield strength, and elongation testing was performed on tubing (pre-processing) used to fabricate the stents. Ultimate tensile strength, yield strength, and elongation testing on pre-processed tubing met product specification. Analysis of SEM images on stent components at various process stages determined that mechanical properties were not altered by processing.	Pass. The mechanical properties were able to be characterized
Stress/Strain Analysis/Fatigue Analysis (Finite Element Analysis)	Using Finite Element Analysis (FEA), stress and strain analysis was performed on the stent to demonstrate acceptable safety is maintained in stress loading environments, simulating nominal and overexpansion, and bending and radial conditions. The FEA evaluated the structural integrity of the stent when subjected to the expected loading conditions generated in coronary arteries. The analysis took into account manufacturing, delivery, implantation, and clinical loading over the implant life, and predicted that fatigue failures will not occur over 400 million cycles (10-years) of loading.	Pass. The FEA testing predicted no fatigue failures over a 10 year evaluation.
Accelerated Durability Testing	The accelerated durability of the stent was evaluated through the stent platform performance in Overlapping Pulsatile Fatigue on a Curve testing and determined that the structural integrity is maintained following exposure to the pulsatile stresses and strains exceeding those typically experienced by a human coronary artery for 10 years (400 million cycles).	Pass. Testing showed that the stent maintained structural integrity in an overlapped, bent configuration for 400 million cycles (10 years).
Particulates Evaluation (Simulated Use)	The system was evaluated for particulates after simulated use through a tortuous vessel model. The product has particulate counts that are similar to VeriFlex stent systems.	Pass. Testing showed that the device had an acceptably low amount of particulates generated after simulated use in a mock vessel.

In Vitro Test	Summary of Results	Results
Magnetic Resonance Imaging (MRI) Safety and Compatibility	<p>Non-clinical testing has demonstrated that the REBEL stent is MR Conditional for single and overlapped conditions up to 74 mm. A patient with this device can be safely scanned in a Magnetic Resonance system meeting the following conditions:</p> <ul style="list-style-type: none"> • Static magnetic field of 3.0 and 1.5 Tesla only • Maximum spatial gradient magnetic field of 2200 gauss/cm (22 T/m) • Maximum Magnetic Resonance system reported, whole body averaged specific absorption rate (SAR) of <2 W/kg (Normal Operating Mode) <p>Under the scan conditions defined above, the REBEL stent is expected to produce a maximum temperature rise of 2.6°C after 15 minutes of continuous scanning. In non-clinical testing, the image artifact caused by the device extends approximately 8 mm from the REBEL stent when imaged with a spin echo pulse sequence and a 3.0 Tesla MRI system. The artifact does not obscure the device lumen.</p>	Pass. The device met conditions to be labeled MR conditional.
Radiopacity	The radiopacity of the stent was assessed through porcine model evaluations of stent positioning, expansion, and delivery system removal. The stent exhibits clinically acceptable radiopacity.	Pass. The device is sufficiently radiopaque to be viewed under fluoroscopic imaging.
Stent Axial Strength	The ability of the stent to withstand axial length change after being subjected to point-load force was tested. The stent design minimizes the potential for longitudinal stent deformation over the OMEGA stent by effectively increasing axial strength at the proximal end.	Pass. The device has sufficient axial strength to help resist against longitudinal deformation.
Delivery System Dimensional and Functional Attributes		
Dimensional Verification	The catheter effective length, overall length, crossing profile, and inner diameter were evaluated and met product specifications.	Pass. All dimensions met specifications.

In Vitro Test	Summary of Results	Results
Delivery, Deployment and Retraction	The delivery, deployment and retraction of stent system was assessed by testing system track, crossing profile, deflated balloon profile, stent deployment, flexibility/kink, guidewire movement, torque strength, and balloon withdrawal from a stent and into the guide catheter. Testing demonstrated that the stent system could be delivered to the target location, deployed, and retracted, thus meeting required acceptance criteria.	Pass. The stent delivery system successfully track, deploy, and retract through the ASTM F2394 Figure X2.4 track model without damage to ancillary devices (guidewire and guide catheter), delivery system, or the stent.
Balloon Rated Burst Pressure	Stent systems were evaluated to demonstrate that the stent system met rated (RBP) burst pressure. Results indicated that the product specifications were met and with 95% confidence that at least 99.9% of balloons will not experience loss of integrity at or below the rated burst pressure.	Pass. The device has a labeled RBP of 18 ATM
Balloon Fatigue	Stent systems across the range of stent/balloon lengths and diameters were evaluated for the ability to complete 10 pressurization cycles to Rated Burst Pressure (RBP). The results indicated that, with 95% confidence, 90% of the catheters will not experience balloon, shaft, or proximal/distal seal loss of integrity at or below the maximum recommended rated balloon burst pressure.	Pass. Testing showed that the device can handle repeated inflations to RBP without damage to the balloon.
Stent Diameter vs. Balloon Pressure	Stent systems were evaluated to determine how the diameter of a deployed stent varies with applied balloon pressures. The stent sizing evaluations verify that the stent systems meet the labeled compliance values.	Pass. The compliance chart is included in the labeling.
Balloon Inflation and Deflation Time	Stent systems across the range of balloon lengths and diameters were evaluated for deflation and inflation times. Results indicated that the product specifications were met.	Pass. Inflation and deflation times increase as stent dimensions increase; however, all times were less than 30s

In Vitro Test	Summary of Results	Results
Catheter Bond Strength	Stent delivery systems were evaluated to determine the balloon bond strength. Results indicated that the product specifications were met or exceed for balloon bond strength.	Pass. All tested samples were well above the acceptable tensile strength of 1.4 lbf.
Tip Pull Test	Stent delivery system were tested to determine the tip bond strength. Results met balloon bond strength product specifications.	Pass. The acceptance criteria for each unit was >0.3 lbf (1.33 N).
Flexibility and Kink Test	Stent delivery systems were evaluated to determine the ability of the delivery system to withstand kinking. Results indicated that the product specifications were met for flexibility and kink testing.	Pass. At a 15mm radius of curvature, the device did not kink.
Torque Strength	Stent delivery systems were evaluated to determine strength of the delivery system catheter when torsional forces were applied. Results indicated that the product specifications were met for torque strength.	Pass. Testing showed that the device can withstand torsional forces seen during use.
Catheter Coating Integrity	The acute coating integrity of the stent delivery system coating was evaluated via the results of a series of acute in vitro tests (baseline and simulated use). The test results demonstrate that the hydrophilic coating displays acceptable acute coating integrity.	Pass. The coating had acceptable integrity after simulated use.
Stent Securement for Unsheathed Stents	Stent systems were evaluated to assess the forces required to displace a stent from the delivery system (1) directly from the delivery catheters, (2) after tracking and then through a simulated lesion. Results indicated that the product specifications were met for stent securement.	Pass. Results indicated that the stent will remain on the delivery system when tracked across a lesion.
Non-Coaxial Withdrawal into a Simulated Guiding Catheter	Stent systems were evaluated for performance during withdrawal of a catheter with a mounted stent non-coaxially into a simulated guide catheter tip following a repeated track conditioning step. Results indicated that the product specifications were met for stent securement.	Pass. The results indicate that the stent can withdraw back into a guide catheter if still mounted to the balloon.

3. Packaging Testing

Packaging verification testing was performed to demonstrate that the design of the REBEL Stent System packaging can withstand the hazards of the distribution environment and that the sterility of the device is maintained throughout the labeled shelf life.

4. Shelf Life Testing

Performance testing was conducted following 3 years of aging for Monorail stent systems and 2 years of aging for Over-the-Wire stent systems to demonstrate that the device and packaging performs within product specifications for a labeled shelf life.

5. Sterilization

The REBEL Stent System is sterilized using ethylene oxide (EO) gas and has been validated per AAMI / ANSI / ISO 11135-1:2007, *Sterilization of health care products - Ethylene oxide - Part 1: Requirements for the development, validation, and routine control of a sterilization process for medical devices*. Results from the sterilization studies show that the product satisfies a minimum Sterility Assurance Level (SAL) of 10^{-6} and residual levels were within acceptable ranges in accordance with ISO 10993-7:2008, *Biological Evaluation of Medical Devices - Part 7: Ethylene Oxide Sterilization Residuals*.

