SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Stent, Superficial Femoral Artery, Drug-Eluting
Device Trade Name:	ELUVIA™ Drug-Eluting Vascular Stent System
Device Procode:	NIU
Applicant's Name and Address:	Boston Scientific Corporation Three Scimed Place Maple Grove, MN 55311
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P180011
Date of FDA Notice of Approval:	September 18, 2018

II. INDICATIONS FOR USE

The ELUVIA Drug-Eluting Vascular Stent System is indicated for improving luminal diameter in the treatment of symptomatic *de-novo* or restenotic lesions in the native superficial femoral artery (SFA) and/or proximal popliteal artery with reference vessel diameters (RVD) ranging from 4.0 - 6.0 mm and total lesion lengths up to 190 mm.

III. CONTRAINDICATIONS

- Women who are pregnant, breastfeeding, or plan to become pregnant in the next 5 years should not receive an Eluvia Drug-Eluting Stent. It is unknown whether paclitaxel will be excreted in human milk, and there is a potential for adverse reaction in nursing infants from paclitaxel exposure.
- Patients who cannot receive recommended anti-platelet and/or anti-coagulant therapy.
- Patients judged to have a lesion that prevents proper placement of the stent or stent delivery system.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the ELUVIA Drug-Eluting Vascular Self-Expanding Stent System labeling.

V. DEVICE DESCRIPTION

The Boston Scientific ELUVIA™ Drug-Eluting Vascular Stent System is a medical device containing an ancillary medicinal substance, which provides a mechanical scaffold for vascular lumen support (the stent component) and a pharmacological agent (paclitaxel) targeted towards reducing the injury response that leads to restenosis after stent implantation.

The ELUVIA Stent System consists of a self-expanding, open mesh, laser-cut nitinol stent with tantalum markers and a triaxial stent delivery system, which includes a middle sheath to protect and constrain the stent. The stent is loaded into the triaxial delivery system. When ready to be implanted, the stent is deployed by retracting the middle sheath of the delivery system. As the stent is exposed to body temperature, it expands to appose the vessel wall.

The ELUVIA Stent System is comprised of the following components:

- Stent Component
- Stent Coating (Polymers and Drug Substance)
- Delivery Catheter

The ELUVIA stent and catheter components are identical in material and design to the BSC Innova Self-Expanding Stent System (reference P140028, approved July 21, 2015). The ELUVIA stent is a laser cut self-expanding stent composed of a nickel titanium alloy (Nitinol). The stent delivery system is a triaxial design and is available in 75 cm and 130 cm working lengths.

The ELUVIA stent coating is composed of a PBMA (poly (n-butyl methacrylate)) polymer primer layer, an active layer consisting of PVDF-HFP (copolymer of vinylidene fluoride and hexafluoropropylene) polymer and anti-proliferative drug paclitaxel.

The ELUVIA Stent System is illustrated in **Figure 1:**

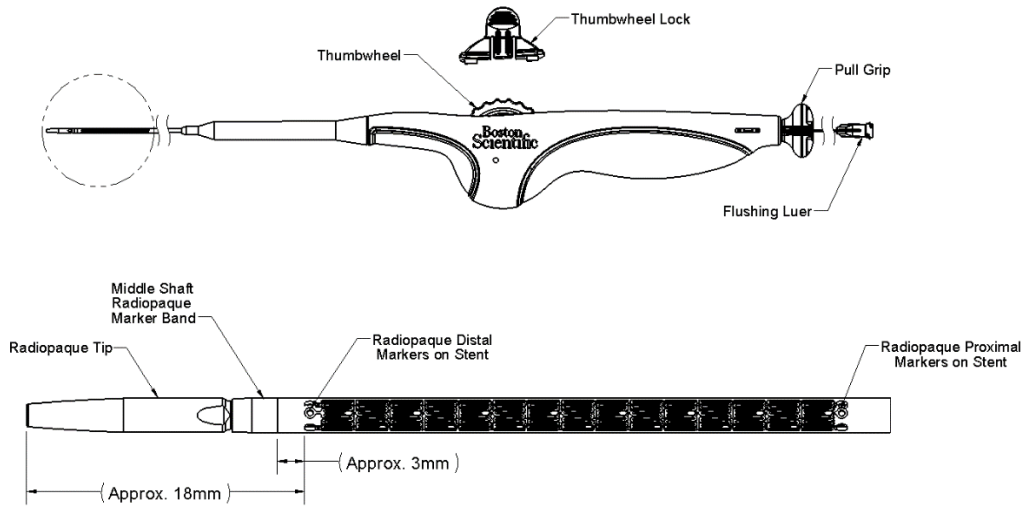

Figure 1: ELUVIA™ Drug-Eluting Vascular Stent System

The ELUVIA™ Drug-Eluting Vascular Stent System is available in multiple stent sizes (diameters and lengths), containing a range of nominal drug doses, as listed in **Table 1** below:

Table 1: ELUVIA™ Drug-Eluting Vascular Stent System Matrix Product Matrix and Nominal Total Loaded Weight of Drug, Primer and Drug Matrix

Stent Model		**Stent Length**				
Design	**Diameter**	**40 mm**	**60 mm**	**80 mm**	**100 mm**	**120 mm**
Total Paclitaxel Dose / Stent (µg)	**6 mm**	135	207	272	344	409
	7 mm	135	207	272	344	409
Primer Coat Weight / stent (µg)	**6 mm**	596	914	1200	1518	1804
	7 mm	596	914	1200	1518	1804
Drug Matrix Coat Weight / Stent (µg)	**6 mm**	1351	2073	2721	3442	4091
	7 mm	1351	2073	2721	3442	4091

Mechanism of Action

Microtubules are integral components of all eukaryotic cells and are involved in various functions including cell proliferation and migration, which are key processes in the formation of neointimal hyperplasia post-stenting.

Paclitaxel promotes the assembly of numerous decentralized and unorganized microtubules from tubulin dimers and stabilizes microtubules by preventing depolymerization. This stability inhibits the normal dynamic reorganization of the microtubule network that is essential for vital interphase and mitotic cellular functions, resulting in reduced proliferation, migration, and signal transduction. This interruption of the restenotic cascade impedes the re-narrowing of the vessel. This antiproliferative property of the drug is the reason for its inclusion in the coating and its addition to the stent.

A stent provides the mechanical capability to dilate the vessel in order to create a larger lumen, and minimize elastic recoil. Paclitaxel is incorporated into a polymer carrier matrix, coated onto the stent and delivered to the inner arterial wall so that a reduction in restenosis may be achieved by locally controlling cell replication. Thus, the primary mode of action of the product is accomplished through mechanical dilatation and the product is assisted in its function through the ancillary pharmacologic action of the drug component, paclitaxel, to inhibit restenosis.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of peripheral artery disease located in the SFA/PPA arteries. These include percutaneous transluminal angioplasty (PTA), PTA accompanied by bare metal stenting, bare metal stenting alone, atherectomy, drug coated balloons, thrombolytic therapy, conservative medical management, exercise therapy, and/or surgical procedures (i.e. bypass surgery). Atherosclerotic risk factors may be reduced through lifestyle modifications such as cessation of smoking, weight reduction, lipid control, blood pressure control, and diabetes management. 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 ELUVIA Drug Eluting Vascular Stent System (Eluvia) received CE Mark on February 18, 2016 for commercial distribution in Europe and is marketed in the countries listed in **Table 2** with a general peripheral indication. In December 2017, the 150 mm stent size was removed from the OUS market as a result of trends in deployment complaints. Eluvia is available in stent diameters of 6 and 7 mm and stent lengths of 40 mm, 60 mm, 80 mm, 100 mm, and 120 mm. All stent sizes are available in both 75 cm and 130 cm catheter lengths.

Table 2: Countries Where the ELUVIA Stent System is Commercially Available

Austria	Baltics	Belgium	Denmark	Finland	France
Germany	Hong Kong	Hungary	Italy	Netherlands	New Zealand
Norway	Poland	Spain	Sweden	Switzerland	United Kingdom
Israel	Macedonia	Columbia	South Korea	Costa Rica	Argentina
Thailand	Australia	Macau	Taiwan	Serbia	Ukraine
Mexico	Saudi Arabia	Egypt	Russia	Vietnam	Indonesia
Philippines	Bolivia				

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) which may be associated with the use of a peripheral stent include but are not limited to:

- Allergic reaction (to drug/polymer, contrast, device or other)
- Amputation
- Arterial aneurysm
- Arteriovenous fistula
- Death

- Embolization (air, plaque, thrombus, device, tissue, or other)
- Hematoma
- Hemorrhage (bleeding)
- Infection/Sepsis
- Ischemia
- Need for urgent intervention or surgery
- Pseudoaneurysm formation
- Renal insufficiency or failure
- Restenosis of stented artery
- Thrombosis/thrombus
- Transient hemodynamic instability (hypotensive/hypertensive episodes)
- Vasospasm
- Vessel injury, including perforation, trauma, rupture and dissection
- Vessel occlusion

Below is a list of the potential adverse effects not captured above that may be unique to the paclitaxel drug coating:

- Allergic/immunologic reaction to drug (paclitaxel or structurally-related compounds) or the polymer stent coating (or its individual components)
- Alopecia
- Anemia
- Gastrointestinal symptoms
- Hematologic dyscrasia (including leukopenia, neutropenia, thromboctyopenia)
- Hepatic enzyme changes
- Histologic changes in vessel wall, including inflammation, cellular damage or necrosis
- Myalgia/Arthralgia
- Peripheral neuropathy

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

IX. SUMMARY OF NON-CLINICAL STUDIES

A series of non-clinical laboratory and pharmacokinetic studies related to the product were performed to evaluate the device.

A. Biocompatibility Studies

A series of Good Laboratory Practice (GLP) biocompatibility tests were conducted to demonstrate that the components of the ELUVIA Stent System are biocompatible.

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, April 2010

- Good Laboratory Practices Regulations (§21 CFR Part 58)
- EN ISO 10993-1, Biological Evaluation of Medical Devices

The tests summarized in **Table 3** have been conducted in support of the ELUVIA stent component as recommended for a permanent implantable device contacting circulating blood for > 30 days.

Table 3: Biocompatibility Tests Performed on Stent

Test Performed / Applicable EN ISO 10993 Part Number	Test Purpose	Results
Cytotoxicity MEM Elution / Part 5	To determine the potential for cytotoxicity	Non-cytotoxic
Guinea Pig Maximization Sensitization/Part 10	To evaluate the allergenic potential or sensitizing capacity of a test article.	Non-sensitizing
Intracutaneous Reactivity/Part 10	To screen test article extracts for potential irritation effects.	Non-irritant
Acute Systemic Injection/Part 11	To screen test article extracts for potential systemic toxic effects.	Non-toxic
Subchronic Toxicity - Systemic Toxicity Study in Rats Following Subcutaneous Implantation, 13 Weeks / Part 11 and Part 6	To evaluate the potential for local and systemic toxicity of a test article implanted subcutaneously in rats for 13 weeks.	Non-toxic
Implantation - Subcutaneous Implantation Study in Rabbits, 4 Weeks / 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 for 4 weeks.	Non-irritant
Material-Mediated Rabbit Pyrogenicity / Part 11	To determine the presence of material-mediated pyrogens in extracts of a test article.	Non-pyrogenic
Ames Mutagenicity /Part 3	To evaluate the mutagenic potential of leachables from the test article.	Non-mutagenic
Mouse Lymphoma /Part 3	To evaluate mutagenicity of the test agents.	Non-mutagenic
Hemolysis Direct and Extract/Part 4	To assess the hemolytic activity of the test article when in direct contact with blood.	Non-hemolytic

Test Performed / Applicable EN ISO 10993 Part Number	Test Purpose	Results
Complement Activation SC5b-9 /Part 4	Measurement of complement activation indicates whether a test article is capable of inducing a complement-induced inflammatory immune response in humans.	Not a complement activator
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.	Non-activator
In vivo thrombogenicity	Assess acute thrombogenic potential of test article in the non-diseased iliac and iliofemoral arteries of domestic swine, as described in Section H below.	Non-thrombogenic
Chemical Characterization Extraction by NVR, LC-MS, GC-MS, ICP-MS	Chemical characterization analysis to identify and semi-quantify extractables found under exhaustive extraction conditions.	Extractables do not pose a concern for genotoxicity, carcinogenicity, or systemic toxicity

The implantation endpoint for the stent was also leveraged from the animal safety study, as described in Section H below. The tests summarized in **Table 4** have been performed in support of the ELUVIA delivery system catheter as recommended for externally communicating device contacting the circulating blood with limited exposure of < 24 hours.

