

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Carotid Stent

Device Trade Name: ENROUTE™ Transcarotid Stent System

Device Procode: NIM

Applicant's Name and Address: Silk Road Medical, Inc.
735 North Pastoria Avenue
Sunnyvale, CA 94085

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P140026

Date of FDA Notice of Approval: May 18, 2015

II. INDICATIONS FOR USE

The ENROUTE™ Transcarotid Stent System used in conjunction with the ENROUTE Transcarotid Neuroprotection System (NPS) is indicated for the treatment of patients at high risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria outlined below.

1. Patients with neurological symptoms and $\geq 50\%$ stenosis of the common or internal carotid artery by ultrasound or angiogram OR patients without neurological symptoms and $\geq 80\%$ stenosis of the common or internal carotid artery by ultrasound or angiogram, AND
2. Patients must have a vessel diameter of 4-9mm at the target lesion, AND
3. Carotid bifurcation is located at minimum 5 cm above the clavicle to allow for placement of the ENROUTE Transcarotid NPS.

III. CONTRAINDICATIONS

Use of the ENROUTE™ Transcarotid Stent System is contraindicated in the following patients:

1. Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated.
2. Patients in whom the ENROUTE Transcarotid NPS is unable to be placed.

3. Patients with uncorrected bleeding disorders.
4. Patients with known allergies to nitinol.
5. Lesions in the ostium of the common carotid artery.

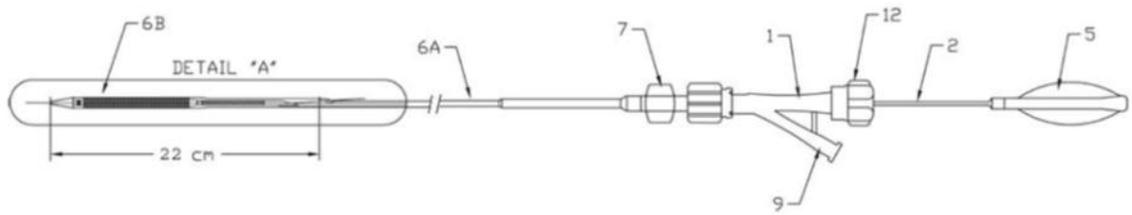
IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the ENROUTE™ Transcarotid Stent System labeling.

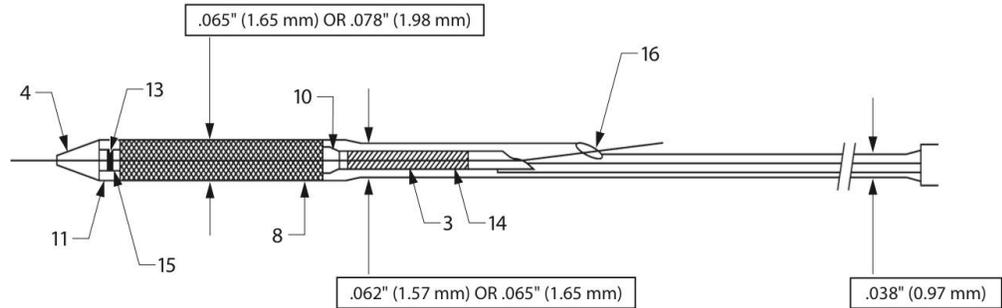
V. DEVICE DESCRIPTION

P030047, submitted by Cordis Corporation (Cordis) for the PRECISE® Nitinol Stent System, was approved on September 22, 2006 for the same use proposed by Silk Road Medical, Inc. The SSED for P030047 is available on the CDRH website and is incorporated by reference here. Silk Road Medical (SRM) has entered into a license and supply agreement with Cordis, whereby SRM has modified the FDA-approved Cordis PRECISE® PRO Rx Nitinol Stent System (PRECISE) for transcarotid delivery when used in conjunction with the ENROUTE™ Transcarotid Neuroprotection System (cleared on February 9, 2015 under 510(k) K143072). The 510(k) Summary for K143072 is also available on the CDRH website. The only difference between the ENROUTE™ Transcarotid Stent System and PRECISE is a shortened stent delivery system length to accommodate introduction directly into the common carotid artery (CCA) versus the traditional femoral approach. Direct access to the CCA permits the stent delivery system to be shortened to a useable length of 57 cm versus the 135 cm of PRECISE. All other aspects of PRECISE and the ENROUTE™ Transcarotid Stent Systems are identical, including the stent, materials, and mechanism of action.