B. Animal Studies

. The versions of the devices (stent and delivery systems) used in the animal studies, the Element, Bare Element and Element BMS were early design iterations of the OMEGA Stent Systems used for the OMEGA clinical study; updates were made prior to the clinical study to improve balloon and stent robustness. The REBEL Coronary Stent System is a design iteration of the OMEGA Coronary Stent system used for the OMEGA clinical study. The OMEGA and REBEL stents share identical primary stent designs, materials, and manufacturing processes, however the REBEL SWH, WH, and LV models have additional connectors at the proximal end to provide more robust performance with relation to axial length change. The Element/OMEGA and REBEL delivery systems share shaft and balloon designs, materials, and manufacturing processes, however the REBEL delivery system has an updated shaft coating and bumper tip to enhance delivery and align with currently marketed devices .

The objective of the animal studies were:

- o To assess the safety and vascular compatibility of uncoated Element stents in comparison to uncoated Liberté stents.
- o To evaluate acute device performance of the Element stent and stent delivery system

Preclinical evaluations of the Element stent using the overlapping and single porcine coronary artery stent models supported safety and vascular compatibility, with comparable results to Liberté (VeriFLEX) in key safety parameters including early and late in-stent healing. Stent and delivery system acute performance as assessed in the porcine model demonstrated acceptable clinical performance. Studies were conducted in accordance with §21 CFR 58 (Good Laboratory Practices).

The results support the conclusion that the stent system is safe based on comparison to a commercially approved product, and is appropriate for commercial release. Summaries of the study designs and results are included in **Table 6**.

Table 6: Summary of Applicable Animal Studies

Test and/or Study Name	Test Article	Stent Size Diameter and Length (mm) and Number of Stent (n)	Total Drug per Stent / Total Carrier per Stent (µg)	Drug Loading Density (µg/mm ²) and Formulation (w% rx)	Vessel Location	Evaluation Time Points	Testing Summary and/or Objectives
GLP Safety Overlap Study 1133-024*	TAXUS Element	2.75 x 12 (30 pairs histology, 9 pairs SEM)	61/638	1.0/8.8	LAD, LCX, RCA	30, 90, 180 Days	Supports safety. No device related mortality or morbidity. Vascular response
	Uncoated Element	2.75 x 12 (30 pairs histology, 9 pairs SEM)	N/A	N/A			

Test and/or Study Name	Test Article	Stent Size Diameter and Length (mm) and Number of Stent (n)	Total Drug per Stent / Total Carrier per Stent (µg)	Drug Loading Density (µg/mm ²) and Formulation (w% rx)	Vessel Location	Evaluation Time Points	Testing Summary and/or Objectives
	TAXUS Liberté Control	2.75 x 12 (30 pairs histology, 9 pairs SEM)	83/865	1.0/8.8			shows early and late healing, vessel stability and patency over 30, 90, and 180 days.
	Uncoated Liberté Controls	2.75 x 12 (30 pairs histology, 9 pairs SEM)	N/A	N/A			
GLP Safety Overlap Study 07-032G	PROMUS Element	3.00 x 8 3.50 x 8 (50 pairs histology, 9 pairs SEM)	43.0 / 254	100 / 1:4.9	LAD, LCX, RCA	7, 30, 90, 180, 270 Days	Supports safety. No device related mortality or morbidity. Vascular response shows acceptable healing, vessel stability and patency over 30, 90, 180 days.
	Polymer Only Element	3.00 x 8 3.50 x 8 (43 pairs histology, 9 pairs SEM)	N/A / 254	N/A			
	Uncoated Element	3.00 x 8 3.50 x 8 (43 pairs histology, 9 pairs SEM)	N/A / N/A	N/A			
	Xience V (PROMUS)	3.00 x 8 3.50 x 8 (46 pairs histology, 9 pairs SEM)	36.5 / 241 52.5 / 347	100 / 1:4.9			
Non-GLP Acute Performance Study 10-046N	Uncoated Element	3.0 x 8 (2) 3.5 x 8 (1) 3.5 x 16 (3) 4.0 x 16 (3) 4.5 x 16 (3)	N/A	N/A	LAD, LCX, RCA, Thoracic Artery	Acute	Stent systems perform at or above acceptable level for all performance criteria.
GLP Acute Performance Study 10-047G	Uncoated Element	2.5 x 8 (5) 3.0 x 8 (4) 4.0 x 8 (5)	N/A	N/A	LAD, LCX, RCA	Acute	Stent systems perform at or above acceptable level for all performance criteria.

Test and/or Study Name	Test Article	Stent Size Diameter and Length (mm) and Number of Stent (n)	Total Drug per Stent / Total Carrier per Stent (μg)	Drug Loading Density ($\mu\text{g}/\text{mm}^2$) and Formulation (w% rx)	Vessel Location	Evaluation Time Points	Testing Summary and/or Objectives
Non-GLP Acute Performance Study 11-112T	Uncoated Element	2.25 x 8 (4)	N/A	N/A	LAD, LCX, RCA	Acute	Stent systems perform at or above acceptable level for all performance criteria.

*Boston Scientific implemented an internal study numbering convention after the completion of the 1133-024 study, and therefore, study 1133-024 is referenced by the contract research organization study number.

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

The applicant collected clinical data through the OMEGA clinical trial (*OMEGA: A Prospective, Multicenter Single-Arm Trial to Assess the OMEGA™ Coronary Stent System for the Treatment of a Single De Novo Coronary Artery Lesion*) and the NG PROMUS clinical trial (*NG PROMUS: A Prospective, Multicenter Trial to Assess the NG PROMUS Everolimus-Eluting Platinum Chromium Coronary Stent System (NG PROMUS Stent System) for the Treatment of Atherosclerotic Lesion(s)*) to evaluate the safety and effectiveness of the REBEL Coronary Stent System for improving coronary luminal diameter in patients with de novo lesions ≤ 28 mm in length in native coronary arteries with a reference vessel diameter (RVD) of ≥ 2.25 mm to ≤ 4.50 mm. The OMEGA clinical trial was evaluated under IDE G110092. Although the OMEGA clinical trial assessed the OMEGA™ Coronary Stent System, the OMEGA and REBEL Coronary Stent Systems utilize the same platinum chromium alloy. The REBEL Coronary Stent System differs from the OMEGA Coronary Stent System in that the REBEL Stent System has supplementary proximal stent connectors for increased axial strength, a short flexible stent delivery system tip, and a PTFE coated proximal hypotube for improved stent deliverability. Given the similarities between the OMEGA and REBEL Coronary Stent Systems and supportive bench and animal study information, the findings from the OMEGA Clinical Trial are applicable to the REBEL Stent System. The NG PROMUS Stent System is the same stent design as the REBEL Stent System, however the NG PROMUS stent is coated with the Everolimus drug. Therefore, data from these clinical trials were the basis for the PMA approval decision. Summaries of the clinical trials are presented below.

A. OMEGA Clinical Trial

A1. Study Design

The OMEGA Clinical Trial is a prospective, single-arm, multicenter study. Eligible patients were to be ≥ 18 years of age and with left ventricular ejection fraction (LVEF) $\geq 30\%$. Lesions were to be coverable by a single study stent and to have visually estimated stenosis $\geq 50\%$ and $< 100\%$ with Thrombolysis in Myocardial Infarction (TIMI) flow > 1 . Patients could have 1 target lesion treated. Patients with a single target lesion could also have 1 de novo native coronary artery lesion within a different epicardial vessel (non-target lesion) treated with a commercially-available treatment (e.g., stent, balloon angioplasty, excluding brachytherapy) during the index procedure. The non-target lesion had to be treated before the target lesion and the treatment had to be a clinical angiographic success (defined as visually assessed stenosis $< 50\%$ [$< 30\%$ for stents] with TIMI 3 flow without prolonged chest pain or electrocardiogram [ECG] changes consistent with MI) before the patient could be enrolled. The protocol mandated antiplatelet therapy compliance in accordance with the 2007 ACC/AHA/SCAI Guidelines for PCI.

Baseline and post-procedure angiographic data were collected and assessed by quantitative analysis at a designated core laboratory. An independent Clinical Events Committee adjudicated major adverse clinical events and stent thrombosis.

A2. Clinical Inclusion and Exclusion Criteria, OMEGA

Subjects were eligible to participate in the study if they met the following inclusion criteria (Table 7).

