SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Percutaneous Transluminal Coronary Angioplasty (PTCA) Scoring Balloon Catheter
Device Trade Name:	Lacrosse NSE ALPHA Coronary Dilatation Catheter (hereinafter "NSE ALPHA")
Device Product Code:	NWX
Applicant's Name and Address:	Infraredx, Inc. 28 Crosby Drive, Suite 100 Bedford, MA, 01730, USA
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P230026
Date of FDA Notice of Approval:	06/06/2024

II. INDICATIONS FOR USE

The Lacrosse NSE ALPHA Coronary Dilatation Catheter is indicated for balloon dilatation of the stenotic portion of the coronary artery including both *de novo* and in-stent restenosis, for the purpose of improving myocardial perfusion.

III. CONTRAINDICATIONS

- Vasculature spasm without significant stenosis.
- Lesions in left main trunk without protection from collateral blood flow, bypass or any other method.
- Lesions located in bifurcation beyond stent struts.
- Lesion located distal to a freshly implanted stent.
- Lesions with stent damage such as fractures, cuts, cracks, bends, etc.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Lacrosse NSE ALPHA Coronary Dilatation Catheter labeling.

V. DEVICE DESCRIPTION

The NSE ALPHA is a rapid exchange (RX) percutaneous transluminal coronary angioplasty (PTCA) balloon catheter. The balloon has nylon threads (protruding elements) that focus dilatation force during inflation (**Figure 1**). The three nylon threads are located at 120° intervals parallel to the shaft and bonded at the distal and proximal ends of the 13 mm long semi-compliant balloon (**Figure 2**). Inside the balloon, two radiopaque markers indicate the working length of the balloon to guide proper positioning in the target lesion.

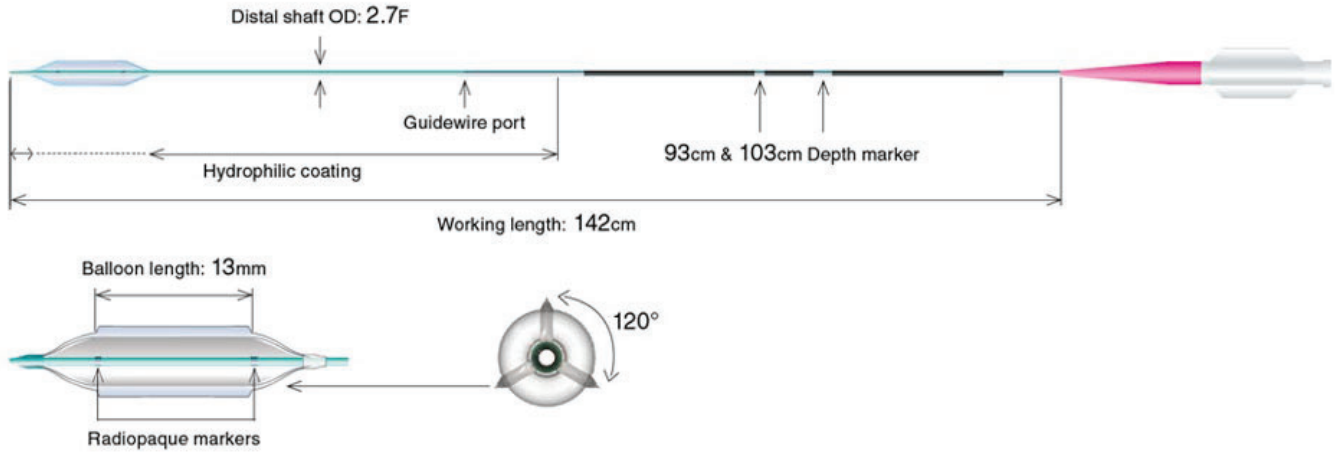

Figure 1: Lacrosse NSE ALPHA Coronary Dilatation Catheter (NSE ALPHA)

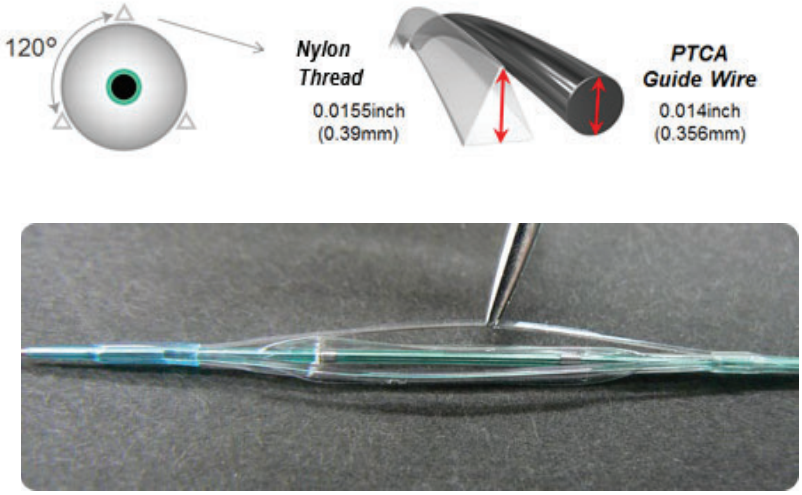

Figure 2: Nylon Threads

The distal section of the 2.7 Fr catheter comprises a dual-lumen shaft; the outer lumen is for balloon dilatation, and the inner lumen allows for rapid exchange of 0.014" or smaller guidewires. A hydrophilic coating is applied to the catheter shaft and tapered distal tip. The proximal shaft contains catheter insertion

depth markers at 93 cm and 103 cm, and the proximal hub enables balloon inflation and deflation using a standard balloon inflation device.

The device is available in balloon diameters ranging from 2.0 to 4.0 mm (**Table 1**). The nominal inflation pressure is 6 atm and the rated burst pressure is 14 atm. A balloon compliance chart is provided in the device instructions for use (IFU). The device is packaged sterile with a balloon protective tube and stylet that are removed prior to use.

Table 1: Sizes of NSE ALPHA

Model #	Balloon size
NSA20013	2.00 mm x 13 mm
NSA22513	2.25 mm x 13 mm
NSA25013	2.50 mm x 13 mm
NSA27513	2.75 mm x 13 mm
NSA30013	3.00 mm x 13 mm
NSA32513	3.25 mm x 13 mm
NSA35013	3.50 mm x 13 mm
NSA40013	4.00 mm x 13 mm

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of coronary artery disease including medical therapy, atherectomy, stenting, bypass graft (CABG) surgery or the use of other commercially available PTCA catheters and scoring balloon catheters. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with their physician to select the method that best meets expectations and lifestyles.

VII. MARKETING HISTORY

The NSE ALPHA was first introduced in Japan in 2007. **Table 2** lists the device approval years in the different markets.

Table 2: NSE ALPHA Approved Markets

Year Approved	Approved Markets
2007	Japan[+]
2012	Singapore

Year Approved	Approved Markets		
2014	Thailand Ecuador	Mexico Indonesia	Columbia Guatemala*
2015	Peru Paraguay*	EU Argentina	Hong Kong
2016	Myanmar Sri Lanka* Vietnam	Malaysia UAE	Kazakhstan* Iran
2017	Egypt*		
2018	Korea	Saudi Arabia	Taiwan
2019	Belarus Israel	Australia	Russia
2020	Bolivia	India	
2021	El Salvador		
2022	Dominican Republic	Philippines	
2023	Bangladesh		
No marketing approval required	New Zealand	Brunei	Chile
	Jordan	Macao	Namibia
	Oman	Palestine	South Africa

+ NSE, a predecessor device of the subject device Lacrosse NSE ALPHA Coronary Dilatation Catheter, was approved by MHLW in 2007. Since the NSE and NSE ALPHA are similar in their design and performance, they are marketed under the same Japanese brand name, Lacrosse NSE PTCA Balloon Catheters. As a result, the MHLW approval notice does not indicate the approval date specifically for the NSE ALPHA.

* A marketing decision was made not to renew the certification. The withdrawal from market is not due to safety or effectiveness of the subject device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Possible adverse events (e.g., complications) associated with the use of the NSE ALPHA include, the following:

- Acute myocardial infarction
- Arrhythmia (including ventricular fibrillation, bradycardia, tachycardia)
- Arterial spasm
- Arteriovenous fistula
- Blood loss from puncture site
- Coronary artery dissection, perforation, rupture, or injury
- Death
- Hemorrhage or hematoma
- Hemorrhagic complications
- Hypo / hypertension
- Infection
- Ischemia caused by long duration inflation
- Nausea or vomiting
- Palpitation

- Reaction (e.g., medicinal reaction or allergic reaction to contrast media)
- Restenosis following angioplasty
- Stroke, air embolization, distal embolization
- Thrombosis
- Total occlusion of the coronary artery or bypass graft
- Unstable angina

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

IX. SUMMARY OF NON-CLINICAL STUDIES

A series of non-clinical laboratory studies were performed with the NSE ALPHA. These evaluations included biocompatibility studies, animal study, bench testing, and sterilization validation. A summary of each of these evaluations is provided below.