The SRM ENROUTE™ Transcarotid Stent System consists of a nitinol self-expanding stent preloaded on a .065 inch (1.65 mm) or .078 inch (1.98 mm) sheathed delivery system. The delivery system consists mainly of an inner shaft and an outer sheath with radiopaque markers, and a Tuohy Borst valve. The distal inner shaft consists of a support member and wire lumen. The proximal portion of the support member is comprised of a hub connected to a stainless steel wire and hypotube and distally of a stainless steel coil. The wire lumen originates distally in a catheter tip and terminates proximally at a guidewire exit port located mid-shaft and designed to accept a .014" (0.36 mm) guidewire. The outer sheath has a proximal shaft and distal outer sheath with a nominal working length of 57 cm. The self-expanding stent is constrained within the space between the inner shaft and the distal outer sheath, located between distal and proximal stent markers on the inner shaft. The stent expands to its unconstrained diameter when released from the deployment catheter into the vessel. Upon deployment, the stent forms an open lattice and pushes outward on the luminal surface, helping to maintain the patency of the vessel. Due to the self-expanding behavior of nitinol, the stents are indicated for placement into vessels that are 1-2 mm smaller in diameter than the unconstrained diameter of the stent. Device depictions and components are provided in Figure 1.



DETAIL "A":



Item	Description
1	Tuohy Borst valve
2	Hypotube
3	Coil
4	Catheter inner shaft tip
5	Inner shaft hub
6A	Proximal shaft
6B	Distal outer sheath
7	Outer shaft Luer hub
8	Pod housing crimped stent
9	Tuohy Borst Y-connection
10	Proximal inner shaft marker (stop) marks trailing end of stent
11	Outer sheath radiopaque marker
12	Proximal valve end
13	Distal inner shaft stent marker
14	Coil sleeve
15	Wire lumen
16	Guidewire exit port

Figure 1: ENROUTE™ Transcarotid Stent System

Table 1 lists the stent configurations. Due to the self-expanding behavior of nitinol, the stents are indicated for placement into vessels that are 1-2mm smaller in diameter than the unconstrained diameter of the stent.

Table 1: Silk Road ENROUTE™ Transcarotid Stent System Catalog Numbers

Catalog Number	Sterilized Packaged Assembly Number	Unconstrained Stent Dimensions Diameter x Length (mm)	Crossing Profile
SR-0520-CS	K0520RXTC	5 x 20	5F (.078", 1.98mm)
SR-0530-CS	K0530RXTC	5 x 30	5F (.078", 1.98mm)
SR-0540-CS	K0540RXTC	5 x 40	5F (.078", 1.98mm)
SR-0620-CS	K0620RXTC	6 x 20	5F (.078", 1.98mm)
SR-0630-CS	K0630RXTC	6 x 30	5F (.078", 1.98mm)
SR-0640-CS	K0640RXTC	6 x 40	5F (.078", 1.98mm)
SR-0720-CS	K0720RXTC	7 x 20	5F (.078", 1.98mm)
SR-0730-CS	K0730RXTC	7 x 30	5F (.078", 1.98mm)
SR-0740-CS	K0740RXTC	7 x 40	5F (.078", 1.98mm)
SR-0820-CS	K0820RXTC	8 x 20	5F (.078", 1.98mm)
SR-0830-CS	K0830RXTC	8 x 30	5F (.078", 1.98mm)
SR-0840-CS	K0840RXTC	8 x 40	5F (.078", 1.98mm)
SR-0920-CS	K0920RXTC	9 x 20	6F (.087", 2.21mm)
SR-0930-CS	K0930RXTC	9 x 30	6F (.087", 2.21mm)
SR-0940-CS	K0940RXTC	9 x 40	6F (.087", 2.21mm)
SR-1020-CS	K1020RXTC	10 x 20	6F (.087", 2.21mm)
SR-1030-CS	K1030RXTC	10 x 30	6F (.087", 2.21mm)
SR-1040-CS	K1040RXTC	10 x 40	6F (.087", 2.21mm)

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternatives to stenting for the correction of carotid artery disease (CAD) include: surgery, medical therapy, or a combination of both. The primary treatment used to prevent stroke in patients with significant CAD is surgery (endarterectomy) to remove plaque from the affected artery. Medical therapy includes use of antiplatelet and/or anticoagulant medicine, as well as antihypertensive and antilipidemic drugs as indicated. Antiplatelet drugs include aspirin, Plavix® (clopidogrel), or Ticlid® (ticlopidine). Anticoagulants include Coumadin® (warfarin). Medical therapy can also include modification of lifestyle risk factors for stroke, such as cigarette smoking and alcohol use. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The ENROUTE™ Transcarotid Stent System (marketed as the KOBİ Transcervical Carotid Stent System) has been commercially available in the following countries since August 2013:

- Great Britain
- Germany
- France
- Spain
- Hungary
- Belgium

As of April 30, 2015, 135 stents have been distributed outside the United States (OUS). No product has been withdrawn from the market in any country for any reason.