Table 7: Inclusion Criteria, OMEGA

<p>Clinical Inclusion Criteria</p>	<p>CI1. Subject must be at least 18 years of age. CI2. Subject (or legal guardian) indicates understanding of the trial requirements and the treatment procedures and provides written informed consent before any trial-specific tests or procedures are performed. CI3. Subject is eligible for PCI. CI4. Subject has symptomatic coronary artery disease or documented silent ischemia. CI5. Subject is an acceptable candidate for coronary artery bypass grafting (CABG). CI6. Subject has a left ventricular ejection fraction (LVEF) $\geq 30\%$ as measured within 60 days prior to enrollment. CI7. Subject is willing to comply with all protocol-required follow-up evaluations.</p>
<p>Angiographic Inclusion Criteria</p>	<p>AI1. Target lesion must be a de novo lesion located in a native coronary artery with a visually estimated reference vessel diameter (RVD) ≥ 2.25 mm and ≤ 4.50 mm. AI2. Target lesion length must measure (by visual estimate) as follows: o ≤ 28 mm for stent diameter lengths of 2.75 mm, 3.00 mm, 3.50 mm, 4.00 mm and 4.50 mm o ≤ 24 mm for stent diameter lengths of 2.25 mm and 2.50 mm AI3. Target lesion must be in a major coronary artery or branch with visually estimated stenosis $\geq 50\%$ and $< 100\%$ with Thrombolysis in Myocardial Infarction (TIMI) flow > 1 AI4. Target lesion must be successfully pre-dilated.</p>

Subjects were ineligible to participate in the study if they met any of the following exclusion criteria (Table 8).

Table 8: Exclusion Criteria, OMEGA

<p>Clinical Exclusion Criteria</p>	<p>CE1. Subject has clinical symptoms and/or electrocardiogram (ECG) changes consistent with acute MI.</p> <p>CE2. Subject with unstable angina or recent MI (clinically diagnosed within 3 days) must have CK/CK-MB or troponin documented prior to the procedure and are excluded if any of the following criteria are met at the time of the index procedure:</p> <ol style="list-style-type: none"> 1. If CK-MB >2× upper limit of normal (ULN), the subject is excluded regardless of the CK Total. 2. If CK Total >2× ULN, CK-MB must be drawn and the subject is excluded if CK-MB is abnormal. 3. If CK/CK-MB results are not available at the time of the procedure, the subject is excluded if troponin >1× ULN and the subject has at least one of the following: <ul style="list-style-type: none"> ○ Subject has ischemic symptoms and ECG changes indicative of ongoing ischemia (e.g., >1 mm ST segment elevation or depression in consecutive leads or new left bundle branch block [LBBB]) ○ Development of pathological Q-waves in the ECG or; ○ Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality <p><i>Note:</i> Subjects who do not have unstable angina or recent MI must still have CK/CK-MB drawn prior to the index procedure. However, the results for these subjects do not need to be available prior to the index procedure and there are no exclusion criteria based on these studies.</p> <p>CE3. Subject is receiving chronic (≥72 hours) anticoagulation therapy (e.g., heparin, coumadin) for indications other than acute coronary syndrome.</p> <p>CE4. Subject has a platelet count <100,000 cells/mm³ or >700,000 cells/mm³.</p> <p>CE5. Subject has a white blood cell (WBC) count <3,000 cells/mm³.</p> <p>CE6. Subject has documented or suspected liver disease, including laboratory evidence of hepatitis.</p> <p>CE7. Subject is on dialysis or has known renal insufficiency (e.g. serum creatinine level >2.0 mg/dL).</p> <p>CE8. Subject has active peptic ulcer disease, an active gastrointestinal (GI) bleed, other bleeding diathesis or coagulopathy or will refuse transfusions.</p> <p>CE9. Subject has had a cerebrovascular accident (CVA) or transient ischemic attack (TIA) within the past 6 months, or has any permanent neurologic defect that may cause non-compliance with the protocol.</p> <p>CE10. Target vessel (including side branches) has been treated with any type of PCI (e.g., balloon angioplasty, stent, cutting balloon, atherectomy) within 12 months prior to the index procedure.</p> <p>CE11. Target vessel has been treated within 10 mm proximal or distal to the target lesion (by visual estimate) with any type of PCI (e.g., balloon angioplasty, stent, cutting balloon, or atherectomy) at any time prior to the index</p>
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Table 8: Exclusion Criteria, OMEGA

	<p>procedure.</p> <p>CE12. Non-target vessel or side branch has been treated with any type of PCI (e.g., balloon angioplasty, stent, cutting balloon, atherectomy) within 1 day prior to the index procedure.</p> <p><i>Note:</i> 1 lesion in a non-target vessel may be treated during the index procedure prior to the treatment of the target (study) lesion.</p> <p>CE13. Planned or actual target vessel treatment with an unapproved device, directional or rotational coronary atherectomy, laser, cutting balloon, or transluminal extraction catheter immediately prior to stent placement.</p> <p>CE14. Planned PCI or CABG after the index procedure.</p> <p>CE15. Subject previously treated at any time with coronary intravascular brachytherapy.</p> <p>CE16. Subject has known allergy to the study stent system or protocol-required concomitant medications (e.g., stainless steel, platinum, chromium, nickel, iron, thienopyridines and ASA) and contrast (that cannot be adequately premedicated).</p> <p>CE17. Subject has any other serious medical illness (e.g., cancer, congestive heart failure) that may reduce life expectancy to less than 12 months.</p> <p>CE18. Subject has current problems with substance abuse (e.g., alcohol, cocaine, heroin, etc.).</p> <p>CE19. Subject has a planned procedure that may cause non-compliance with the protocol or confound data interpretation.</p> <p>CE20. Subject is participating in another investigational drug or device clinical trial that has not reached its primary endpoint or intends to participate in another investigational drug or device clinical trial within 12 months after the index procedure.</p> <p>CE21. Subject is female of childbearing potential with a positive pregnancy test within 14 days before the index procedure, is lactating, or intends to become pregnant during the study.</p> <p>CE22. Subject has more than 1 target lesion, or more than 1 target lesion and 1 non-target lesion, which will be treated during the index procedure.</p>
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Table 8: Exclusion Criteria, OMEGA

<p>Angiographic Exclusion Criteria (visual estimate)</p>	<p>AE1. Target lesion meets any of the following criteria:</p> <ul style="list-style-type: none"> ○ Aorto-ostial location (i.e., lesion located within 5 mm of the ostium by visual estimate) ○ Left main location ○ Located within 5 mm of the origin of the left anterior descending (LAD) coronary artery or left circumflex (LCx) coronary artery or RCA by visual estimate ○ Located within a saphenous vein graft or an arterial graft ○ Will be accessed via a saphenous vein graft or an arterial graft ○ Involves a side branch ≥ 2.0 mm in diameter by visual estimate ○ Involves a side branch < 2.0 mm in diameter by visual estimate that has a clinically significant stenosis at the ostium ○ TIMI flow 0 (total occlusion) or TIMI flow 1 prior to guide wire crossing ○ Excessive tortuosity proximal to or within the lesion ○ Extreme angulation proximal to or within the lesion ○ Target lesion and/or target vessel proximal to the target lesion is moderately to severely calcified by visual estimate ○ Restenotic from previous intervention ○ Thrombus, or possible thrombus, present in the target vessel ○ Target lesion cannot be covered by a single study stent (unplanned bailout stenting is allowed) <p>AE2. Non-target lesion to be treated during the index procedure meets any of the following criteria:</p> <ul style="list-style-type: none"> ○ Located within the target vessel ○ Located within a bypass graft (venous or arterial) ○ Left main location ○ Chronic total occlusion ○ Involves a complex bifurcation (e.g., bifurcations requiring treatment with more than 1 stent) ○ Requires additional unplanned stents (treatment of the non-target lesion with more than one stent is permitted as long as the stents are initially planned) ○ Treatment not deemed a clinical angiographic success ○ Treatment not completed prior to treatment of target lesion <p>AE3. Subject has unprotected left main coronary artery disease ($> 50\%$ diameter stenosis).</p> <p>AE4. Subject has protected left main coronary artery disease and a target lesion in the LAD or LCx.</p> <p>AE5. Subject has an additional clinically significant lesion(s) in the target vessel for which an intervention within 12 months after the index procedure may be required.</p>
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A3. Follow-up Schedule, OMEGA

Enrolled patients underwent clinical follow-up in hospital and at 30 days, 9 months and 12 months after the index procedure. Final 12-month follow-up for the OMEGA trial was

completed on January 7, 2014. Follow-up included clinical assessments at 30 days, 9 and 12 months post-index procedure.

A4. Clinical Endpoints, OMEGA

Adverse events are collected throughout the study with a prespecified subset of events adjudicated by an independent Clinical Events Committee.

