

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Drug-eluting percutaneous transluminal coronary angioplasty catheter
Device Trade Name:	SELUTION SLR™ 014 PTCA Drug-Eluting Balloon Catheter
Device Prococode:	OOB
Applicant's Name and Address:	MedAlliance LLC 4 Jenner, Suite 190 Irvine, CA 92618
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P250041
Date of FDA Notice of Approval:	September 18, 2026
Breakthrough Device:	Granted breakthrough device status on February 21, 2019 because the combination product and proposed indication for use met the criteria outlined in FDA Guidance Document "Breakthrough Devices Program."

II. INDICATIONS FOR USE

The SELUTION SLR™ 014 PTCA Drug-Eluting Balloon Catheter is intended to be used after appropriate vessel preparation in adult patients undergoing percutaneous coronary intervention (PCI) in coronary arteries 2.25 mm to 4.50 mm in diameter and lesions $\leq$ 26 mm in length for the purpose of improving myocardial perfusion when treating in-stent restenosis (ISR).

III. CONTRAINDICATIONS

The SELUTION SLR™ PTCA Drug Eluting Balloon Catheter is contraindicated for use in:

- Patients with known allergies or hypersensitivities to sirolimus (or analogs).
- Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy.
- Patients with unprotected native left main coronary artery disease
- Patients with coronary artery spasm in the absence of a significant stenosis
- Neurovasculature

IV. **WARNINGS AND PRECAUTIONS**

The warnings and precautions can be found in the SELUTION™ SLR PTCA Drug Eluting Balloon Catheter labeling.

V. **DEVICE DESCRIPTION**

The SELUTION SLR™ 014 PTCA Drug Eluting Balloon Catheter (hereafter referred to as SELUTION DEB or SELUTION) is a device-drug combination product consisting of a standard rapid exchange (RX) semi-compliant percutaneous coronary intervention (PCI) catheter compatible with 0.014 inch guidewires; the balloon portion is coated with a micro-encapsulated drug formulation (sirolimus as the active pharmaceutical ingredient, and a three-lipid system comprising a PEG-lipid, a structural phosphatidylcholine, and a cholesterol derivative, combined in a proprietary molar ratio as the excipient). It is designed to improve myocardial perfusion and decrease the incidence of restenosis in previously stented coronary arteries by (1) physically opening the artery through the mechanical inflation of the balloon and (2) inhibiting restenosis through the anti-proliferative and anti-stenotic actions of sirolimus.

The distal end of the catheter has a coaxial dual lumen design. The outer lumen is used for inflation of the balloon to conform to the vessel wall, and the inner lumen permits the use of a guidewire to facilitate advancement of the catheter. The proximal remainder of the catheter continues with one lumen that is used for balloon inflation. The semi-compliant balloon is designed to provide an inflatable segment of known diameter and length at recommended pressures. The balloon has two radiopaque markers that indicate the balloon working length and aid in the positioning of the balloon relative to the stenosis. The catheter tip is tapered to facilitate advancement of the catheter to the treatment area and through the stenosis. The proximal shaft consists of a stainless steel hypotube and is marked with exit markers. The distal shaft is partially coated with a hydrophilic coating for lubricity. **Figure 1** shows a schematic drawing of the SELUTION DEB.

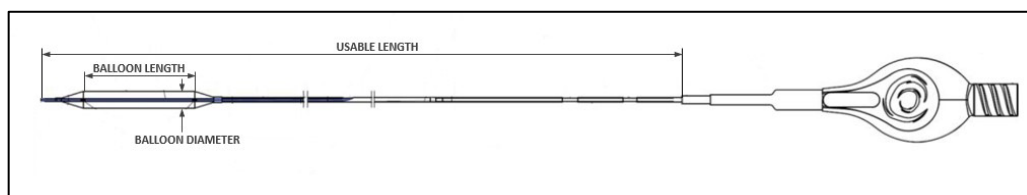


Figure 1: Schematic Drawing of the SELUTION DEB

The SELUTION DEB is available in balloon diameters between 2.25 - 4.50 mm and in balloon lengths between 15 and 30 mm. The effective or usable length of the catheter is 140 cm.

Mechanism of Action

SELUTION DEB's primary mode of action is mechanical dilation of the stenotic lesion with a secondary inhibition of restenosis through the application of sirolimus to the coronary vessel wall.

Drug Coating Description

The drug coating for the SELUTION DEB consists of sirolimus (the active pharmaceutical ingredient) encapsulated in poly(lactic-co-glycolic acid) (PLGA) polymer microspheres within a lipid-based excipient (the inactive ingredients).

Drug Substance – Sirolimus

The active pharmaceutical ingredient in the proprietary SELUTION DEB coating is sirolimus (CAS no. 53123-88-9). Sirolimus is a drug that acts both as an anti-proliferative agent and as an anti-inflammatory immunosuppressant. Sirolimus inhibits T and B-lymphocyte activation and smooth muscle and endothelial cell proliferation in response to cytokine and growth factor stimulation. Sirolimus is used as a cell growth inhibiting compound in both medicinal products (drug products) and combination products (device/drug products).

The chemical name for sirolimus is :

(3*S*,6*R*,7*E*,9*R*,10*R*,12*R*,14*S*,15*E*,17*E*,19*E*,21*S*,23*S*,26*R*,27*R*,34*AS*)-9,10,12,13,14,21,22,23,24,25,26,27,32,33,34,34*A*-hexadecahydro-9,27-dihydroxy-3-((1*R*)-2-((1*S*,3*R*,4*R*)-4-hydroxy-3-methoxycyclohexyl)-1-methylethyl)-10,21-dimethoxy-6,8,12,14,20,26-hexamethyl-23,27-epoxy-3*H*-pyrido(2,1-*C*)-(1,4)oxaazacyclohentriacontine-1,5,11,28,29-(4*H*,6*H*,31*H*)-pentone.

Sirolimus has a molecular weight of 914.17 g/mol and chemical formula C₅₁H₇₉NO₁₃. The stereochemical structure of sirolimus molecules are shown in **Figure 2** below:

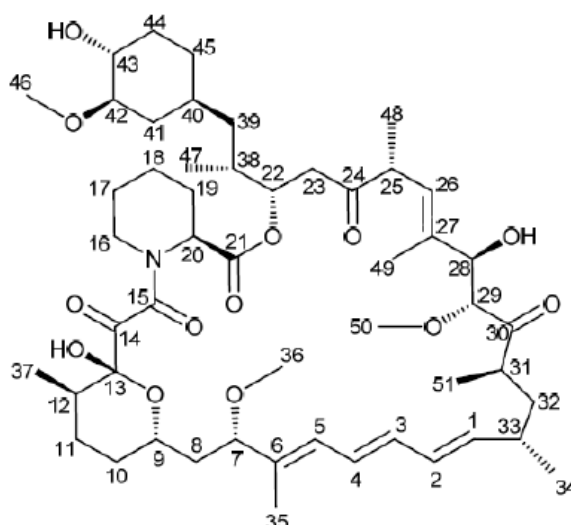


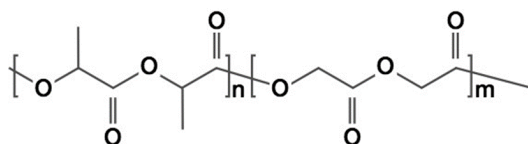
Figure 2: Sirolimus Chemical Structure

Excipients

The inactive ingredients in the SELUTION DEB coating are PLGA and a three-lipid system comprising a PEG-lipid, a structural phosphatidylcholine, and a cholesterol derivative, combined in a proprietary molar ratio in which the PLGA microspheres are suspended.

PLGA

The PLGA used in the SELUTION DEB coating is a co-polymer made of DL-lactide and glycolide in a 75:25 molar ratio. PLGA is a biodegradable polymer that is used widely for medical devices and drug delivery. The PLGA microspheres are 4 μm in diameter and help to regulate the release of sirolimus, which is loaded into the polymers at 41% by weight, as the polymer breaks down over time. The chemical structure of PLGA is shown in **Figure 3**. An illustration of the drug-loaded microspheres is shown in **Figure 4**.



Poly(DL-lactide-co-glycolide)

Figure 3: Chemical Structure of PLGA

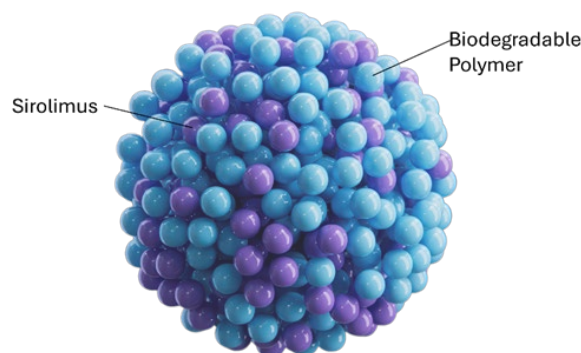


Figure 4: Drug loaded microspheres

Lipid Blend

The lipid blend is made of a three-lipid system comprising a PEG-lipid, a structural phosphatidylcholine, and a cholesterol derivative, combined in a proprietary molar ratio. This blend aids in reducing drug coating wash-off in the bloodstream during insertion, tracking and lesion crossing. The blend also improves drug transfer to the tissue during the short-term balloon dilatation and helps the microspheres adhere to the surrounding tissue after SELUTION DEB treatment.

Drug Dose

The nominal drug dose density on the SELUTION DEB is 1.0 $\mu\text{g}/\text{mm}^2$ of cylindrical balloon surface. The drug content for each size is defined by the product of the balloon surface area and the nominal drug dose density. The total amount of sirolimus for each balloon size is provided in **Table Table** /Error! Reference source not found..

Table 1: Nominal Sirolimus Content (µg) Per Balloon Size

Nominal Balloon Diameter (mm)	Nominal Balloon Length (mm)			
	15	20	25	30
2.25	106	141	177	212
2.50	118	157	196	236
2.75	130	173	216	259
3.00	141	188	236	283
3.25	153	204	255	306
3.50	165	220	275	330
4.00	188	251	314	377
4.50	212	283	353	424

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of coronary in-stent restenosis, including:

- Medical therapy and risk factor modification (e.g., diet, exercise, smoking cessation)
- Coronary artery bypass graft (CABG) surgery
- Vascular brachytherapy
- Plain old balloon angioplasty (POBA; angioplasty with a balloon with no drug coating)
- Additional drug-eluting stent
- Drug-coated or drug-eluting balloon catheters

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

A version of the SELUTION DEB (using the identical drug coating but a different base catheter) has been commercially available for distribution in the European Union (EU) since receiving CE Mark in May 2020. Since that time, the SELUTION DEB has been commercially available in the countries identified in **Table 2**. During this time, the device has not been withdrawn from marketing for any reason related to its safety or effectiveness.

Table 2: List of Approved Countries

Armenia	Egypt	Indonesia	Kuwait	Philippines	Slovenia
Austria	Finland	Iran	Lebanon	Poland	South Africa
Bangladesh	France	Iraq	Luxembourg	Portugal	Spain
Belarus	Georgia	Ireland	Malaysia	Qatar	Switzerland
Belgium	Germany	Israel	Morocco	Russia	Taiwan
Brunei	Greece	Italy	Netherlands	Saudi Arabia	Uzbekistan
Canary Islands	Hong Kong	Jordan	New Zealand	Serbia	Vietnam
Croatia	Hungary	Kazakhstan	Northern Ireland	Singapore	
Czech Republic	India	Kenya	Oman	Slovakia	

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the SELUTION DEB or the angioplasty procedure.