Table 4: Biocompatibility Tests Performed on ELUVIA Delivery System Catheter

Test Performed / Applicable EN ISO 10993 Part Number	Test Purpose	Results
Cytotoxicity MEM Elution / Part 5	To determine the potential for cytotoxicity	Non -cytotoxic
Intracutaneous Reactivity/Part 10	To screen test article extracts for potential irritation effects.	non-irritant
Guinea Pig Maximization Sensitization/Part 10	To evaluate the allergenic potential or sensitizing capacity of a test article.	Non-sensitizing

Test Performed / Applicable EN ISO 10993 Part Number	Test Purpose	Results
Acute Systemic Injection/Part 11	To screen test article extracts for potential systemic toxic effects.	Non-toxic
Material-Mediated Rabbit Pyrogenicity / Part 11	To determine the presence of material-mediated pyrogens in extracts of a test article.	Non-pyrogenic
Hemolysis Direct and Extract	To assess the hemolytic activity of the test article when in direct/indirect contact with blood.	Non-hemolytic
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.	Non-activator
Complement Activation SC5b-9 and C3a/Part 4	Measurement of complement activation indicates whether a test article is capable of inducing a complement-induced inflammatory immune response in humans.	Not a complement activator
In vivo Thrombogenicity	Assess acute thrombogenic potential of test article in the non-diseased femoral arteries of domestic swine, as described in Section H below.	Non-thrombogenic

B. *In Vitro* Engineering Testing

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

- *FDA Guidance for Industry and FDA Staff: Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, April 18, 2010*
- *FDA Guidance for Industry and Staff: Establishing Safety and Compatibility of Passive Implants in the Magnetic Resonance (MR) Environment,* December 11, 2014

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

Test	Test Purpose	Acceptance Criteria	Results
Material Composition	To verify the composition of nitinol and tantalum stent materials and to measure the composition and thickness of the surface passivation layer.	The stent material must conform to ASTM F2063-00 for the nitinol material and to ASTM F560-04 for the tantalum material. The stent material must exhibit surface composition and passive layer depth consistent with published literature for nitinol surfaces.	Pass
Shape Memory and Superelasticity of Intravascular Stents	To determine the Austenite finish transition temperature (Af) of the stent.	The stent must have an Af temperature ≤ 34°C when tested per ASTM F2082 to ensure the stent will expand to its intended size and shape under normal body temperatures.	Pass
Stent Corrosion Resistance - Post 10-year Pulsatile Fatigue Cycling	To document the potential for fretting, pitting and crevice corrosion of the stent.	Fretting corrosion and crevice and pitting corrosion are evaluated and characterized on stents after 10-year pulsatile fatigue cycling (400 million cycles). The stent must exhibit no evidence of pitting when tested per ASTM F2129.	Pass
Stent Corrosion Resistance – Galvanic Corrosion	To document the potential for galvanic corrosion when coupled with stents of dissimilar materials.	The resistance to galvanic corrosion was characterized when the stent was coupled separately with dissimilar material stent. Testing shall result in "very low" or "negligible" current post testing.	Pass
Stent Dimensional Verification	To characterize the unconstrained diameter of the stent.	The unconstrained expanded diameter must be within -0.25 mm/+0.75 mm of its labeled diameter.	Pass
Percent Surface Area	To characterize the metal to lumen ratio of the stent.	The metal to lumen must be ≤ 30% for all stent sizes.	Pass
Foreshortening	To determine the foreshortening of the stent from the catheter constrained diameter to use diameter.	The change in stent length from catheter constrained diameter to length post deploy shall be ±10%.	Pass
Stent Integrity	To determine the stent's resistance to fracture upon deployment.	The stent must not exhibit strut fractures upon deployment.	Pass
Outward Radial Force	To characterize the minimum and maximum outward radial force for the stent within use range.	The outward radial force must be ≥ 2.9 g/mm..	Pass

Test	Test Purpose	Acceptance Criteria	Results
Mechanical Properties – Preprocessing	To evaluate nitinol material prior to processing.	The mechanical properties of the nitinol material must meet the following specifications. • Loading Plateau > 60ksi • Unloading Plateau > 17ksi • Ultimate Tensile Strength > 150ksi • Strain at Peak Load > 10% • Unrecovered Strain (permanent set after 8% strain) < 0.5%	Pass
Mechanical Properties – Post Processing	To verify the permanent set of the nitinol material post-thermal processing.	The permanent set of the nitinol material post-thermal processing must be <1.5%.	Pass
Stress/Strain Analysis/Fatigue Analysis (Finite Element Analysis)	To evaluate the durability and integrity of the stent using Finite Element Analysis (FEA). The FEA analysis simulated physiological conditions in the SFA.	The FEA analysis must demonstrate that the stent maintains acceptable fatigue safety using the Goodman fatigue analysis with a safety factor > 1.	Pass
Accelerated Durability Testing	To characterize the accelerated durability of overlapping stents after 10-year pulsatile fatigue cycling.	No stent shall have type II or greater fracture occurrence after 400 million cycles (10 year simulation).	Pass
Accelerated Durability Testing	To characterize the accelerated durability of stents after 10-year fatigue cycling with relative SFA physiological motions.	Stents shall demonstrate fatigue integrity after 10 year simulated axial, twist, bend, and compression fatigue testing.	Pass
Magnetic Resonance Imaging (MRI) Safety and Compatibility	To evaluate the stent for magnetically induced force, magnetically induced torque, image artifact, and radio frequency (RF) induced heating when placed in field strengths of 1.5 and 3.0 Tesla.	The stent must meet the requirements of *Guidance for Industry and FDA Staff: Establishing Safety and Compatibility of Passive Implants in the MR (Magnetic Resonance) Environment*, ASTM F2052, ASTM F2213, ASTM F2182, and ASTM 2119 standards for MR Conditional. The conditions under which the device can be safely scanned are reflected in the Directions for Use (DFU).	Pass
Radiopacity	To assess the radiopacity of the stent.	The radiopacity of the stent while loaded in the delivery system and post stent deployment must be clinically acceptable when assessed during animal testing.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Crush Resistance	To verify the ability of the stent to recover to its size and shape after applying an external load.	The recovery of the stent diameter post compression must be 90% or greater for both parallel plate and focal compression testing.	Pass
Kink Resistance	To characterize the smallest radius of curvature the stent can withstand without kinking.	The minimum gage pin diameter that the stent can be bent around without kinking or experiencing a diameter reduction of at least 50% in the bent condition shall be characterized.	Pass
Stent Marker Securement	To characterize the force required to dislodge the tantalum marker from the stent.	The force to dislodge the marker from the stent much be $\geq$ 0.70 lbs.	Pass
Delivery System Dimensional Verification	To document dimensional characteristics of the delivery system.	The delivery system working length must be ± 1.0cm of the labeled delivery system working length. The delivery system working profile must be 6F. The delivery system must track and exchange over 0.035" guide wire.	Pass
Delivery, Deployment and Retraction	To assess the ability of the delivery system to deliver the stent to the intended location and deploy the stent.	The delivery system must track through a simulated anatomical model, deliver the stent and be withdrawn remaining fully intact. The delivery system must fully deploy the stent.	Pass
Deployment Force	To ensure that the amount of force required to deploy the stent remains within intended limits.	The delivery system must deploy the stent with an acceptable deployment force.	Pass
Deployment Accuracy	To assess the ability of the delivery system to place the stent in the intended location in the vessel.	The delivery system must deploy the stent with an acceptable deployment accuracy.	Pass
Catheter Bond Strength	To evaluate the tensile strength of the delivery system bonds.	The delivery system must be able to withstand forces which may be experienced clinically.	Pass
Delivery System Flexibility and Kink Test	To determine the susceptibility of the delivery system to kink.	The delivery system must not kink and maintain guidewire movement when simulating worst-case clinical use.	Pass
Torque Strength	To assess the ability of the delivery system to withstand torsional forces.	The delivery system must be able to be subjected to clinically-relevant rotation without catheter failure.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Delivery System Radiopacity	To assess the radiopacity of the delivery system.	The delivery system markers must exhibit clinically acceptable radiopacity.	Pass

C. Coating Characterization Testing

The following tests were developed to characterize and set specifications for the ELUVIA Drug-Eluting Stent System. The coating characterization testing conducted on the device is summarized in **Table 6** below.

Table 6: Coating Characterization Testing

Test	Test Purpose	Acceptance Criteria	Results
Coating Thickness	To characterize coating thickness measured on the stent cross sections from the distal, middle, and proximal stent areas.	The coating thickness should be uniform and consistent along the stent's length, as well as on different stent surfaces (inner, outer, cut faces).	Pass
Coating Adhesion and Cohesion	To characterize the cohesive strength between polymer layers and the adhesive strength of the coating to the stent substrate.	The coating should demonstrate acceptable and consistent cohesive and adhesive strength.	Pass
Particulate Identification	To chemically identify particles recovered during particulate testing.	The Eluvia drug coating and catheter should be a minimal source of particulates.	Pass
Coating Uniformity	To characterize drug coating uniformity across stent length and circumference.	All measurements should be within 15% of target drug content values to demonstrate uniformity of across stent length and circumference.	Pass
Acute Coating Integrity	Measure the coating integrity at baseline and after tracking through a simulated use model	The coating should demonstrate a uniform coating along the length and circumference of the stent. All measurements should be within 15.0% percent bare area.	Pass
Chronic Coating Integrity	Measure the coating integrity of worst case model of overlapping stents deployed following tracking in an anatomical model and fatigue conditioning.	The coating should demonstrate a uniform coating along the length and circumference of the stent. All measurements should be within of 15.0% percent bare area.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Acute and Chronic Particulates	To evaluate the total number and size of particulates generated after worst case model of overlapping stents deployed following tracking in an anatomical model and fatigue conditioning.	Acute: Device to not exceed requirements per USP 788 guidance: ≥ 10µm: 6,000 ≥ 25µm: 600 Chronic: The number of downstream particulates collected must be consistent with clinical safety thresholds as shown by pre-clinical studies and a baseline uncoated stent of the same design. Identification of particulates must show that significant particulate matter is not generated by the stent or coating.	Pass

D. Chemistry, Manufacturing and Controls (CMC) Testing

Where applicable, International Conference on Harmonization (ICH) guidelines were followed for testing routinely performed on the ELUVIA stent as part of CMC. The purpose and specifications for this routine testing is summarized in **Table 7** below. Information relating to ELUVIA stability testing is provided in **Section IX-F**.

Table 7: ELUVIA Stent CMC Specifications and Testing

Test	Test Purpose	Acceptance Criteria
Appearance	A visual inspection is conducted to ensure the stent is retained within the middle sheath until deployment. Upon deployment, stent has metallic appearance.	Product packaging must be intact and stent is retained within the middle sheath until deployment. Upon deployment, stent has metallic appearance.
Paclitaxel Identity	Assay is conducted to verify the identity of the drug substance, paclitaxel via high performance liquid chromatography (HPLC). For positive identity, the retention time and the UV spectrum of the main peak obtained from the sample preparation must correspond to that obtained from the standard preparation. Tested per ICH Q6A.	The retention time of paclitaxel as sampled from product must be ±1% of the retention time of a paclitaxel reference standard. The spectrum (between 195 nm and 350 nm) of the sample must match the spectrum of a paclitaxel reference standard. This is defined by the spectra matching in overall appearance and the peak maxima (around 230 nm) agree to within +/- 5 nm.

Test	Test Purpose	Acceptance Criteria
Drug Content Assay	Paclitaxel content is specified and quantitatively verified to ensure product contains the labeled dose via high performance liquid chromatography (HPLC). Tested per ICH Q6A.	The arithmetic mean Paclitaxel content for ten (10) stents must be greater than or equal to (≥) 90.0% and less than or equal to (≤) 110.0% of the nominal content.
Drug Degradants and Impurities	The stent must have acceptable levels of drug degradants and impurities with the use of high performance liquid chromatography (HPLC).	Total Paclitaxel degradants and related substances must be ≤ 2.0% of the total area of the test sample. Individual Paclitaxel degradants or related substances must be ≤ 1.0% of the total area of the test sample.
Drug Content Uniformity	Paclitaxel content is specified to ensure product contains the labeled dose within limits for individual dosage units defined by the formula in USP <905>. Tested per ICH Q6A and USP 905	The requirements for Paclitaxel drug content uniformity are met if the acceptance value of the first 10 dosage units is less than or equal to L1. If the acceptance value is greater than L1, test the next 20 units, and calculate the acceptance value. The requirements are met if the final acceptance value of the 30 dosage units is less than or equal to L1, and no individual content of any dosage unit is less than [1 - (0.01)(L2)] M nor more than [1 + (0.01)(L2)] M Acceptance value = | M – Xavg | + ks M = Xavg when 98.5% ≤ Xavg ≤ 101.5% M = 98.5% when Xavg < 98.5% M = 101.5% when Xavg > 101.5% Xavg is average of individual contents as percent of nominal Paclitaxel drug content k = 2.4 when sample size is 10 k = 2.0 when sample size is 30 s = sample standard deviation L1 = 15.0 L2 = 25.0

Test	Test Purpose	Acceptance Criteria
Kinetic Drug Release (Average and Individual Kinetic Drug Release)	Drug release is specified to ensure the product releases drug consistently within limits. This performance feature is linked to product efficacy. Tested per USP 711	Level L1: No individual value lies outside each of the stated ranges and no individual value is less than the stated amount at the final specified time point. (6 samples – Drug Release: Cumulative Release of Paclitaxel as percent of label claim) Time (hours) 5 24 72 LSL: 32% 60% 80% USL: 52% 80% N/A Level L2: The average value of the 12 units (L1+L2) does not lie outside of the stated ranges and is not less than the stated amount at the final specified time point; no individual value is more than 10% of labeled content outside each of the stated ranges; and no individual value is below the stated amount at the final specified time point – (6 additional samples (12 samples in total) Drug Release Cumulative Release of Paclitaxel as percent of label claim) Average: Time (hours) 5 24 72 LSL: 32% 60% 80% USL: 52% 80% N/A Individuals: Time (hours) 5 24 72 LSL: 22% 50% 70% USL: 62% 90% N/A Level L3: The average value of the 24 units (L1+L2+L3) does not lie outside of the stated ranges, and is not less than the stated amount at the final specified time point; no more than 2 of the 24 units are more than 10% of labeled content outside each of the stated ranges; no more than 2 of the 24 units are more than 10% of labeled content below the stated amount at the final specified time point; and no individual unit is more than 20% of labeled content outside each of the stated ranges or more than 20% of labeled content below the stated amount at the final specified time point.