The primary endpoint was the rate of target lesion failure (TLF), defined as any ischemia-driven revascularization of the target lesion (TLR), myocardial infarction (MI; Q-wave and non-Q-wave) related to the target vessel, or cardiac death, at 9 months post-index procedure. The rate of the primary endpoint was compared to a predefined performance goal (PG) of 21.2%, which was calculated based on historical bare metal stent (BMS) results. The PG equals the historical BMS 9-month TLF rate adjusted for differences in the non-Q-wave MI definition (15.2%) + margin (6.0%). A one-group exact binomial test was used to test the hypothesis that the primary endpoint rate in the OMEGA cohort is less than the PG.

A5. Accountability of PMA Cohort, OMEGA

A total of 328 patients were enrolled (the ITT analysis set) at 37 sites in the United States and Europe in the OMEGA Trial. Clinical follow-up or death at 9-months was 98.2% (322/328). Four patients were lost to follow-up and 2 patients missed their 9-month visit. Details of 9-month follow-up compliance are provided in **Table 9**.

Clinical follow-up or death at 12-months was 97.6% (320/328). Seven patients were lost to follow-up and 1 patient missed their 12-month visit.

Table 9: Subject Disposition, Clinical Follow-up Compliance Intent-to-Treat, All Subjects (N=328)

	Subjects
Subjects enrolled (Intent-to-Treat analysis set)	328
Death ≤ 300 days with no 9-Month Clinical Follow-up Performed	6
Eligible for 9-Month Clinical Follow-up^a	322
9-Month Clinical Follow-up Performed^b	98.1% (316/322)
Office Visit	286
Telephone Contact	30
No 9-Month Clinical Follow-up Performed	6
Prematurely Discontinued	4
Death > 300 days	0
Withdrew Consent	0
Lost to Follow-up	4
Adverse Event	0
Investigator Discretion	0
Transplant or Removal of Target Organ	0
Other	0
Missed 9-Month Visit	2
With Later Follow-up Visit Performed	2
No Later Follow-up Visit Performed	0
9-Month Clinical Follow-up or Death^c	98.2% (322/328)
9-Month Clinical Follow-up Patient Accountability^d	96.3% (316/328)

Numbers are n or % (count/sample size).

	Subjects
a: Patients who died prior to completion of follow-up window and prior to completing a 9-month clinical follow-up visit are considered censored and are excluded from calculation of proportion of patients who completed clinical follow-up visit.	
b: Based on patients eligible for 9-month clinical follow-up (excludes patients who died within 300 days with no 9-month follow-up).	
c: Includes patients who have died in both the numerator and the denominator; based on ITT analysis set.	
d: All patients with 9-month follow-up out of all Intent-to-Treat patients.	
Abbreviation: ITT=intent-to-treat	

A6. Study Population and Baseline Parameters, OMEGA

Table 10 and Table 11 present demographics and baseline clinical characteristics for the ITT analysis set (N=328). The ITT population was predominantly male (67.7%) with a history of medically treated hyperlipidemia (70.8%) and hypertension (75.0%). Medically treated diabetic subjects accounted for 17.4% of ITT subjects. Unstable angina was reported for 33.8% of subjects and 29.6% had a history of MI.

Table 10: Baseline Demographics and General Medical History, ITT Analysis Set (N=328 Subjects)

Parameter	OMEGA (N=328)	[95% CI]
Male	67.7% (222/328)	[62.3%, 72.7%]
Age (yr)	65.46±11.23 (328) (32.00, 95.00)	[64.25, 66.68]
Ethnicity and Race		
American Indian or Alaska native	0.0% (0/328)	[0.0%, 1.1%]
Asian	0.0% (0/328)	[0.0%, 1.1%]
Black, of African heritage	2.7% (9/328)	[1.3%, 5.1%]
Caucasian	77.4% (254/328)	[72.5%, 81.8%]
Hispanic or Latino	0.6% (2/328)	[0.1%, 2.2%]
Native Hawaiian or other Pacific Islander	0.0% (0/328)	[0.0%, 1.1%]
Other	0.6% (2/328)	[0.1%, 2.2%]
Not disclosed	18.6% (61/328)	[14.5%, 23.2%]
Smoking, Ever	66.1% (211/319)	[60.7%, 71.3%]
Current	28.2% (90/319)	[23.3%, 33.5%]
Previous	37.9% (121/319)	[32.6%, 43.5%]
Medically Treated Diabetes	17.4% (57/328)	[13.4%, 21.9%]
Insulin Requiring	5.5% (18/328)	[3.3%, 8.5%]
Non-Insulin Requiring	11.9% (39/328)	[8.6%, 15.9%]
Diabetes Treated with Diet Only	7.0% (23/328)	[4.5%, 10.3%]
Hyperlipidemia Requiring Medication	70.8% (230/325)	[65.5%, 75.7%]
Hypertension Requiring Medication	75.0% (243/324)	[69.9%, 79.6%]
History of Bleeding Disorder	2.5% (8/326)	[1.1%, 4.8%]
Gastrointestinal	2.5% (8/326)	[1.1%, 4.8%]
Hematologic Dyscrasia	0.0% (0/326)	[0.0%, 1.1%]
History of TIA or CVA	7.7% (25/326)	[5.0%, 11.1%]
History of TIA	3.7% (12/326)	[1.9%, 6.3%]
History of CVA	4.3% (14/326)	[2.4%, 7.1%]
History of Renal Disease	4.3% (14/326)	[2.4%, 7.1%]

Parameter	OMEGA (N=328)	[95% CI]
History of PVD	6.4% (21/326)	[4.0%, 9.7%]

Numbers are presented as mean±standard deviation (n) or % (count/sample size), or mean±SD (n) (minimum, maximum).

Abbreviation: ITT=intent-to-treat

Abbreviation: TIA=transient ischemic attack, CVA=cerebrovascular event, PVD=peripheral vascular disease

Table 11: Cardiac History, ITT Analysis Set (N=328 Subjects)

Parameter	OMEGA (N=328)	[95% CI]
Stable Angina	55.5% (182/328)	[49.9%, 60.9%]
Angina Class (CCS)		
1	14.0% (46/328)	[10.5%, 18.3%]
2	27.4% (90/328)	[22.7%, 32.6%]
3	11.9% (39/328)	[8.6%, 15.9%]
4	1.8% (6/328)	[0.7%, 3.9%]
Unknown	0.3% (1/328)	[0.0%, 1.7%]
Unstable Angina	33.8% (111/328)	[28.7%, 39.2%]
Braunwald Classification		
IA	0.9% (3/328)	[0.2%, 2.6%]
IB	5.5% (18/328)	[3.3%, 8.5%]
IC	0.3% (1/328)	[0.0%, 1.7%]
IIA	0.3% (1/328)	[0.0%, 1.7%]
IIB	18.3% (60/328)	[14.3%, 22.9%]
IIC	0.3% (1/328)	[0.0%, 1.7%]
IIIA	0.3% (1/328)	[0.0%, 1.7%]
IIIB	5.5% (18/328)	[3.3%, 8.5%]
IIIC	0.6% (2/328)	[0.1%, 2.2%]
Unknown	1.8% (6/328)	[0.7%, 3.9%]
No Angina	10.7% (35/328)	[7.5%, 14.5%]
Silent Ischemia	19.9% (54/272)	[15.3%, 25.1%]
Family History of CAD	43.4% (131/302)	[37.7%, 49.2%]
Previous MI	29.6% (94/324)	[24.7%, 34.9%]
History of CHF	6.4% (21/327)	[4.0%, 9.6%]
New York Heart Association Classification		
I	1.5% (5/327)	[0.5%, 3.5%]
II	3.4% (11/327)	[1.7%, 5.9%]
III	0.9% (3/327)	[0.2%, 2.7%]
IV	0.3% (1/327)	[0.0%, 1.7%]
Unknown	0.3% (1/327)	[0.0%, 1.7%]
History of PCI	29.1% (95/326)	[24.3%, 34.4%]
History of CABG	4.6% (15/327)	[2.6%, 7.5%]
History of Arrhythmia	12.3% (40/326)	[8.9%, 16.3%]
Left Ventricular Ejection Fraction (LVEF, %)	58.50±9.25 (325) (30.00, 88.00)	[57.50, 59.51]
LVEF not Measured or not Known	0.9% (3/328)	[0.2%, 2.6%]
History of Multivessel Disease	28.5% (93/326)	[23.7%, 33.8%]

Parameter	OMEGA (N=328)	[95% CI]
History of Left Main Disease	1.8% (6/327)	[0.7%, 4.0%]

Numbers are presented as mean±standard deviation (n) or % (count/sample size), or mean±SD (n) (minimum, maximum).