- Additional interventions, including surgical intervention
- Allergic reaction (e.g., to contrast medium, medications, device components, drug coating and its components)
- Arrhythmias
- Bleeding (including hemorrhage or hematoma possibly requiring transfusion or additional intervention)
- Chest pain (angina)
- Death
- Embolism (of tissue, plaque, thrombus, device, drug coating)
- Fever
- Hypertension
- Hypotension
- Infection/sepsis
- Inflammation
- Myocardial infarction/ischemia
- Pain or tenderness at the vascular access site
- Pericardial effusion/cardiac tamponade
- Kidney injury/failure
- Shock
- Stroke or transient ischemic attack (TIA)
- Vessel injury (dissection, perforation, rupture, arteriovenous fistula, aneurysm or pseudoaneurysm)
- Vessel occlusion (spasm, abrupt closure/recoil, slow flow/no reflow, thrombosis, restenosis)

Potential adverse events not captured above that have been associated with oral administration of sirolimus (the drug in the SELUTION DEB coating) at systemic doses include the following:

- Abnormal liver enzymes
- Anemia
- Arthralgia (joint pain)
- Diarrhea
- Hypercholesterolemia (high cholesterol)
- Hypersensitivity, including anaphylactic/anaphylactoid type reactions
- Hypertriglyceridemia (high triglycerides)
- Hypokalemia (low blood potassium)
- Infection
- Interstitial lung disease
- Leukopenia (low white blood cell count)
- Lymphoma and other cancers
- Thrombocytopenia (low platelet count)

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

IX. SUMMARY OF NON-CLINICAL STUDIES

A. Laboratory Studies

A series of non-clinical laboratory studies related to the product were performed to evaluate the device, including: biocompatibility studies, bench testing, coating characterization testing, chemistry, manufacturing and controls (CMC) testing, sterilization testing, packaging testing, shelf-life testing, and Good Laboratory Practice (GLP) animal studies.

i. Biocompatibility

Biocompatibility testing of the SELUTION DEB was conducted in accordance with ISO 10993-1 *Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing within a Risk Management Process*, FDA Guidance – *Use of International Standard ISO 10993-1 – Guidances for Industry and Food and Drug Administration Staff* as summarized in **Table 3**.

To ensure any potential effects of the drug coating component on biocompatibility could be differentiated from any potential effects of the device component, testing was conducted on three separate test articles:

- 1) the final, drug-coated SELUTION DEB catheter
- 2) the excipient-coated balloon catheter (no drug)
- 3) the uncoated PTCA balloon catheter

Table 3: Summary of Biocompatibility Testing

Test	Applicable Standard	Test Article			Results
		1	2	3	
Cytotoxicity - ISO MEM Elution Method	ISO 10993-5	X	X	X	Not concerning*
Sensitization	ISO 10993-10	X	-	X	Non-sensitizing
Intracutaneous Reactivity	ISO 10993-10	X	X	X	Not concerning*
Hemolysis (Direct and Extract)	ISO 10993-4	X	X	X	Not concerning*
SC5b9 Complement Activation	ISO 10993-4:2017 (E)	X	-	X	Not a complement activator**
Partial Thromboplastin Time (PTT)	ISO 10993-4	X	-	-	Met requirements
Acute Systemic Toxicity	ISO 10993-11:2017(E)	X	-	X	Non-toxic
Material-Mediated Pyrogenicity	ISO 10993-11:2017 (E)	X	-	X	Non-pyrogenic

Test	Applicable Standard	Test Article			Results
		1	2	3	
Genotoxicity Bacterial Mutagenicity Test - AMES Assay	ISO 10993-3:2014 (E)	X	-	-	Not concerning*
Genotoxicity In-Vitro Mouse Lymphoma Assay	ISO 10993-3:2014	X	X	-	Not concerning*
Chemical Characterization/ Toxicological Risk Assessment	ISO 10993-18:2020	X	X	X	Extractables do not pose toxicity concerns for the endpoints of carcinogenicity, genotoxicity, and subchronic/chronic systemic toxicity.
*Although cytotoxic, genotoxic, irritation, and hemolytic response was noted for the neat extract of the finished SELUTION DEB and excipient coated balloons, the results are considered acceptable following extract dilutions and based on acceptable implantation response from the GLP animal studies as described in section B. **SELUTION DEB did not meet the acceptance criteria for SC5b-9 Complement Activation. However, the GLP animal safety study (section B) found no pathological evidence to suggest that uncontrolled complement activation occurred in-vivo and thus, the results were considered acceptable.					

This biocompatibility assessment concluded that the SELUTION DEB demonstrated acceptable biological risk under its intended use.

Thrombogenicity, Implantation, Sub-chronic/Chronic Toxicity and Carcinogenicity endpoints, per ISO 10993-4, -6, -11 and -3, respectively, were leveraged from the GLP animal safety study using the SELUTION drug coated balloon catheter. The outcomes related to these endpoints were found to be acceptable.

ii. Bench Testing

A summary of the bench testing studies to support the SELUTION DEB is provided in **Table 4**. All testing was completed in accordance with relevant standards and FDA guidance documents, as applicable, to support the approved indication.

Table 4: Summary of Bench Testing

Test	Objective	Acceptance Criteria	Results
Dimensional and Functional Attributes	Demonstrate accurate dimensions, including crossing profile, effective length, and balloon length. Demonstrate guidewire and accessory device compatibility consistent with the product label.	Compatible with labeled dimensions.	Pass
Rated Burst Pressure (constrained and unconstrained)	Ensure burst pressures are above the labeled range, including when inflated inside of a previously deployed stent.	The burst pressure must be ≥ 14 atm.	Pass
Balloon Compliance	Establish an accurate compliance chart by measuring the balloon diameter at multiple pressures.	Characterization	Acceptable
Balloon Inflation and Deflation Time	Ensure the balloon can inflate and deflate sufficiently quickly to avoid prolonged obstruction of blood flow.	The balloon must inflate in less than 10 seconds and deflate in less than 30 seconds.	Pass
Balloon Fatigue (constrained and unconstrained)	Ensure freedom from leakage or damage after multiple inflations, including when inflated inside of a previously deployed stent.	Must be able to withstand 10 inflation/deflation cycles.	Pass
Catheter Bond Strength	Ensure all bonds can withstand clinically relevant tensile forces.	0.44-126.9N, depending on the bond	Pass
Flexibility and Kink	Ensure catheter can withstand flexural forces typical of clinical use in tortuous vasculature.	The catheter demonstrates a kink radius ≤ 15 mm.	Pass
Torque Strength	Ensure catheter can withstand torsional forces typical of clinical use without fractures.	The catheter withstands a minimum of three (3) 180° rotations of the proximal hub.	Pass
Balloon Preparation, Delivery, and Retraction (Simulated Use)	Demonstrate that the balloon catheter can be safely and reliably prepared, tracked, and deployed in a stented mock vessel, then retracted out of the model without damage to the product as per the instructions for use.	The device can be prepared, tracked, deployed, and retracted with no damage.	Pass
Radiopacity	Ensure marker bands are visible under fluoroscopy to aid in placement of the balloon.	Marker bands must be radiopaque.	Pass (determined during in vivo animal studies)

Test	Objective	Acceptance Criteria	Results
Hydrophilic Coating Integrity	Demonstrate the hydrophilic coating remains largely intact after simulated use.	Characterize	Acceptable

iii. Coating Characterization Testing

Coating characterization testing performed to evaluate characteristics of the SELUTION DEB drug coating are summarized in **Table 5**.

Table 5: Summary of Coating Characterization

Test	Description	Results
Acute Coating Integrity	High magnification imaging was used to inspect drug coated balloons and surface appearance.	Acceptable Outcomes
Coating Adhesion	A tape test was conducted to evaluate coating adhesion.	Acceptable Outcomes
Coating Thickness	The coating thickness was measured at the distal, middle, and proximal locations of each balloon.	Acceptable Outcomes
Drug Coating Circumferential Uniformity	The drug present in each circumferential segment was analyzed to demonstrate uniformity across the balloon.	Acceptable Outcomes
Drug Coating Length Uniformity	The drug present in each longitudinal segment was analyzed to demonstrate uniformity across the balloon.	Acceptable Outcomes
Particulate Quantification (Track & Deploy)	Track and deploy particulate testing quantified the particulate released from the coated balloon.	Acceptable Outcomes

iv. Chemistry, Manufacturing, and Controls (CMC)

The established requirements for ongoing SELUTION DEB release batch and stability testing are summarized in **Table 6**.

Table 6: SELUTION DEB CMC Testing Requirements

Test	Objective	Acceptance Criteria
Appearance	Packaging inspected for damage and visual inspection of the drug coating conducted to verify that it meets the appearance specification.	Must meet visual standard
Drug Identity	The identity of the drug substance, sirolimus, is confirmed by high performance liquid chromatography (HPLC) analysis and its UV spectrum.	Identity must be confirmed

Test	Objective	Acceptance Criteria
Drug Content	Sirolimus content is quantified by HPLC to ensure product contains the labeled dose.	Drug content mean value should be 90.0 – 110.0% of label claim
Drug Content Uniformity	Sirolimus content is quantified by HPLC to ensure individual devices contain the labeled dose.	USP <905>
Impurities	The levels of drug degradants and impurities are quantified by HPLC to ensure they remain within acceptable levels.	ICH Q3B(R2)
Residual Solvent	The amount of residual solvents (cyclohexane, ethanol, heptane, and methylene chloride) is verified to be within the established specification limits using gas chromatography.	The device met the established specification limits for residual solvents (<5-24 ug depending on balloon size).
Dissolution/Drug Release	The released sirolimus is quantified by HPLC to ensure it is within limits.	The drug release at multiple timepoints must be within limits
Endotoxin	Endotoxin levels are evaluated per AAMI ST72 to ensure they are within established safety guidelines.	AAMI ST72
Particulates	Particulate sizes and counts measured for the SELUTION SLR PTCA DEB using light obscuration on particulates released during simulated use testing.	Particulate sizes and counts must be within limits per USP 788
Polymer Molecular Weight (MW)	Determine PLGA MW by gel permeability chromatography (GPC).	Molecular weight must meet specification

v. *In Vitro* Polymer Degradation Studies

GPC was used to determine the change in MW and mass of PLGA used in the SELUTION DEB. Under clinically relevant conditions (37°C), PLGA underwent expected hydrolytic degradation, where 88% of its MW and 97% of its mass was lost over 210 days.

vi. Sterilization

The SELUTION DEB is sterilized using electron beam (E-beam) sterilization with a radiation dose range of 22.5-30.0 kGy. This cycle is validated using the VDmax^{SD} method and controlled in accordance with ISO TIR13004 and ISO 11137-1:2006 (Sterilization of Health Care Products - Radiation - Requirements for Development, Validation and Routine Control of Sterilization Process for Medical Devices) to provide a Sterility Assurance Level (SAL) of at least 10⁻⁶.

vii. Packaging

Packaging verification testing was performed to demonstrate that the SELUTION DEB packaging can withstand the hazards of distribution and the environment, and that the sterility of the device is maintained throughout the labeled shelf life. Package integrity testing included a visual assessment, seal width, bubble leak testing, and seal strength testing. Testing was conducted at baseline and aged conditions after preconditioning, including thermal cycling per ASTM D4332 and transportation testing per ASTM D4169.

viii. Shelf Life

Shelf-life studies evaluating the effects of aging on the mechanical properties of the catheter, packaging, and the stability of the drug were conducted to establish a shelf life/expiration date for the SELUTION DEB product. The data generated supports an 18-month shelf life for the SELUTION DEB device and the product is labeled accordingly.

B. Animal Studies

The following animal studies were conducted to evaluate the safety and pharmacokinetics (PK) of the SELUTION DEB. Four GLP animal studies were conducted in compliance with 21 CFR 58 (Good Laboratory Practices) and one animal study was not conducted in accordance with 21 CFR 58.

Animal studies are summarized in **Table 7**.