Test	Test Purpose	Acceptance Criteria
Endotoxin (Pyrogens)	The average endotoxin level shall be less than 20 Endotoxin Units (EU) per device. (Where 'device' refers to the average endotoxin level per coated stent plus the average endotoxin level per delivery catheter). Regulatory requirement to ensure endotoxin levels are within established safety guidelines.	The average endotoxin level shall be less than 20 Endotoxin Units (EU) per device. (Where 'device' refers to the average endotoxin level per coated stent + the average endotoxin level per delivery catheter).
Particulate Matter	Particulate matter is quantified for quality control and product safety measures. Tested per USP 788	The total system particulates of each of three (3) individual stent delivery systems must not exceed the following limits. **Size** **Upper Specification Limit** ≥ 10 µm 6,000 ≥ 25 µm 600
Residual Solvents	The amount of Cyclohexanone and acetone on the ELUVIA stent is measured to ensure that residual levels of the solvent used in the manufacturing process are within specification limits established for the finished stent release. Tested per ICH Q3B	Cyclohexanone content must be ≤ 2 µg/stent Acetone content must be ≤ 9.7 µg/stent

E. Packaging Testing

Packaging verification testing was performed to demonstrate that the design of the ELUVIA 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. Package integrity testing included a visual assessment, bubble leak testing, and seal strength testing at both the baseline condition and for packages aged to the products shelf life.

F. Stability/Shelf Life Testing

A formal stability study for the drug product was conducted to help establish a shelf life expiration date for the ELUVIA Stent System. This testing included appearance of stent, paclitaxel identity, drug assay, drug degradants and impurities, drug uniformity, drug release, sterility, endotoxin, and particulates.

Functional device and container closure performance testing was conducted following 18 months of aging to demonstrate that the device and packaging performs within product specifications for a labeled shelf life of 18 months.

This testing in combination supports the shelf life of 18 months.

G. Sterilization

The ELUVIA Stent System is sterilized using ethylene oxide (EO) gas and has been validated per AAMI / ANSI / ISO 11135:2007, 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 EN ISO 10993-7:2008, Biological Evaluation of Medical Devices - Part 7: Ethylene Oxide Sterilization Residuals.

H. Animal Studies

Drug Release Testing and Pharmacokinetics

The objectives of BSC's preclinical pharmacokinetic evaluations were to investigate the local target tissue and systemic blood levels of paclitaxel and to histopathologically evaluate downstream muscle beds following stent implantation. The polymer carrier of PTx for all stents tested was a copolymer of poly(vinylidene fluoride-co-hexafluoropropylene) (PVDF).

Local Tolerance

The objective of the preclinical program for Eluvia stents was to assess the safety and vascular compatibility of Eluvia stents and to show comparability of results to the uncoated Innova stents. Safety of single and overlapped implant configurations of the stents types listed below was assessed using the non-injured porcine iliofemoral peripheral artery model.

- Single stent configurations
  - Bare Epic stents
  - Bare Innova stents
  - Epic stents coated with the Eluvia formulation
  - Epic stents coated with four other polymers plus drug formulations
  - Eluvia stents
- Overlap sent configurations
  - Eluvia stents
  - Innova stents

Delivery System Assessments

The objective of the study was to evaluate the acute performance of the Innova Over-the-Wire Self-Expanding Stent System, which is the identical delivery system with an uncoated stent, in an *in vivo* model. The secondary objective of the study was to demonstrate that the Innova Over-the-Wire Self-Expanding Stent System conformed to the user needs and intended uses.

Acute performance of the Innova stent delivery system was assessed using the non-injured porcine iliofemoral peripheral artery model.

The results of the pre-clinical studies support the conclusion that the ELUVIA Stent System is safe and appropriate for intended use. Summaries of the study designs and results are included in the **Table 8** below.

Table 8: ELUVIA Animal Studies - PK

Test and/or Study Name	Test Article	Stent (Diameter and Length in mm) and Number of Stents (n)	Total Paclitaxel per Stent (µg)	Paclitaxel Density (µg/mm^2); Paclitaxel % / Coat Wt. (mg)	Vessel Location	Paclitaxel Systemic and Tissue Levels	Evaluation Time Points	Endpoints Met
Pharmacokinetic (PK) Studies								
PK Study 14-088G	Eluvia	6.0 x 40 (40) 7.0 x 40 (35)	135	0.167 µg/mm^2	Iliac artery, profunda artery femoral artery	Measured in stents, and iliac, profunda and femoral artery, (tissue), and blood (systemic)	1, 3, 7, 14, 30, 90, 180 and 270 Days	Yes
PK Study 08-044N	Test: 2% PTx DES	5.0 x 20 (0) 6.0 x 2 0 (19) 7.0 x 20 (19)	40	2/2.0	Iliac artery, femoral artery	Measured in stents, and iliac and femoral artery, (tissue), and blood (systemic)	4, 10, 30, 60, 90 and 180 Days	Yes
	Test: 10% PTx DES (Eluvia Formulation)	5.0 x 20 (0) 6.0 x 2 0 (25) 7.0 x 20 (23)	50	10/ 0.5				
	Test: 7% PTx DES	5.0 x 20 (0) 6.0 x 2 0 (18) 7.0 x 20 (18)	105	7/1.5				

Test and/or Study Name	Test Article	Stent (Diameter and Length in mm) and Number of Stents (n)	Total Paclitaxel per Stent (μg)	Paclitaxel Density (μg/mm^2); Paclitaxel % / Coat Wt. (mg)	Vessel Location	Paclitaxel Systemic and Tissue Levels	Evaluation Time Points	Endpoints Met
	Test: 12% PTx DES (Safety Margin Formulation)	5.0 x 20 (0) 6.0 x 2 0 (19) 7.0 x 20 (17)	180	12/1.5				
	Test 4% PTx DES	5.0 x 20 (0) 6.0 x 2 0 (18) 7.0 x 20 (20)	12	4/0.3				

Table 9: ELUVIA Animal Studies - Safety and Acute Performance

Test and/or Study Name	Test Article	Stent (Diameter and Length in mm) and Number of Stents (n)	Total Paclitaxel per Stent (μg)	Paclitaxel Density (μg/mm^2); Paclitaxel % / Coat Wt. (mg)	Vessel Location	Paclitaxel Systemic and Tissue Levels	Evaluation Time Points	Endpoints Met
Animal Testing for Safety and Preliminary Effectiveness								
Safety Study 14-089G (Overlap stent configuration)	DES SFA (Eluvia Formulation)	6.0 x 40 (4) 6.0 x 60 (4) 7.0 x 40 (11) 7.0 x 60 (11)	135 207 135 207	0.167	Iliofemoral artery	None – Histology study	14 and 90 Days	Yes

Test and/or Study Name	Test Article	Stent (Diameter and Length in mm) and Number of Stents (n)	Total Paclitaxel per Stent (μg)	Paclitaxel Density (μg/mm^2); Paclitaxel % / Coat Wt. (mg)	Vessel Location	Paclitaxel Systemic and Tissue Levels	Evaluation Time Points	Endpoints Met
	Innova	6.0 x 40 (2) 6.0 x 60 (2) 7.0 x 40 (14) 7.0 x 60 (14)	NA – Uncoated stents	NA – Uncoated stents				
Safety Study 09-117G (Single stent configuration)	Eluvia	6.0 x 80 (4) 7.0 x 80 (24) 8.0 x 80 (9)	273 272 280	0.167	Iliofemoral artery	None – Histology study	30, 90 and 180 Days	Yes
	Innova	6.0 x 80 (3) 7.0 x 80 (20) 8.0 x 80 (13)	N/A Uncoated stents	N/A Uncoated stents				
Dose Finding Study 08-043N (Single stent configuration)	Test: Polymer-only	5.0 x 20 (1) 6.0 x 2 0 (13) 7.0 x 20 (10)	N/A No Paclitaxel in coating	N/A No Paclitaxel in coating	Iliac artery, femoral artery	None – Histology study	30, 90 and 180 Days	Yes
	Test: 2% PTx DES	5.0 x 20 (0) 6.0 x 2 0 (14) 7.0 x 20 (10)	20	2/2.0				

Test and/or Study Name	Test Article	Stent (Diameter and Length in mm) and Number of Stents (n)	Total Paclitaxel per Stent (μg)	Paclitaxel Density (μg/mm^2); Paclitaxel % / Coat Wt. (mg)	Vessel Location	Paclitaxel Systemic and Tissue Levels	Evaluation Time Points	Endpoints Met
	Test: 10% PTx DES (Eluvia Formulation)	5.0 x 20 (3) 6.0 x 2 0 (7) 7.0 x 20 (13)	50	10/ 0.5				
	Test: 7% PTx DES	5.0 x 20 (0) 6.0 x 2 0 (13) 7.0 x 20 (11)	105	7/1.5				
	Test: 12% PTx DES (Safety Margin Formulation)	5.0 x 20 (0) 6.0 x 2 0 (12) 7.0 x 20 (12)	180	12/1.5				
	Test: 4% PTx DES	5.0 x 20 (1) 6.0 x 2 0 (11) 7.0 x 20 (12)	12	4/0.3				
	Control: Bare Metal Epic	5.0 x 20 (2) 6.0 x 2 0 (12) 7.0 x 20 (10)	N/A Uncoated stents	N/A Uncoated stents				
Acute Performance study								
Acute Performance Study 14-101G	Innova	5.0 x 40 (2) 6.0 x 40 (3) 7.0 x 40 (1) 5.0 x 120 (1) 6.0 x 120 (7) 7.0 x 120 (1)	NA – Uncoated stents	NA – Uncoated stents	Iliac artery, femoral artery	None -- Acute Performance study	Acute	Yes

X. SUMMARY OF PRIMARY CLINICAL TRIAL

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of stenting with the ELUVIA Drug-Eluting Vascular Stent System to improve luminal diameter in the treatment of symptomatic *de-novo* or restenotic lesions in the native SFA and/or PPA with reference vessel diameters (RVD) ranging from 4.0 - 6.0 mm and total lesion lengths up to 190 mm in the US, Canada, Japan, New Zealand, and Europe under IDE G150171. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between December 3, 2015 and February 15, 2017. The database for this PMA reflected data collected through April 4, 2018 and included 524 patients. The primary endpoint analysis was conducted when there were sufficient patients evaluable to meet the statistical requirements, as specified in the statistical analysis plan. The database for the primary endpoint analysis reflected data collected through January 24, 2018 and included 421 patients. There were 65 investigational sites.

The IMPERIAL Trial was a global, prospective, multicenter, 2:1 randomized (ELUVIA vs Zilver PTX), controlled, single-blind, non-inferiority trial (RCT). It also included a concurrent, non-blinded, non-randomized, single-arm, pharmacokinetic (PK) substudy and a concurrent, non-blinded, non-randomized, Long Lesion (LL) substudy. Subjects whose eligibility was confirmed were enrolled in the study and treated with the ELUVIA Drug-Eluting Vascular Stent System (test device) or the Zilver PTX stent (control device) on the day of the index procedure. After the index procedure, all subjects were followed to investigate the safety and effectiveness of the ELUVIA Drug-Eluting Vascular Stent System.

A Clinical Events Committee (CEC) was used to adjudicate any reported death, Target Lesion Revascularization (TLR), Target Vessel Revascularization (TVR), amputation or stent thrombosis that occurred during the IMPERIAL trial. The CEC further determined which of these events met protocol definition of a major adverse event (MAE) for the IMPERIAL trial.

1. Clinical Inclusion and Exclusion Criteria

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

   1. Subjects age 18 and older.
   2. Subject (or Legal Guardian if applicable) is willing and able to provide consent before any study-specific test or procedure is performed, signs the consent form, and agrees to attend all required follow-up visits. NOTE: For subjects less than 20 years of age enrolled at a Japanese center, the subject's

legal representative, as well as the subject, must provide written informed consent.

3. Chronic, symptomatic lower limb ischemia defined as Rutherford categories 2, 3 or 4.
4. Stenotic, restenotic or occlusive lesion(s) located in the native SFA and/or PPA:
   a. Degree of stenosis ≥70% by visual angiographic assessment
   b. Vessel diameter ≥ 4 and ≤ 6 mm
   c. Total lesion length (or series of lesions) ≥ 30 mm and ≤ 140 mm (Note: Lesion segment(s) must be fully covered with one ELUVIA stent or up to two Zilver PTX stents)

      Long Lesion Substudy: Total lesion length (or series of lesions) >140 mm and ≤ 190 mm (Note: Lesion segment(s) will require overlapping of two ELUVIA stents).
   d. For occlusive lesions requiring use of re-entry device, lesion length ≤ 120 mm

      Long Lesion Substudy**:** For occlusive lesions requiring use of re-entry device, lesion length > 120 mm and ≤ 170 mm
   e. Target lesion located at least three centimeters above the inferior edge of the femur
5. Patent infrapopliteal and popliteal artery, i.e., single vessel runoff or better with at least one of three vessels patent (<50% stenosis) to the ankle or foot with no planned intervention.

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

1. Previously stented target lesion/vessel.
2. Target lesion/vessel previously treated with drug-coated balloon < 12 months prior to randomization/enrollment.
3. Subjects who have undergone prior surgery of the SFA/PPA in the target limb to treat atherosclerotic disease.
4. Use of atherectomy, laser or other debulking devices in the target limb SFA/PPA during the index procedure.
5. History of major amputation in the target limb.
6. Documented life expectancy less than 24 months due to other medical co-morbid condition(s) that could limit the subject's ability to participate in the clinical trial, limit the subject's compliance with the follow-up requirements, or impact the scientific integrity of the clinical trial.
7. Known hypersensitivity or contraindication to contrast dye that, in the opinion of the investigator, cannot be adequately pre-medicated.
8. Known hypersensitivity/allergy to the investigational stent system or protocol related therapies (e.g., nitinol, paclitaxel, or structurally related compounds, polymer or individual components, and antiplatelet, anticoagulant, thrombolytic medications).