Abbreviation: ITT=intent-to-treat; CAD=coronary artery disease; MI=myocardial infarction; CHF=congestive heart failure; PCI=percutaneous coronary intervention; CABG=coronary artery bypass graft surgery; LVEF= Left Ventricular Ejection Fraction

A7. Safety and Effectiveness Results, OMEGA

The principal safety and effectiveness results through 9 months are summarized below and presented in Tables 12 and 13.

- For the primary endpoint analysis, the ITT 9-month rate of target lesion failure was 11.5% (37/323) with a one-sided upper confidence bound of 14.79%, significantly less than the performance goal of 21.2% (P<0.0001)
- Similar results were found when the primary endpoint was analyzed on a per protocol or intent-to-treat basis
- There were 4 cardiac deaths (1.2%), 12 myocardial infarctions (3.7%), and 2 patients experienced definite stent thrombosis (0.6%) through 9 months
- The technical success rate was 98.5% (332/337)
- The clinical procedural success rate was 95.4% (313/328)

Table 12: Primary Endpoint: TLF at 9 Months

Population	OMEGA	95% Confidence Interval	95% UCB ^a	Performance Goal ^b	1-sided P value
ITT ^c (N=328)	11.5% (37/323)	[8.2%, 15.4%]	14.79%	21.2%	<0.0001
Per-protocol (N=325)	11.6% (37/320)	[8.3%, 15.6%]	14.93%	21.2%	<0.0001

P value is based on the exact binomial test.

a: One-sided 95% Clopper-Pearson upper confidence bound

b: Based on historical BMS results

c: Primary analysis

Abbreviations: ITT=intent-to-treat; TLF=target lesion failure (including any ischemia-driven revascularization of the target lesion, myocardial infarction [Q-wave and non-Q-wave] related to the target vessel, or cardiac death); UCB=upper confidence bound

Table 13: Principal Effectiveness and Safety Results (9 Months), ITT Analysis Set

Parameter	OMEGA (N=328)	95% Confidence Interval
9-Month Clinical Endpoints		
All death, MI, TVR	12.9% (42/325)	[9.5%, 17.1%]
All death or MI	5.5% (18/325)	[3.3%, 8.6%]
All death	1.8% (6/325)	[0.7%, 4.0%]
Cardiac death ^a	1.2% (4/325)	[0.3%, 3.1%]
Non-cardiac death	0.6% (2/325)	[0.1%, 2.2%]
MI ^{a, b}	3.7% (12/325)	[1.9%, 6.4%]
TVR ^c	8.6% (28/325)	[5.8%, 12.2%]
TLR ^c	7.4% (24/325)	[4.8%, 10.8%]
Non-TLR TVR ^c	1.8% (6/325)	[0.7%, 4.0%]
Cardiac death or MI	4.9% (16/325)	[2.8%, 7.9%]
TLF	11.5% (37/323)	[8.2%, 15.4%]
TVF	12.4% (40/323)	[9.0%, 16.5%]
ARC stent thrombosis (definite/probable) ^d	0.6% (2/318)	[0.1%, 2.3%]
Peri-procedural Endpoints		
Clinical procedural success ^e	95.4% (313/328)	[92.6%, 97.4%]
Technical success ^f	98.5% (332/337)	[96.6%, 99.5%]

Numbers are % (counts/sample size)

a: All events were related to the target vessel

b: All MI were target vessel-related non-Q-wave MI

c: All revascularizations were by PCI.

d: All stent thromboses were determined to be ARC definite stent thromboses.

e: Mean lesion diameter stenosis <30% in 2 near-orthogonal projections with TIMI 3 flow, as visually assessed by the physician, without the occurrence of in-hospital MI, TVR, or cardiac death

f: Technical success is successful delivery and deployment of the study stent to the target vessel, without balloon rupture or stent embolization.

Abbreviations: ARC=Academic Research Consortium; ITT=intent-to-treat; TLF=target lesion failure (including any ischemia-driven revascularization of the target lesion [TLR], myocardial infarction [MI; Q-wave and non-Q-wave] related to the target vessel, or cardiac death); TVF=target vessel failure (any ischemia-driven revascularization of the target vessel [TVR], MI related to the target vessel, or death related to the target vessel).

The principal safety and effectiveness results through 12 months are summarized in Table 14. There were 4 cardiac deaths (1.2%), 13 myocardial infarctions (4.0%), and 2 patients experienced definite stent thrombosis (0.6%) through 12 months post-index procedure. These results support the continued safety and effectiveness of the OMEGA stent through 12 months of follow-up.

Table 14 Principal Effectiveness and Safety Results (12 Months), ITT Analysis Set

Parameter	OMEGA (N=328)	95% Confidence Interval
12-Month Clinical Endpoints		
All death, MI, TVR	14.3% (46/322)	[10.7%, 18.6%]

Table 14 Principal Effectiveness and Safety Results (12 Months), ITT Analysis Set

Parameter	OMEGA (N=328)	95% Confidence Interval
All death or MI	5.9% (19/322)	[3.6%, 9.1%]
All death	1.9% (6/322)	[0.7%, 4.0%]
Cardiac death ^a	1.2% (4/322)	[0.3%, 3.1%]
Non-cardiac death	0.6% (2/322)	[0.1%, 2.2%]
MI ^{a, b}	4.0% (13/322)	[2.2%, 6.8%]
TVR ^c	9.9% (32/322)	[6.9%, 13.7%]
TLR ^c	8.4% (27/322)	[5.6%, 12.0%]
Non-TLR TVR ^c	2.2% (7/322)	[0.9%, 4.4%]
Cardiac death or MI	5.3% (17/322)	[3.1%, 8.3%]
TLF	12.8% (41/320)	[9.4%, 17.0%]
TVF	13.8% (44/320)	[10.2%, 18.0%]
ARC stent thrombosis (definite/probable) ^d	0.6% (2/314)	[0.1%, 2.3%]

Numbers are % (counts/sample size)

a: All events were related to the target vessel

b: All MI were target vessel-related non-Q-wave MI

c: All revascularizations were by PCI.

d: All stent thromboses were determined to be ARC definite stent thromboses.

Abbreviations: ARC=Academic Research Consortium; ITT=intent-to-treat; TLF=target lesion failure (including any ischemia-driven revascularization of the target lesion [TLR], myocardial infarction [MI; Q-wave and non-Q-wave] related to the target vessel, or cardiac death); TVF=target vessel failure (any ischemia-driven revascularization of the target vessel [TVR], MI related to the target vessel, or death related to the target vessel).

A8. Subgroup Analyses, OMEGA

OMEGA data were evaluated retrospectively for possible gender-based differences in clinical outcomes. OMEGA was not designed or powered to study safety or effectiveness of the OMEGA Stent in gender-specific subgroups, so these analyses were performed post hoc and are considered hypothesis-generating.

In the OMEGA ITT population, of the 328 enrolled patients, 222 patients were male (67.7%) and 106 patients were female (32.3%).

In the United States, an estimated 15.4 million adults of 20 years and older (7.9% of men and 5.1% of women) suffer from coronary artery disease (CAD)¹. However, it is estimated that only about 33% of the annual PCIs are performed in women. In PCI clinical trials, women represent only 25-35% of the enrolled populations, and there are relatively little gender-specific data. The disproportionate enrollment distribution in this study may be partly attributable to gender differences in pathophysiology, risk factors and symptoms which may lead to under-diagnosis and under-referral of female patients with CAD^{2,3}. Once diagnosed and treated, poorer revascularization outcomes have been reported in women due to smaller coronary arteries and increased prevalence of baseline comorbidities including advanced age, diabetes, hypertension, and peripheral vascular disease compared with men.

In patients treated with the OMEGA stent, the 9-month rate of TLF was 12.3% in males and 9.6% in females. This post hoc analysis shows similar treatment effect between genders for

the primary endpoint of 9-month TLF and its components. This suggests that the overall conclusions of the trial regarding both safety and effectiveness of the OMEGA stent can be generalized to males and females.

Table 15 OMEGA 9-Month TLF Results by Gender, Intent-to-Treat, All Patients (N=328)

Event	OMEGA Females (N=106)	[95% CI]	OMEGA Males (N=222)	[95% CI]
9-Month TLF	9.6% (10/104)	[4.7%, 17.0%]	12.3% (27/219)	[8.3%, 17.4%]

This trial was not sized to determine the rate of low frequency events with a pre-specified precision. Numbers are % (count/sample size). 9-Month TLF is the proportion of patients who experience a target lesion failure (defined as any ischemia-driven revascularization of the target lesion [TLR], MI [Q-wave and non-Q wave] related to the target vessel, or cardiac death) up to 270 days post-procedure out of the population that have been followed for at least 240 days or who have experienced a TLF up to 270 days post-procedure.