A. Biocompatibility Studies

The biocompatibility of the NSE ALPHA was evaluated per the requirements of ISO 10993-1 and the FDA guidance titled *Use of International Standard ISO 10993-1, Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process*, issued on September 4, 2020. For the purpose of this testing, the device was categorized as an externally communicating device with limited contact duration (<24 hours) with circulating blood. A summary of the biocompatibility tests and their results can be found in **Table 3**. All test results indicate that the final, sterilized NSE ALPHA device is biocompatible and suitable for their intended use.

Table 3: Summary of Biocompatibility Testing for NSE ALPHA

Endpoint	Test Description	Referenced Standard	Results
Cytotoxicity	L929 Neutral Red Uptake Test	ISO 10993-5: 2009	Non-cytotoxic
Sensitization	Klingman Maximization Test	ISO 10993-10: 2010 USP 43-NF38: 2020 <1184>	Non-sensitizing
Intracutaneous Reactivity (Irritation)	Intracutaneous Injection Test	ISO 10993-10: 2010	Non-irritating
Material Mediated Pyrogenicity	Rabbit Pyrogen Test	ISO 10993-11: 2017 USP 43-NF38: 2020 <151>	Non-pyrogenic
Acute Systemic Toxicity	Systemic Injection Test	ISO 10993-11: 2017	Non-toxic
Hemocompatibility	Hemolysis Test	ISO 10993-4: 2017 ASTM F756-17	Non-hemolytic
	SC5B-9 Complement Activation Test	ISO 10993-4: 2017	Not a complement activator

B. Animal Study

An *in vivo* animal study was performed to evaluate the acute performance and safety of the NSE ALPHA using a porcine model.

Overview

This study was conducted in compliance with the Food and Drug Administration Good Laboratory Practice Regulations, as set forth in 21 CFR Part 58. Ten female Yorkshire swine underwent interventional testing on Day 0 in which at least 1 test (NSE ALPHA) and 1 control device (EMERGE™ PTCA Dilatation Catheter, Boston Scientific Inc.) were inflated for 60 seconds in 3 coronary arteries (RCA, LAD, and LCX or branches thereof). Angiography was performed and recorded during procedures. Thrombogenicity and acute performance characteristics of the system were evaluated, including assessment of the delivery, placement, and retrieval. Aspirin and clopidogrel were generally administered daily or every other day until euthanasia for antiplatelet therapy. Activated clotting times were monitored during the interventional procedures. Animal health, including incision site and clinical observations, body weights/condition, and clinical pathology were monitored at pre-determined, regular intervals. On Day 0 (n=5) and Day 30 (n=5), animals were euthanized, subjected to a comprehensive necropsy, and the treated arteries and downstream myocardium were collected for pathologic evaluation.

Results and Conclusion

This study demonstrated that the NSE ALPHA performed similarly to the control device with respect to device acute performance. Angiographic assessments showed no effect on blood flow or causing vascular injury. Thrombogenicity testing showed no adherent material on the balloon catheters after use. There were no health or clinical problems associated with the treatments, and all animals survived until their scheduled endpoint. Histologically, the test device was associated with favorable tissue responses and no evidence of adverse effects at both time points. Histological results, with minimal endothelialization/endothelial loss noted at Day 0 and neointima noted at Day 30, were comparable between test and control devices at both time points. There were no histological observations of embolic material or changes in all examined downstream myocardial sections. Overall, this study supports the conclusion that acute performance and safety of the NSE ALPHA in a swine coronary artery model compares favorably with the control device, and there were no safety concerns 30 days post treatment.

C. Bench Testing

Table 4 provides an overview of the bench testing supporting the NSE ALPHA. The table includes the test performed, acceptance criteria, results, and analysis type. Additionally, the NSE ALPHA's 3-year shelf life has been supported by the functional performance tests (denoted by asterisk *) which passed after 3-year accelerated aging.

Table 4: Summary of Bench Testing for NSE ALPHA

Test	Acceptance Criteria		Results	Analysis Type
Packaging				
Label Integrity*	Approved labels shall be affixed to the sterilization pouch and the packaging box.		Pass	Attribute
	Labels shall remain in place and legible.		Pass	
IFU Integrity*	IFU shall be included in the packaging box.		Pass	Attribute
	IFU shall remain legible.		Pass	
Accessory Integrity*	Flush Device shall be included in pouch and fixed to the catheter hoop.		Pass	Attribute
	Catheter Clip shall be included in the pouch and fixed to the compliance chart.		Pass	
	Compliance Chart shall be included in the packaging box and remain legible.		Pass	
Air Leak Test*	No leak.		Pass	Attribute
Dye Penetration Test*	No leak.		Pass	Attribute
Seal Strength Test*	Min. 1.5N.		Pass	Variable
Catheter				
Visual Verification*	The distal tip shall be smooth, rounded, tapered.		Pass	Attribute
	The external surface of the effective length of the catheter shall appear free from extraneous matter.		Pass	
	The external surface of the effective length of the catheter, including the distal end, shall be free from process and surface defects.		Pass	
	The lubricant shall not be visible as drops of fluid on the external surface.		Pass	
	Product name and model printed on the hub shall remain legible.		Pass	
Dimensional Verification*	Crossing profile shall meet the dimensional specification.		Pass	Attribute
	Element Height shall meet the dimensional specification.		Pass	Variable
	Other components shall meet the dimensional specifications.		Pass	Attribute
Balloon Rated Burst Pressure (RBP) & Balloon Compliance (Diameter vs. Pressure)*	Balloon RBP	Min. 14 atm	Pass	Variable
	Center Body Burst Pressure	Catheter Body shall not burst/leak prior to balloon or Min.20atm	Pass	Attribute
	Balloon Compliance	Balloon OD must meet specifications at 6 and 14 atm	Pass	Variable
Balloon RBP in Stent*	Balloon RBP	Min. 14 atm	Pass	Variable
Balloon Fatigue*	Balloon durability, Element adherence and durability	No Burst/ Leak of the catheter and No Failure (detachment/ tear) of the protruding elements	Pass	Attribute
Balloon Fatigue in Stent / Calcified Model*	Balloon durability, Element adherence and durability in Stent	No Burst/ Leak of the catheter and No Failure (detachment/ tear) of the protruding elements	Pass	Attribute
	Balloon durability, Element adherence and durability in Calcified Model	No Burst/ Leak of the catheter and No Failure (detachment/ tear) of the protruding elements	Pass	Attribute
Balloon Inflation/ Deflation Time, Balloon Working Length*	Balloon Working Length	13 ± 1 mm at 6 atm	Pass	Attribute
	Inflation Time	Max. 10 seconds	Pass	Attribute
	Deflation Time	Max. 25 seconds	Pass	Attribute
Tensile for Bonds*	Balloon Proximal Bond	Min. 5N	Pass	Variable

Test	Acceptance Criteria		Results	Analysis Type
	Guidewire port	Min. 8.9N	Pass	Attribute
	D+P Bond	Min. 8.9N	Pass	Variable
	Hub Bond	Min. 10N	Pass	Variable
Tip Tensile*	Tip Bond	Min. 2.25N	Pass	Variable
Flexibility & Kink*	Max. 15 mm (Bend radius)		Pass	Attribute
Torque Strength*	Min. 5 rotations		Pass	Attribute
Element Bond Tensile*	All element bonds must meet the specifications.		Pass	Attribute
Coating Integrity	N/A, Coating integrity characterization only.			
Particulate Evaluation	N/A, Particulate testing is characterization only.			
Corrosion Resistance	Metallic components of the catheter intended for fluid path contact shall show no signs of corrosion.		Pass	Attribute
Simulated Use Test*	All procedures, including device preparation and operation, must be performed with ease of use including, opening the packaging, removing device, deployment, trackability to lesion site, and withdrawal. Additionally, damage shall not be observed on the test catheters and the accessories.		Pass	Attribute

* The product shelf life of 3 years is supported by functional tests. Functional specifications were met after 3-year accelerated aging.

D. Sterilization Study

The NSE ALPHA is sterilized with ethylene-oxide (EO). The sterilization validation was completed in accordance with ANSI/AAMI/ISO 11135:2014/AMD 1:2018 *Sterilization of health care products — Ethylene oxide — Part 1: Requirements for development, validation, and routine control of a sterilization process for medical devices.* The validation demonstrated that the sterility assurance level (SAL) of 10^{-6} or less was achieved and that the EO residuals are below the maximum allowable limits per ISO 10993-7:2008 *Biological evaluation of medical devices – Part 7: Ethylene oxide*.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of NSE ALPHA Coronary Dilatation Catheter for subjects undergoing percutaneous coronary intervention (PCI) who have stenotic coronary arteries. The EXPANSE-PTCA study was performed in the United States under an approved IDE (G210195). 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 17th, 2021 and December 16th, 2022. The database for this PMA reflected data collected through May 24th, 2023 and included 200 subjects. There were 10 investigational sites.