9. Platelet count < 80,000 mm^3 or > 600,000 mm^3 or history of bleeding diathesis.
10. Concomitant renal failure with a serum creatinine > 2.0 mg/dL.
11. Receiving dialysis or immunosuppressant therapy.
12. History of myocardial infarction (MI) or stroke/cerebrovascular accident (CVA) within 6 months prior to randomization/enrollment.
13. Unstable angina pectoris at the time of randomization/enrollment.
14. Pregnant, breast feeding, or plan to become pregnant in the next 5 years.
15. Current participation in another investigational drug or device clinical study that has not completed the primary endpoint at the time of randomization/enrollment or that clinically interferes with the current study endpoints (Note: studies requiring extended follow-up for products that were investigational, but have become commercially available since then are not considered investigational studies).
16. Septicemia at the time of randomization/enrollment.
17. Presence of other hemodynamically significant outflow lesions in the target limb requiring intervention within 30 days of randomization/enrollment.
18. Presence of aneurysm in the target vessel.
19. Acute ischemia and/or acute thrombosis of the SFA/PPA prior to randomization/enrollment.
20. Perforated vessel as evidenced by extravasation of contrast media prior to randomization/enrollment.
21. Heavily calcified lesions.

2. Follow-Up Schedule

All patients were scheduled to return for follow-up examinations at 1 month, 6 months, 12 months, 24 months, 36 months (via telephone or in office), 48 months (via telephone or in office) and 60 months postoperatively.

Preoperatively and during the index procedure, an inclusion/exclusion criteria assessment, medication assessment, angiogram, and adverse event assessment was performed. Postoperatively, the objective parameters measured during the study included a Rutherford Classification, Ankle-Brachial Index (ABI) measurements, a Walking Impairment Questionnaire (WIQ), EQ-5D Questionnaire, 6 Minute Hall Walk (only at 12 months), Medication Assessment, Adverse Event Assessment, Duplex Ultrasound, and X-Ray. Adverse events and complications were recorded at all visits. PK substudy subjects had baseline venous blood drawn followed by blood draws at 10 minutes, 30 minutes, 1, 2, 3, 4, 6, 12, and 24 hours and one final blood draw at either 48 hours or 72 hours after placement of the final ELUVIA stent.

The key time points are shown in **Table 10** below and are included in the tables summarizing safety and effectiveness.

Table 10: Study Event Schedule Procedures and Assessments

Procedure/Assessment	Pre-procedure [2]	During Index Procedure	Pre-Discharge	1-month (30±7 days)	6-month (182±30 days)	12-month (365±30 days)	24-month (730±30 days)	36-month[5] (1095±30 days)	48-month[5] (1460 ± 30 days)	60-month (1825 ± 30 days)
Informed Consent[1]	X									
Confirm Inclusion/Exclusion	X	X								
Demographics and Medical History, Height and Weight	X									
Serum Creatinine	X									
Pregnancy Test[2]	X									
CBC and platelet count	X									
ABI Measurements	X			X[3]	X	X	X			X
Rutherford Categorization	X			X	X	X	X			X
Walking Impairment Questionnaire (WIQ)	X			X	X	X	X			X
EQ-5D Questionnaire	X			X	X	X	X			X
6 Minute Hall Walk (6MHW)	X					X				
Angiogram[4]		X								
Randomization		X								
Venous blood draw for subjects in PK sub-study		X[6]	X							
Medication Assessment	X	X	X	X	X	X	X	X	X	X
Adverse Events Assessment		X	X	X	X	X	X[7]	X[7]	X[7]	X[7]
Duplex Ultrasound[4]					X	X	X			X
X-Ray[4]						X	X			X

[1] Subject's consent obtained and informed consent form signed prior to any study-specific tests or procedures
[2] Performed within 30 days of procedure, except urine or blood pregnancy test required for females of childbearing potential performed within 7 days of procedure
[3] ABI measurement may be collected immediately post-procedure through 1 Month Follow-up window (Day 0 – 37).
[4] Angiograms, Ultrasounds and X-rays will be sent to the respective core lab for analysis. Follow-up angiograms, ultrasounds and x-rays will not be required for any subject who underwent bypass surgery of the target lesion during the 60-month follow-up timeframe, or has a documented occluded stent.
[5] The 36 month and 48 month visit may be conducted in the office or by telephone.
[6] Up to 24 hours prior to stent placement.
[7] Reporting required through the end of trial for SAEs, UADEs and ADEs/Device Deficiencies. AEs not related to the investigational device or procedure reported only through 12 month follow-up visit.

3. Clinical Endpoints

With regards to safety, the primary safety endpoint assessed the occurrence of Major Adverse Events (MAEs) defined as all causes of death through 1 month, target limb major amputation through 12 months and/or target lesion revascularization (TLR) through 12 months. This safety endpoint was designed to demonstrate that the 12-month MAE-free rate for the ELUVIA treatment group is non-inferior to the Zilver PTX control group. ELUVIA will be concluded to be non-inferior to Zilver PTX for device safety if the one-sided lower 95% confidence bound on the difference between treatment groups (ELUVIA – Zilver PTX) in 12-month MAE-free is greater than -0.1 (or -10%). The primary safety endpoint analysis was conducted when there were sufficient patients evaluable to meet the statistical requirements, as specified in the statistical analysis plan, and did not include the full patient cohort.

With regards to effectiveness, the primary effectiveness endpoint assessed primary patency at 12 months post-procedure. This effectiveness endpoint was designed to demonstrate that the 12-month primary patency for the ELUVIA treatment group is non-inferior to the Zilver PTX control group. ELUVIA will be concluded to be non-inferior to Zilver PTX for device effectiveness if the one-sided lower 95% confidence bound on the difference between treatment groups (ELUVIA – Zilver PTX) in 12-month primary patency is greater than -0.1 (or -10%). The primary effectiveness endpoint analysis was conducted when there were sufficient patients evaluable to meet the statistical requirements, as specified in the statistical analysis plan, and did not include the full patient cohort.

Primary vessel patency was defined as the percentage of lesions (target stented segments) that reached the endpoint without a hemodynamically significant stenosis on duplex ultrasound (DUS) (Peak Systolic Velocity Ratio {PSVR} is $\leq$ 2.4), and without clinically-driven TLR or bypass of the target lesion before or on the DUS follow up visit. All DUS readings were assessed by an independent core laboratory.

Additional Secondary Endpoints

- Technical success defined as delivery and deployment of the assigned study stent to the target lesion to achieve residual angiographic stenosis no greater than 30% assessed visually
- Procedural success defined as technical success with no MAEs noted within 24 hours of the index procedure
- MAE rate at 1 month post-index procedure defined as all causes of death, target limb major amputation and/or TLR
- Primary Patency and Assisted Primary Patency at 6 months, 12 months, 24 months and 60 months using different PSVRs
- Clinically-driven TLR and Target Vessel Revascularization (TVR) Rate at each time point

- Adverse Event Rates (unanticipated, major, serious, device/procedure-related) at each time point
- Non-serious non-device/procedure-related Adverse Event Rates at each time point through 12 months
- Stent Fracture Rate at 12 months, 24 months and 60 months utilizing VIVA definitions
- Distribution of Rutherford Classification during follow-up as compared to baseline at 1 month, 6 months, 12 months, 24 months and 60 months
- Rate of Primary and Secondary Sustained Clinical Improvement as assessed by changes in Rutherford Classification from baseline at 1 month, 6 months, 12 months, 24 months and 60 months
- Rate of Hemodynamic Improvement as assessed by changes in Ankle-Brachial Index (ABI) from baseline at 1 month, 6 months, 12 months, 24 months and 60 months
- Walking Improvement at12 months assessed by change in Six Minute Hall Walk (6MHW) from baseline
- Walking Improvement and Patient Utility Values assessed at 1 month, 6 months, 12 months, 24 months and 60 months assessed by change in Walking Impairment Questionnaire and EQ-5D from baseline
- Changes in healthcare utilization over time
- PK parameters calculated for subjects in the PK substudy

The secondary endpoint analyses were conducted on the full patient cohort at the associated time points.

Long Lesion substudy

The Long Lesion substudy primary effectiveness endpoint assessed primary patency at 12 months post-procedure. There was a non-statistically driven performance goal (60%) which was developed from the historical long stent performance of the Innova Bare Metal Stent System and the expected enhanced performance (10%) for the ELUVIA Stent System. If the observed 12-month primary patency is greater than or equal to 60%, the ELUVIA Stent System will be considered to have acceptable effectiveness performance in the long lesion population.

The Long Lesion substudy primary safety endpoint assessed the 12-month MAE-free rate. It was expected that the MAE-free rate would be similar to the rates observed by the ELUVIA stent group in the RCT.

With regard to success/failure criteria, both the primary endpoints needed to be met, demonstrating non-inferiority to the control device.

B. Accountability of Full Cohort

At the time of database lock, of the 524 subjects enrolled in the PMA study, 94.6% (440) RCT subjects, 98% (49) LL substudy subjects and 92.3% (12) PK substudy subjects were available for analysis at the completion of the study, the 12 month post-operative visit. **Table 11**, **Table 12** and **Table 13** display subject disposition at each follow-up visit for the RCT, LL substudy, and PK substudy, respectively.

Table 11: Subject Disposition - RCT

	Eluvia N=309 Subjects	**Zilver PTX N=156 Subjects**	**Overall N=465 Subjects**
Intent to Treat (All Enrolled Subjects)	309	156	465
Eligible for 1-Month Clinical Follow-up	307	155	462
Not Eligible for 1-Month Clinical Follow-up	2	1	3
Death ≤ 37 Days with no 1-Month Clinical Follow-up Performed	0	0	0
Withdrawal	2	1	3
Adverse Event	0	0	0
Investigator Discretion	0	0	0
Lost to Follow-up	0	0	0
Withdrew Consent	2	1	3
Did not meet eligibility criteria	0	0	0
Other	0	0	0
1-Month Visit Missed	2	1	3
1-Month Clinical Follow-up Performed	305	154	459
1-Month Clinical Follow-up or Death (Evaluable)	305	154	459
1-Month Clinical Follow-up Compliance[1]	98.7% (305/309)	98.7% (154/156)	98.7% (459/465)
Eligible for 6-Month Clinical Follow-up	303	150	453
Not Eligible for 6-Month Clinical Follow-up	6	6	12
Death ≤ 212 Days with no 6-Month Clinical Follow-up Performed	2	3	5
Withdrawal	4	3	7
Adverse Event	0	0	0
Investigator Discretion	0	0	0
Lost to Follow-up	0	0	0
Withdrew Consent	4	3	7
Did not meet eligibility criteria	0	0	0
Other	0	0	0
6-Month Visit Missed	11	5	16
6-Month Clinical Follow-up Performed	292	145	437
6-Month Clinical Follow-up or Death (Evaluable)	294	148	442
6-Month Clinical Follow-up Compliance[1]	95.1% (292/307)	94.8% (145/153)	95.0% (437/460)
6-Month Duplex Ultrasound Follow-up Compliance[2]	92.2% (283/307)	94.1% (144/153)	92.8% (427/460)

	Eluvia N=309 Subjects	Zilver PTX N=156 Subjects	Overall N=465 Subjects
Eligible for 12-Month Clinical Follow-up *(Full Cohort)*	294	146	440
Not Eligible for 12-Month Clinical Follow-up	15	10	25
Death ≤ 395 Days with no 12-Month Clinical Follow-up Performed	6	6	12
Withdrawal	9	4	13
Adverse Event	2	0	2
Investigator Discretion	0	0	0
Lost to Follow-up	0	0	0
Withdrew Consent	6	4	10
Did not meet eligibility criteria	0	0	0
Other	1	0	1
12-Month Visit Missed	12	4	16
12-Month Clinical Follow-up Performed	282	142	424
12-Month Clinical Follow-up or Death (Evaluable)	288	148	436
12-Month Clinical Follow-up Compliance[1]	93.1% (282/303)	94.7% (142/150)	93.6% (424/453)
12-Month Duplex Ultrasound Follow-up Compliance[2]	92.7% (281/303)	94.7% (142/150)	93.4% (423/453)
12-Month X-ray Follow-up Compliance[2]	92.1% (279/303)	90.7% (136/150)	91.6% (415/453)
12-Month Disposition: Primary Endpoint Cohort			
12-Month Safety Primary Endpoint Evaluable	273	133	406
Subjects with (TLR/Major Amputation/last follow up > 335) with no 12-Month Clinical Follow-up Performed	6	2	8
Subjects with 12-Month Clinical Follow-up Performed	267	131	398
12-Month Safety Primary Endpoint Non-Evaluable	10	10	20
Death ≤ 365 Days with no 12-Month Clinical Follow-up Performed	5	5	10
12-month clinical follow-up unavailable for analysis	5	5	10
12-Month Primary Effectiveness Endpoint Evaluable	266	130	396
Subjects with CD TLR but no 12-Month Clinical Follow-up Performed	2	1	3
Subjects with 12-Month Clinical Follow-up Performed	264	129	393
12-Month Primary Effectiveness Endpoint Non-Evaluable	16	12	28
Death ≤ 365 Days with no 12-Month Clinical Follow-up Performed	6	6	12
12-month clinical follow-up unavailable for analysis	5	5	10
Missing 12 month DUS	5	1	6

[1]Death prior to the visit window does not contribute to the denominators and numerators of the compliance rate
[2]All duplex ultrasounds and x-ray imaging apply, including anyone without interpretable image

Table 12: Subject Disposition - LL sub-study

	Eluvia N=50 Subjects
Intent to Treat (All Enrolled Subjects)	50
Eligible for 1-Month Clinical Follow-up	50
Not Eligible for 1-Month Clinical Follow-up	0
Death ≤ 37 Days with no 1-Month Clinical Follow-up Performed	0
Withdrawal	0
Adverse Event	0
Investigator Discretion	0
Lost to Follow-up	0
Withdrew Consent	0
Did not meet eligibility criteria	0
Other	0
1-Month Visit Missed	0
1-Month Clinical Follow-up Performed	50
1-Month Clinical Follow-up or Death (Evaluable)	50
1-Month Clinical Follow-up Compliance[1]	100.0% (50/50)
Eligible for 6-Month Clinical Follow-up	50
Not Eligible for 6-Month Clinical Follow-up	0
Death ≤ 212 Days with no 6-Month Clinical Follow-up Performed	0
Withdrawal	0
Adverse Event	0
Investigator Discretion	0
Lost to Follow-up	0
Withdrew Consent	0
Did not meet eligibility criteria	0
Other	0
6-Month Visit Missed	1
6-Month Clinical Follow-up Performed	49
6-Month Clinical Follow-up or Death (Evaluable)	49
6-Month Clinical Follow-up Compliance[1]	98.0% (49/50)
6-Month Duplex Ultrasound Follow-up Compliance[2]	94.0% (47/50)
Eligible for 12-Month Clinical Follow-up	49
Not Eligible for 12-Month Clinical Follow-up	1
Death ≤ 395 Days with no 12-Month Clinical Follow-up Performed	0
Withdrawal	1
Adverse Event	0
Investigator Discretion	0
Lost to Follow-up	0
Withdrew Consent	1
Did not meet eligibility criteria	0
Other	0
12-Month Visit Missed	2
12-Month Clinical Follow-up Performed	47