Table 16 shows OMEGA 9-Month clinical results for male and female patients. Given the small number of patients enrolled, no conclusions can be drawn from these data.

Table 16 9-Month Clinical Endpoints by Gender, Intent-to-Treat, All Patients

	OMEGA Female Patients (N=106)	OMEGA Male Patients (N=222)
Efficacy		
TVR, Overall	7.6% (8/105)	9.1% (20/220)
TLR, Overall	6.7% (7/105)	7.7% (17/220)
TLR, PCI	6.7% (7/105)	7.7% (17/220)
TLR, CABG	0.0% (0/105)	0.0% (0/220)
Non-TLR TVR, Overall	2.9% (3/105)	1.4% (3/220)
Non-TLR TVR, PCI	2.9% (3/105)	1.4% (3/220)
Non-TLR TVR, CABG	0.0% (0/105)	0.0% (0/220)
Safety		
All Death	1.0% (1/105)	2.3% (5/220)
Cardiac Death or MI	3.8% (4/105)	5.5% (12/220)
Cardiac Death	0.0% (0/105)	1.8% (4/220)
MI	3.8% (4/105)	3.6% (8/220)
Q-wave MI	0.0% (0/105)	0.0% (0/220)
Non-Q-wave MI	3.8% (4/105)	3.6% (8/220)
ARC Stent Thrombosis	1.0% (1/104)	0.5% (1/214)
Definite or Probable	1.0% (1/104)	0.5% (1/214)
Definite	1.0% (1/104)	0.5% (1/214)
Probable	0.0% (0/104)	0.0% (0/214)
Peri-Procedural Endpoints		
Procedural Success	95.3% (101/106)	95.5% (212/222)
Technical Success ^a	99.1% (106/107)	98.3% (226/230)

a: denominator is number of study stents attempted

Numbers are % (count/sample size).

This trial was not sized to determine the rate of low frequency events with a pre-specified precision.

Abbreviations: ARC=Academic Research Consortium; CABG=coronary artery bypass graft; MI=myocardial infarction; PCI=percutaneous coronary intervention; TLR=target lesion revascularization; TVR=target vessel revascularization.

B. NG PROMUS Clinical Trial

B.1. Study Design: NG PROMUS was a prospective, single arm, multicenter, observational study designed to evaluate clinical and periprocedural angiographic and IVUS outcomes for the Promus PREMIER Everolimus-Eluting Platinum Chromium Coronary Stent System in the treatment of subjects with atherosclerotic lesions ≤ 34 mm in length (by visual estimate) in native coronary arteries ≥ 2.50 mm to ≤ 4.00 mm in diameter (by visual estimate).

B2. Clinical Inclusion and Exclusion Criteria, NG PROMUS

Subjects were eligible to participate in the study if they met the following inclusion criteria (Table 17).

Table 15: Inclusion Criteria, NG PROMUS

Clinical Inclusion Criteria	<p>CI1. Subject must be at least 18 years of age</p> <p>CI2. Subject (or legal guardian) understands the trial requirements and the treatment procedures and provides written informed consent before any trial-specific tests or procedures are performed</p> <p>CI3. Subject is eligible for percutaneous coronary intervention (PCI)</p> <p>CI4. Subject has symptomatic coronary artery disease with objective evidence of ischemia or silent ischemia</p> <p>CI5. Subject is an acceptable candidate for coronary artery bypass grafting (CABG)</p> <p>CI6. Subject is willing to comply with all protocol-required follow-up evaluation</p>
Angiographic Inclusion Criteria	<p>AI1. Target lesion(s) must be located in a native coronary artery with a visually estimated reference vessel diameter (RVD) ≥ 2.50 mm and ≤ 4.0 mm</p> <p>AI2. Target lesion(s) length must be ≤ 34 mm (by visual estimate)</p> <p>AI3. Target lesion(s) must have visually estimated stenosis $\geq 50\%$ and $< 100\%$ with thrombolysis in Myocardial Infarction (TIMI) flow > 1 and one of the following (stenosis $\geq 70\%$, abnormal fractional flow reserve (FFR), abnormal stress test or imaging stress test, or elevated biomarkers) prior to procedure</p> <p>AI4. Coronary anatomy is likely to allow delivery of a study device to the target lesions(s)</p> <p>AI5. The first lesion treated must be successfully pre-dilated/pretreated</p> <p><i>Note:</i> Successful pre-dilatation/pretreatment refers to dilatation with a balloon catheter of appropriate length and diameter, or pretreatment with directional or rotational coronary atherectomy, laser or cutting/scoring balloon with no greater than 50% residual stenosis and no dissection greater than National Heart, Lung, Blood Institute (NHLBI) type C.</p>

Subjects were ineligible to participate in the study if they met any of the following exclusion criteria (Table 18).

Table 16: Exclusion Criteria, NG PROMUS

Clinical Exclusion Criteria	<p>CE1. Subject has clinical symptoms and/or electrocardiogram (ECG) changes consistent with acute ST elevation MI (STEMI)</p> <p>CE2. Subject has cardiogenic shock, hemodynamic instability requiring inotropic or mechanical circulatory support, intractable ventricular arrhythmias, or ongoing intractable angina</p> <p>CE3. Subject has received an organ transplant or is on a waiting list for an organ transplant</p>
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Table 16: Exclusion Criteria, NG PROMUS

	<p>CE4. Subject is receiving or scheduled to receive chemotherapy within 30 days before or after the index procedure</p> <p>CE5. Planned PCI (including staged procedures) or CABG after the index procedure</p> <p>CE6. Subject previously treated at any time with intravascular brachytherapy</p> <p>CE7. Subject has a known allergy to contrast (that cannot be adequately premedicated) and/or the trial stent system or protocol-required concomitant medications (e.g., platinum, platinum-chromium alloy, stainless steel, everolimus or structurally related compounds, polymer or individual components, all P2Y12 inhibitors, or aspirin)</p> <p>CE8. Subject has one of the following (as assessed prior to the index procedure):</p> <ul style="list-style-type: none"> • Other serious medical illness (e.g., cancer, congestive heart failure) with estimated life expectancy of less than 24 months • Current problems with substance abuse (e.g., alcohol, cocaine, heroin, etc.) • Planned procedure that may cause non-compliance with the protocol or confound data interpretation <p>CE9. Subject is receiving chronic (≥ 72 hours) anticoagulation therapy (i.e., heparin, coumadin) for indications other than acute coronary syndrome</p> <p>CE10. Subject has a platelet count $< 100,000$ cells/mm³ or $> 700,000$ cells/mm³</p> <p>CE11. Subject has a white blood cell (WBC) count $< 3,000$ cells/mm³</p> <p>CE12. Subject has documented or suspected liver disease, including laboratory evidence of hepatitis</p> <p>CE13. Subject is on dialysis or has baseline serum creatinine level > 2.0 mg/dL ($177\mu\text{mol/L}$)</p> <p>CE14. Subject has a history of bleeding diathesis or coagulopathy or will refuse blood transfusions</p> <p>CE15. Subject has had a history of cerebrovascular accident (CVA) or transient ischemic attack (TIA) within the past 6 months</p> <p>CE16. Subject has an active peptic ulcer or active gastrointestinal (GI) bleeding</p> <p>CE17. Subject has signs or symptoms of active heart failure (i.e., NYHA class IV) at the time of the index procedure</p> <p>CE18. Subject is participating in another investigational drug or device clinical trial that has not reached its primary endpoint</p> <p>CE19. Subject intends to participate in another investigational drug or device clinical trial within 12 months after the index procedure</p> <p>CE20. Subject with known intention to procreate within 12 months after the index procedure (women of child-bearing potential who are sexually active must agree to use a reliable method of contraception from the time of screening through 12 months after the index procedure)</p> <p>CE21. Subject is a woman who is pregnant or nursing (a pregnancy test must be performed within 7 days prior to the index procedure in women of child-bearing potential)</p>
<p>Angiographic Exclusion Criteria (visual estimate)</p>	<p>AE1. Planned treatment of more than 3 lesions.</p> <p>AE2. Planned treatment of lesions in more than 2 major epicardial vessels</p> <p>AE3. Planned treatment of a single lesion with more than 1 stent</p> <p>AE4. Subject has 2 target lesions in the same vessel that are separated by less than 15 mm (by visual estimate)</p> <p>AE5. Target lesion(s) is located in the left main</p> <p>AE6. Target lesion(s) is located within 3 mm of the origin of the left anterior descending (LAD) coronary artery or left circumflex (LCx) coronary artery by visual estimate.</p> <p>AE7. Target lesion(s) is located within a saphenous vein graft or an arterial graft</p> <p>AE8. Target lesion(s) will be accessed via a saphenous vein graft or arterial graft</p>