Table 7: Summary of Animal Studies

Study ID	Number & Animal Type	Local Drug Dose	Balloon Size (mm x mm)	Time Points	Major Endpoints	Endpoints Met
Safety Study (CR 2648-205G)	n=75 Yucatan Swine	1X, 3X, excipient only, 2X overlap, POBA (control)	3.00 x 15 3.50 x 15 3.00 x 40 (overlap)	ISR: 3d, 30d, 90d, 180d de novo: 3d, 30d, 90d, 180d, 270d	Device Performance, Quantitative Angiography, Animal Health, Histopathology and Pathology	Yes
Safety Study Confirmatory (APS SEB008-IS07)	n=19 Yorkshire Cross Domestic Swine	1X, POBA (control)	3.00 x 20	de novo: 30d, 90d	Animal Health, Quantitative Angiography, Histopathology and Pathology	Yes

Study ID	Number & Animal Type	Local Drug Dose	Balloon Size (mm x mm)	Time Points	Major Endpoints	Endpoints Met
Embolitic Safety APS (SEB009-IS07)	n=6 Yorkshire Cross Domestic Swine	3X, POBA (control)	3.00 x 20	30d	Animal Health, Quantitative Angiography, Histopathology and Pathology	Yes
Embolitic Safety (100664590)	n=12 Yorkshire Cross Domestic Swine	5X, POBA (control)	3.00 x 40 3.50 x 40	28d	Animal Health, Quantitative Angiography, Histopathology and Pathology	Yes
PK Study (CR 2649-205G)	n=51 Yucatan Mini Swine	1X	3.00 x 15	de novo: 1h, 6h, 1d, 3d, 7d, 14d, 30d, 60d, 90d, 105d ISR: 1h, 1d, 30d, 60d	Plasma and Tissue Analysis	Yes

The primary animal safety study, CR 2648-205, demonstrated the following:

- Successful delivery of the device to the target treatment location without major procedural or device related complications, such as acute thrombosis, major bleeding, or flow-limiting dissection.
- All but one treated animals survived until scheduled euthanasia; one animal died on Day 0 due to complications during the balloon treatment. Cause of death was attributed to the balloon procedure and not a direct result of the SELUTION DEB device.
- No thrombosis was observed after treatment on any of the devices evaluated.
- All treated arteries were evaluated with no observations of aneurysm, dissection, lumen narrowing in the non-treated region, or thrombosis.
- The primary safety study identified deep granulomatous inflammation observed inconsistently across all test and control groups, including animals treated with PTCA balloon angioplasty
 - A second safety study, SEB008-IS07, was performed to address this and no granulomas or deep inflammation were observed for any group at any time point.
- The downstream embolic studies showed no abnormalities suggestive of drug, embolic, and/or particulates activity in the arterioles in any of heart/myocardium sections examined.

The preclinical PK study (CR-2649-205G) demonstrated effective drug delivery and uptake into arterial tissues at the therapeutic dose of 1.0 µg/mm² with no evidence of drug toxicity demonstrated as follows:

- Sirolimus was detectable in blood as early as 3 minutes after deployment. The maximum median concentration was reached after 6 hours. After 2 weeks, no sirolimus was quantifiable in blood.
- In the treated arteries, the maximum median sirolimus concentration was reached 1 hour after balloon deployment with a medium C_{max} of 1.10 ng/mL. Sirolimus was undetectable in the treated artery tissue at 90 days.
- Sirolimus distributed into some non-target, peripheral tissues, with the highest median concentration in the left caudal lobe of the lung. With the exception of the lung, no sirolimus was quantifiable in the non-target peripheral tissues after 60 days. Sirolimus was no longer detectable in the lungs at 105 days. Animals were monitored up to 270 days and there was no evidence of systemic or local tissue toxicity.
- The PK profiles of SELUTION DEB in treated vessel, blood, and downstream tissues and organs were similar between the de novo and in-stent restenosis animal models. Based on this data, the de novo model was found to be sufficient to represent and predict the paclitaxel PK profiles and arterial concentrations in an in-stent restenosis model.

Pharmacokinetic data demonstrated localization of sirolimus with limited systemic and non-target tissue exposure. Histopathology data demonstrated an acceptable drug dose and embolic load safety margin for the intended therapeutic dose of 1.0 µg/mm² and range of allowable balloon sizes.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study, SELUTION4ISR, to establish a reasonable assurance of safety and effectiveness of the SELUTION DEB in patients with coronary in-stent restenosis (ISR). The study was conducted in the United States (US), Canada, Brazil, Belgium, France, Italy, and the Netherlands under IDE # G220237. 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 July 6, 2020 and July 16, 2024. The database for this PMA reflected data collected through August 15, 2025 and included 418 patients. There were 48 enrolling investigational sites: 34 sites in the United States, 1 site in Belgium, 2 sites in Brazil, 1 site in Canada, 4 sites in France, 3 sites in Italy, and 3 sites in the Netherlands.

The SELUTION4ISR Study was a prospective, multicenter, randomized, single-blind, noninferiority clinical study to assess the safety and effectiveness of the SELUTION DEB as compared to the standard of care (described below) in patients with ISR.

The study was designed to enroll 418 randomized patients (including 60 subjects in an angiographic and optical coherence tomography [OCT] sub-study), stratified by study center, drug-eluting stent (DES) or bare metal stent (BMS) ISR, and whether there were currently one (first stent restenosis) or two (second stent restenosis) implanted stent layers at the target lesion. Randomization occurred in a 1:1 ratio to receive the SELUTION DEB or standard of care (SOC). Patients randomized to the standard of care were treated with either an FDA-approved zotarolimus- or everolimus-eluting stent or with plain balloon angioplasty (POBA) without stenting.

The intent of including POBA as an option in the SOC arm was to ensure patients with lesions with clinical justification for avoiding implantation of another stent could be enrolled in the study, particularly those with two existing implanted stent layers. The protocol stated that POBA was an acceptable alternative to stenting if clinically justified, but investigator justifications were not required to be recorded. Investigators were required to declare which SOC option they would use prior to randomization. A maximum of 20% of patients randomized to SOC were allowed to be treated with POBA. At the time of the protocol approval, in the US, no DCBs were approved for use in coronary applications.

The trial was designed to assess the non-inferiority of the SELUTION DEB compared to the current SOC with respect to the primary endpoint of 12-month target lesion failure (TLF), defined as cardiac death, target vessel myocardial infarction (MI), or clinically-driven target lesion revascularization (TLR).

Statistical assessment for the primary hypothesis was conducted using a statistical test for non-inferiority of proportions based on posterior probability. The criterion for success was based on the posterior probability of the alternative hypothesis (i.e., of noninferiority being met).

The sample size was determined using the following assumptions:

- A true 12-month TLF rate of 12% for both study arms
- A true 12-month TLF rate of 9% in patients with one layer of previous stent in both DES and SELUTION DEB treatment groups
- 80% DES use and 20% POBA use in the SOC
- An absolute non-inferiority margin of 10%
- Posterior probability of 97.5% to meet the primary endpoint alternative hypothesis
- Posterior probability of 95% to meet the hypothesis-driven secondary endpoint.

A total of 396 patients had 84% power to reject the primary endpoint null hypothesis at the final analysis. To account for loss to follow-up (expected to be approximately 5%), a total of 418 patients were required to be randomized.

The non-inferiority margin of 10% was selected to maintain at least 50% of the absolute risk difference between DES and POBA based on a meta-analysis of TLF rates from historical trials of subjects with ISR treated with DES or POBA.

An angiographic core laboratory and optical coherence tomography (OCT) core laboratory were used for independent analysis of data. A Data Safety Monitoring Board

(DSMB) had the responsibility to monitor safety aspects of the study. A Clinical Events Committee (CEC) developed specific criteria for categorization of clinical events and clinical endpoints in the trial and adjudicated events according to these criteria.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the SELUTION4ISR study was limited to patients who were ≥ 18 years with no chance of being pregnant who presented with a chronic coronary syndrome such as documented stable or unstable angina or stabilized non-ST elevated myocardial infarction (STEMI) whose clinical history indicated treatment with PCI and for whom an intervention was planned. Subjects also needed to be eligible for dual antiplatelet therapy (DAPT) with aspirin plus clopidogrel, prasugrel, or ticagrelor. Patients should have had a life expectancy > 1 year in opinion of investigator and needed to be willing and able to provide informed consent and comply with study procedures and required follow-up evaluations.

To be enrolled in the study, these patients also needed to meet the following imaging criteria. The target lesion must be within a native coronary artery or major branch < 26 mm in length with a reference vessel diameter (RVD) ≥ 2.00 mm and ≤ 4.50 mm. The lesion must be within a previously placed BMS or DES which is 50-99% restenosed, and the lesion must not extend further than 5 mm beyond either the proximal or distal edge of the stent. Up to two non-target lesions in non-target vessels could be treated, but successful PCI of the non-target lesions must be completed before treatment of the target lesion. Successful PCI was defined as no greater than 30% residual stenosis based on the operator's visual estimate, no dissection greater than National Heart, Lung, Blood Institute (NHLBI) type C, and Thrombolysis in Myocardial Infarction (TIMI) grade flow in the non-target lesion > 2 . The target lesion must be successfully pre-dilated/pre-treated, defined as dilation or pre-treatment that achieves stent expansion of approximately 80% of the distal RVD (at the discretion of the investigator) based on intravascular ultrasound (IVUS)/optical coherence tomography (OCT) and no greater than 30% residual stenosis by visual estimate and no dissection greater than NHLBI type C. TIMI grade flow in the target lesion must be > 2 .

Patients were not permitted to enroll in the SELUTION4ISR study if they met any of the following clinical or imaging exclusion criteria:

Clinical Exclusion Criteria

1. Known hypersensitivity or allergy to sirolimus or other pharmacologic agents required for the procedure.
2. STEMI within 30 days.
3. Planned treatment of additional lesions in the target vessel, or more than two non-target lesions within non-target vessels, during the index procedure.
4. Target lesion located within a bifurcation with planned treatment of side branch vessel.
5. More than two layers of stent present at any segment of the target lesion.
6. Any previous vascular brachytherapy treatment of target vessel, or planned to undergo brachytherapy at index procedure.
7. Previous PCI of the target vessel within 30 days.

8. Planned PCI of a non-target vessel, or a non-target lesion in the target vessel, within 30 days of randomization.
9. Chronic renal insufficiency (dialysis dependent, or glomerular filtration rate [GFR] ≤ 30 ml/min/1.73 m² within 30 days of index procedure) or undergone renal transplantation.
10. Acute renal insufficiency confirmed by 50% increase of serum creatinine within 48 hours before procedure and/or decrease in urine output.
11. History of active peptic ulcer or gastrointestinal bleeding within prior 6 months or other inability to comply with the recommended duration of DAPT.
12. Pregnant, breast-feeding, or not using appropriate contraceptives to avoid becoming pregnant.
13. Documented left ventricular ejection fraction (LVEF) <25%.
14. Currently participating in another investigational drug or device study that has not completed primary endpoint follow-up.

Imaging Exclusion Criteria

1. Target lesion is a total occlusion or has evidence of thrombus.
2. Target lesion involves an unprotected left main coronary artery.
3. Target lesion has >30% residual stenosis by visual estimate or dissection greater than NHLBI type C after pre-dilation/pre-treatment.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at hospital discharge, 30 days, 6 months, 1 year, and then annually between 2 and 5 years post-procedure.

Pre-procedure, patients were assessed for medical history, physical exam, angina status, complete blood count, kidney function (using serum creatinine), cardiac enzymes, COVID-19 status, cardiac rhythm (using electrocardiogram (ECG)), and use of cardiovascular and diabetic medications. Post-procedure, the objective parameters measured during the study included angina status, cardiac rhythm, cardiac enzymes (pre-discharge only), and use of cardiovascular and diabetic medications. Patients participating in the imaging sub-study were assessed using angiography and IVUS/OCT one year post-procedure. Adverse events and clinical endpoints were monitored and recorded at all visits. The schedule of pre-procedure and post-procedure evaluations is included in **Table 8** below.