	Eluvia N=50 Subjects
12-Month Clinical Follow-up or Death (Evaluable)	47
12-Month Clinical Follow-up Compliance[1]	94.0% (47/50)
12-Month Duplex Ultrasound Follow-up Compliance[2]	94.0% (47/50)
12-Month X-ray Follow-up Compliance[2]	90.0% (45/50)

[1]Death prior to the visit window does not contribute to the denominators and numerators of the compliance rate
[2]All duplex ultrasounds and x-ray imaging apply, including anyone without interpretable images

Table 13: Subject Disposition - PK sub-study

	Eluvia N=13 Subjects
Intent to Treat (All Enrolled Subjects)	13
Eligible for 1-Month Clinical Follow-up	13
Not Eligible for 1-Month Clinical Follow-up	0
Death ≤ 37 Days with no 1-Month Clinical Follow-up Performed	0
Withdrawal	0
Adverse Event	0
Investigator Discretion	0
Lost to Follow-up	0
Withdrew Consent	0
Did not meet eligibility criteria	0
Other	0
1-Month Visit Missed	0
1-Month Clinical Follow-up Performed	13
1-Month Clinical Follow-up or Death (Evaluable)	13
1-Month Clinical Follow-up Compliance[1]	100.0% (13/13)
Eligible for 6-Month Clinical Follow-up	13
Not Eligible for 6-Month Clinical Follow-up	0
Death ≤ 212 Days with no 6-Month Clinical Follow-up Performed	0
Withdrawal	0
Adverse Event	0
Investigator Discretion	0
Lost to Follow-up	0
Withdrew Consent	0
Did not meet eligibility criteria	0
Other	0
6-Month Visit Missed	0
6-Month Clinical Follow-up Performed	13
6-Month Clinical Follow-up or Death (Evaluable)	13
6-Month Clinical Follow-up Compliance[1]	100.0% (13/13)
6-Month Duplex Ultrasound Follow-up Compliance[2]	100.0% (13/13)
Eligible for 12-Month Clinical Follow-up	12
Not Eligible for 12-Month Clinical Follow-up	1
Death ≤ 395 Days with no 12-Month Clinical Follow-up Performed	1

	Eluvia N=13 Subjects
Withdrawal	0
Adverse Event	0
Investigator Discretion	0
Lost to Follow-up	0
Withdrew Consent	0
Did not meet eligibility criteria	0
Other	0
12-Month Visit Missed	0
12-Month Clinical Follow-up Performed	12
12-Month Clinical Follow-up or Death (Evaluable)	13
12-Month Clinical Follow-up Compliance[1]	100.0% (12/12)
12-Month Duplex Ultrasound Follow-up Compliance[2]	100.0% (12/12)
12-Month X-ray Follow-up Compliance[2]	100.0% (12/12)

[1]Death prior to the visit window does not contribute to the denominators and numerators of the compliance rate
[2]All duplex ultrasounds and x-ray imaging apply, including anyone without interpretable images

C. Study Population Demographics and Baseline Characteristics

The demographics of the study population are typical for pivotal study performed in the US. **Table 14**, **Table 15** and **Table 16** provide a summary of baseline demographics and medical history of all subjects enrolled in the RCT, PK substudy, and LL substudy, respectively. In the RCT, the baseline demographics and medical history of subjects randomized to the treatment group (Eluvia) are similar to those of the subjects randomized to the control group (Zilver PTX).

Table 14: Baseline Demographics and Medical History – RCT (N=465)

Subject Characteristic	Eluvia N=309 Subjects	Zilver PTX N=156 Subjects
Demographics		
Age (Year)	68.5±9.5 (309) (39.0, 90.0)	67.8±9.4 (156) (38.0, 87.0)
Male Gender	66.0% (204/309)	66.7% (104/156)
Race/Ethnicity[1]		
Hispanic or Latino	5.8% (18/309)	3.8% (6/156)
Caucasian	66.3% (205/309)	69.2% (108/156)
Asian	18.4% (57/309)	17.9% (28/156)
Japanese	18.1% (56/309)	17.9% (28/156)
Black, or African heritage	6.8% (21/309)	7.1% (11/156)
Native Hawaiian or other Pacific Islander	0.3% (1/309)	0.0% (0/156)
American Indian or Alaska Native	0.6% (2/309)	1.3% (2/156)
Other	1.0% (3/309)	0.6% (1/156)
Not Disclosed	0.6% (2/309)	0.0% (0/156)
General Medical History		
History of Smoking		

Subject Characteristic	Eluvia N=309 Subjects	Zilver PTX N=156 Subjects
Current	35.3% (109/309)	40.4% (63/156)
Previous	50.8% (157/309)	43.6% (68/156)
Never	13.6% (42/309)	14.1% (22/156)
Unknown	0.3% (1/309)	1.9% (3/156)
Current Diabetes Mellitus	41.7% (129/309)	43.6% (68/156)
Type 1	2.3% (3/129)	4.4% (3/68)
Type 2	92.2% (119/129)	94.1% (64/68)
Unknown	5.4% (7/129)	1.5% (1/68)
Current Method of Treatment		
Diet	31.0% (40/129)	25.0% (17/68)
Diet (only)	9.3% (12/129)	4.4% (3/68)
Medically Treated	89.9% (116/129)	94.1% (64/68)
Oral Agent	72.1% (93/129)	75.0% (51/68)
Insulin	38.0% (49/129)	38.2% (26/68)
Other	1.6% (2/129)	0.0% (0/68)
Unknown	0.8% (1/129)	1.5% (1/68)
History of Hyperlipidemia requiring medication	76.3% (235/308)	75.6% (118/156)
History of Hypertension requiring medication	82.2% (254/309)	85.3% (133/156)
History of Chronic Obstructive Pulmonary Disease	15.6% (48/308)	18.1% (28/155)
Cardiac History		
History of Coronary Artery Disease	50.8% (156/307)	45.2% (70/155)
History of Myocardial Infarction (MI)	19.6% (60/306)	17.5% (27/154)
History of Congestive Heart Failure	8.5% (26/307)	7.8% (12/154)
New York Heart Assoc. (NYHA) Classification		
I	19.2% (5/26)	25.0% (3/12)
II	23.1% (6/26)	41.7% (5/12)
III	15.4% (4/26)	8.3% (1/12)
IV	0.0% (0/26)	0.0% (0/12)
Unknown	42.3% (11/26)	25.0% (3/12)
History of Percutaneous Coronary Intervention (PCI)	32.5% (100/308)	34.2% (53/155)
History of Coronary Artery Bypass Graft (CABG) Surgery	14.0% (43/308)	13.5% (21/156)
Current Anginal Status		
Stable Angina	10.4% (32/309)	12.2% (19/156)
Unstable Angina	0.0% (0/309)	0.0% (0/156)
None	86.7% (268/309)	86.5% (135/156)
Unknown	2.9% (9/309)	1.3% (2/156)
Neurologic/Renal History		
History of Transient Ischemic Attacks (TIA)	4.5% (14/308)	3.9% (6/155)
History of Cerebrovascular Accident (CVA)	9.7% (30/309)	9.0% (14/156)
History of Renal Insufficiency	8.1% (25/309)	7.1% (11/156)
History of Renal Percutaneous Intervention	1.9% (6/309)	0.6% (1/155)

Subject Characteristic	Eluvia N=309 Subjects	Zilver PTX N=156 Subjects
Peripheral Vascular History		
History of Peripheral Vascular Surgery	12.9% (40/309)	9.6% (15/156)
History of endovascular interventions in Target vessel	8.7% (27/309)	11.0% (17/155)
Type of interventions		
Atherectomy	1.3% (4/309)	3.2% (5/156)
Drug Coated Balloon	2.6% (8/309)	1.9% (3/156)
Percutaneous Transluminal Angioplasty (PTA)	6.1% (19/309)	7.7% (12/156)
Stenting	0.6% (2/309)	0.0% (0/156)
Other	1.0% (3/309)	1.9% (3/156)
History of Other Peripheral Endovascular Interventions (other than Target Vessel)	36.2% (112/309)	31.6% (49/155)
Type of most recent Intervention		
Atherectomy	8.4% (26/309)	7.7% (12/156)
Drug Coated Balloon	9.4% (29/309)	7.7% (12/156)
Percutaneous Transluminal Angioplasty (PTA)	16.8% (52/309)	12.8% (20/156)
Stenting	23.9% (74/309)	21.8% (34/156)
Other	0.6% (2/309)	2.6% (4/156)
History of Claudication	98.4% (303/308)	97.4% (151/155)

[1]Subjects that are having more than one race will be considered only once in the sub category where less number of subjects are available. For example, if a subject has races ticked as "Caucasian" and "Hispanic or Latino", the subject will be considered in "Hispanic or Latino" as this sub category has less number of subjects.

Table 15: Baseline Demographics and Medical History – PK (N=13)

Subject Characteristic	Eluvia N=13 Subjects
Demographics	
Age (Year)	66.4±6.1 (13) (57.0, 78.0)
Male Gender	76.9% (10/13)
Race/Ethnicity[1]	
Hispanic or Latino	0.0% (0/13)
Caucasian	100.0% (13/13)
Asian	0.0% (0/13)
Japanese	0.0% (0/13)
Black, or African heritage	0.0% (0/13)
Native Hawaiian or other Pacific Islander	0.0% (0/13)
American Indian or Alaska Native	0.0% (0/13)
Other	0.0% (0/13)
Not Disclosed	0.0% (0/13)
General Medical History	
History of Smoking	

Subject Characteristic	Eluvia N=13 Subjects
Current	23.1% (3/13)
Previous	76.9% (10/13)
Never	0.0% (0/13)
Unknown	0.0% (0/13)
Current Diabetes Mellitus	53.8% (7/13)
Type 1	0.0% (0/7)
Type 2	100.0% (7/7)
Unknown	0.0% (0/7)
Current Method of Treatment	
Diet	42.9% (3/7)
Diet (only)	14.3% (1/7)
Medically Treated	85.7% (6/7)
Oral Agent	71.4% (5/7)
Insulin	71.4% (5/7)
Other	0.0% (0/7)
Unknown	0.0% (0/7)
History of Hyperlipidemia requiring medication	92.3% (12/13)
History of Hypertension requiring medication	92.3% (12/13)
History of Chronic Obstructive Pulmonary Disease	15.4% (2/13)
Cardiac History	
History of Coronary Artery Disease	53.8% (7/13)
History of Myocardial Infarction (MI)	15.4% (2/13)
History of Congestive Heart Failure	7.7% (1/13)
New York Heart Assoc. (NYHA) Classification	
I	0.0% (0/1)
II	100.0% (1/1)
III	0.0% (0/1)
IV	0.0% (0/1)
Unknown	0.0% (0/1)
History of Percutaneous Coronary Intervention (PCI)	25.0% (3/12)
History of Coronary Artery Bypass Graft (CABG) Surgery	23.1% (3/13)
Current Anginal Status	
Stable Angina	0.0% (0/13)
Unstable Angina	0.0% (0/13)
None	92.3% (12/13)
Unknown	7.7% (1/13)
Neurologic/Renal History	
History of Transient Ischemic Attacks (TIA)	7.7% (1/13)
History of Cerebrovascular Accident (CVA)	30.8% (4/13)
History of Renal Insufficiency	15.4% (2/13)
History of Renal Percutaneous Intervention	0.0% (0/13)
Peripheral Vascular History	
History of Peripheral Vascular Surgery	7.7% (1/13)
History of endovascular interventions in Target vessel	7.7% (1/13)

Subject Characteristic	Eluvia N=13 Subjects
Type of interventions	
Atherectomy	0.0% (0/13)
Drug Coated Balloon	0.0% (0/13)
Percutaneous Transluminal Angioplasty (PTA)	7.7% (1/13)
Stenting	0.0% (0/13)
Other	0.0% (0/13)
History of Other Peripheral Endovascular Interventions (other than Target Vessel)	38.5% (5/13)
Type of most recent intervention	
Atherectomy	0.0% (0/13)
Drug Coated Balloon	0.0% (0/13)
Percutaneous Transluminal Angioplasty (PTA)	38.5% (5/13)
Stenting	30.8% (4/13)
Other	0.0% (0/13)
History of Claudication	100.0% (13/13)

[1]Subjects that are having more than one race will be considered only once in the sub category where less number of subjects are available. For example, if a subject has races ticked as "Caucasian" and "Hispanic or Latino", the subject will be considered in "Hispanic or Latino" as this sub category has less number of subjects.