The clinical study was a prospective, multi-center, single arm clinical study that followed subjects through hospital discharge. The population for this study was adult subjects (18 years and older) with

stenotic coronary artery disease who were suitable candidates for PTCA. An angiographic core lab was used for image acquisition, processing instructions to sites, and independent assessment of angiographic imaging. There was no control group in this clinical study.

Clinical Inclusion and Exclusion Criteria

Enrollment in the clinical study was limited to patients who met the following inclusion criteria.

General inclusion criteria

1. Age 18 years or older.
2. Willing to provide written informed consent and written HIPAA authorization prior to initiation of study-related procedures.
3. Agree to not participate in any other clinical study, during hospitalization for the index procedure that would interfere with the endpoints of this study.
4. Clinical evidence of ischemic heart disease, stable/unstable angina, or silent ischemia.
5. Acceptable candidate for PCI and emergency coronary artery bypass grafting and is planned for possible PTCA and/or stent placement.

Angiographic inclusion criteria

6. *De novo* or restenotic lesion(s) in native coronary arteries, including in-stent restenosis.
7. A maximum of two lesions, including at least one target lesion, in single or double vessel coronary artery disease.
   a) If two target lesions are defined, then no non-target lesions can be treated.
   b) If a single target lesion is defined, then a single non-target lesion may be treated, but if so, it must be located in a different coronary artery from the target lesion.
8. Target lesion(s) must have a reference vessel diameter between 2.0 mm and 4.0 mm by visual estimation.
9. Target lesion(s) must have a diameter stenosis of (a) ≥70% by visual estimation or (b) >50% by visual estimation and a fractional flow reserve (FFR) of <0.80 or resting full-cycle ratio (RFR) or instantaneous wave-free ratio (iFR) <0.9.
10. Treatment of non-target lesion, if any, must be completed prior to treatment of target lesion; must not, in the opinion of the investigator, impact the conduct or completion of the index procedure; and must be deemed a clinical angiographic success as visually assessed by the investigator.

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

General exclusion criteria

1. Known hypersensitivity or contraindication to aspirin, heparin, bivalirudin, anti-platelet medications, a clopidogrel non-responder, or sensitivity to contrast media that cannot be adequately pre-medicated or replaced with a clinically suitable alternative.
2. Known diagnosis of type I myocardial infarction (resulting from primary reduction of flow from a culprit lesion likely to have a thrombotic component) within 7 days prior to the index procedure.
3. Known pregnancy or is nursing. Women of child-bearing potential should have a documented negative pregnancy test within 7 days prior to index procedure.
4. Planned target lesion treatment with atherectomy (rotational, orbital or laser), cutting balloon, thrombectomy, lithotripsy or an unapproved device during the index procedure.
5. Serum creatinine >2.0 mg/dl within 7 days prior to the index procedure.
6. Cerebrovascular accident within 6 months prior to the index procedure.
7. Active peptic ulcer or active gastrointestinal bleeding within 6 months prior to the index procedure.
8. Left ventricular ejection fraction <30% based on most recent measurement within a year of the index procedure (if LVEF is not available in the medical records, it may be obtained at the time of the index procedure, prior to enrollment).
9. Target lesion located within a bypass graft (venous or arterial) or graft anastomosis.
10. Previous percutaneous intervention, within 9 months before the study procedure, on lesions in a target vessel (including side branches) that are located within 10 mm from the current target lesion.
11. Target lesion(s) with complete total occlusion (CTO) defined as the complete obstruction of a native coronary artery, exhibiting TIMI 0 or TIMI 1 flow, with an occlusion duration of at least 3 months.
12. Unstable hemodynamics or shock.
13. Other medical condition which might, in the opinion of the investigator, put the patient at risk or confound the results of the study.

Angiographic exclusion criteria

14. Target lesion(s) longer than 32 mm by visual estimation.
15. Extreme angulation (90º or greater) within 5 mm of the target lesion.
16. Target lesion(s) demonstrating flow limiting dissection (NHLBI Grade C or higher) prior to deployment of the Lacrosse NSE ALPHA.
17. Unprotected left main coronary artery disease (>50% diameter stenosis).
18. Coronary artery spasm of the target vessel in the absence of a significant stenosis.
19. Target lesion(s) with angiographic presence of probable or definite thrombus.
20. Target lesion(s) involves a bifurcation requiring treatment with more than one stent or pre-dilatation of a side branch >2.0 mm in diameter.
21. Target lesion(s) located in bifurcation beyond stent struts.
22. Target lesion(s) located distal to an implanted stent.

23. Target lesion(s) with stent damage.
24. Non-target lesion that meets any of the following criteria:
    - Located within a bypass graft (venous or arterial)
    - Located in an unprotected left main coronary artery
    - A CTO
    - Involves a bifurcation

Follow-up Schedule

All study subjects that participated in the EXPANSE-PTCA study were followed through hospital discharge. The table below summarizes the schedule of procedures.

Table 5: Schedule of Procedures

Evaluations	Screening / Baseline	Treatment Procedure[1]	Post-Procedure/ Discharge
Subject informed consent	X		
Inclusion/exclusion assessment - general	X		
Demographics & medical/surgical history[2]	X		
Pregnancy test[3, 4]	X		
Serum creatinine[4]	X		
Coronary angiography (send to core lab)[5]		X	
Inclusion/exclusion assessment – angio[5]		X	
PCI procedure		X	
Device performance assessment		X	
Device deficiency assessment		X	
Adverse event assessment[6]		X	X
Catheter performance questionnaire			X

[1] Within 30 days of screening/baseline.
[2] Medical history collected within 14 days of the index procedure.
[3] If female with child-bearing potential.
[4] Completed within 7 days of the index procedure.
[5] Angiography occurs in cath lab, prior to treatment, to determine enrollment eligibility.
[6] Adverse event assessment begins at the time of enrollment.

Clinical Endpoints

Primary Endpoint

The primary endpoint for the EXPANSE-PTCA study was device procedural success, defined as:

- Successful delivery, inflation, deflation, and withdrawal of the study balloon; and
- No evidence of device-related vessel perforation, flow limiting dissection (grade C or higher, per Clinical Events Committee (CEC) adjudication) or reduction in TIMI flow from baseline (per core laboratory assessment); and

- Final TIMI flow grade of 3 at the conclusion of the PCI procedure per core laboratory assessment.

The following hypotheses were used for primary endpoint analysis:

- H0: $r \leq PG$
- HA: $r > PG$,

where r was the proportion of endpoint successes and PG was the performance goal of 87.7% which was chosen based on data from studies of comparable products. The hypotheses were tested at a one-sided alpha level of 0.05 and endpoint success was based on whether the performance goal was met. For primary analysis, this endpoint was tested on all subjects with available data, with a worst-case sensitivity analysis also incorporated as noted within the statistical analysis plan. Success would be achieved if the lower 95% confidence interval was greater than the stated PG.

Secondary Endpoints

The secondary endpoints for the study were:

- Angiographic procedural success, defined as final diameter stenosis ≤50% in at least one of the Lacrosse NSE ALPHA attempted lesions following completion of the interventional procedure, including adjunctive stenting per core laboratory assessment.
- MACE through hospital discharge per CEC adjudication. MACE is defined as a composite of:
  - All-cause death
  - Myocardial infarction (MI)
  - Clinically indicated target lesion revascularization (TLR)
- Stent thrombosis (ST) within the target vessel(s) through hospital discharge using ARC-2 definitions for definite & probable, per CEC adjudication.
- Clinically significant arrhythmia (defined as those requiring intervention) through hospital discharge, per CEC adjudication.
- Occurrence of Lacrosse NSE ALPHA balloon rupture, per device deficiency eCRF.
- Change in minimum lumen diameter (MLD) following use of the Lacrosse NSE ALPHA catheter, measured by quantitative coronary angiography (QCA) per core laboratory assessment.
- Device procedural success defined as for the primary endpoint, calculated and presented per target lesion.

B. Accountability of PMA Cohort

At the time of database lock, a total of 200 subjects were enrolled from a pool of 927 subjects that consented and were screened for the EXPANSE-PTCA study, resulting in a 21.6% enrollment rate. The majority of screen failures were related to failure to meet angiographic eligibility criteria.