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 device.

- Air embolism
- Allergic/anaphylactoid reaction
- Aneurysm
- Angina/coronary ischemia
- Arrhythmia (including bradycardia, possibly requiring need for a temporary or permanent pacemaker)
- Arterial occlusion/restenosis of the treated vessel
- Arterial occlusion/thrombus, at puncture site
- Arterial occlusion/thrombus, remote from puncture site
- Arteriovenous fistula
- Bacteremia or septicemia
- Cerebral edema
- Death
- Embolization, arterial
- Embolization, stent
- Emergent repeat hospital intervention
- Fever
- GI bleeding from anticoagulation/antiplatelet medication
- Hematoma bleed, access site
- Hematoma bleed, remote site
- Hemorrhage
- Hyperperfusion syndrome
- Hypotension/hypertension
- Infection
- Intimal injury/dissection
- Ischemia/infarction of tissue/organ
- Local infection and pain at insertion site
- Malposition (failure to deliver the stent to the intended site)
- Myocardial infarction
- Pain
- Pseudoaneurysm
- Renal failure
- Restenosis of the vessel (> 50% obstruction)
- Seizure
- Severe unilateral headache
- Stent migration

- Stent thrombosis
- Stroke
- Transient ischemic attack
- Transient intolerance to reverse flow
- Vasospasm
- Venous occlusion/thrombosis, at puncture site
- Venous occlusion/thrombosis, remote from puncture site
- Vessel rupture, dissection, perforation

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

IX. SUMMARY OF PRECLINICAL STUDIES

Because the ENROUTE™ Transcarotid Stent System is identical to the Cordis PRECISE device with the exception of the shortened delivery system length, the following pre-clinical tests were leveraged from the P030047 approval for PRECISE to support this approval: Biocompatibility, Shelf Life, Package Shelf Life, Sterilization Validation; EO Residual Qualification, Chronic Animal Studies, Acute Animal Studies, and the following bench data:

Delivery System	Stent
<ul style="list-style-type: none"> • Crossing profile • Wire lumen ID • SDS Tip ID • Luer fitting • Air embolized • Ability to aspirate • Deployment accuracy • Tip OD • OM hub/hemovalve joint torque • Pod/body fuse joint pull strength & elongation • Brite tip/pod fuse joint strength • OM Proximal OM Body elongation pull strength • Wire lumen tip pull strength • OM hub pull strength 	<ul style="list-style-type: none"> • Expanded Stent Length and Flare • Deployed Stent Uniformity • Deployed Stent Outer Diameter • Radial Resistive Force • Chronic Outward Force • Stent Mechanical and Thermal Properties • Stent Finite Element Analysis • Balloon Tacking • Stent Corrosion • Stent MRI Compatibility • Stent AF Temperature Verification • Stent Recoil • Stent Expansion • Stent Flaw Size Detection • Stent Crush Fatigue • Stent Pulsatile Fatigue • Stent Length vs. Diameter • Stent Dimensional Verification • Stent Open Area • Stent Kinking

Please see the P030047 SSED for details of the non-clinical testing that was conducted to obtain approval of PRECISE and leveraged herein, with the permission of Cordis.

In addition, a series of non-clinical laboratory studies were performed to evaluate the change to the delivery system length. These evaluations included *in vitro* engineering studies, including simulated use testing. Table 2 contains a summary of this testing.