Table 16: Baseline Demographics and Medical History – LL (N=50)

Subject Characteristic	Eluvia N=50 Subjects
Demographics	
Age (Year)	68.2±8.9 (50) (51.0, 84.0)
Male Gender	64.0% (32/50)
Race/Ethnicity[1]	
Hispanic or Latino	6.0% (3/50)
Caucasian	60.0% (30/50)
Asian	22.0% (11/50)
Japanese	22.0% (11/50)
Black, or African heritage	12.0% (6/50)
Native Hawaiian or other Pacific Islander	0.0% (0/50)
American Indian or Alaska Native	0.0% (0/50)
Other	0.0% (0/50)
Not Disclosed	0.0% (0/50)
General Medical History	
History of Smoking	
Current	32.0% (16/50)
Previous	52.0% (26/50)
Never	16.0% (8/50)
Unknown	0.0% (0/50)
Current Diabetes Mellitus	40.0% (20/50)

Subject Characteristic	Eluvia N=50 Subjects
Type 1	5.0% (1/20)
Type 2	90.0% (18/20)
Unknown	5.0% (1/20)
Current Method of Treatment	
Diet	20.0% (4/20)
Diet (only)	5.0% (1/20)
Medically Treated	95.0% (19/20)
Oral Agent	85.0% (17/20)
Insulin	40.0% (8/20)
Other	0.0% (0/20)
Unknown	0.0% (0/20)
History of Hyperlipidemia requiring medication	82.0% (41/50)
History of Hypertension requiring medication	92.0% (46/50)
History of Chronic Obstructive Pulmonary Disease	18.0% (9/50)
Cardiac History	
History of Coronary Artery Disease	56.0% (28/50)
History of Myocardial Infarction (MI)	18.0% (9/50)
History of Congestive Heart Failure	16.0% (8/50)
New York Heart Assoc. (NYHA) Classification	
I	25.0% (2/8)
II	50.0% (4/8)
III	0.0% (0/8)
IV	0.0% (0/8)
Unknown	25.0% (2/8)
History of Percutaneous Coronary Intervention (PCI)	36.0% (18/50)
History of Coronary Artery Bypass Graft (CABG) Surgery	14.3% (7/49)
Current Anginal Status	
Stable Angina	10.0% (5/50)
Unstable Angina	0.0% (0/50)
None	88.0% (44/50)
Unknown	2.0% (1/50)
Neurologic/Renal History	
History of Transient Ischemic Attacks (TIA)	10.0% (5/50)
History of Cerebrovascular Accident (CVA)	18.0% (9/50)
History of Renal Insufficiency	6.0% (3/50)
History of Renal Percutaneous Intervention	0.0% (0/50)
Peripheral Vascular History	
History of Peripheral Vascular Surgery	4.0% (2/50)
History of endovascular interventions in Target vessel	4.0% (2/50)
Type of interventions	
Atherectomy	2.0% (1/50)
Drug Coated Balloon	0.0% (0/50)
Percutaneous Transluminal Angioplasty (PTA)	2.0% (1/50)
Stenting	0.0% (0/50)
Other	0.0% (0/50)

Subject Characteristic	Eluvia N=50 Subjects
History of Other Peripheral Endovascular Interventions (other than Target Vessel)	40.0% (20/50)
Type of most recent intervention	
Atherectomy	16.0% (8/50)
Drug Coated Balloon	12.0% (6/50)
Percutaneous Transluminal Angioplasty (PTA)	26.0% (13/50)
Stenting	26.0% (13/50)
Other	0.0% (0/50)
History of Claudication	98.0% (49/50)

[1]Subjects that are having more than one race will be considered only once in the sub category where less number of subjects are available. For example, if a subject has races ticked as "Caucasian" and "Hispanic or Latino", the subject will be considered in "Hispanic or Latino" as this sub category has less number of subjects

Angiographic Core Lab baseline measurements are summarized in **Table 17** (RCT), **Table 18** (PK substudy) and **Table 19** (LL substudy). The majority of stents were implanted in the middle and distal regions of the SFA. The lesion length eligible for participation into the IMPERIAL RCT was ≥ 30 to ≤ 140 mm, and > 140 to ≤ 190 mm in the LL substudy. The average overall lesion length treated in the RCT was assessed by the core lab to be 86.5 mm for the treatment group (Eluvia) and 81.8 mm for the control group (Zilver PTX). The average overall lesion length treated in the PK substudy and LL substudy was assessed by the core lab to be 94.6 mm and 162.8 mm, respectively.

Table 17: Baseline Angiographic Core Lab Reported Lesion Characteristics – RCT (N=465)

	Eluvia N=309 Subjects	Zilver PTX N=156 Subjects
Treated Limb		
Right leg	51.5% (159/309)	55.1% (86/156)
Left leg	48.5% (150/309)	44.9% (70/156)
Arterial Segments[a]		
Ostial	1.6% (5/309)	0.6% (1/156)
Proximal	12.9% (40/309)	10.3% (16/156)
Mid	65.0% (201/309)	66.7% (104/156)
Distal	66.3% (205/309)	65.4% (102/156)
Proximal Popliteal Artery	18.0% (37/205)	12.7% (13/102)
mm from Ostium (mm)	168.0±73.4 (270) (0.0, 379.6)	168.5±71.2 (126) (4.4, 343.1)
Length (mm)	86.5±36.9 (308) (12.6, 171.3)	81.8±37.3 (154) (12.6, 164.6)
Lesion Type		
Eccentric Lesion	66.9% (206/308)	67.1% (104/155)
Concentric Lesion	33.1% (102/308)	32.9% (51/155)
Bend (degrees)		
>45 degrees	0.0% (0/308)	0.0% (0/155)
>90 degrees	0.0% (0/308)	0.0% (0/155)
Thrombus[b]		

	Eluvia N=309 Subjects	Zilver PTX N=156 Subjects
Grade 0	100.0% (308/308)	100.0% (155/155)
Grade 1	0.0% (0/308)	0.0% (0/155)
Grade 2	0.0% (0/308)	0.0% (0/155)
Grade 3	0.0% (0/308)	0.0% (0/155)
Grade 4	0.0% (0/308)	0.0% (0/155)
Grade 5	0.0% (0/308)	0.0% (0/155)
Calcification		
None/Mild	36.5% (112/307)	32.3% (50/155)
Moderate	22.8% (70/307)	34.8% (54/155)
Severe	40.1% (123/307)	32.3% (50/155)
Unknown	0.7% (2/307)	0.6% (1/155)
Ulceration (Present)	5.2% (16/309)	2.6% (4/156)
Aneurysm (Present)	0.0% (0/309)	2.6% (4/156)
Patency to Foot	94.8% (293/309)	93.6% (146/156)
Anterior Tibial Artery (Patent)	42.1% (130/309)	47.4% (74/156)
Posterior Tibial Artery	57.9% (179/309)	60.9% (95/156)
Peroneal Artery	71.5% (221/309)	64.7% (101/156)
Profunda Femoris Artery	83.2% (257/309)	82.7% (129/156)
% Diameter Stenosis	80.7±16.5 (308) (30.4, 100.0)	80.8±16.4 (155) (39.0, 100.0)
<50%	1.6% (5/308)	1.9% (3/155)
50%-<100%	67.2% (207/308)	67.7% (105/155)
100%(Occlusion)	31.2% (96/308)	30.3% (47/155)

[a] Subjects under "Arterial Segments" may have checked more than one location present.
[b]Thrombus could have subjects with "N/A" response as allowed by CRF so percentages may not add up to 100%

Table 18: Baseline Angiographic Core Lab Reported Lesion Characteristics – PK (N=13)

	Eluvia N=13 Subjects
Treated Limb	
Right leg	76.9% (10/13)
Left leg	23.1% (3/13)
Arterial Segments[a]	
Ostial	7.7% (1/13)
Proximal	30.8% (4/13)
Mid	61.5% (8/13)
Distal	84.6% (11/13)
Proximal Popliteal Artery	9.1% (1/11)
mm from Ostium (mm)	156.2±92.2 (12) (0.0, 290.9)
Length (mm)	94.6±60.3 (12) (21.6, 222.9)
Lesion Type	
Eccentric Lesion	53.8% (7/13)
Concentric Lesion	46.2% (6/13)

	Eluvia N=13 Subjects
Bend (degrees)	
>45 degrees	0.0% (0/13)
>90 degrees	0.0% (0/13)
Thrombus[b]	
Grade 0	100.0% (13/13)
Grade 1	0.0% (0/13)
Grade 2	0.0% (0/13)
Grade 3	0.0% (0/13)
Grade 4	0.0% (0/13)
Grade 5	0.0% (0/13)
Calcification	
None/Mild	15.4% (2/13)
Moderate	38.5% (5/13)
Severe	46.2% (6/13)
Unknown	0.0% (0/13)
Ulceration (Present)	0.0% (0/13)
Aneurysm (Present)	0.0% (0/13)
Patency to Foot	100.0% (13/13)
Anterior Tibial Artery (Patent)	61.5% (8/13)
Posterior Tibial Artery	53.8% (7/13)
Peroneal Artery	53.8% (7/13)
Profunda Femoris Artery	84.6% (11/13)
%Diameter Stenosis	81.7±20.1 (13) (45.4, 100.0)
<50%	15.4% (2/13)
50%-<100%	46.2% (6/13)
100%(Occlusion)	38.5% (5/13)

[a] Subjects under "Arterial Segments" may have checked more than one location present.
[b]Thrombus could have subjects with "N/A" response as allowed by CRF so percentages may not add up to 100%

Table 19: Baseline Angiographic Core Lab Reported Lesion Characteristics – LL (N=50)

	Eluvia N=50 Subjects
Treated Limb	
Right leg	64.0% (32/50)
Left leg	36.0% (18/50)
Arterial Segments[a]	
Ostial	2.0% (1/50)
Proximal	54.0% (27/50)
Mid	90.0% (45/50)
Distal	76.0% (38/50)
Proximal Popliteal Artery	18.4% (7/38)
mm from Ostium (mm)	93.5±58.6 (46) (0.0, 260.5)

	Eluvia N=50 Subjects
Length (mm)	162.8±34.7 (49) (55.6, 243.8)
Lesion Type	
Eccentric Lesion	64.0% (32/50)
Concentric Lesion	36.0% (18/50)
Bend (degrees)	
>45 degrees	0.0% (0/50)
>90 degrees	0.0% (0/50)
Thrombus[b]	
Grade 0	100.0% (50/50)
Grade 1	0.0% (0/50)
Grade 2	0.0% (0/50)
Grade 3	0.0% (0/50)
Grade 4	0.0% (0/50)
Grade 5	0.0% (0/50)
Calcification	
None/Mild	28.0% (14/50)
Moderate	42.0% (21/50)
Severe	28.0% (14/50)
Unknown	2.0% (1/50)
Ulceration (Present)	8.0% (4/50)
Aneurysm (Present)	2.0% (1/50)
Patency to Foot	100.0% (50/50)
Anterior Tibial Artery (Patent)	40.0% (20/50)
Posterior Tibial Artery	56.0% (28/50)
Peroneal Artery	72.0% (36/50)
Profunda Femoris Artery	86.0% (43/50)
%Diameter Stenosis	81.9±15.0 (50) (49.8, 100.0)
<50%	2.0% (1/50)
50%-<100%	66.0% (33/50)
100%(Occlusion)	32.0% (16/50)

[a] Subjects under "Arterial Segments" may have checked more than one location present.
[b]Thrombus could have subjects with "N/A" response as allowed by CRF so percentages may not add up to 100%

D. Safety and Effectiveness Results

1. Primary Safety Results

The analysis of safety was based on the intent-to-treat (ITT) cohort of 421 RCT patients available for the 12-month evaluation. The primary safety endpoint analysis was conducted when there were sufficient patients evaluable to meet the statistical requirements, as specified in the statistical analysis plan, and did not include the full patient cohort (N=465). The key safety outcomes for this study are presented below in **Table 20**.

The MAE-free rate at 12 months was determined to be 94.9% in the treatment group (Eluvia) and 91.0% in the control group (Zilver PTX), with the one-sided lower 95% confidence bound of -0.46% on the difference between the treatment groups being greater than -10 (non-inferiority p-value <.0001). Therefore, the primary safety endpoint was met and Eluvia is concluded to be non-inferior to Zilver PTX for device safety.

Table 20: Primary Safety Endpoints – RCT

Intent-To-Treat (N=421 Subjects)	Eluvia N=280 Subjects	Zilver PTX N=141 Subjects	Difference [95% CI]	One-sided 95% Farrington-Manning Lower Confidence Bound	Non-Inferiority Margin (Delta)	Non-Inferiority P-value[2]
12-Month MAE[1]-Free	94.9% (259/273)	91.0% (121/133)	3.9% [-1.6%, 9.4%]	- 0.46%	-10%	<.0001

[1]Twelve-Month Major Adverse Events (MAEs) defined as all causes of death through 1 month, target limb major amputation through 12 months and/or target lesion revascularization through 12 months.
[2]P-value is from the Farrington-Manning test and is based on the standard normal distribution.A two-group Farrington-Manning test is used to test the one-sided hypothesis of non-inferiority in proportions. If the P-value from the one-sided Farrington-Manning test is <0.05, Eluvia is concluded to be non-inferior to Zilver PTX.

Table 21 shows the individual components of the primary safety endpoint: all causes of death through 1 month, target limb major amputation through 12 months and target lesion revascularization (TLR) through 12 months for the full patient cohort (N=465). The rate of TLR at 12 months was 4.5% in the treatment group (Eluvia) and 9.0% in the control group (Zilver PTX). One major amputation occurred in the treatment group (Eluvia).

Table 21: Safety Endpoints through 12 Months – Full Cohort RCT (N=465)

	Eluvia N=309 Subjects	Zilver PTX N=156 Subjects
Primary Safety Endpoint		
12-Month MAE[1]-Free	95.1% (273/287)	91.0% (132/145)
12-Month MAE[1] and Components		
12-Month MAE[1] (Composite Endpoint)	4.9% (14/287)	9.0% (13/145)
All Causes of Deaths at 1 Month	0.0% (0/287)	0.0% (0/145)
Target Limb Major Amputation	0.3% (1/287)	0.0% (0/145)
Target Lesion Revascularization	4.5% (13/287)	9.0% (13/145)
Clinically-Driven	4.5% (13/287)	9.0% (13/145)
Non-Clinically-Driven	0.0% (0/287)	0.0% (0/145)

[1]Twelve-Month Major Adverse Events (MAEs) defined as all causes of death through 1 month, target limb major amputation through 12 months and/or target lesion revascularization through 12 months.