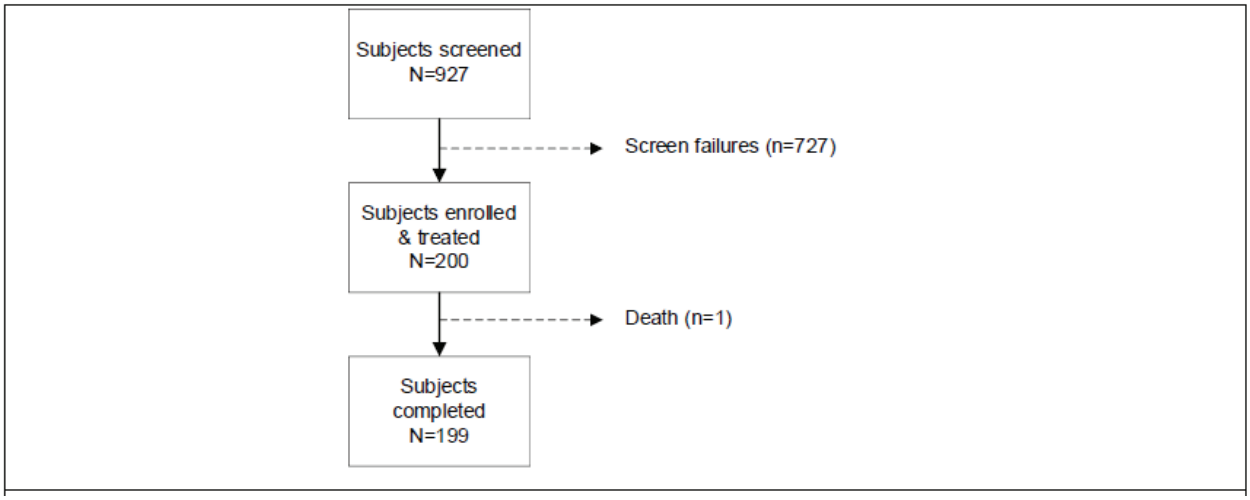

Figure 3: Patient Accountability Tree for Subject Enrollment

C. Study Population Demographics and Baseline Parameters

Baseline Demographics & Medical History

Subject baseline demographics and medical history are presented in **Table 6**. The median subject age was 69.5 years and 78.5% were male. Nearly half (42.5%) had undergone a prior coronary intervention and 24.0% had a prior myocardial infarction. The demographics of the study population are typical for interventional cardiology studies performed in the US.

Table 6: Baseline Demographics & Medical History

Characteristic	Subjects (%) (N=200)
Baseline Demographics	
Age (years) (median/range)	69.5 (32.0 - 93.0)
Sex at birth	
Male	157 (78.5%)
Female	43 (21.5%)
Height (cm) (median/range)	175.0 (135.0 - 198.0)
Weight (kg) (median/range)	90.7 (50.0 – 147.0)
Race	

Characteristic	Subjects (%) (N=200)
White	171 (85.5%)
Other	10 (5.0%)
Black or African American	8 (4.0%)
Subject chose not to disclose	7 (3.5%)
Asian	3 (1.5%)
American Indian or Alaska Native	1 (0.5%)
Ethnicity	
Not Hispanic or Latino	183 (91.5%)
Hispanic or Latino	7 (3.5%)
Subject chose not to disclose	10 (5.0%)
Medical History	
Prior coronary intervention(s)	85 (42.5%)
PCI	77 (38.5%)
CABG	18 (9.0%)
Prior myocardial infarction(s)	48 (24.0%)
Diabetes mellitus	
None	121 (60.5%)
Type I	3 (1.5%)
Type II	76 (38.0%)
Insulin required	30 (15.0%)
Dyslipidemia requiring treatment	183 (91.5%)
Hypertension requiring treatment	166 (83.0%)
Cigarette smoking	
Never	99 (49.5%)
Quit ≥ 6 months ago	80 (40.0%)
Current (w/in last 30 days)	20 (10.0%)
Quit > 1 month to < 6 months ago	1 (0.5%)
Chronic kidney disease	18 (9.0%)
Ejection fraction (%) (median/range)	55.0 (30.0 - 82.0)
Acute coronary syndrome	20 (10.0%)
Cardiac status (current)	
Chronic stable angina	89 (44.5%)
Ambiguous or abnormal symptoms with noninvasive functional study or FFR/iFR	65 (32.5%)
Unstable (accelerated) angina	31 (15.5%)

Characteristic	Subjects (%) (N=200)
Stabilized acute coronary syndrome – stabilized patient 24-72 hours post STEMI	3 (1.5%)
Other	12 (6.0%)

Procedural and Lesion Characteristics

A summary of procedural characteristics as reported by the site is provided in **Table 7.** The majority of subjects (89.0%) underwent attempted treatment of a single target lesion, and 13.5% underwent treatment of a non-target lesion. The predominant arterial access approach was radial (66.7%), and 92.3% of lesions were stented after use of the study device.

Table 7: Procedural Characteristics

Characteristic	Subjects (%) (N=200)
Number of target lesions treated	
1	178 (89.0%)
2	22 (11.0%)
Number of non-target lesions treated	
None	173 (86.5%)
1	27 (13.5%)
Total fluoroscopy time (minutes, median/range)	13.0 (3.0 - 71.0)
Radiation exposure (milligray, median/range)	1094.0 (18.0 - 5345.0)
	Target Lesions (N=222)
Access approach[1]	
Radial	148 (66.7%)
Femoral	75 (33.8%)
Other (ulnar)	1 (0.5%)
Reason NSE Alpha chosen	
Severe stenosis	104 (46.8%)
Calcified lesion	92 (41.4%)
Bulky lesion	42 (18.9%)
In-stent restenosis	31 (14.0%)
Long lesion	24 (10.8%)
Other	18 (8.1%)
Other balloon dilatation performed on target lesion before use of study balloon (and before other treatment, e.g., stent)[2,3]	98 (44.1%)
Other balloon used after study balloon (i.e., balloon and stenting; or balloon and no stenting)[2,4]	134 (60.4%)
Additional intervention on target lesion	
Stent	205 (92.3%)
Other balloon (after other treatment, e.g., stent)	135 (60.8%)
Other[5]	26 (11.7%)

Atherectomy	6 (2.7%)
Cutting balloon	1 (0.5%)

1. Some lesions had more than one access approach.
2. Categories are not mutually exclusive and will not sum to N=222 lesions.
3. Patient 390-006 is missing pre-dilatation data.
4. Balloon may be before or after stent.
5. Includes additional stent(s) (n=14), other non-study balloons (n=5), intravascular lithotripsy (n=5), brachytherapy (n=1) and brachytherapy and intravascular lithotripsy (n=1).

A summary of pre-procedure target lesion characteristics as assessed by the core lab is provided in **Table 8**. The left anterior descending artery was the most commonly treated vessel (48.6% of lesions). The median lesion length was 12.3 mm with a median reference vessel diameter of 2.9 mm. Most lesions were *de novo* (84.1%) and a majority (75%) had complex (B2 or C) lesion morphology. Severe calcification was seen in 55.0% of the lesions.

Table 8: Pre-procedure Target Lesion Characteristics and Morphology (Core Lab)

Characteristic	**n (%) (N = 220[1] Lesions)**
Vessel location[2]	
Left anterior descending	107 (48.6%)
Right coronary artery	65 (29.5%)
Left circumflex	47 (21.4%)
Left main	1 (0.5%)
Lesion location	
Proximal	75 (34.1%)
Mid	95 (43.2%)
Distal	42 (19.1%)
Ostial	8 (3.6%)
Lesion type	
De novo	185 (84.1%)
In-stent restenosis (ISR)	35 (15.9%)
ISR: stented length (mm) (median/range)	32.1 (9.7 - 114.9)
ISR: pattern	
IB	15 (42.9%)
IC	10 (28.6%)
ID	2 (5.7%)
II	6 (17.1%)
III	2 (5.7%)
Lesion morphology classification	
A	13 (5.9%)

Characteristic	n (%) (N = 220[1] Lesions)
B1	41 (18.6%)
B2	124 (56.4%)
C	41 (18.6%)
Unknown	1 (0.5%)
Eccentricity	
Concentric	162 (73.6%)
Eccentric	57 (25.9%)
Unknown	1 (0.5%)
Bend (degrees) (median/range)	18.0 (0.0 - 88.0)
Thrombus	1 (0.5%)
Tortuosity	
None	197 (89.5%)
Moderate	19 (8.6%)
Severe	3 (1.4%)
Unknown	1 (0.5%)
Ulcerated	1 (0.5%)
Calcification	
None/mild	37 (16.8%)
Moderate	56 (25.5%)
Severe	121 (55.0%)
Unknown	6 (2.7%)
Aneurysm present	0 (0.0%)
Ectasia present	7 (3.2%)
Side branch present	71 (32.3%)
Bifurcations, Medina type	
0,0,1	1 (0.5%)
0,1,0	39 (17.7%)
1,0,0	16 (7.3%)
1,0,1	1 (0.5%)
1,1,0	14 (6.4%)
RVD - user defined[3] (mm) (median/range)	2.9 (1.7 - 4.9)
Lesion length (mm) (median/range)	12.3 (4.2 - 45.9)
Focal (≤10 mm)	70 (31.8%)
Long (>10 - 20 mm)	110 (50.0%)
Diffuse (>20 mm)	38 (17.3%)
Unknown	2 (0.9%)

Characteristic	n (%) (N = 220[1] Lesions)
MLD (mm) (median/range)	0.9 (0.0 - 2.3)
Diameter stenosis (%) (median/range)	67.6 (31.1 - 100.0)

[1] The number of lesions analyzed by the core lab (N = 220) differs from the number of lesions reported by the sites (N = 222) The sites reported two (2) target lesions in the same vessel for two subjects that the core lab measured as one contiguous lesion.
[2] CASS breakdowns by artery: right coronary artery, CASS 1-10; left main, CASS 11; left anterior descending, CASS 12-17 & 29; left circumflex,CASS 18-28.
[3] User defined is average of the proximal and distal reference vessel diameter.