Table 8: Evaluation and Data Collection Time Points

Assessment	Screening / Baseline		Index Procedure	Post-Procedure / Discharge	1 Month ± 10 Days	6 Months ± 14 Days	12 Months ± 30 Days	2, 3, 4, 5 Years ± 60 Days	Un-scheduled Visit
	Within 7 days Prior to Procedure	Within 24 hours Prior to Procedure			Clinic Visit	Clinic or Telephone Visit	Clinic Visit	Clinic or Telephone Visit	
Informed consent form	X								
Demographic, medical, and cardiac history	X								
Physical examination	X								
Angina status	X			X	X	X	X	X	X
CBC	X								
Creatinine	X								
CKMB or troponin T ¹		X		X					X ³
Pregnancy test	X								
COVID-19 status (if available)		X		X	X	X	X	X	X
ECG		X		X			X		X ³
Coronary angiography			X				X ²		X ³
IVUS/OCT			X						R
OCT (imaging sub-group only)			X ²				X ²		
AE/SAE monitoring			X	X	X	X	X	X	X
Device Deficiency			X						
Concomitant Medication ⁴		X		X	X	X	X	X	X

AE: adverse event; CBC: complete blood count; CKMB: creatine kinase-muscle/brain; ECG: electrocardiogram; IVUS: intravascular ultrasound; OCT: Optical coherence tomography; R: recommended; SAE: serious adverse event.

¹ CKMB or Troponin T preferred (Troponin I was not accepted after CIP Rev 7, adopted August 3, 2021). Obtained at baseline and 4-24 hours post-procedure; if the biomarker was elevated, then repeat levels at 4-6 hours were obtained to assess the peak value.

² Imaging subset only. Required after 12-month clinical follow-up completed. May be performed up to 30 days after clinical follow-up was completed, but not before clinical follow-up. However,

patients who underwent clinically indicated angiography after 6 months (180 days) were considered compliant and did not require repeat 12-month angiography.

³ Obtained for repeat visits where ischemic event was suspected.

⁴ All cardiovascular and diabetic medications administered were recorded from 24 hours pre-procedure through the 12-month follow-up assessment. Use of antiplatelet/anticoagulant therapy was recorded throughout the 5-year follow-up period.

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

3. Clinical Endpoints

The primary endpoint, which included components for both safety and effectiveness, is the 12-month rate of target lesion failure (TLF) defined as a composite of:

- Cardiac death
- Target vessel myocardial infarction (MI)
- Clinically-driven target lesion revascularization (TLR)

MI included spontaneous (Type 1) MI using the 4th Universal Definition of Myocardial Infarction (UDMI) and peri-procedural MI using the Society for Cardiac Angiography and Intervention (SCAI) definition. CK-MB and troponin T were the preferred cardiac biomarkers.

An additional safety and effectiveness composite hypothesis-driven secondary endpoint, which was to be evaluated if the primary endpoint was met, was the incidence of TLF at 12 months comparing the SELUTION DEB arm to the DES cohort of the SOC arm among patients with one previous layer of stent.

With regards to safety, additional endpoints included all-cause death, cardiovascular death, MI, stent thrombosis per Academic Research Consortium (ARC) definitions, and bleeding (to 12 months).

With regards to effectiveness, additional endpoints included device, lesion, and procedural success, TLR, and target vessel revascularization (TVR).

With regard to success/failure criteria, the study was considered a success if the SELUTION DEB was shown to be non-inferior to the SOC control for the primary endpoint of TLF at one year.

A statistical test for noninferiority of proportions based on posterior probability was to be used to test the following hypotheses:

$$\begin{aligned}H_0: \text{TLF}_{\text{DEB}} - \text{TLF}_{\text{SOC}} &\geq \delta \\H_1: \text{TLF}_{\text{DEB}} - \text{TLF}_{\text{SOC}} &< \delta\end{aligned}$$

where TLF_{DEB} and TLF_{SOC} are the 12-month TLF rates in the SELUTION DEB group and comparator SOC group, respectively, and $\delta = 10\%$ is the noninferiority margin. A

uniform prior was assumed for each group. The SELUTION DEB was to be declared noninferior to the SOC group if the posterior probability of the alternative hypothesis H_1 was greater than 97.5%.

The primary analysis set for the primary endpoint was the per-protocol (PP) analysis population. Results are presented for this population unless otherwise specified.

B. Accountability of PMA Cohort

At the time of database lock, of 418 patients enrolled in the PMA study, 94.7% (396/418) of patients were eligible for analysis at the completion of the primary endpoint, the 12-month post-procedure visit. **Table 9** and **Figure 5** show patient disposition from randomization through 12 months for the intent-to-treat (ITT) population (all enrolled patients).

Table 9: Patient Disposition Through 12 Months

	SELUTION SLR PTCA DEB (N=210)	SOC (N=208)	Total (N=418)
All Randomized	210	208	418
Active ¹	197	199	396
Discontinued ²	13	9	22
Withdrew consent	1	1	2
Death	9	5	14
Lost to follow-up	1	0	1
Other ³	2	3	5
1. A patient is active if they have had their procedure, have not discontinued the study, and are alive. 2. Within one year of procedure date. 3. “Other” includes “site closing and voluntarily withdrawing subject(s)” and “withdrawal with consent for continued electronic medical record and public records review.”			

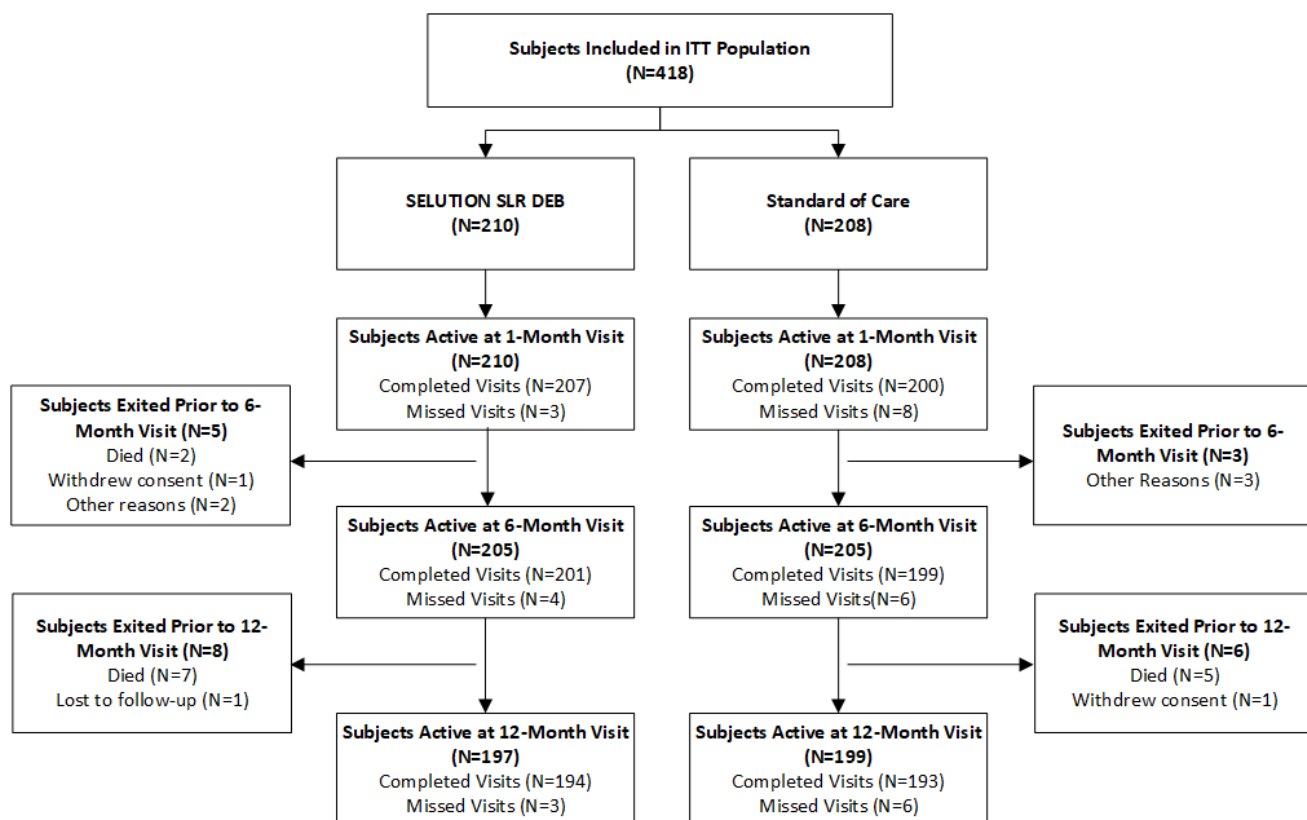
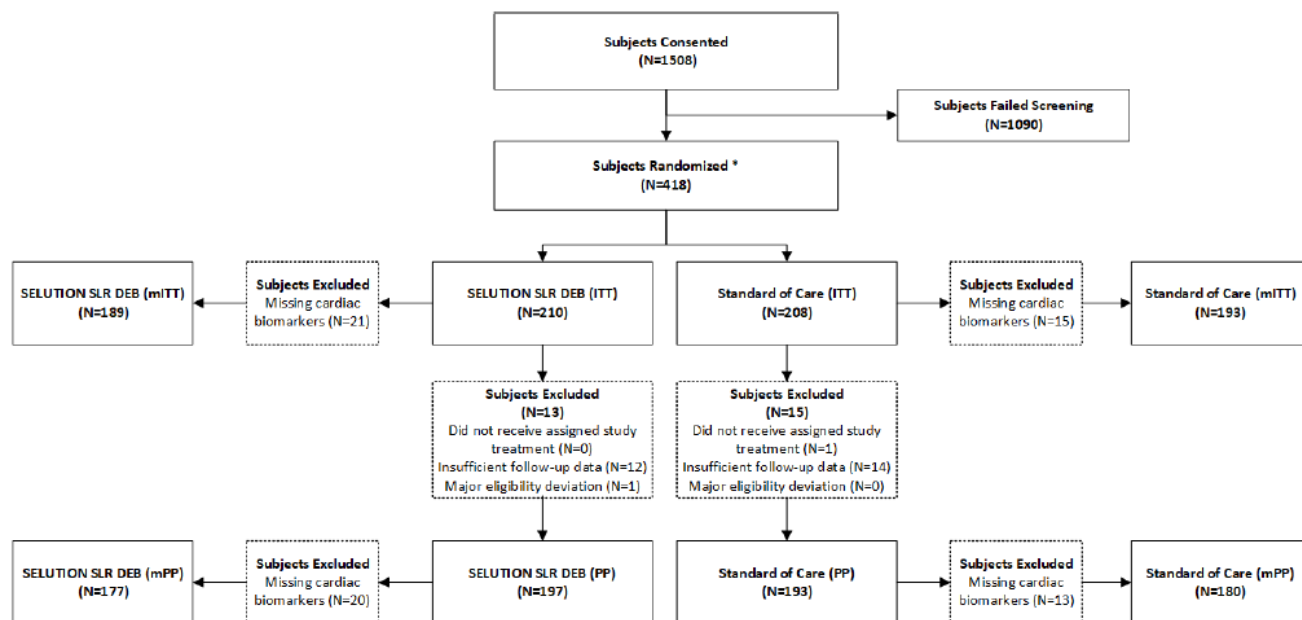


Figure 5: Patient Disposition Flow Diagram



*Two non-randomized subjects were treated with the investigational device. These subjects were not enrolled in the study and followed for safety only.

Figure 6: Subject Enrollment Flow Diagram

C. Study Population Demographics and Baseline Parameters

The known demographics of the study population are typical for an interventional cardiovascular study performed in the US; information on patient race was not collected. **Table 10** presents demographics for the PP analysis set. The treatment arms were well-balanced with no significant differences in any parameters, except for the prevalence of peripheral vascular disease, which was significantly higher in the SELUTION SLR PTCA DEB group compared with the SOC group (19.80% vs. 11.40%; $p=0.026$). The mean patient age was 69 years and 22% of patients were female.

Given the lower enrollment of female patients and the unknown race of the study participants, a post approval surveillance study will be initiated for an all-comers patient population with specific focus and analyses for these groups. See **Section XIV** below for details on the post-approval surveillance study.