Table 16: Exclusion Criteria, NG PROMUS

	<p>AE9. Target lesion(s) with a TIMI flow 0 (total occlusion) or TIMI flow 1 prior to guide wire crossing</p> <p>AE10. Target lesion(s) treated during the index procedure that involves a complex bifurcation (e.g., bifurcation lesion requiring treatment with more than 1 stent)</p> <p>AE11. Target lesion(s) is restenotic from a previous stent implantation or study stent would overlap with a previous stent</p> <p>AE12. Subject has unprotected left main coronary artery disease (>50% diameter stenosis)</p> <p>AE13. Subject has been treated with any type of PCI (i.e., balloon angioplasty, stent, cutting balloon atherectomy) within 24 hours prior to the index procedure</p> <p>AE14. Thrombus, or possible thrombus, present in the target vessel (by visual estimate)</p>
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B3. Follow-up Schedule, NG PROMUS

Clinical follow-up by telephone at 30 days

B4. Clinical Endpoints, NG PROMUS

Adverse events are collected throughout the study with a prespecified subset of events adjudicated by an independent Clinical Events Committee.

The Primary Endpoint is technical success rate, defined as successful delivery and deployment of the study stent to the target lesion, without balloon rupture or stent embolization, and post-procedure diameter stenosis of <30% assessed in 2 near-orthogonal projections with TIMI 3 flow in the target lesion, as visually assessed by the physician

B5. Accountability of PMA Cohort, NG PROMUS

Table 19 shows subject disposition. There were 100 subjects enrolled (intent-to-treat [ITT] analysis set) and implanted (as-treated analysis set) at 9 investigative centers in Australia, New Zealand, and Singapore from 20-Nov-2012 to 12-Mar-2013.

Clinical follow-up at 30 days was 99.0% (98/99). One subject died before the 30-day follow-up window and 1 subject missed the 30-day visit.

Table 17: Subject Disposition, Clinical Follow-up Compliance Intent-to-Treat, All Subjects (N=100)

	Subjects
Subjects enrolled (Intent-to-Treat analysis set)	100
Subjects treated with at least 1 study stent	100
Death ≤30 days with no 30-day clinical follow-up performed	1
Eligible for 30-day clinical follow-up ^a	99
30-Day clinical follow-up visit completed ^b	99.0% (98/99)
Office Visit	11
Telephone contact	87
No 30-Day clinical follow-up performed	1
Premature discontinuation	0
Withdrew consent	0
Lost to follow-up	0
Adverse event	0
Investigator discretion	0
Other	0
Death >30 days	0
Missed 30-day follow-up visit	1
30-Day clinical follow-up or death ^c	99.0% (99/100)

Numbers are n or % (count/sample size).

a: Patients who died prior to completion of follow-up window and prior to completing a 30-day clinical follow-up visit are considered censored and are excluded from calculation of proportion of patients who completed clinical follow-up visit.

b: Based on patients eligible for 30-day clinical follow-up (excludes deaths before 30 days)

c: Includes patients who have died in both the numerator and the denominator

Abbreviation: ITT=intent-to-treat

B6. Study Population and Baseline Parameters, NG PROMUS

Table 20 presents demographics and baseline clinical characteristics for the ITT analysis set (N=100). The ITT population was predominantly male (85.0%) with a history of medically treated hyperlipidemia (78.0%) and hypertension (70.0%). Medically treated diabetic subjects accounted for 16.0% of ITT subjects. Unstable angina was reported for 25.0% of subjects and 16.0% had a history of MI.

Table 18: Baseline Demographics and General Medical History, ITT Analysis Set (N=100 Subjects)

Parameter	NG PROMUS
Male	85.0% (85/100)
Age (years)	61.72±9.73 (100) (38, 81)
Weight (kg)	87.94±19.85 (100) (50, 179)
Ethnicity and Race	
Hispanic or Latino	2.0% (2/100)
Caucasian	72.0% (72/100)
Asian	13.0% (13/100)
Black, of African Heritage	1.0% (1/100)
Native Hawaiian or Other Pacific Islander	5.0% (5/100)
American Indian or Alaska Native	0.0% (0/100)
Other	6.0% (6/100)
Not disclosed	1.0% (1/100)
Medical History	

Parameter	NG PROMUS
Smoking Status	
Current	14.0% (14/100)
Previous	42.0% (42/100)
Never	44.0% (44/100)
Unknown	0.0% (0/100)
Current diabetes mellitus	
Diabetes treated with diet only	6.0% (6/100)
Diabetes (medically treated)	16.0% (16/100)
Insulin	2.0% (2/100)
Oral medications (no insulin)	16.0% (16/100)
Injectable agent (other than insulin)	0.0% (0/100)
Diabetes with treatment unknown	0.0% (0/100)
History of hyperlipidemia (medically treated)	78.0% (78/100)
History of hypertension (medically treated)	70.0% (70/100)
History of bleeding disorder	0.0% (0/100)
Gastrointestinal	0.0% (0/100)
Hematologic dyscrasia	0.0% (0/100)
Cardiac History	
Family history of coronary artery disease	51.0% (51/100)
History of myocardial infarction	16.0% (16/100)
History of congestive heart failure	2.0% (2/100)
Current Angina Status	
Angina, stable	51.0% (51/100)
Angina, unstable	25.0% (25/100)
Angina, none	21.0% (21/100)
Angina, unknown	3.0% (3/100)
Silent ischemia	6.0% (6/100)
Previous percutaneous coronary intervention	23.0% (23/100)
Previous coronary artery bypass graft	5.0% (5/100)
History of arrhythmia	6.0% (6/100)
Left ventricular ejection fraction (%)	63.57±11.22 (49) (40.00, 90.00)
History of multivessel disease	32.0% (32/100)
Neurologic History	
Transient ischemic attack	1.0% (1/100)
Cerebrovascular accident	2.0% (2/100)
Renal and Peripheral History	
History of renal disease	1.0% (1/100)
History of peripheral vascular disease	3.0% (3/100)

Numbers are presented as mean±standard deviation (n) or % (count/sample size).

Abbreviation: ITT=intent-to-treat

B7. Safety and Effectiveness Results, NG PROMUS

Principal safety and efficacy results through 30-Days are summarized below and in Table 21: Technical success was 99.2% (118/119 lesions)

- Clinical procedural success was 99.0% (99/100)
- There was a single death, which was adjudicated by the CEC as a cardiac death.
- Through 30 days, the protocol MI rate was 9.0% (9/100) and the PLATINUM MI rate was 1.0% (1/100); all of the MIs occurred in hospital and all were non-Q-wave MIs.
- There were no revascularizations and no stent thromboses.

Table 19: NG PROMUS 30-Day Clinical Results, Intent-to-Treat Patients N= 100

Parameter	NG PROMUS (N=100)	
Primary endpoint (technical success)	99.2% (118/119 lesions)	
Clinical endpoints	In-Hospital	30 Days
All death, MI, TVR	1.0% (1/100)	2.0% (2/100)
All death or MI	1.0% (1/100)	2.0% (2/100)
All death	0.0% (0/100)	1.0% (1/100)
Cardiac death	0.0% (0/100)	1.0% (1/100)
Non-cardiac death	0.0% (0/100)	0.0% (0/100)
MI	1.0% (1/100)	1.0% (1/100)
Q-wave MI	0.0% (0/100)	0.0% (0/100)
Non-Q wave MI	1.0% (1/100)	1.0% (1/100)
TVR, overall	0.0% (0/100)	0.0% (0/100)
TLR, overall	0.0% (0/100)	0.0% (0/100)
Cardiac death, MI	1.0% (1/100)	2.0% (2/100)
TLF	1.0% (1/100)	2.0% (2/100)
TVR	1.0% (1/100)	2.0% (2/100)
ARC ST (definite/probable)	0.0% (0/100)	0.0% (0/100)
Peri-procedural endpoints	NG PROMUS (N=100)	
Clinical procedural success	99.0% (99/100)	
Quantitative coronary angiography (N=119 Lesions, N=127 Stents)		
Pre-procedure		
Lesion length (mm)	16.05 ± 7.14 (119)	
Reference vessel diameter (mm)	2.78 ± 0.45 (119)	
MLD, in-lesion (mm)	0.85 ± 0.29 (119)	
Diameter stenosis (%)	69.12 ± 9.69 (119)	
Post-procedure		
MLD, in-stent (mm)	2.69 ± 0.43 (119)	
MLD, in-segment (mm)	2.31 ± 0.46 (119)	
Acute gain, in-stent (mm)	1.84 ± 0.45 (119)	
Acute gain, in segment (mm)	1.46 ± 0.47 (119)	
Diameter stenosis, in-stent (%)	3.86 ± 8.43 (119)	
Diameter stenosis, in-segment (%)	18.14 ± 7.90 (119)	
Intravascular ultrasound		
Incomplete stent apposition	12.9% (13/101)	
Vessel area (mm ²)	15.10 ± 4.34 (99) (7.57, 28.35)	
Stent area (mm ²)	7.83 ± 2.38 (101) (3.72, 15.89)	
Lumen area (mm ²)	7.76 ± 2.25 (100) (3.72, 13.51)	
Vessel volume (mm ³)	354.34 ± 181.60 (99) (98.40, 975.05)	
Stent volume (mm ³)	185.30 ± 91.75 (101) (49.23, 460.78)	
Lumen volume (mm ³)	182.62 ± 87.93 (100) (49.23, 459.36)	
In-stent net volume obstruction (%)	0.00 ± 0.01 (100) (1.00, 0.12)	
Numbers are presented as % (count/sample size) or mean ± standard deviation (n). MLD=minimum lumen diameter		