D. Safety and Effectiveness Results

1. Safety Results

Adverse Events & Device Deficiencies

Adverse Events

A summary of adverse events (AEs) is provided in **Table 9**. A total of 57 AEs were reported in 46 subjects. There were no unanticipated adverse device effects (UADEs). In total, 20 events in 17 subjects (8.5%) were serious, of which 14 events were procedure-related, 1 event was both device- and procedure-related, and 5 were not related.

Table 9: Summary of Adverse Events

Characteristic	Number of AEs	Subjects (%) with AE (N=200)
All AEs	57	46 (23.0%)
Unanticipated adverse device effects (UADE)	0	0 (0.0%)
Serious	20	17 (8.5%)
Procedure-related only	14	12 (6.0%)
Device-related only	0	0 (0.0%)
Device- and procedure-related	1	1 (0.5%)
Not procedure or device related	5	5 (2.5%)
Non-serious	37	32 (16.0%)
AEs by relationship to device		
Related	6	6 (3.0%)
Not related	51	40 (20.0%)
AEs by relationship to procedure		
Related	47	42 (21.0%)
Not related	10	10 (5.0%)

Characteristic	Number of AEs	Subjects (%) with AE (N=200)
AEs by outcome		
Resolved	53	43 (21.5%)
Death	2[1]	1 (0.5%)
Resolved with sequelae	2	1 (0.5%)
Ongoing	0	0 (0.0%)
Ongoing at study completion	0	0 (0.0%)

[1] One subject had 2 adverse events that contributed to death outcome.

Deaths

As noted in the table above, one subject died during the EXPANSE-PTCA study. One subject experienced an arterial dissection of the aorta related to guide catheter use before the study device was deployed, with subsequent Q-wave myocardial infarction and periprocedural death. These events were independently adjudicated as a MACE, resulting in a MACE rate of 0.5% (1/200 subjects). Both the dissection and myocardial infarction were assessed to be related to the procedure and unrelated to the study device.

Device-Related AEs

Of the six AEs that were related to the study device, all were arterial dissections. None of the device-related dissection AEs were flow-limiting. Five of the six dissections were non-serious and one dissection was adjudicated by the CEC as anatomically serious due to its proximal location, although it resulted in no short- or long-term clinical events.

Adverse Events by Diagnosis & Seriousness

A summary of all AEs by diagnosis and seriousness (ordered by percent of total subjects with the event) is provided in **Table 10**. The most frequently reported adverse event was arterial dissection, reported in 10.5% (21/200) of subjects.

Table 50: Adverse Events by Diagnosis & Seriousness

	Non-serious		Serious		Total	
Diagnosis	No. of AEs	Number (%) of Subjects with AE (N=200)	No. of AEs	Number (%) of Subjects with AE (N=200)	No. of AEs	Number (%) of Subjects with AE (N=200)
Total events[1]	**37**	**28 (14.0%**	**20**	**20 (10.0%**	**57**	**46 (23.0%**
Arterial dissection	17	17 (8.5%)	4	4 (2.0%)	21	21 (10.5%)
Hematoma, access site, >5 cm	3	3 (1.5%)	2	2 (1.0%)	5	5 (2.5%)
Blood loss from puncture site	2	2 (1.0%)	2	2 (1.0%)	4	4 (2.0%)

Diagnosis	Non-serious		Serious		Total	
	No. of AEs	Number (%) of Subjects with AE (N=200)	No. of AEs	Number (%) of Subjects with AE (N=200)	No. of AEs	Number (%) of Subjects with AE (N=200)
Chest pain, non-cardiac	2	2 (1.0%)	1	1 (0.5%)	3	3 (1.5%)
Hypotension	1	1 (0.5%)	2	2 (1.0%)	3	3 (1.5%)
Arrhythmia, bradycardia	0	0 (0.0%)	2	2 (1.0%)	2	2 (1.0%)
Arrhythmia, other	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.5%)
Arrhythmia, tachycardia	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.5%)
Arterial perforation	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.5%)
Hypertension	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.5%)
Myocardial infarction	0	0 (0.0%)	1	1 (0.5%)	1	1 (0.5%)
Nausea or vomiting	1	1 (0.5%)	0	0 (0.0%)	1	1 (0.5%)
Other, specify	10	9 (4.5%)	3	3 (1.5%)	13[2`]	12 (6.0%)

[1] Columns may not add to total as subjects may have experienced more than one event.
[2] Includes plaque shift (n=3), chest pain (n=2), groin pain (n=2), and 1 each of arterial occlusion, ecchymosis, hematemesis, shortness of breath, urinary retention, and vasovagal event.

Dissection Adverse Events

The three events assessed by the CEC as flow-limiting (grade C or higher) were not related to the study device. Four of the dissection events were serious and one of these was adjudicated by the CEC as device-related and anatomically serious due to its proximal location, although it resulted in no short- or long-term clinical events.

Device Deficiencies and Protocol Deviations

One device deficiency was reported in the EXPANSE-PTCA study (1/228 devices used, 0.4%). This subject had two target lesions, and the study balloon burst during the second inflation of the device within the calcified mid-LAD lesion. The first inflation was at 20 atm for 25 seconds, and the second inflation was at 20 atm for 38 seconds. The balloon ruptured at the end of this second inflation. Another study balloon of the same size was opened and used successfully for the final two inflations of 20 atm for 21 and 30 seconds.

A total of 8 deviations related to study balloon overinflation were reported. The IFU for NSE ALPHA lists a rated burst pressure of 14 atm, and any inflation over the burst rating was reported as a deviation. One over-inflation resulted in a balloon bursting. There were no associated adverse clinical events, and this was reported as a device deficiency.

A total of 7 deviations related to eligibility criteria were reported. Four of these deviations involved a non-target lesion in the same vessel as the target lesion (inclusion criterion 7b). The following table summarizes the protocol deviations:

Table 11: Summary of Protocol Deviation

Deviation Category	n	% of Deviations
Balloon inflation >14 atm	8	47.1%
Eligibility criteria not met	7	41.2%
Interval-related (visit completed outside of window)	1	5.9%
Same study device used in both target lesions	1	5.9%
Total	**17**	

1. Effectiveness Results

Primary Endpoint Analysis

The primary endpoint of procedural success, a composite of successful use of the study balloon, freedom from device-related injury or reduction in TIMI flow and final post-procedural TIMI 3 flow was achieved in 89.8% (176/196) of subjects (**Table 12**). The study protocol defined a performance goal of 87.7% based on data from studies of comparable products. As shown in **Table 12**, the primary endpoint success rate (89.8%) was numerically higher than the performance goal (87.7%); however, the lower end of the 95% confidence interval was 85.5%, and therefore, the statistical objective was not met and thus, the study failed to meet its primary endpoint.

All of the primary endpoint failures included failure of the technical component of the endpoint (successful delivery, inflation, deflation, and withdrawal of study balloon), specifically the inability to cross the target lesion. One subject also experienced reduction of TIMI flow and final TIMI 2 flow due to non-study device-related aortic dissection, with subsequent Q-wave myocardial infarction and periprocedural death. However, the CEC adjudicated these adverse events as unrelated to the study device.

Per the statistical analysis plan, a sensitivity analysis was performed on the primary endpoint where missing data was considered a failure, resulting in procedural success of 88.0% (176/200).

A more detailed description of each component of the primary endpoint is included after **Table 12**.

Table 12: Summary of Primary Endpoint – Procedure Success (by Subject)

Characteristic	n (%) 90% CI (N=196)[1,5]
Met overall primary endpoint (procedure success)[2]	176 (89.8%)

	[85.5%, 93.1%]
Components of primary endpoint	
Successful delivery, inflation, deflation, and withdrawal of study balloon	176 (89.8%) [85.5%, 93.1%]
No evidence of device-related vessel perforation, device-related flow-limiting dissection, or reduction in TIMI flow from baseline[4]	195 (99.5%)[3] [97.6%, 100.0%]
Final TIMI flow grade of 3 at the conclusion of the PCI procedure[4]	195 (99.5%)[3] [97.6%, 100.0%]

[1] Four (4) subjects had no final TIMI assessed by either the core lab or the site so are not included in the assessment of primary endpoint. One of the four subjects was a "no-cross" subject.
[2] If a subject had greater than one target lesion, they needed to be a success in both lesions to be counted a study success.
[3] One subject had a reduction of TIMI flow and final TIMI II flow due to non-study device-related aortic dissection, with subsequent Q-wave myocardial infarction and periprocedural death.
[4] If final TIMI was not assessed by the core laboratory, due to missing imaging, site-reported data was used.
[5] Hypothesis testing for the primary endpoint was completed using a one-sided alpha level of 0.05. The 90% confidence interval is calculated using the Clopper-Pearson (Exact) method.