Table 10: Patient Demographics (PP)

Patient Characteristic	SELUTION (N=197)	SOC (N=193)	P-value ¹
Age (years) Mean $\pm$ SD (N)	68.2 $\pm$ 9.0 (197)	69.6 $\pm$ 9.0 (193)	0.13
>75	21.3% (42/197)	27.5% (53/193)	0.19
Sex			
Female	18.3% (36/197)	26.0% (50/193)	0.09
Ethnicity			0.06
Hispanic or Latino	4.6% (9/197)	7.8% (15/193)	
Non-Hispanic or non-Latino	70.0% (137/197)	75.1% (145/193)	
Not disclosed	25.9% (51/197)	17.1% (33/193)	
1. P-value calculated using ANOVA for continuous variables and Fisher's exact test for categorical variables.			

Table 11 shows the baseline clinical characteristics and cardiac history of the patient population. Approximately 43% of patients had diabetes, 48% had a history of MI, and 33% presented with acute coronary syndrome (ACS). In general, baseline clinical characteristics were comparable between the SELUTION DEB and SOC control groups.

Table 11: Baseline Clinical Characteristics and Cardiac History (PP)

Baseline Characteristic	SELUTION (N=197)	SOC (N=193)	P-value
Body Mass Index (kg/m ²) (Mean ± SD (N))	28.8 ± 5.5 (196)	29.4 ± 5.5 (193)	0.27
Clinical Characteristics			
Smoking History			0.896
Current Smoker	15.2% (30/197)	14.0% (27/193)	
Ex-Smoker	42.1% (83/197)	41.4% (80/193)	
Diabetes	43.1% (85/197)	42.5% (82/193)	0.92
Renal Insufficiency	16.8% (33/197)	11.4% (22/193)	0.15
Undergoing Dialysis	0.5% (1/197)	1.0% (2/193)	0.62
Hyperlipidemia	90.9% (179/197)	88.6% (171/193)	0.51
Hypertension	92.9% (183/197)	93.3% (180/193)	1.00
Peripheral Vascular Disease	19.8% (39/197)	11.4% (22/193)	0.03
History of Stroke or TIA	9.6% (19/197)	6.2% (12/193)	0.26
Cardiac History			
Prior MI	47.7% (94/197)	48.2% (93/193)	1.00
Prior STEMI	21.8% (43/197)	19.2% (37/193)	0.46
Prior PCI	100% (197/197)	100.0% (193/193)	1.00
Treated with DES	90.4% (178/197)	95.8% (185/193)	0.07
Treated with Bare Metal Stent (BMS)	19.3% (38/197)	13.0% (25/193)	0.10
Prior CABG	22.3% (44/197)	20.7% (40/193)	0.71
Baseline Cardiac Status			
Angina Status			0.98
Stable Angina	62.4% (123/197)	61.7% (119/193)	
Unstable Angina	30.5% (60/197)	30.0% (58/193)	
No Angina (Silent Ischemia)	7.1% (14/197)	8.3% (16/193)	
CCS classification			0.24
I	15.2% (30/197)	18.6% (36/193)	
II	35.0% (69/197)	26.4% (51/193)	
III	34.0% (67/197)	39.4% (76/193)	
IV	8.6% (17/197)	6.7% (13/193)	
ACS ²	34.5% (68/197)	32.1% (62/193)	0.67
2. Defined as: Patients with unstable angina or any elevated cardiac enzymes at baseline (any pre-procedure CK, CKMB, or troponin out of normal range).			

Baseline lesion characteristics as assessed by the angiographic core laboratory are summarized in **Table 12**. Most characteristics were similar between arms, including the presence of two-layer in-stent restenosis (22% in both arms). Severe calcification was observed in 2.59% (5/193) of lesions treated with SOC; no lesions randomized to the SELUTION DEB arm had severe calcification. The number of severely calcified lesions in this study was too small to draw meaningful conclusions about the impact of calcification on the study results.

Table 12: Baseline Target ISR Lesion Characteristics as Determined by the Angiographic Core Laboratory (PP)

Measure	SELUTION (N=197)	SOC (N=193)	P-value ¹
Number of Existing Stent Layers			0.90
One	77.7% (153/197)	78.2% (151/193)	
Two	22.3% (44/197)	21.8% (42/193)	
Target Lesion Vessel			0.30
RCA	34.5% (68/197)	33.7% (65/193)	
LAD	39.6% (78/197)	39.4% (76/193)	
LCX	25.4% (50/197)	23.3% (45/193)	
Left Main	0.5% (1/197)	3.1% (6/193)	
Minimal Lumen Diameter (mm) (Mean ± SD (N))	0.9 ± 0.35 (108)	0.9 ± 0.37 (102)	0.73
RVD (mm) (Mean ± SD (N))	2.5 ± 0.48 (106)	2.6 ± 0.50 (101)	0.06
RVD			0.831
RVD ≤ 2.75 mm	67.0% (132/197)	65.8% (127/193)	
RVD > 2.75 mm	33.0% (65/197)	34.2% (66/193)	
% Diameter Stenosis (Mean ± SD (N))	64.6 ± 12.0 (106)	65.1 ± 11.7 (101)	0.76
Pre-Procedure TIMI Flow			0.21
0	0.0% (0/197)	1.0% (2/193)	
1	0.0% (0/197)	0.5% (1/193)	
2	4.1% (8/197)	2.1% (4/193)	
3	94.9% (187/197)	94.8% (183/193)	
Severe Calcification	0.0% (0/197)	2.6% (5/193)	0.02
Vessel Angulation			0.19
None or Mild (<45 degrees)	84.8% (167/197)	88.6% (171/193)	
Moderate (≥45 - <90 degrees)	14.2% (28/197)	9.8% (19/193)	
Severe (≥90 degrees)	0.5% (1/197)	0.0% (0/193)	
Vessel Tortuosity			1.00
None or Mild	98.5% (194/197)	99.5% (192/193)	
Moderate	0.5% (1/197)	0.0% (0/193)	
Bifurcation Lesion	37.6% (74/197)	35.8% (69/193)	0.75
Eccentric	55.3% (109/197)	60.1% (116/193)	0.35
Length, mm			
Mean ± SD (N)	12.4 ± 6.0 (196)	11.9 ± 5.6 (190)	0.42
Length			0.72
Length ≤ 26 mm	97.0% (191/197)	96.9% (187/193)	
Length > 26 mm	2.5% (5/197)	1.6% (3/193)	
1. P-values calculated using ANOVA for continuous variables and Fisher's exact test for categorical variables.			

Table 13 presents the procedural characteristics for the PP analysis set. Differences between study groups were seen in procedure time, study device length, study device inflation pressure, study device inflation time, prevalence of post-dilatation, post-procedure reference vessel diameter, post-procedure minimal lumen diameter, and post-procedure residual stenosis. Most differences can be attributed to the fundamental procedural differences between stenting and balloon angioplasty.

Procedures in the SELUTION DEB group were shorter on average (54 minutes) compared with the SOC group (60 minutes). Lesion lengths were similar across groups and the average SELUTION DEB device length (21.6 ± 6.0 mm) was similar to the average DES device length (20.4 ± 7.8 mm). The average SELUTION DEB device length was longer than the plain balloon angioplasty device length (15.2 ± 3.6 mm). This is not unexpected, as BA is primarily used for mechanical dilatation of the focal restenotic areas of a lesion while a drug-eluting balloon is designed to apply drug up to 5 mm beyond the lesion. The average inflation pressure was 10.2 ± 3.7 atm in the SELUTION DEB group compared to 16.1 ± 5.6 atm in the SOC group. This is also not unexpected as the rated burst pressure (RBP) of the SELUTION DEB is 12 atm while the RBPs of most control devices was greater. The mean inflation time was 69.2 ± 28.1 seconds for the SELUTION DEB group and 22.9 ± 19.8 seconds for the SOC group. A longer inflation time for the SELUTION DEB group was recommended in the clinical investigation protocol (minimum inflation time of 30 seconds, recommended inflation time of 60 seconds).

Post-dilatation was performed for 1.5% of SELUTION SLR PTCA DEB patients and 48.2% of SOC patients; post-dilation in patients treated with SELUTION occurred only when bailout stenting was needed. All bailout stents were placed due to persistent dissection $\geq$ NHLBI grade C.

Table 13: Procedural Characteristics (PP)

Characteristic	SELUTION (N=197)	SOC (N=193)	P-value ¹
Non-target lesion(s) treated	10.7% (21/197)	11.4% (22/193)	0.87
Procedure Time (min) (Mean $\pm$ SD (N))	54.0 $\pm$ 23.8 (197)	60.2 $\pm$ 31.4 (193)	0.03
Pre-dilatation device ²			0.43
PTCA	87.3% (172/197)	83.9% (162/193)	
Cutting Balloon	28.4% (56/197)	35.8% (69/193)	
Scoring Balloon	15.7% (31/197)	17.1% (33/193)	
Number of SELUTION devices used			
1	90.4% (178/197)	N/A	
2	8.1% (16/197)	N/A	
3	1.0% (2/197)	N/A	
Number of control DES used			
1	N/A	90.9% (140/154)	
2	N/A	8.4% (13/154)	
3	N/A	0.6% (1/154)	
Number of control POBA devices used			

Characteristic	SELUTION (N=197)	SOC (N=193)	P-value ¹
1	N/A	84.6% (33/39)	
2	N/A	10.3% (4/39)	
3	N/A	2.6% (1/39)	
4	N/A	2.6% (1/39)	
Treatment device diameter (mm) ³ (Mean ± SD (N))	3.3 ± 0.4 (197)	3.3 ± 0.6 (193)	1.00
Treatment device length (mm) ³ (Mean ± SD (N))	21.6 ± 6.0 (197)	19.3 ± 7.5 (193)	<0.001
Inflation pressure (atm) ⁴ (Mean ± SD (N))	10.2 ± 3.7 (197)	16.1 ± 5.6 (191)	<0.001
Inflation time (s) ⁵ (Mean ± SD (N))	69.2 ± 28.1 (197)	22.9 ± 19.8 (190)	<0.001
Post-dilatation performed after stenting	1.5% (3/197)	48.2% (93/193)	<0.001
Bailout stenting occurred	1.5% (3/197)	0.5% (1/193)	0.62
1. P-value calculated using ANOVA for continuous variables and Fisher's exact test for categorical variables. 2. A patient may have had more than one type of pre-treatment device used, so subgroups may sum to more than total. 3. If multiple treatment devices were present in the dataset, the final entry was used to summarize device diameter and length. 4. If multiple treatment devices were present in the dataset, the maximum inflation pressure (atm) was used. 5. If multiple treatment devices were present in the dataset, the inflation times were summed to present total inflation time.			

Use of dual antiplatelet therapy (DAPT; aspirin plus a P2Y₁₂ inhibitor) at baseline (pre-procedure), one month, six months, and one year post-procedure is shown in Table 11. Although most patients in the SOC group received a stent, the percentage of patients treated with DAPT was similar between the two groups at each time point.

Table 14: Dual Antiplatelet Medication Usage Through 1 Year, ITT (N=390) Procedural Characteristics (PP)

Medication	SELUTION (N=197)	SOC (N=193)
DAPT (Aspirin and one of Clopidogrel, Prasugrel, Ticagrelor, Ticlopidine)		
Baseline	56.4% (111/197)	57.0% (110/193)
1 month follow-up	75.3% (149/197)	82.9% (160/193)
6 month follow-up	71.1% (140/197)	76.7% (148/193)
1 year follow-up	60.4% (119/197)	62.7% (121/193)

D. Safety and Effectiveness Results

The primary analysis of safety and effectiveness was based on the PP cohort of the 390 patients available for the 12-month evaluation of target lesion failure.