Adverse effects that occurred in the PMA clinical study:

The Clinical Events Committee (CEC) adjudicated any site-reported AEs that could potentially meet the IMPERIAL protocol-specified MAE definitions plus stent thrombosis. MAEs include all causes of death, target limb major amputation and TLR. **Table 22** summarizes the CEC adjudicated events experienced by the full cohort of RCT subjects during the 12-month follow-up period.

Table 22: CEC Adjudicated Events through 12 Months – Full Cohort RCT (N=465)

CEC Adjudicated Events	Eluvia N=309 Subjects	Zilver PTX N=156 Subjects
1 Month		
All Deaths	0.0% (0/306)	0.0% (0/156)
Target Lesion Revascularization	0.3% (1/306)	0.6% (1/156)
Target Vessel Revascularization	0.7% (2/306)	0.6% (1/156)
Target Limb Amputation	0.0% (0/306)	0.6% (1/156)
Stent Thrombosis	0.7% (2/306)	0.6% (1/156)
6 Months		
All Deaths	0.7% (2/302)	1.9% (3/155)
Target Lesion Revascularization	1.3% (4/302)	3.2% (5/155)
Target Vessel Revascularization	2.3% (7/302)	3.2% (5/155)
Target Limb Amputation	0.0% (0/302)	0.6% (1/155)
Stent Thrombosis	1.0% (3/302)	1.9% (3/155)
12 Months		
All Deaths	2.1% (6/292)	4.0% (6/150)
Target Lesion Revascularization	4.5% (13/292)	8.7% (13/150)
Target Vessel Revascularization	6.8% (20/292)	8.7% (13/150)
Target Limb Amputation	0.3% (1/292)	1.3% (2/150)
Stent Thrombosis	1.7% (5/292)	4.0% (6/150)

Note: Denominators for the cumulative rate were based on 1) subjects with events, and 2) subjects with no events but their follow-up time reached on (or beyond) the earliest visit window. Subjects under "1-Month" column should have a minimum follow up of 23 days.

The CEC reviewed a total of 12 deaths, 6 in each treatment group that were reported within the first year of follow-up. Within the Eluvia treatment group, the CEC adjudicated 3 deaths as cardiovascular related and 3 deaths as non-cardiovascular related. The investigators determined 1 death (unknown cause) as unlikely to be related to the procedure or device. All other deaths were determined to be unrelated to procedure/device. Within the Zilver PTX treatment group, the CEC adjudicated 5 deaths as cardiovascular related and 1 death as vascular related. The investigators determined 1 death (unknown cause) as unlikely to be related to the procedure or device. All other deaths were determined to be unrelated to procedure/device. Three subjects (one in the treatment group (Eluvia) and two in the control group (Zilver PTX)) experienced an amputation of the target limb. Thirty-three (33) subjects had TVRs that were reviewed. Twenty-six (26) subjects had TLRs. Five (5) subjects in the treatment group (Eluvia) and six (6) subjects in the control group (Zilver PTX) experienced a stent thrombosis. The observed stent thrombosis rate remains low at 12 months.

Table 23 displays the frequency of Serious Adverse Events (SAE) by MedDRA System/Organ Class that were reported as of the data snapshot date of April 4, 2018 for the full cohort.

Table 23: Frequency of Site-Reported Serious Adverse Events to 12 Months – Full Cohort RCT (N=465)

Serious Adverse Event		Eluvia (N=309 Subjects)		Zilver PTX (N=156 Subjects)	
MedDRA System Organ Class	**MedDRA Preferred Term**	**Events**	**Rate of Subjects with Event**	**Events**	**Rate of Subjects with Event**
Total	Total	242	41.4% (128/309)	140	42.3% (66/156)
Vascular disorders	Total	93	22.3% (69/309)	55	25.0% (39/156)
Cardiac disorders	Total	32	7.4% (23/309)	20	9.6% (15/156)
Infections and infestations	Total	18	3.9% (12/309)	21	8.3% (13/156)
Musculoskeletal and connective tissue disorders	Total	14	4.2% (13/309)	7	3.8% (6/156)
Gastrointestinal disorders	Total	14	3.9% (12/309)	3	1.9% (3/156)
Nervous system disorders	Total	12	3.6% (11/309)	7	3.8% (6/156)
Respiratory, thoracic and mediastinal disorders	Total	10	2.6% (8/309)	4	2.6% (4/156)
Injury, poisoning and procedural complications	Total	9	2.6% (8/309)	7	4.5% (7/156)
General disorders and administration site conditions	Total	9	1.9% (6/309)	4	2.6% (4/156)
Blood and lymphatic system disorders	Total	9	2.3% (7/309)	0	0.0% (0/156)
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	Total	7	1.9% (6/309)	3	1.9% (3/156)
Skin and subcutaneous tissue disorders	Total	3	1.0% (3/309)	2	1.3% (2/156)
Renal and urinary disorders	Total	3	1.0% (3/309)	1	0.6% (1/156)
Endocrine disorders	Total	3	1.0% (3/309)	0	0.0% (0/156)
Metabolism and nutrition disorders	Total	2	0.6% (2/309)	2	1.3% (2/156)
Psychiatric disorders	Total	1	0.3% (1/309)	2	0.6% (1/156)

Serious Adverse Event		Eluvia (N=309 Subjects)		Zilver PTX (N=156 Subjects)	
MedDRA System Organ Class	**MedDRA Preferred Term**	**Events**	**Rate of Subjects with Event**	**Events**	**Rate of Subjects with Event**
Ear and labyrinth disorders	Total	1	0.3% (1/309)	1	0.6% (1/156)
Eye disorders	Total	1	0.3% (1/309)	1	0.6% (1/156)
Reproductive system and breast disorders	Total	1	0.3% (1/309)	0	0.0% (0/156)

"Events" numbers are total episodes of each type of event among all subjects.
"Rate of Subjects with Event" numbers are percent of subjects who experienced one or more episodes of the event.
"Events" numbers for "TOTAL" are the sum of the individual event category totals.
"Rate of Subjects with Event" numbers for "TOTAL" is the percent of subjects who experienced an adverse event

Unanticipated Adverse Device Effects (UADEs)

No UADEs have been reported.

Stent Fractures

An X-ray exam 1 year after the index procedure was performed for all enrolled subjects to evaluate stent integrity. All X-rays were sent to the X-ray core lab for an initial reading. If the X-ray core lab detected a suspected fracture, the film was sent to the angiography core lab for review against the procedural angiographic images.

The X-ray core lab identified four stents with a possible fracture during the 12-month follow-up period (two stents in the RCT and two stents in the LL substudy). The angiography core lab confirmed three of these fractures, after comparing the X-rays against the procedural angiographic film. The fourth stent was not fractured but showed severe stent deformation, most likely due to heavy calcification. The stent fracture rate in the RCT was 0.6% in the treatment group (Eluvia) and 0.0% in the control group (Zilver PTX). The stent fracture rate was 2.1% in the LL subgroup.

2. Primary Effectiveness Results

The analysis of effectiveness was based on the 421 RCT available patients for the 12-month time point. The primary effectiveness endpoint analysis was conducted when there were sufficient patients evaluable to meet the statistical requirements, as specified in the statistical analysis plan, and did not include the full patient cohort (N=465). Key effectiveness outcomes are presented in **Table 24**.

Primary patency at 12 months was determined to be 86.8% in the treatment group (Eluvia) and 81.5% in the control group (Zilver PTX), with the one-sided lower 95% confidence bound of -0.66% on the difference between the treatment groups being greater than -10% (non-inferiority p-value <.0001). Therefore, the primary

effectiveness endpoint was met and Eluvia is concluded to be non-inferior to Zilver PTX for device effectiveness.

Table 24: Primary Effectiveness Endpoint – RCT

Intent-To-Treat (N=421 Subjects)	Eluvia N=280 Subjects	Zilver PTX N=141 Subjects	Difference [95% CI]	One-sided 95% Farrington-Manning Lower Confidence Bound	Non-Inferiority Margin (Delta)	Non-Inferiority P-value[2]
12-Month Primary Patency[1]	86.8% (231/266)	81.5% (106/130)	5.3% [-2.5%, 13.1%]	- 0.66%	-10%	<.0001

[1]Primary Patency: percentage (%) of lesions (target stented segments) that reach endpoint without a hemodynamically significant stenosis on DUS and without clinically-driven TLR or, bypass of the target lesion before or on the DUS follow-up visit. All evaluable 12M DUS data have been taken into account, irrespective of the visit window.
[2]P-value is from the Farrington-Manning test and is based on the standard normal distribution. A two-group Farrington-Manning test is used to test the one-sided hypothesis of non-inferiority in proportions. If the P-value from the one-sided Farrington-Manning test is <0.05, Eluvia is concluded to be non-inferior to Zilver PTX.

Table 25 presents vessel patency through 12 months for all evaluable subjects in the full cohort of the RCT group.

Primary patency at 12 months was determined to be 86.8% in the treatment group (Eluvia) and 77.5% in the control group (Zilver PTX).

Table 25: Vessel Patency Analysis through 12 Months – Full Cohort RCT (N=465)

	Eluvia N=309 Subjects	Zilver PTX N=156 Subjects
Patency at 6 Months		
Primary Patency[1]	94.5% (274/290)	91.2% (135/148)
Assisted Primary Patency[2]	96.5% (274/284)	95.2% (138/145)
Patency at 12 Months		
Primary Patency[1]	86.8% (243/280)	77.5% (110/142)
Assisted Primary Patency[2]	92.9% (249/268)	86.9% (119/137)

[1]Primary Patency: percentage (%) of lesions (target stented segments) that reach endpoint without a hemodynamically significant stenosis on DUS and without clinically-driven TLR or, bypass of the target lesion before or on the DUS follow-up visit.
[2]Assisted Primary Patency: percentage (%) of lesions (target stented segments) without clinically-driven TLR and those with clinically-driven TLR (not due to complete occlusion or by-pass) that reach endpoint without restenosis The subjects with available diagnostic DUS images are included for the analysis.

3. Additional Secondary Analyses

Full cohort analysis of secondary endpoints for procedural/technical success, MAE rate at 1 month, non-serious non-device/procedure-related AE rates, rate of primary and secondary sustained clinical improvement as assessed by changes in Rutherford Classification from baseline, rate of hemodynamic improvement as assessed by changes in Ankle-Brachial Index (ABI), walking improvement and patient utility values assessed by change in Walking Impairment Questionnaire and EQ-5D, fracture rate, distribution of Rutherford Classification during follow-up as compared to baseline, rate of hemodynamic improvement as assessed by changes in Ankle-Brachial Index (ABI) from baseline, Walking Improvement at 12 months assessed by change in Six Minute Hall Walk (6MHW) from baseline, changes in healthcare utilization over time, and PK parameters calculated for subjects in the PK substudy were observational and demonstrated similar outcomes in both treatment arms.

4. Subgroup Analyses

Primary safety and effectiveness endpoints were evaluated for the following subgroups: region, race, gender, age, diabetic status and stent(s) used. These sub-groups were not statistically powered to make claims on the potential differences seen between groups. No statistically significant differences in terms of the treatment by subgroup interaction were identified.

Long Lesion Substudy (LL)

Table 26 presents the primary effectiveness endpoint of the IMPERIAL LL substudy. Primary patency at 12 months was determined to be 87.0%.

Table 26: Vessel Patency Analysis through 12 Months – LL (N=50)

	Eluvia N=50 Subjects
Patency at 6 Months	
Primary Patency[1]	93.9% (46/49)
Assisted Primary Patency[2]	97.9% (47/48)
Patency at 12 Months	
Primary Patency[1]	87.0% (40/46)
Assisted Primary Patency[2]	93.3% (42/45)

[1]Primary Patency: percentage (%) of lesions (target stented segments) that reach endpoint without a hemodynamically significant stenosis on DUS and without clinically-driven TLR or, bypass of the target lesion before or on the DUS FU visit. All evaluable 12M DUS data have been taken into account, irrespective of the visit window.
[2]Assisted Primary Patency: percentage (%) of lesions (target stented segments) without clinically-driven TLR and those with clinically-driven TLR (not due to complete occlusion or bypass) that reach endpoint without restenosis

Table 27: presents the primary safety endpoint of the IMPERIAL LL substudy. The 93.5% MAE-free rate observed in the LL substudy is similar to the 94.9% MAE-free rate observed in the treatment group (Eluvia) in the RCT. The composite rate of

MAEs, including all causes of death through 1 month, target limb major amputation and target lesion revascularization (TLR) through 12 months, was 6.5%. The only MAEs that occurred in the LL substudy were TLRs; there were no deaths or major amputations.

Table 27: Safety Endpoints Through 12 Months – LL (N=50)

	Eluvia N=50 Subjects
Primary Safety Endpoint	
12-Month MAE[1]-Free	93.5% (43/46)
12-Month MAE[1] and Components	
12-Month MAE[1] (Composite Endpoint)	6.5% (3/46)
All Causes of Deaths at 1 Month	0.0% (0/46)
Target Limb Major Amputation	0.0% (0/46)
Target Lesion Revascularization	6.5% (3/46)
Clinically-Driven	6.5% (3/46)
Non-Clinically-Driven	0.0% (0/46)

[1]Twelve-Month Major Adverse Events (MAEs) defined as all causes of death through 1 month, target limb major amputation through 12 months and/or target lesion revascularization through 12 months.

Table 28 summarizes the CEC adjudicated events experienced by LL subjects during the 12-month follow-up period. The CEC reviewed 3 TLRs that were reported within the first 12 months of follow-up. No deaths, target limb amputations or stent thromboses occurred in this substudy population.