Primary Endpoint Component 1: Successful Device Usage

Analysis of the components of the primary endpoint showed device delivery was unsuccessful in 20 subjects. One additional subject was not included in the primary endpoint analysis due to missing final TIMI measurement, resulting in 21 "no-cross" subjects.

All of the device usage failures were related to inability to deliver the balloon through the lesion (here-in referred to as "no-cross" or "failure to cross"). There were no technical failures relating to the other technical components such as device inflation, deflation or withdrawal when lesions were crossed.

Primary Endpoint Component 2: No Evidence of Device-related Perforation or Flow Limiting Dissection (grade C or higher), or Reduction in TIMI Flow from Baseline

One subject did not meet this component of the primary endpoint, had a reduction in TIMI from 3 pre-procedure to 2 at procedure end due to non-study device-related aortic dissection, with subsequent Q-wave myocardial infarction and periprocedural death.

The safety component of the primary endpoint includes assessment of device-related vessel perforation and flow limiting dissection (grade C or higher), per CEC adjudication.

Figure 4 summarizes the number of subjects with perforations and dissections and shows that there were no device-related arterial perforations or device-related flow-limiting dissections of grade C or higher in the study.

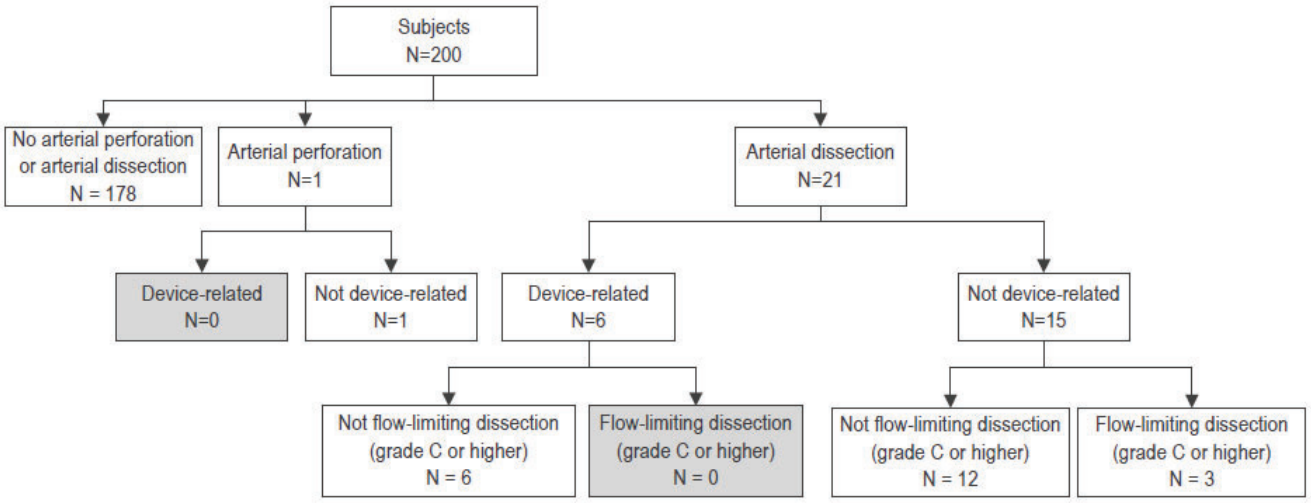

Figure 4: Flow Diagram of Device-Related Perforation & Dissection

Primary Endpoint Component 3: TIMI Flow

Final achievement of TIMI 3 was observed in 99.5% of lesions (215/216) as shown in **Table 13**. One subject had a final TIMI flow grade 2 at procedure end due to non-study device-related aortic dissection, with subsequent Q-wave myocardial infarction and periprocedural death.

Table 13: TIMI Summary by Lesion

Timepoint	N	TIMI Score			
		0	1	2	3
Pre-Procedure	220	1 (0.5%)[1]	2 (0.9%)	28 (12.7%)	189 (85.9%)
Post-Study Device	199	0 (0.0%)	0 (0.0%)	3 (1.5%)	196 (98.5%)
Final	216	0 (0.0%)	0 (0.0%)	1 (0.5%)	215 (99.5%)

[1] The site reported pre-procedure TIMI of II (i.e., subject met study criteria as determined by the investigator at the time of enrollment).

Secondary Endpoints Analysis

A summary of secondary endpoint data is provided in the following two tables:

Table 14: Summary of Secondary Endpoints

Endpoint	N	n (%)
Angiographic procedural success (final diameter stenosis ≤50%) in at least one of the NSE ALPHA attempted lesions following completion of the procedure[2]	197 subjects[1]	197 (100.0%)

Endpoint	N	n (%)
Increase in MLD following use of NSE ALPHA[2]	158 lesions[4]	158 (100.0%)
Increase in MLD at the end of the procedure by target lesion[2, 3]	208 lesions[4]	208 (100.0%)
MACE through hospital discharge	200 subjects	1 (0.5%)
Death, all-cause	200 subjects	1 (0.5%)
Myocardial infarction	200 subjects	1 (0.5%)
Clinically indicated target lesion revascularization	200 subjects	0 (0.0%)
Stent thrombosis through hospital discharge	200 subjects	0 (0.0%)
Clinically significant arrhythmia through hospital discharge	200 subjects	4 (2.0%)
Occurrence of NSE ALPHA rupture	200 subjects	1 (0.5%)
Device procedural success by target lesion	216 lesions[5]	193 (89.4%)

[1] Three subjects were missing final diameter stenosis (both core lab and site data).
[2] If final diameter stenosis or MLD was not assessed by the core laboratory, due to missing imaging, site-reported data was used.
[3] Additional analysis of MLD at the end of the procedure is included, due to the missing data at the post-study device time point.
[4] Reference available number of lesions as indicated in Table 15.
[5] Includes only those lesions in the subjects included in the primary endpoint analysis (N=196 subjects)

Table 15: Minimum Lumen Diameter & Diameter Stenosis (by Lesion, per Core Lab)

Timepoint	Number of Lesions	Diameter Stenosis (%)	Minimum Lumen Diameter (mm)
Pre-procedure	219	67.6 (31.1 - 100.0)	0.9 (0.0 - 2.3)
Post-study device	158	38.5 (2.7 - 60.8)	1.7 (1.0 - 3.2)
Final	208	11.6 (2.1 - 25.5)	2.6 (1.7 - 4.1)
Values presented as median (min, max)			

The study did not require prospective collection of pre procedure (baseline) cardiac enzymes per study protocol. Cardiac enzymes were only recorded if available. Post-procedure enzymes were collected on one patient (who was symptomatic). This patient met the ARC-2 MI definition, and cardiac troponin I was collected.

Post Hoc Additional Analyses – "No-Cross" Subjects

"No-Cross" Overview

Analysis of the components of the primary endpoint showed device delivery was unsuccessful in 20 subjects. One additional subject had unsuccessful device delivery and was not included in the primary endpoint analysis due to missing final TIMI measurement, resulting in 21 "no-cross" subjects. Of the 21 no-cross subjects, lesions in 20 of the subjects were successfully crossed with an alternative device.

Of note, a single attempt was made by the investigator to cross the target lesion in 12 of the 21 "no-cross" patients (57%). Six of the 12 cases (50%) were from one site.

Post Hoc Clinical Events Committee Review of "No-Cross" Cases

A review of "no-cross" cases was conducted by four high-enrolling study investigators, the national principal investigator, and the angiographic core laboratory. This review included review of the angiographic images, and characterization of the anatomic lesion characteristics (tortuosity, calcium, diffuse) and the operator technique (guide catheter support, device sequencing, etc.). A summary of these discussions are provided in **Table 16**.

Overall, 81.0% (17/21) of "no-cross" subjects were identified as having notable anatomic complexity (e.g., tortuosity, calcification, diffusely diseased). Operator technical discretion (e.g., operator decision not to retry the study device after other pre-dilation, guide catheter extension usage/selection) played a role in the failure to cross in 38.1% (8/21) of the "no-cross" cases.

Scenario	Number of Patients
Anatomical Complexity (Tortuosity, calcification, distal location, diffusely diseased, etc.)	**11**
Operator Discretion (Decision not to retry study device after another pre-dilation of addition of guide catheter extension, etc.)	**2**
Anatomical Complexity and Operator Discretion	**6**
Other (Not identified by investigators as scenario 1 or 2)	**2**

Table 16: "No-Cross" Investigator Review

Guide Catheter Extension Usage

Based on the clinical review of the "no-cross" cases, a review of guide catheter extension usage was completed and is included in **Table 17**. The usage was analyzed to understand which lesions, at the discretion of the treating investigator, required additional guide catheter back up support for adequate delivery of devices. Additional guide catheter support may be needed when using the device for more complex procedures with severe lesion characteristics including calcification and tortuosity.