The study primary endpoint was met. SELUTION DEB was noninferior to SOC as the posterior probability of noninferiority was above the defined success threshold of 97.5% in the PP population. As shown in **Table 14**, 16.2% (32/197) of patients treated with SELUTION DEB and 14.5% (28/193) of the SOC treated subjects experienced TLF by 1 year. The difference between the two groups was 1.7% with a corresponding 95% Bayesian credible interval of (-5.5%, 8.9%). The upper bound of the credible interval (8.9%) was therefore below the predefined noninferiority margin of 10%.

Table 14: Primary Endpoint Results

12-Month TLF	SELUTION (N=197)	SOC (N=193)	Difference [95% Credible Interval]	Posterior Probability of Non-inferiority
PP	16.2% (32/197)	14.5% (28/193)	1.1% [-5.5%,8.9%]	98.80%

Figure 7 depicts Kaplan Meier curves illustrating the percentage of patients free from TLF over time in each treatment group.

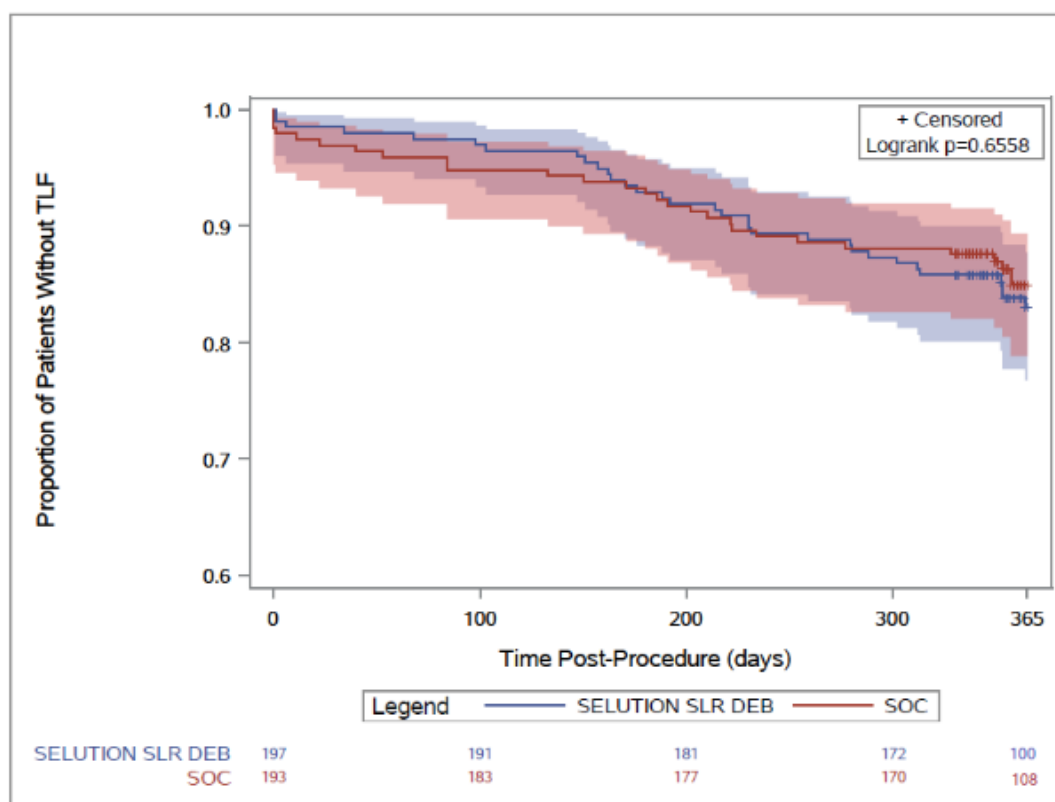


Figure 7: Kaplan-Meier Analysis (PP)

Intention-to-treat (ITT) analysis was also performed, and the result again demonstrated noninferiority. Sensitivity analysis of the primary endpoint, and multiple analyses for missing data, were conducted and confirmed the robustness of the primary analysis set findings. Some data was missing at 12 months follow-up for 5.7% (12/210) of patients in the SELUTION DEB group and 6.7% (14/208) of patients in the SOC group.

Sensitivity analyses were conducted for the primary endpoint using a Bayesian analysis on the mPP cohort and on the ITT cohort after using a logistic regression model to account for the missing data. All analyses found that the SELUTION DEB was non-inferior to the SOC with a posterior probability of non-inferiority of >97%.

The hypothesis-driven secondary endpoint, incidence of TLF at 12 months comparing the SELUTION DEB arm to the DES cohort of the SOC arm among the cohort of patients with one previous layer of stent, was not met. As shown in **Table 15**, in the SELUTION DEB group, 14.2% (22/155) of patients with one previous stent layer experienced TLF within 12 months, compared to 6.5% (9/138) of DES patients with one previous stent layer in the SOC control group. The difference between the two groups was 7.5% with a corresponding 95% Bayesian credible interval of (0.6%, 14.6%). The posterior probability of non-inferiority was 76.1%, which was below the predefined success threshold of 95%. Similar results were seen in the ITT analysis population.

Table 15: Hypothesis-Driven Secondary Endpoint

12-Month TLF	SELUTION (1 Previous Stent Layer) (N=155)	DES (1 Previous Stent Layer) (N=138)	Difference [95% Credible Interval]	Posterior Probability of Non-inferiority
PP	14.2% (22/155)	6.5% (9/138)	7.5% [0.6%, 14.6%]	76.1%

The intent of this analysis was to directly compare outcomes of the SELUTION DEB to those of implanting an additional DES in patients with ISR. However, as investigators chose whether patients in the SOC arm were treated with DES or POBA, the two groups in this analysis were not randomized against each other. While it was anticipated that POBA would primarily be used to treat patients with more than one previous stent layer, 20 of the 39 patients chosen to be treated with POBA in the SOC group before the POBA enrollment cap was reached had only one previous stent layer.

1. Safety Results

The analysis of safety was based on the PP cohort of 390 patients available for the 12-month evaluation. The key safety outcomes for this study for all currently available timepoints are presented below in **Table 16**. Serious adverse events (SAEs) that were present at a rate of $\geq 0.95\%$ are reported in **Table 17**.

Table 16: Summary of Secondary Safety Endpoints by Timepoint (PP)

Secondary Endpoints	SELUTION (N=197)	SOC (N=193)
In-Hospital		
Death	0.0% (0/197)	0.0% (0/193)
MI	1.5% (3/197)	1.0% (2/193)
Bleeding ¹	2.0% (4/197)	2.6% (5/193)
1-Month Follow-up		
Death	0.0% (0/197)	0.0% (0/193)
MI	2.5% (5/197)	2.6% (5/193)
Bleeding ¹	2.0% (4/197)	3.6% (7/193)
6-Month Follow-up		
Death	0.5% (1/197)	0.0% (0/193)
Cardiovascular death	0.5% (1/197)	0.0% (0/193)
Non-cardiovascular death	0.0% (0/197)	0.0% (0/193)
MI	6.1% (12/197)	4.7% (9/193)
Bleeding ¹	5.1% (10/197)	5.7% (11/193)
1-Year Follow-up		
Death	2.5% (5/197)	1.6% (3/193)
Cardiovascular death	2.0% (4/197)	1.6% (3/193)
Non-cardiovascular death	0.5% (1/197)	0.0% (0/193)
MI	8.1% (16/197)	6.7% (13/193)
Bleeding ¹	7.6% (15/197)	9.3% (18/193)
Stent thrombosis	2.0% (4/197)	2.1% (4/193)
1. Bleeding according to Bleeding Academic Research Consortium (BARC) classification 2-5.		

Adverse effects that occurred in the PMA clinical study:

There were 432 adverse events reported in 143 patients in the SELUTION DEB group, compared to 395 adverse events reported in 134 patients in the SOC control group through 12 months of follow up. The frequency and nature of adverse events observed in the SELUTION DEB group were similar to those observed for the SOC control group.

Serious adverse events (SAEs) that occurred in the SELUTION4ISR study impacting $\geq 1.0\%$ of patients in either group are presented in **Table 17**. Serious adverse events are defined as events that resulted in death, were life-threatening, required inpatient hospitalization or caused prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, or required intervention to prevent life-threatening illness or injury or permanent impairment. Adverse events were coded using MedDRA preferred terms. Only categories of serious adverse events occurring at a rate of $\geq 1.0\%$ in either treatment group are reported; thus, the listed events may not add up to the total amount in each group or overall.

Table 17: Patients with Serious Adverse Events Through 1 Year with Event Rate $\geq 1.0\%$ (ITT)

SAEs to 365 Days	MedDRA High-Level Group Term	MedDRA Preferred Term	SELUTION (N=210)	SOC (N=208)
Any SAE	Total	Total	37.1% (78/210)	43.8% (91/208)
Cardiac disorders	Total	Total	21.9% (46/210)	24.0% (50/208)
	Coronary artery disorders	Total	18.1% (38/210)	17.8% (37/208)
		Angina pectoris	5.7% (12/210)	8.2% (17/208)
		Acute myocardial infarction	7.1% (15/210)	5.3% (11/208)
		Angina unstable	3.8% (8/210)	1.9% (4/208)
		Arteriosclerosis coronary artery	1.0% (2/210)	2.4% (5/208)
		Coronary artery disease	1.0% (2/210)	1.9% (4/208)
		Myocardial infarction	1.0% (2/210)	1.0% (2/208)
		Coronary artery dissection	1.0% (2/210)	0.5% (1/208)
		Coronary artery stenosis	1.0% (2/210)	0.5% (1/208)
		Myocardial ischaemia	1.0% (2/210)	0.0% (0/208)
	Heart failures	Total	4.8% (10/210)	2.4% (5/208)
		Cardiac failure congestive	1.9% (4/210)	1.4% (3/208)
		Cardiac failure	1.9% (4/210)	0.5% (1/208)
		Cardiac failure acute	1.0% (2/210)	0.5% (1/208)
		Cardiac failure chronic	1.0% (2/210)	0.0% (0/208)
	Cardiac arrhythmias	Total	4.8% (10/210)	6.7% (14/208)
		Atrial fibrillation	3.8% (8/210)	1.4% (3/208)
		Ventricular tachycardia	0.0% (0/210)	2.4% (5/208)
		Cardiac arrest	0.5% (1/210)	1.0% (2/208)
		Atrial flutter	0.0% (0/210)	1.0% (2/208)
		Atrioventricular block complete	0.0% (0/210)	1.0% (2/208)
		Bradycardia	1.0% (2/210)	0.0% (0/208)
	Cardiac valve disorders	Total	0.0% (0/210)	1.0% (2/208)
		Aortic valve stenosis	0.0% (0/210)	1.0% (2/208)

SAEs to 365 Days	MedDRA High-Level Group Term	MedDRA Preferred Term	SELUTION (N=210)	SOC (N=208)
Respiratory, thoracic and mediastinal disorders	Total	Total	6.2% (13/210)	4.3% (9/208)
	Respiratory disorders NEC	Total	5.2% (11/210)	2.4% (5/208)
		Respiratory failure	2.4% (5/210)	0.5% (1/208)
		Dyspnoea	1.9% (4/210)	0.0% (0/208)
		Acute respiratory failure	0.0% (0/210)	1.4% (3/208)
	Bronchial disorders (excl neoplasms)	Total	1.0% (2/210)	0.5% (1/208)
		Chronic obstructive pulmonary disease	1.0% (2/210)	0.5% (1/208)
Infections and infestations	Total	Total	4.3% (9/210)	4.8% (10/208)
	Infections – pathogen unspecified	Total	2.9% (6/210)	3.4% (7/208)
		Urinary tract infection	1.0% (2/210)	1.4% (3/208)
		Pneumonia	1.0% (2/210)	0.5% (1/208)
		Septic shock	0.5% (1/210)	1.0% (2/208)
	Bacterial infectious disorders	Total	1.9% (4/210)	1.0% (2/208)
	Viral infectious disorders	Total	0.0% (0/210)	1.0% (2/208)
Injury, poisoning and procedural complications	Total	Total	5.2% (11/210)	7.2% (15/208)
	Procedural related injuries and complications NEC	Total	4.8% (10/210)	4.3% (9/208)
		Coronary artery restenosis	0.5% (1/210)	1.4% (3/208)
		Vascular access site haematoma	1.0% (2/210)	0.5% (1/208)
		Vascular access site haemorrhage	0.5% (1/210)	1.0% (2/208)
	Injuries NEC	Total	0.5% (1/210)	1.4% (3/208)
	Bone and joint injuries	Total	0.0% (0/210)	1.4% (3/208)
		Femur fracture	0.0% (0/210)	1.0% (2/208)
General disorders and administration site conditions	Total	Total	6.2% (13/210)	5.3% (11/208)
	General system disorders NEC	Total	2.4% (5/210)	3.8% (8/208)
		Chest pain	1.4% (3/210)	3.4% (7/208)
		Non-cardiac chest pain	1.0% (2/210)	0.0% (0/208)
	Complications associated with device	Total	2.9% (6/210)	1.4% (3/208)
		Vascular stent stenosis	2.4% (5/210)	1.4% (3/208)