Table 28: CEC Adjudicated Events through 12 Months – LL (N=50)

CEC Adjudicated Events	**Eluvia N=50 Subjects**
1 Month	
All Deaths	0.0% (0/50)
Target Lesion Revascularization	0.0% (0/50)
Target Vessel Revascularization	0.0% (0/50)
Target Limb Amputation	0.0% (0/50)
Stent Thrombosis	0.0% (0/50)
6 Months	
All Deaths	0.0% (0/50)
Target Lesion Revascularization	2.0% (1/50)
Target Vessel Revascularization	2.0% (1/50)
Target Limb Amputation	0.0% (0/50)
Stent Thrombosis	0.0% (0/50)
12 Months	
All Deaths	0.0% (0/46)
Target Lesion Revascularization	6.5% (3/46)
Target Vessel Revascularization	8.7% (4/46)
Target Limb Amputation	0.0% (0/46)
Stent Thrombosis	0.0% (0/46)

Note: Denominators for the cumulative rate will be based on 1) subjects with events, and 2) subjects with no events but their follow-up time reached on (or beyond) the earliest visit window. Subjects under "1-Month" column should have a minimum follow up of 23 days.

Table 29 displays the frequency of Serious Adverse Events (SAE) in the long lesion substudy by MedDRA System/Organ Class that were reported as of the data snapshot date of April 4, 2018.

Table 29: Frequency of Site-Reported Serious Adverse Events to 12 Months – LL (N=50)

Serious Adverse Event		Eluvia (N=50 Subjects)	
MedDRA System Organ Class	**MedDRA Preferred Term**	**Events**	**Rate of Subjects with Event**
Total	Total	26	30.0% (15/50)
Vascular disorders	Total	8	14.0% (7/50)
Cardiac disorders	Total	5	10.0% (5/50)
Gastrointestinal disorders	Total	5	6.0% (3/50)
Infections and infestations	Total	2	4.0% (2/50)
Injury, poisoning and procedural complications	Total	2	2.0% (1/50)
Blood and lymphatic system disorders	Total	1	2.0% (1/50)
General disorders and administration site conditions	Total	1	2.0% (1/50)
Nervous system disorders	Total	1	2.0% (1/50)
Respiratory, thoracic and mediastinal disorders	Total	1	2.0% (1/50)

"Events" numbers are total episodes of each type of event among all subjects.
"Rate of Subjects with Event" numbers are percent of subjects who experienced one or more episodes of the event.
"Events" numbers for "TOTAL" are the sum of the individual event category totals.
"Rate of Subjects with Event" numbers for "TOTAL" is the percent of subjects who experienced an adverse event

Table 30 presents the primary patency and MAE rates grouped by lesion length tertiles.

Table 30: 12-Month Vessel Patency and MAE Rates for Lesion Length Tertiles

Lesion Length Tertiles	Eluvia ALL(N=50)	Eluvia T1 (N=13)	Eluvia T2 (N=15)	Eluvia T3 (N=22)
12-Month Primary Patency	87.0%(40/46) [73.7%,95.1%]	91.7%(11/12)	86.7%(13/15)	84.2%(16/19)
12-Month MAE-Free	93.5%(43/46) [82.1%,98.6%]	92.3%(12/13)	92.9%(13/14)	94.7%(18/19)

T1:- "<=150 mm"; T2:- " >150 mm to <=170 mm"; T3:- " >170 mm"
Site reported lesion length is considered for analysis for the subject with missing core lab lesion length.

In Vivo Pharmacokinetics-IMPERIAL-PK Sub-Study

The PK profile of the ELUVIA stent was analyzed for subjects enrolled in the PK substudy. PK substudy subjects had baseline venous blood drawn followed by blood draws at 10 minutes, 30 minutes, 1, 2, 3, 4, 6, 12, and 24 hours and one final blood draw at either 48 hours or 72 hours after placement of the final ELUVIA stent.

The analysis results showed that all samples were negative for paclitaxel (< 10 ng/mL). An alternate test method to test to a lower detection limit (< 1 ng/mL) was developed and all samples were retested. All samples but two, which were determined to have a concentration of 1.60 ng/mL and 1.44 ng/mL at the 10 minute time point, were again negative for paclitaxel (< 1 ng/mL).

Table 31 provides an overview of the CEC adjudicated events experienced by PK subjects during the 12-month follow-up period. The CEC reviewed 1 TLR that was reported within the first 12 months (365 days) of follow-up. No deaths, target limb amputations or stent thromboses occurred in this substudy population.

Table 31: CEC Adjudicated Events at 12 Months – PK (N=13)

Event	Eluvia N=13 Subjects	
	Rate	Events
All Death, Amp, TVR	7.7% (1/13)	1
All Death, Amp, TLR	7.7% (1/13)	1
All Deaths	0.0% (0/13)	0
Cardiac	0.0% (0/13)	0
Vascular	0.0% (0/13)	0
Non-Cardiovascular	0.0% (0/13)	0
Amputation	0.0% (0/13)	0
Major	0.0% (0/13)	0
Minor	0.0% (0/13)	0
TVR	7.7% (1/13)	1
TLR	7.7% (1/13)	1
Clinically-Driven	7.7% (1/13)	1
Non-Clinically Driven	0.0% (0/13)	0
Stent Thrombosis	0.0% (0/13)	0
Complete Occlusion	0.0% (0/13)	0
Flow-Limiting	0.0% (0/13)	0

Note: Denominators are based on 1) subjects with events, and 2) subjects with no events but have follow-up at least 335 days. Events that occurred after 365 days are not included.

5. Pediatric Extrapolation

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

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 trial included 75 Principal Investigators (266 sub-investigators) none of which were full-time or part-time employees of the sponsor and 2 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: 0
- Significant payment of other sorts: 1
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 1

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

The global, prospective, randomized, multi-center IMPERIAL trial was designed to determine whether the ELUVIA Drug-Eluting Vascular Stent System shows acceptable performance in long-term (12-month) safety rates and vessel patency when treating femoropopliteal lesions. The primary objective of the study was to demonstrate that the 12-month primary patency rate and the 12-month MAE-free rate for the treatment group (Eluvia) were non-inferior to the control group (Zilver PTX).

A. Effectiveness Conclusions

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 18 months.

The primary effectiveness endpoint in the pivotal clinical study was the 12-month primary patency, as defined as the percentage of stented segments without a hemodynamically significant stenosis on DUS (PSVR ≤ 2.4), and without clinically-driven TLR or bypass of the target lesion. Primary patency at 12 months was determined to be 86.8% in the treatment group (Eluvia) and 81.5% in the control group (Zilver PTX), with the one-sided lower 95% confidence bound of -0.66% on the difference between the treatment groups being greater than -10% (non-inferiority p-value <.0001). Therefore, the primary effectiveness endpoint was met and Eluvia is concluded to be non-inferior to Zilver PTX for device effectiveness.

In the Long Lesion substudy (LL), primary patency at 12 months was determined to be 87.0%, with an expected trend in reduced patency with increased lesion length. This rate met the pre-defined performance goal of 60%. However, limitations with the LL substudy include a lack of blinding and an active comparator. The data from this cohort were found to be sufficient to support an indication to include lesions up to 190 mm in length.

The Eluvia Stent System was demonstrated to be a non-inferior treatment alternative for SFA/PPA lesions in consideration to its similar patency and reintervention rates through 1 year. Full cohort analysis of secondary endpoints demonstrated similar outcomes in both treatment arms at the 12 month time point. Rates and changes from baseline were as expected for this device type.

B. Safety Conclusions

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

The IMPERIAL clinical trial evaluated the safety of the ELUVIA Stent System in the treatment of femoropopliteal artery stenosis in de novo or restenotic lesions. The primary safety endpoint, as define as the MAE-free rate at 12 months, was determined to be 94.9% in the treatment group (Eluvia) and 91.0% in the control group (Zilver PTX), with the one-sided lower 95% confidence bound of -0.46% on the difference between the treatment groups being greater than -10% (non-inferiority p-value <.0001). Therefore, the primary safety endpoint was met and Eluvia is concluded to be non-inferior to Zilver PTX for device safety. The ELUVIA Stent System demonstrated an adequate safety profile in the IMPERIAL trial. The composite rate of major adverse events (MAEs), including all causes of death through 1 month, target limb major amputation and target lesion revascularization (TLR) through 12 months, was 4.9% in the RCT and 6.5% in the LL substudy. This rate was driven mainly by TLR, as no deaths were observed during the first 30 days and only one major amputation occurred through 12 months. The Eluvia Stent System was demonstrated to be a non-inferior treatment alternative for SFA/PPA lesions in consideration of its similar adverse event rates.

C. Benefit-Risk Conclusion

The probable benefits of the device are based on data collected in the clinical study conducted to support PMA approval, as described above. The probable benefits of the ELUVIA Drug-Eluting Vascular Stent System include improving or restoring blood flow in patients with peripheral arterial disease to improve the patient symptoms and quality of life.

The probable risks of the device are also based on data collected in the clinical study conducted to support PMA approval, as described above, and the frequency and types of the adverse events reported throughout the pivotal clinical study are in alignment with what might be expected in the studied patient population and therapeutic area. No unanticipated adverse device effects were reported in the study.

Additional factors that were considered in determining probable risks and benefits for the ELUVIA Drug-Eluting Vascular Stent System included:

- Patient follow-up was satisfactory with adequate follow-up to 12 months to evaluate safety and effectiveness. Follow-up will continue for 5 years to evaluate the longer-term device performance, such as the duration of the benefit and long term adverse event rates.
- The pivotal study was a multi-center study conducted in the United States, Canada, Japan, New Zealand and Europe. The results obtained are expected to be sufficiently representative of US clinical performance.
- The device is intended for use in subjects with peripheral vascular disease of the superficial femoral and proximal popliteal arteries. The results adequately support general use in the identified population. Most patients with the disease have symptoms only, but some patients may have more extensive disease involvement. The device treats the hemodynamic consequences of the disease to improve perfusion and function. The disease is chronic and affects the mobility of the patient and the quality of life. It is treatable but not curable.
- Patient risk is minimized by limiting use to operators who have the necessary training to use the device safely and effectively and by adherence to recommended peri-procedural medications regimens.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for using the device to improve luminal diameter in symptomatic patients with *de-novo* or restenotic native lesions or occlusions of the superficial femoral artery and/or proximal popliteal artery with reference vessel diameters ranging from 4.0 mm to 6.0 mm and total lesion lengths up to 190 mm.

1. Patient Perspectives

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

D. Overall Conclusions

The clinical and non-clinical data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The results of the IMPERIAL trial show that the ELUVIA Stent System is non-inferior to Zilver PTX with regards to effectiveness and safety and confirm that the ELUVIA Stent System is appropriate for the treatment of SFA and PPA lesions when used in accordance with the labeling and Directions for Use (DFU).

XIII. CDRH DECISION

CDRH issued an approval order on September 18, 2018. The final conditions of approval cited in the approval order are described below.

1) *IMPERIAL Continued Follow-Up Study:* This study will evaluate the long-term safety and effectiveness of the Eluvia Drug-Eluting Vascular Stent System in 524 subjects from the premarket study (IMPERIAL trial). The IMPERIAL trial was designed as a global, multicenter, single-blind, prospective, randomized (2:1 Eluvia DES to Zilver DES) trial. Subjects will be followed annually through 5 years post-procedure with no more than 15% attrition. Data is to be provided for both study arms.

   The primary effectiveness endpoint is primary patency of the target lesion at 24 months.

   The primary safety endpoint is freedom from Major Adverse Events defined as all causes of death through 1 month and target limb major amputation and/or target lesion revascularization at 24 months.

   The endpoints to be assessed through 60 months post-procedure are rate of: (1) major adverse events (MAE), (2) clinically-driven target lesion revascularization (CD-TLR), (3) clinically-driven target vessel revascularization (CD-TVR), (4) primary patency (60 months), (5) stent fracture rate (24 and 60 months), (6) change in walking impairment questionnaire (WIQ) (24 and 60 months), and (7) change in quality of life assessment by EQ-5D questionnaire (24 and 60 months).

2) *REGAL and EMINENT Long-Term Follow-Up Studies*: These studies will evaluate the long-term safety and effectiveness of the Eluvia Drug-Eluting Vascular Stent System, including in patients with long lesions.

   a. The REGAL trial was designed as a European, multicenter, prospective, single-arm, post-market trial. 500 subjects will be enrolled and followed through 24 months post-procedure.

      The primary effectiveness endpoint is primary patency of the target lesion at 6, 12, and 24 months.

The primary safety endpoint is freedom from Major Adverse Events defined as all causes of death through 1 month and target limb major amputation and/or target lesion revascularization at 6, 12, and 24 months.

Additional endpoints to be assessed through 24 months post-procedure are rate of: (1) clinically-driven target lesion revascularization (CD-TLR), (2) clinically-driven target vessel revascularization (CD-TVR), (3) change in walking impairment questionnaire (WIQ), and (4) change in quality of life assessment by EQ-5D questionnaire.

b. The EMINENT trial was designed as a European, multicenter, prospective, randomized (2:1 Eluvia DES to BMS) trial. 750 subjects will be enrolled and followed through 36 months post-procedure. Data is to be provided for both study arms.

   The primary effectiveness endpoint is primary patency of the target lesion at 12 months.

   The primary safety endpoint is freedom from Major Adverse Events defined as all causes of death through 1 month and target limb major amputation and/or target lesion revascularization at 12 months.

   Additional endpoints to be assessed through 36 months post-procedure are rate of: (1) major adverse events (MAE), (2) clinically-driven target lesion revascularization (CD-TLR), (3) clinically-driven target vessel revascularization (CD-TVR), (4) primary patency, (5) stent fracture rate (12 and 24 months only), (6) change in walking impairment questionnaire (WIQ), and (7) change in quality of life assessment by EQ-5D questionnaire.

The applicant's manufacturing facilities were 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.