A guide catheter extension was involved in only 8.6% (17/197) of successfully crossed lesions and in 73.9% (17/23) of "no-cross" lesions. However, of these 17 "no-cross" lesions, the study device was not retried after placement of a guide catheter extension in 47.1% (8/17) of these lesions.

Table 67: Guide Catheter Extension Usage by Crossing Success (by Lesion)

Characteristic	Successful Crossing N=197 Lesions	"No-Cross" N=23[1] Lesions
Guide catheter extension used in procedure		
No	180 (91.4%)	6 (26.1%)
Yes	17 (8.6%)	17 (73.9%)
Was successful study device crossing achieved after placement of guide extension catheter?	**N = 17**	**N = 17**
Yes	13 (76.5%)	0 (0.0%)
No	0 (0.0%)	9 (52.9%)
NA – study device not retried after guide extension catheter placed	0 (0.0%)	8 (47.1%)
NA – study device crossed lesion prior to guide extension catheter use	4 (23.5%)	0 (0.0%)

[1] Two of the 21 "no-cross" subjects had 2 target lesions that were not crossed, resulting in n=23 "no-cross" lesions; in one lesion, the study device was tried but was unsuccessful in crossing, and in the other lesion, the study device was not tried after the initial "no-cross" of the first lesion.

Lesion Characteristics by Crossing Success

To further understand lesion characteristics in the "no-cross" group, an expanded lesion characteristics table is provided below including data by crossing success (**Table 18**).

A comparison of the "no-cross" versus successfully crossed lesion characteristics showed higher rates of moderate/severe tortuosity (39.1% versus 6.6%) and moderate/severe calcification (95.7% versus 78.7%) in the "no-cross" lesions. These characteristics may have contributed to the inability to cross the lesions.

Table 78: Lesion Characteristics by Crossing Success (N=220 lesions)

Characteristic	Successful Crossing N=197 lesions	"No-Cross" N=23[1] Lesions
Vessel location[2]		
Left anterior descending	105 (53.3%)	2 (8.7%)
Right coronary artery	51 (25.9%)	14 (60.9%)
Left circumflex	40 (20.3%)	7 (30.4%)
Left main	1 (0.5%)	0 (0.0%)
Lesion location		
Proximal	67 (34.0%)	8 (34.8%)
Mid	84 (42.6%)	11 (47.8%)
Distal	38 (19.3%)	4 (17.4%)
Ostial	8 (4.1%)	0 (0.0%)
Lesion type		

Characteristic	Successful Crossing N=197 lesions	"No-Cross" N=23[1] Lesions
De novo	164 (83.2%)	21 (91.3%)
In-stent restenosis (ISR)	33 (16.8%)	2 (8.7%)
ISR: stented length (mm) (median/range)	34.1 (9.7 - 114.9)	12.7 (10.4 - 15.0)
ISR: pattern		
IB	15 (45.5%)	0 (0.0%)
IC	9 (27.3%)	1 (50.0%)
ID	1 (3.0%)	1 (50.0%)
II	6 (18.2%)	0 (0.0%)
III	2 (6.1%)	0 (0.0%)
Lesion morphology classification		
A	13 (6.6%)	0 (0.0%)
B1	40 (20.3%)	1 (4.3%)
B2	104 (52.8%)	20 (87.0%)
C	39 (19.8%)	2 (8.7%)
Unknown	1 (0.5%)	0 (0.0%)
Eccentricity		
Concentric	147 (74.6%)	15 (65.2%)
Eccentric	49 (24.9%)	8 (34.8%)
Unknown	1 (0.5%)	0 (0.0%)
Bend (degrees) (median/range)	18.0 (0.0 - 88.0)	29.0 (0.0 - 83.0)
Thrombus	1 (0.5%)	0 (0.0%)
Tortuosity		
None	183 (92.9%)	14 (60.9%)
Moderate	11 (5.6%)	8 (34.8%)
Severe	2 (1.0%)	1 (4.3%)
Unknown	1 (0.5%)	0 (0.0%)
Ulcerated	1 (0.5%)	0 (0.0%)
Calcification		
None/mild	36 (18.3%)	1 (4.3%)
Moderate	52 (26.4%)	4 (17.4%)
Severe	103 (52.3%)	18 (78.3%)
Unknown	6 (3.0%)	0 (0.0%)
Aneurysm present	0 (0.0%)	0 (0.0%)
Ectasia present	6 (3.0%)	1 (4.3%)
Side branch present	66 (33.5%)	5 (21.7%)
Bifurcations, Medina type		

Characteristic	Successful Crossing N=197 lesions	"No-Cross" N=23[1] Lesions
0,0,1	1 (0.5%)	0 (0.0%)
0,1,0	35 (17.8%)	4 (17.4%)
1,0,0	16 (8.1%)	0 (0.0%)
1,0,1	1 (0.5%)	0 (0.0%)
1,1,0	13 (6.6%)	1 (4.3%)
RVD - user defined[3] (mm) (median/range)	2.8 (1.7 - 4.9)	2.9 (2.2 - 3.7)
Lesion length (mm) (median/range)	12.2 (4.2 - 45.4)	12.7 (4.7 - 45.9)
Focal (≤10mm)	65 (33.0%)	5 (21.7%)
Long (>10 - 20 mm)	94 (47.7%)	16 (69.6%)
Diffuse (>20mm)	36 (18.3%)	2 (8.7%)
Unknown	2 (1.0%)	0 (0.0%)
MLD (mm) (median/range)	0.9 (0.0 - 2.3)	0.7 (0.2 - 2.0)
Diameter stenosis (%) (median/range)	66.1 (31.1 - 100.0)	74.7 (45.4 - 90.2)

[1] Two of the 21 "no-cross" subjects had 2 target lesions that were not crossed, resulting in n=23 "no-cross" lesions; in one lesion, the study device was tried but was unsuccessful in crossing, and in the other lesion, the study device was not tried after the initial "no-cross" of the first lesion.
[2] CASS breakdowns by artery: right coronary artery, CASS 1-10; left main, CASS 11; left anterior descending, CASS 12-17 & 29; left circumflex,CASS 18-28.
3 User defined is average of the proximal and distal reference vessel diameter.

No-cross Rates by Tortuosity and Calcification

Additional analysis of "no-cross" rates by lesion tortuosity and calcification is presented in **Table 19** and **Table 20**. Severely calcified lesions with any level of tortuosity had a 64.3% "no-cross rate" (9/14) compared to a 6.8% (14/206) "no-cross" rate in all other lesions ($p<0.001$). This analysis of core laboratory-assessed data is concordant with the expert review of no-cross cases, in that the presence of anatomical complexity was highly associated with no-cross occurrences.

Table 19: "No-Cross" Rates by Tortuosity and Calcification (N=220 lesions)

		Tortuosity		
		None	Moderate/Severe	Unknown
Calcification	None/Mild	2.9% (1/35)	0.0% (0/2)	--
	Moderate	8.0% (4/50)	0.0% (0/6)	--
	Severe	8.4% (9/107)	64.3% (9/14)	--
	Unknown	0.0% (0/5)	--	0.0% (0/1)

Table 20: Lesion "No-Cross" Rates by Tortuosity/Calcification Subgroup

Subgroup	N	"No-Cross" Rate	P-value
Severely calcified and tortuous lesions	14	64.3% (9/14)	<0.001
All other lesions	206	6.8% (14/206)	

Primary Endpoint by Calcification Burden

Further analysis of relationship between calcification burden and the primary endpoint is included in **Table 21** (post-hoc analysis). The burden of calcification was negatively associated with the primary endpoint success rate, with success rates declining as calcification increased. For example, as the calcification burden changes from "None/Mild" to "Moderate" to "Severe," the percentage of subjects meeting the primary endpoint decreases from 97.2% to 92.7% to 85.5%, respectively.

Table 21: Post-hoc Analysis of Primary Endpoint by Calcification Burden (by Lesion)

Characteristic	Calcification Burden (N=214)[1]			
	None/Mild (N=36 lesions)	Moderate (N=55 lesions)	Severe (N=117 lesions)	Unknown (N=6 lesions)
Met overall primary endpoint (procedure success)	35 (97.2%)	51 (92.7%)	100 (85.5%)	6 (100.0%)
Components of primary endpoint				
Successful delivery, inflation, deflation, and withdrawal of study balloon	35 (97.2%)	51 (92.7%)	100 (85.5%)	6 (100.0%)
No evidence of device-related vessel perforation, device-related flow limiting dissection (grade C or higher), or reduction in TIMI flow from baseline	36 (100.0%)	55 (100.0%)	117 (100.0%)	6 (100.0%)
Final TIMI flow grade of 3 at the conclusion of the PCI procedure[2]	36 (100.0%)	55 (100.0%)	117 (100.0%)	6 (100.0%)

[1] This table includes subjects assessed for the primary endpoint (N=196); data on 6 of the total 220 lesions are not included.
[2] If final TIMI was not assessed by the core laboratory, due to missing imaging, site-reported data was used.