SAEs to 365 Days	MedDRA High-Level Group Term	MedDRA Preferred Term	SELUTION (N=210)	SOC (N=208)
Nervous system disorders	Total	Total	4.3% (9/210)	5.3% (11/208)
	Neurological disorders NEC	Total	1.0% (2/210)	3.4% (7/208)
		Syncope	0.5% (1/210)	1.9% (4/208)
	Central nervous system vascular disorders	Total	2.9% (6/210)	1.4% (3/208)
		Cerebrovascular accident	1.9% (4/210)	0.0% (0/208)
	Neuromuscular disorders	Total	1.0% (2/210)	0.0% (0/208)
Gastrointestinal disorders	Total	Total	3.3% (7/210)	4.8% (10/208)
	Gastrointestinal haemorrhages NEC	Total	1.4% (3/210)	1.9% (4/208)
		Rectal haemorrhage	1.0% (2/210)	1.0% (2/208)
		Gastrointestinal haemorrhage	0.0% (0/210)	1.0% (2/208)
	Gastrointestinal stenosis and obstruction	Total	0.5% (1/210)	1.9% (4/208)
		Small intestinal obstruction	0.5% (1/210)	1.9% (4/208)
	Gastrointestinal signs and symptoms	Total	1.0% (2/210)	0.5% (1/208)
Renal and urinary disorders	Total	Total	3.3% (7/210)	3.8% (8/208)
	Renal disorders (excl nephropathies)	Total	2.9% (6/210)	2.4% (5/208)
		Acute kidney injury	1.4% (3/210)	1.9% (4/208)
	Urolithiases	Total	0.5% (1/210)	1.0% (2/208)
		Nephrolithiasis	0.5% (1/210)	1.0% (2/208)
Vascular disorders	Total	Total	4.8% (10/210)	3.4% (7/208)
	Decreased and nonspecific blood pressure disorders and shock	Total	2.4% (5/210)	0.5% (1/208)
		Hypotension	1.4% (3/210)	0.5% (1/208)
		Orthostatic hypotension	1.0% (2/210)	0.0% (0/208)
	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	Total	1.9% (4/210)	1.0% (2/208)
		Aortic stenosis	1.0% (2/210)	0.0% (0/208)
	Vascular hypertensive disorders	Total	0.5% (1/210)	1.0% (2/208)
Investigations	Total	Total	2.4% (5/210)	1.0% (2/208)
	Enzyme investigations NEC	Total	1.4% (3/210)	0.5% (1/208)
		Troponin increased	1.0% (2/210)	0.5% (1/208)

SAEs to 365 Days	MedDRA High-Level Group Term	MedDRA Preferred Term	SELUTION (N=210)	SOC (N=208)
Metabolism and nutrition disorders	Total	Total	2.4% (5/210)	1.0% (2/208)
	Glucose metabolism disorders (incl diabetes mellitus)	Total	1.0% (2/210)	0.5% (1/208)
	Diabetic complications	Total	1.0% (2/210)	0.0% (0/208)
		Diabetic ketoacidosis	1.0% (2/210)	0.0% (0/208)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Total	Total	1.4% (3/210)	1.9% (4/208)
	Gastrointestinal neoplasms malignant and unspecified	Total	1.0% (2/210)	0.0% (0/208)
Blood and lymphatic system disorders	Total	Total	1.4% (3/210)	0.5% (1/208)
	Anaemias nonhaemolytic and marrow depression	Total	1.4% (3/210)	0.5% (1/208)
		Anaemia	1.4% (3/210)	0.0% (0/208)
Surgical and medical procedures	Total	Total	2.4% (5/210)	0.5% (1/208)
	Arterial therapeutic procedures (excl aortic)	Total	1.0% (2/210)	0.0% (0/208)
		Arterial revascularisation	1.0% (2/210)	0.0% (0/208)
Musculoskeletal and connective tissue disorders	Total	Total	1.4% (3/210)	1.0% (2/208)
	Musculoskeletal and connective tissue disorders NEC	Total	1.4% (3/210)	0.5% (1/208)
Skin and subcutaneous tissue disorders	Total	Total	1.0% (2/210)	0.5% (1/208)
	Skin and subcutaneous tissue disorders NEC	Total	1.0% (2/210)	0.0% (0/208)
Eye disorders	Total	Total	0.5% (1/210)	1.0% (2/208)
	Anterior eye structural change, deposit and degeneration	Total	0.0% (0/210)	1.0% (2/208)
		Cataract	0.0% (0/210)	1.0% (2/208)
Psychiatric disorders	Total	Total	1.0% (2/210)	0.0% (0/208)

2. Effectiveness Results

The primary analysis of effectiveness, which was a component of the primary endpoint, was based on the PP cohort of 390 evaluable patients at the 12-month time point as described above. Additional effectiveness outcomes, including components of the primary endpoints as well as procedural endpoints, are presented in **Table 18**.

Patients with available angiographic core lab data were analyzed for device, lesion, and/or procedure success. Device success was defined as attainment of <30% residual stenosis of the target lesion using the assigned study device only. Lesion

success was defined as attainment of <30% residual stenosis of the target lesion using any percutaneous method. Procedure success was defined as the attainment of <30% residual stenosis of the target lesion using the assigned study device only without the occurrence of in-hospital major adverse cardiac events (all-cause death, MI, or clinically driven TLR). Acute success rates were comparable in both groups and as expected in this in-stent restenosis population.

The rate of clinically driven target lesion revascularization (TLR) at 12 months was similar between groups (12.7% versus 12.4% in the SELUTION DEB and SOC arms, respectively.)

Table 18: Summary of Effectiveness Outcomes

	SELUTION SLR PTCA DEB (N=197)	SOC (N=193)
Acute Success		
Device Success	89.9% (152/169)	90.4% (122/135)
Lesion Success	91.1% (154/169)	90.4% (122/135)
Procedure Success	88.8% (150/169)	88.2% (119/135)
Revascularization Events to 1 Month		
TVR	1.0% (2/197)	1.6% (3/193)
TLR	0.5% (1/197)	1.0% (2/193)
Revascularization Events to 6 Months		
TVR	7.1% (14/197)	5.7% (11/193)
TLR	5.1% (10/197)	5.2% (10/193)
Revascularization Events to 1 Year		
TVR	15.8% (31/197)	13.5% (26/193)
TLR	12.7% (25/197)	12.4% (24/193)

Imaging (Angiographic and OCT) Sub-study Results

The trial enrolled 60 of the randomized subjects in an angiographic and optical coherence tomography (OCT) sub-study. Subjects in the imaging sub-study had to meet the same inclusion and exclusion criteria as the main study subjects. The baseline and lesion characteristics of this sub-study were similar to the full study population. At the 12-month follow-up visit, several secondary endpoints were assessed by angiography, including binary angiographic restenosis, in-stent and in-segment percent diameter stenosis, in-stent and in-segment late lumen loss (LLL), and in-stent and in-segment MLD. OCT was used to evaluate neointimal hyperplasia, neo-atherosclerosis, and stent underexpansion (**Table 19**). Binary angiographic restenosis was identified in more patients treated with the SELUTION DEB (31.2%, 10/32) than the SOC control (18.8%, 3/16) although these differences were not statistically significant. Similarly, neoatherosclerosis was detected by OCT in more patients treated with the SELUTION DEB (26.9%, 7/26) than the SOC control (7.7%, 1/13) although these results were likewise not statistically significant.

Table 19: Secondary Imaging Endpoints at 12 Months

Secondary Endpoint	SELUTION SLR PTCA DEB (N=36)	SOC (N=24)
Treated segment percent diameter stenosis Mean +/- SD (N)	37.1 +/- 23.5 (32)	27.7 +/- 18.3 (16)
Binary angiographic restenosis % (n/N)	31.2% (10/32)	18.8% (3/16)
Treated segment late lumen loss (LLL) Mean +/- SD (N)	0.6 +/- 0.6 (32)	0.5 +/- 0.5 (16)
Treated segment minimum lumen diameter (MLD) Mean +/- SD (N)	1.6 +/- 0.6 (32)	1.7 +/- 0.9 (18)
OCT study assessments		
Neointimal hyperplasia	57.7% (15/26)	61.5% (8/13)
Neoatherosclerosis	26.9% (7/26)	7.7% (1/13)
Underexpansion	15.4% (4/26)	23.1% (3/13)

3. Subgroup Analyses

The following baseline characteristics were pre-specified and evaluated for potential association with safety and effectiveness outcomes:

- 2 stent layers ISR vs 1 stent ISR (present in lesion prior to procedure)
- BMS ISR vs. no BMS ISR
- DES ISR vs. no DES ISR
- Diabetes vs. No Diabetes
- RVD ≤ 2.75 mm vs. >2.75 mm
- Lesion length ≤ 26 mm vs. > 26 mm
- Focal vs diffuse lesions
- ISR (< 1 year after stent implant vs > 1 year after stent implant)
- COVID-19 positive vs negative

The following additional baseline characteristics were not pre-specified but were also evaluated for potential association with safety and effectiveness outcomes:

- Age
- Sex
- Ethnicity

Information on patient race was not collected during the study and therefore no presentation of outcomes by race is possible.

The SELUTION4ISR Study was not designed or powered to study safety or effectiveness of the SELUTION SLR PTCA DEB versus SOC in these subgroups, so these analyses are considered hypothesis-generating. The primary endpoint results for

these subgroups are included in **Table 20** below.

Subgroup analyses of the primary endpoint demonstrated no significant interactions with treatment effect.

Table 20: Primary Endpoint Subgroup Analyses (PP)

Subgroup	SELUTION DEB (N=197)	SOC (N=193)	P-value for Interaction ¹
Stent Layers			0.167
1	14.2% (22/155)	10.2% (16/157)	
2	23.8% (10/42)	33.3% (12/36)	
BMS ISR			0.878
Yes	10.5% (4/38)	8.0% (2/25)	
No	17.7% (28/158)	15.6% (26/167)	
DES ISR			0.359
Yes	16.8% (30/178)	15.1% (28/185)	
No	11.1% (2/18)	0.0% (0/8)	
Diabetes			0.492
Yes	25.9% (22/85)	20.7% (17/82)	
No	8.9% (10/112)	9.9% (11/111)	
RVD			0.341
> 2.75mm	16.9% (11/65)	10.6% (7/66)	
≤ 2.75mm	15.9% (21/132)	16.5% (21/127)	
Lesion Length			0.433
> 26mm	20.0% (1/5)	0.0% (0/3)	
≤ 26mm	16.2% (31/192)	14.7% (28/190)	
Lesion Type			0.528
Focal	16.4% (12/73)	17.1% (13/76)	
Diffuse	8.8% (5/57)	14.0% (7/50)	
ISR			0.668
< 1 year	21.7% (13/60)	20.6% (13/63)	
≥ 1 year	14.0% (17/121)	10.7% (13/122)	
Covid-19			N/A
Yes	N/A	0.0% (0/1)	
No	20.6% (7/34)	11.5% (3/26)	
Age			0.513
≤ 75 years	16.1% (25/155)	12.9% (18/140)	
> 75 years	16.7% (7/42)	18.9% (10/53)	
Sex			0.891
Male	16.2% (26/161)	14.7% (21/143)	
Female	16.7% (6/36)	14.0% (7/50)	
Ethnicity			0.441
Hispanic or Latino	0.0% (0/9)	13.3% (2/15)	
Not Hispanic or Latino	19.7% (27/137)	15.9% (23/145)	
1. Interaction was assessed using the Breslow-Day test.			