*The MI rates shown in the table are based on the Platinum Trial MI definition. The Platinum definitions for MI were as follows:

- Peri-procedural Q-wave MI: Development of new pathological Q-waves in 2 or more leads with post-procedure CK-MB levels >ULN. If Troponin was only available enzyme, it must be >ULN and the baseline must have been <ULN.
- Peri-procedural Non-Q-wave MI: Elevation of total CK levels >3x ULN without the presence of

new Q-waves. If CK-MB is performed it must be >ULN. If Troponin was only available enzyme, it must be >3x ULN, and the baseline must have been <ULN (there must also be one of the following: ECG changes indicative of new ischemia, imaging evidence of new loss of myocardium or new regional wall abnormality).

- Spontaneous MI definitions are the same as the peri-procedural, with the exception of requiring CK-MB (or Troponin, if the only available enzyme) to be >2x ULN.

The following MI definitions were also evaluated and adjudicated in the NG PROMUS Study protocol only:

- Peri-procedural Q-wave MI: Development of new pathological Q-waves.
- Peri-procedural Non-Q-wave MI: Elevation of CK-MB levels >3x ULN, or if CKMB is not performed total CK must be >2x ULN, or if Troponin was only available enzyme, it must be >3x ULN. There must also be no evidence of pre-procedure biomarker elevations, or one of the following must be true: $\geq 50\%$ increase in cardiac biomarker result, or evidence that cardiac biomarker values were decreasing prior to suspected MI.
- Spontaneous MI definition: Detection of rise and/or fall of CK-MG or Troponin with at least one value above 99th percentile of ULN, together with evidence of myocardial ischemia and at least one of the following: symptoms of ischemia, ECG changes indicative of new ischemia, development of new pathological Q-waves, imaging evidence of new loss of myocardium or new regional wall abnormality.

The MI rate in the NG PROMUS Study based on these MI definitions was 9.0% (9/100). All MIs were peri-procedural Non-Q wave events utilizing this more sensitive MI definition, and there were no additional clinical sequelae in these patients through 30 days follow-up.

C. 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 37 principal 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)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Cardiovascular 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

The safety and effectiveness of the REBEL Platinum Chromium Coronary Stent System are based on the results obtained from: evaluation of biocompatibility; *in vitro* engineering testing; *in vivo* animal testing; sterilization information; shelf life testing; and clinical studies. These studies revealed the following:

A. Safety and Effectiveness Conclusions

The biocompatibility and *in vivo* animal testing demonstrated that the acute and chronic *in vivo* performance characteristics of the REBEL Stent System provide reasonable assurance of safety and acceptability for clinical use.

The *in vitro* engineering testing conducted on the stent and delivery system demonstrated that the performance characteristics met the product specifications.

The test results obtained from the sterilization 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 3 years for Monorail stent systems and 2 years for Over-the-Wire stent systems.

The OMEGA clinical study evaluated the safety and efficacy of the OMEGA Coronary Stent System for the treatment of subjects with a de novo atherosclerotic coronary artery lesion ≤ 28 mm in length (by visual estimate) in a native coronary artery ≥ 2.25 mm to ≤ 4.50 mm in diameter (by visual estimate). The primary endpoint was met as the rate of 9-month TLF with the intent-to-treat analysis set was 11.5% (37/323) with a one-sided upper confidence bound of 14.79%, significantly less ($P < 0.0001$) than the prespecified performance goal of 21.2%. There were four (4) cardiac deaths (1.2%), 12 myocardial infarctions (3.7%), and two (2) patients experienced definite stent thrombosis (0.6%) through 9 months.

The OMEGA trial met its primary endpoint, supporting the safety and effectiveness of the OMEGA Coronary Stent System for the treatment of de novo atherosclerotic coronary artery lesions ≤ 28 mm in length in a native coronary arteries ≥ 2.25 mm to ≤ 4.50 mm in diameter. The 9 month TLF rate was 11.5% and the upper 1-sided 95% confidence bound of 14.79% was less than the prespecified PG of 21.2% ($p < 0.0001$). The objective of the NG PROMUS trial was to evaluate the impact of specific design changes relative to the acute deliverability of the device. This confirmatory trial

consisted of clinical and peri-procedural angiographic and intravascular ultrasound (IVUS) outcomes for the NG PROMUS Stent System in the treatment of subjects with atherosclerotic lesion(s) ≤ 34 mm in length (by visual estimate) in native coronary arteries ≥ 2.50 mm to ≤ 4.00 mm in diameter (by visual estimate).

The NG PROMUS trial met its primary endpoint, supporting the safety and efficacy of the NG PROMUS Stent System for the treatment of subjects with atherosclerotic lesion(s) ≤ 34 mm in length (by visual estimate) in native coronary arteries ≥ 2.50 mm to ≤ 4.00 mm in diameter (by visual estimate). The lesion-based technical success, was 99.2% (118/119).

B. Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in a clinical studies conducted to support PMA approval as described above.

- Device TLF was well inside the success margin.
- There were a low amount of safety events
- Technical Success for the stent design was 99.2%

Additional factors to be considered in determining probable risks and benefits for the REBEL Coronary Stent System included:

- The data can be regarded as robust. The pivotal OMEGA study met its PG by a considerable margin for the important clinical endpoint of TLF at 9 mos. In addition, the performance of this bare metal stent (BMS) in terms of safety profile and technical and procedural success rates are in line with expectations. BMS have been in use for the treatment of ischemic coronary syndromes for several years.
- The OMEGA trial was a well-designed prospective, single arm trial with a PG (TLF at 9 months) which was based on analysis of BMS performance from several prior well executed trials involving BMS. Only 4 patients out of 328 were lost to follow up. The NG PROMUS Trial was a well-executed trial with one death but no patients lost to follow up.
- This study is not first of a kind for either the device being studied or the design of the trial. The findings are in line with expectations when compared with other studies involving other bare metal stents.
- With the caveat that women (1/3 approx.) and sizeable US minority groups (very few) were not well represented there is a reasonable expectation that this stent device will perform as expected when applied to the wider population of patients with coronary artery disease. Proportions of women and minorities in the OMEGA trial are similar to the proportions seen in historical coronary stent trials, as well as to the trials used to formulate the OMEGA Performance Goal.

- Patients with symptomatic ischemic coronary syndromes may also be managed medically or by CABG (coronary artery bypass graft) surgery. Each strategy has its own set of pros and cons and for different subsets of patients with coronary artery disease, one or other of these options may have a particular advantage. Stents have the advantage of requiring significantly less recovery time in comparison to CABG and relative to medical management are more effective at controlling angina. Patients with established coronary disease, especially if advanced and symptomatic, are likely to eventually succumb to this disease. Terminal events are frequently the result of a myocardial infarction, congestive heart failure and/or a lethal arrhythmia.
- The risks associated with use of BMS are already well established. Patient tolerance of the stent device in these studies was good and in line with expectations.

In conclusion, given the available information above, the data support that for improving coronary luminal diameter in patients with *de novo* lesions ≤ 28 mm in length in native coronary arteries with a reference vessel diameter (RVD) of ≥ 2.25 to ≤ 4.50 mm, the probable benefits outweigh the probable risks.

C. Overall Conclusions

The clinical and preclinical testing support the 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 June 27, 2014.

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.

XV. REFERENCES

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