1. Additional Subgroup Analyses

The study was not specifically powered for sex, gender, or race subgroups. No analyses were performed for any subgroups.

2. Pediatric Extrapolation

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

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 IDE clinical study included ten (10) investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

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 Devices 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

The preclinical safety and effectiveness of the NSE ALPHA have been demonstrated by results obtained from biocompatibility testing, bench testing, *in vivo* animal testing, sterilization and shelf-life testing. The results of the US clinical study demonstrate that the NSE ALPHA is safe and effective in coronary artery lesions, consistent with its intended use. Together, the clinical and non-clinical test results provide reasonable assurance that the NSE ALPHA is safe and effective when used as indicated and in accordance with the instructions for use (IFU).

Effectiveness Conclusions

In the EXPANSE-PTCA study, the primary endpoint of procedural success was achieved in 89.8% of subjects, with the lower 95% confidence interval of 85.5%. The EXPANSE-PTCA study thus failed to reject the null hypothesis in favor of the alternative that the proportion of primary endpoint successes was greater than the predetermined performance goal of 87.7%. The failure to meet the primary endpoint was primarily the result of device failure to cross the lesion. Aside from one subject experiencing both failures to cross and a subsequent final TIMI of 2, there were no instances of failure due to other primary endpoint components. Operator escalation of guide catheter support, guide catheter extenders, use of additional guidewires, atherectomy devices and lithotripsy produced successful revascularization in most of these cases despite the initial failure of the study device to cross the target lesion. Qualitative comparative post-hoc analysis of the anatomy included in the EXPANSE-PTCA study cohort demonstrated that certain lesions maintained more advanced disease severity (calcification and tortuosity) than in other studies that evaluated cutting/scoring devices. Specifically, severe calcification was reported in 55.3% of EXPANSE-PTCA lesions as compared to 23.5% in the Scoreflex study and 6.3% in the AngioSculpt study (1, 2). These differences in lesion complexity in prior studies, in conjunction with the significant amount of complexity observed in the EXPANCE-PTCA study, may not have been fully accounted for and/or anticipated, which presented challenges for the Lacrosse device to successfully meet the predefined primary endpoint performance

goal. Further, complex lesion crossing may be more likely when the device is used with support devices including guide catheters.

Safety Conclusions

The risks of the device are based on non-clinical laboratory and animal studies as well as data collected in a clinical study to support PMA approval as described above. As noted in the clinical study, the safety profile of the study device showed acceptable freedom from device-related injury with no device-related perforations or device-related flow-limiting dissections, and a single device-related serious adverse event which was a dissection adjudicated by the CEC as anatomically serious due to its proximal location, but resulted in no short- or long-term clinical events. One death, not related to the study device, was observed during the EXPANSE-PTCA study. This safety profile is similar to that of other devices for similar indications, and in line with the clinical expectations for this patient population, thus there are no new safety risks of concern. Further, both the animal study and non-clinical performance data provides further assurance that the NSE Alpha is safe when used as indicated and in accordance with the instructions for use supplied with the device.

Benefit-Risk Determination

The probable benefits and risks of the device are based on data collected in the in vivo animal and clinical study to support PMA approval.

The probable benefits of the NSE ALPHA are the same as other scoring/cutting balloons. Aside from failure to cross, patients treated with the NSE ALPHA had a high rate of procedural success, acceptable flow post-procedure, and did not experience any device failures including device-related vessel perforation, flow-limiting dissections, or device-related reduction in TIMI flow. Additional factors to be considered in determining probable risk and benefits for the NSE ALPHA Coronary Dilatation Catheter include:

- The device is intended for use in subjects with de novo stenotic coronary arteries or in-stent restenosis.
- The frequency and types of adverse events reported throughout the pivotal clinical study are what might be expected in the studied patient population and therapeutic area. No unanticipated adverse device effects were reported in the study.
- While there was no evidence of increased risk associated with the use of the NSE ALPHA, because the trial failed to meet its predefined performance goal this led to some remaining uncertainty. The primary endpoint failures can be attributed to failure to cross the lesion and the high proportion of complex lesions in EXPANSE-PTCA appears to have contributed to this. In addition, device performance was acceptable when the lesion was successfully crossed. To mitigate this risk, cautionary language was added to the device Instructions for Use to encourage the clinical operator to consider use of support devices including guide catheters and pre-dilatation when using the device in complex lesions.
- A post-approval study will be conducted to further evaluate the performance of NSE Alpha for crossing and scoring stenotic lesions in standard and complex lesions, with specific a focus on

understanding success of lesion crossing after physicians use of extra delivery support in complex lesions.

- Patient risk is minimized by limiting use to operators who have the necessary training to use the device safety and effectively and adhere to the recommended precaution regarding the fact that anatomical complexity was associated with no-cross occurrences in the clinical evaluation of the Lacrosse NSE ALPHA Coronary Dilatation Catheter in the EXPANSE-PTCA Study.

Therefore, the totality of the available information overall supports the conclusion that the probable benefits of the NSE ALPHA for improving patient outcomes outweigh the probable risks associated with the use of the device.

Patient Perspective

This submission did not include specific information on patient perspectives, and therefore, did not serve as part of the basis of the decision to approve or deny the PMA for the NSE ALPHA.

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 preclinical safety and effectiveness of the NSE ALPHA have been demonstrated by results obtained from biocompatibility testing, engineering bench testing, *in vivo* animal testing, sterilization testing, packaging testing, and shelf-life testing. Considering the EXPANSE-PTCA study did not meet its primary effectiveness endpoint, careful consideration was given to ensure that the totality of data was evaluated to support the marketing decision. To address the residual uncertainty regarding the rate of device failure associated with complex lesion cases, the device IFU maintains cautionary language to encourage the use of supporting devices when treating complex lesions and will be further investigated by a post approval study as outlined in the conditions of approval below.

XV. CDRH DECISION

CDRH issued an approval order on June 6, 2024.The final clinical conditions of approval cited in the approval order are described below.

Lacrosse NSE Alpha Coronary Dilatation Catheter New Enrollment Post Approval Study: This new enrollment study is a prospective, multicenter, single-arm, post-approval study to further evaluate the Lacrosse NSE Alpha coronary dilation catheter in patients with stenotic coronary artery disease who are suitable candidates for percutaneous transluminal coronary angioplasty. The purpose of the study is to further evaluate the performance of Lacrosse NSE Alpha for crossing and scoring stenotic lesions in standard and complex lesions, with specific focus on understanding success of lesion crossing after encouraging physicians to plan for the use of extra delivery support in complex (moderate to severely calcified and/or tortuous) lesions. Patients will be consecutively enrolled and at least 30 patients will have both severe calcification and moderate/severe tortuosity.

The study will collect data on the following outcomes:

A. Similar to EXPANSE-PTCA, the primary endpoint will include:
   - Successful delivery, inflation, deflation, and withdrawal of the study balloon; and
   - No evidence of device-related vessel perforation, flow limiting dissection (grade C or higher, per Clinical Events Committee (CEC) adjudication) or reduction in TIMI flow from baseline (per core laboratory assessment); and
   - Final TIMI flow grade of 3 at the conclusion of the PCI procedure per core laboratory assessment.

B. In addition to the secondary endpoints noted in EXPANSE-PTCA, the PAS will evaluate:
   - Rate of device success and failure to cross lesions, including how this may relate to specific lesion characteristics (i.e., calcified and/or tortuous); and
   - Number of crossing attempts with the device, if any complications with crossing are observed; and
   - Details regarding the use of support catheters and/or additional devices to enable lesion crossing after failure from use of device.
   - Physician a priori evaluation of crossing complexity

At least 100 patients with clinical characteristics described above, including at least 30 patients with complex lesion characteristics will be enrolled and followed through discharge. More than 100 patients may be needed if the 30 patient minimum for complex lesions hasn't been achieved during consecutive enrollment. Outside of the minimum 30 patients enrolled for severe calcification and moderate/severe tortuosity, the remaining patients will maintain complex lesion characteristics i.e., lesions characterized on a spectrum of moderate to severe calcification or tortuosity.

The following Subgroup and Sensitivity Analyses will be performed for the primary outcome:

- Lesion complexity (overall); by operator grading and angiography
- Support catheter use (overall)
- Support catheter use in complex lesions

The data will be evaluated descriptively to better understand and inform use in complex lesions.

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

XVI. 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.

XVII. REFERENCES

1. Kandzari D, Hearne S, Kumar G, Sachdeva R, et al. Procedural effectiveness with a focused force scoring angioplasty catheter: Procedural and clinical outcomes from the Scoreflex NC trial. Cardiovasc Revasc Med. 2021 Mar 20:S1553-8389(21)00147-0. doi: 10.1016/j.carrev.2021.03.013. Epub ahead of print. PMID: 33781677
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