SOC Subgroup (POBA or DES)

Primary endpoint results broken down by SOC subgroup (DES and POBA) in patients with 1 or 2 existing stent layers are shown in **Table 21**. Investigators were permitted to choose DES or POBA for patients randomized to the control group until the 20% POBA enrollment cap was reached.

Table 21: 12-Month TLF in the SELUTION DEB, POBA, and DES

Endpoint	SELUTION DEB	SOC	SOC: POBA	SOC: DES
One-Layer ISR				
TLF at 12 Months	14.2% (22/155)	10.2% (16/157)	36.8% (7/19)	6.5% (9/138)
Cardiac Death	1.9% (3/155)	1.3% (2/157)	0.0% (0/19)	1.4% (2/138)
Target Vessel MI ¹	7.7% (12/155)	3.8% (6/157)	15.8% (3/19)	2.2% (3/138)
CD-TLR	9.7% (15/155)	7.6% (12/157)	26.3% (5/19)	5.1% (7/138)
Two-Layer ISR				
TLF at 12 Months	23.8% (10/42)	33.3% (12/36)	50.0% (10/20)	12.5% (2/16)
Cardiac Death	2.4% (1/42)	2.8% (1/36)	0.0% (0/20)	6.2% (1/16)
Target Vessel MI ¹	7.1% (3/42)	11.1% (4/36)	10.0% (2/20)	12.5% (2/16)
CD-TLR	23.8% (10/42)	33.3% (12/36)	50.0% (10/20)	12.5% (2/16)
1. Target vessel MI includes spontaneous (Type 1) MI using the 4th Universal Definition of Myocardial Infarction (UDMI) and peri-procedural MI using the Society for Cardiac Angiography and Intervention (SCAI) definition.				

4. Pediatric Extrapolation

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

5. Clinical Pharmacokinetics

The pharmacokinetic (PK) profile of sirolimus following treatment with the SELUTION DEB was evaluated in 17 patients treated with SELUTION devices coated with 118-400 µg of sirolimus. Mean whole blood concentration (mean C_{max} = 1.81 ng/mL) peaked immediately post-procedure (median T_{max} = 10 minutes) and decreased steadily over time with 6 of the 17 subjects having quantifiable concentrations at one day after administration and no subjects having quantifiable levels beyond three days after administration. These data indicate that treatment with the SELUTION DEB provides low systemic exposure to sirolimus that clears rapidly.

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included

276 investigators of which 1 was a full-time or part-time employee of the sponsor and 1 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: 2
- 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.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The SELUTION4ISR Study was a prospective, multi-center, randomized controlled trial comparing the SELUTION DEB with the standard of care (80% DES, 20% POBA) for the treatment of coronary ISR. The study met its primary endpoint, including effectiveness components, demonstrating non-inferiority to SOC with TLF rates of 16.2% (SELUTION DEB) and 14.5% (SOC), with a posterior probability of noninferiority of 98.8% in the primary PP analysis set. Target lesion revascularization (TLR) rates at 12 months were 12.7% in the SELUTION DEB arm and 12.4% in the SOC arm, showing comparable effectiveness in preventing the need for reintervention. Additional effectiveness endpoints such as device, lesion, and procedural success demonstrated the SELUTION SLR PTCA DEB's acceptable acute performance.

The SELUTION4ISR Study did not demonstrate non-inferiority to DES among patients with one previous layer of stent. In the SELUTION DEB group, 14.2% (22/155) of patients with one previous stent layer experienced TLF within 12 months, compared to 6.5% (9/138) of DES patients in the SOC control group. The hypothesis-driven secondary endpoint was not met, as indicated by the posterior probability of non-inferiority of 76.1% in the PP and 82.9% in the ITT cohorts, which were both below the predefined success threshold of 95%. This analysis, though prespecified, does have limitations due to the non-randomization of SOC patients to treatment with POBA or DES. Therefore, it is not possible to determine the degree to which differences in baseline characteristics may have influenced outcomes in this analysis.

While patients were randomized to either the SELUTION DEB or the SOC groups,

within the SOC group patients were not randomized to POBA or DES. Prior to the 20% POBA cap being reached, if a patient was randomized to the SOC group, clinicians could choose to treat the patient with either POBA or DES. After the 20% POBA cap was reached, all SOC patients were treated with DES. This may have skewed the patient population, as after the POBA cap was reached some clinicians may have opted not to enroll patients who were not considered to be suitable candidates for stents.

These results support the effectiveness of the SELUTION DEB for percutaneous coronary intervention (PCI) in coronary arteries 2.00 mm to 4.50 mm in diameter and lesions ≤ 26 mm in length for the purpose of improving myocardial perfusion when treating in-stent restenosis (ISR). Patient selection is also a key consideration and, given the results summarized above, the SELUTION DEB may be most suitable for patients in which the operator, based on clinical or lesion factors, determines that it is not in the best interest of the patient to implant additional stents.

B. Safety Conclusions

The risks of the SELUTION DEB are based on the results obtained from biocompatibility testing; *in vivo* pre-clinical safety and pharmacokinetics testing; *in vitro* engineering testing; coating characterization; chemistry, manufacturing and controls information; sterilization testing; stability testing; and data collected in the clinical study conducted to support PMA approval, as described above. These tests revealed the following information:

- The biocompatibility, *in vivo* pharmacokinetics, and *in vivo* animal safety testing demonstrate the acute and chronic safety of the product and support its acceptability for clinical use.
- The *in vitro* engineering testing demonstrated that the performance characteristics met the product specifications.
- The coating characterization testing adequately characterized the SELUTION DEB's drug coating and demonstrated that the coating can be applied consistently and uniformly.
- The chemistry, manufacturing, and controls information ensures that only product meeting analytical specifications will be released.
- The test results obtained from the sterilization testing demonstrated that the product can be adequately sterilized and is acceptable for commercial use.
- The functional shelf life and drug stability testing demonstrated that the product can be labeled with a shelf life of 18 months.
- The clinical testing conducted demonstrated that the product provides a reasonable assurance of safety when used as indicated in accordance with the Instructions for Use. In the IDE study, adverse event rates, including mortality and MI, observed with use of SELUTION DEB to treat coronary ISR lesions were comparable to the control arm and were in line with expectations for this patient population.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval, as described above. Patients treated with the SELUTION DEB experienced similar revascularization events, MI events, and cardiac death events as compared with patients treated in the SOC arm. As compared to 80% of patients in the SOC arm, the SELUTION DEB also provides the benefit of not implanting an additional layer of stent, which may preserve future treatment options.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval, as described above. The risks of using the SELUTION DEB to treat in-stent restenosis appear similar to the risks of treating with the SOC and the risks of PCI for in-stent restenosis in general. No unanticipated adverse device effects were reported in the study.

Additional factors considered in determining probable risks and benefits included:

- 1) The clinical study was a high quality randomized, controlled trial, with a prespecified statistical analysis plan. Therefore, uncertainty and potential for bias were reduced.
- 2) The randomized comparator for this study was a blended control of treatment with DES (80%) or POBA (20%), with the choice of control left to the operator's discretion prior to reaching the POBA enrollment cap. While the design was intended to allow greater enrollment of patients with two previous existing stent layers, the use of multiple control treatments with different associated outcomes added uncertainty when evaluating the risks and benefits of the three treatments.
- 3) The hypothesis-driven secondary endpoint, comparing the SELUTION DEB to DES in subjects with one previous stent layer, was not met. The data suggest that the SELUTION DEB may be most suitable when implantation of an additional stent is determined to be not in the best interest of the patient.
- 4) The clinical study provided adequate follow-up (to 12 months) to evaluate safety and effectiveness.
- 5) Patient risk is minimized by limiting the use to operators who have the necessary training to use the device safely and effectively. This includes appropriate lesion selection, adequate lesion preparation, and adherence to the recommended periprocedural medication regimens.

1. Patient Perspective

This submission either did not include specific information on patient perspectives, or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for the treatment of coronary ISR the probable benefits outweigh the probable risks.

D. Overall Conclusions

The 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 clinical study results of the SELUTION DEB showed non-inferior outcomes compared to the blended control arm (POBA and DES) for the treatment of coronary ISR. Given all available data, it is reasonable to conclude that the benefits of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the labeling and Instructions for Use (IFU).

XIV. CDRH DECISION

CDRH issued an approval order on September 18, 2026.

The final conditions of approval cited in the approval order are described below.

1. Long-term drug stability studies will be completed on three total finished product batches representing the commercial process each year, evaluating one lot of the largest-longest device size, one lot of an intermediate size, and one lot of the shortest-smallest device size manufactured during that time period. All batches for these studies will be stored at Long Term Conditions of $25^{\circ}\text{C} \pm 2^{\circ}\text{C}/60\% \text{ RH} \pm 5\%$, per ICH Q1A(R2). Testing for all studies will occur at 0, 3, 6, 9, 12, and 18 months.
2. Additional testing will be completed to determine percent free sirolimus of one batch of the 4.5 x 30 mm balloon size after aging to 18 months. This testing will use the same methodology, storage conditions, and acceptance criteria as those provided under P250041/A001.
3. *The SELUTION4ISR Continued Follow-Up Study*: This study will evaluate the long-term safety and effectiveness of the SELUTION SLR PTCA DEB in 418 subjects from the premarket study (SELUTION4ISR). The SELUTION4ISR study was designed as a global, multicenter, single blind, randomized (1:1 Selution to blended SOC control (80:20 DES:POBA)) trial. Subjects will be followed annually through 5 years post-procedure, and all efforts must be made to minimize the amount of missing long-term data (a minimum of 75% of subjects should be evaluable for the primary endpoint at 3 years, and a minimum of 90% of subjects should have a documented mortality status at 5 years).

The primary endpoint is the target lesion failure (TLF) rate, defined as clinically-driven target lesion revascularization (CD-TLR), target vessel myocardial infarction (TV-MI, Q-wave and non-Q-wave) or cardiac death. The MI events include PPMI according to the SCAI MI definition and spontaneous MI according to the 4th Universal MI definition.

The endpoints to be assessed through 5 years post-procedure are the rates of: (1) serious adverse events (SAE), (2) death (including all-cause and cardiovascular death), (3) MI (Q-wave and non-Q-wave) (PPMI per the SCAI definition and spontaneous MI per 4th Universal Definition), (4) stent thrombosis, (5) target lesion

failure (TLF), (6) target lesion revascularization (TLR), and (7) target vessel revascularization (TVR).

4. *SELUTION SLR PTCA DEB Post-Approval Surveillance Analysis*: This surveillance will be carried out to assess the real-world safety and effectiveness of the SELUTION SLR PTCA DEB, including in patient populations underrepresented or on whom no information was collected in the SELUTION4ISR pivotal trial (i.e., women and racial and ethnic groups). It will involve all consecutive patients treated within the first 2 years following device approval who are entered into the SELUTION4ALL Global Registry and treated at a US site (approximately 3,500 patients followed through 2 years). It will capture information about physicians' decision-making process and their intent to treat through a PCI strategy section in the electronic clinical registry form (eCRF). Endpoints include in-hospital major adverse cardiac events, all-cause death, myocardial infarction, and revascularization through 2 years follow up. Comparative outcomes in women and across racial and ethnic groups with in-stent restenosis will be specifically evaluated.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820), which was in effect at the time of the inspection. As of February 2, 2026, the revised part 820, referred to as the Quality Management System Regulation (QMSR), is effective.

XV. 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.