Table 2: *In Vitro* Engineering Testing

Test	Description of Test	Acceptance Criteria	Conclusion
SDS Visual Inspection	To ensure the stent delivery system is free of damage and contamination. All stent delivery systems met the specifications.	The SDS must be free of surface damage, kinks, marks, and cuts, melted or collapsed tubing, and not exposed distally of the Outer Member Tip. Loose contamination should be <1/32", embedded contamination should be <0.050".	Pass
Label Content Verification	To ensure the label has the correct information, including variable after the label is printed. All labels met the specification.	Labeling and print must be verified as correct per the label specifications.	Pass
Usable Length	To measure usable length of the carotid stent system. All ENROUTE Transcarotid Stent Systems met the specification.	Usable length of 57cm +1.2/-2.0cm	Pass
Exit Port Location	To measure the distance of the exit port location from the tip All ENROUTE Transcarotid Stent Systems met the specification.	Exit Port Location is located at 18cm to 32cm from the tip.	Pass
Marker Band Placement	To measure the distance from the distal edge of the proximal maker band (the stop) to the distal edge of the brite tip. All ENROUTE Transcarotid Stent Systems met the specification.	<u>5F SDS stents</u> 20mm stent: ≤ 1.11" [28.2mm] 30mm stent: ≤ 1.58" [40.1mm] 40mm stent: ≤ 2.04" [51.8mm] <u>6F SDS stents</u> 20mm stent: ≤ 1.09" [27.7mm] 30mm stent: ≤ 1.50" [38.1mm] 40mm stent: ≤ 1.92" [48.8mm]	Pass
Pre-Deployment	To measure the distance between the proximal edge of the stent and the distal edge of the brite tip. All ENROUTE Transcarotid Stent Systems met the specification.	<u>5F SDS Stents</u> 20mm stent: ≥ 0.90" [22.8mm] 30mm stent: ≥ 1.36" [34.6mm] 40mm stent: ≥ 1.83" [46.4mm] <u>6F SDS Stents</u> 20mm stent: ≥ 0.85" [21.6mm] 30mm stent: ≥ 1.27" [32.3mm] 40mm stent: ≥ 1.69" [42.9mm]	Pass
Stroke Length	To measure the distance between the proximal edge of the hemovalve and the distal edge of the support member hub. All ENROUTE Transcarotid Stent Systems met the specification.	20mm stents: ≥ 40mm (1.57") 30mm stents: ≥ 50mm (1.97") 40mm stents: ≥ 60mm (2.36")	Pass
Hub/Hypotube Pull Strength	To evaluate the ability of the Hub/Hypotube joint to withstand the applied tensile forces. All ENROUTE Transcarotid Stent Systems met the specification.	Hub/Hypotube Pull Strength: ≥ 2.2 lbs	Pass

Test	Description of Test	Acceptance Criteria	Conclusion
Hub/Proximal Wire Pull Strength	To evaluate the ability of the Hub/Proximal Wire joint to withstand the applied tensile forces. All ENROUTE Transcarotid Stent Systems met the specification.	Support member Hub/Proximal Wire Pull Strength: ≥ 3.0 lbs	Pass
Wire lumen/PET/Proximal Wire sleeve pull strength	To evaluate the ability of the wire lumen / PET sleeve / proximal wire joint to withstand the applied tensile forces. All ENROUTE Transcarotid Stent Systems met the specification.	Wire lumen/Proximal Wire/PET sleeve pull Strength: ≥ 3.0 lbs	Pass
Proximal Wire /Hypotube Pull Strength	This test evaluates the ability of the proximal wire/spiral hypotube weld joint to withstand the applied tensile forces. All ENROUTE Transcarotid Stent Systems met the specification.	≥ 4.0 lbs after subjected to a compressive load pre-conditioning	Pass
Stop Pull Strength	This test evaluates the ability of the stop/spiral hypotube weld joint to withstand the applied tensile forces. All ENROUTE Transcarotid Stent Systems met the specification.	≥ 0.7 lbs after subjected to a compressive load pre-conditioning	Pass
Simulated Use	To verify that the ENROUTE Transcarotid Stent System can be prepared and tracked to a location from which the stent can be deployed using adequate force. Verify the delivery system can be retracted after stent deployment. All ENROUTE Transcarotid Stent System met the specification.	<ul style="list-style-type: none"> • Device Preparation: Device can be prepared per IFU • Device Delivery: Devices can be tracked to location in tortuous path model (10929) • Device Deployment Force: <ul style="list-style-type: none"> ○ 5F: ≤ 3.8 lb (Maximum) ○ 6F: ≤ 5.0 lb (Maximum) • Device Retraction: No adverse effect on SDS or MICHI Arterial sheath integrity • Post-Deployment Stent Inspection: <ul style="list-style-type: none"> ○ Stent is fully expanded (no bottlenecks) ○ No kinks ○ No broken struts • Post-Deployment Delivery System Inspection: <ul style="list-style-type: none"> ○ Tip of SDS is attached. ○ No visual damages to portion of SDS engaged during the test. 	Pass
MR Compatibility	To verify the ENROUTE Transcarotid Stent can be labeled for MR Compatibility with 1.5 and 3 Tesla MRI systems. The ENROUTE Transcarotid is MR Conditional for 1.5 and 3.0 Tesla MR Systems.	To meet the FDA Guidance document “Establishing Safety and Compatibility of Passive Implants in the Magnetic Resonance (MR) Environment”.	Pass

The non-clinical data reviewed under P030047, along with the newly conducted testing reviewed in this PMA, were found to be adequate to support the safety and effectiveness of the ENROUTE™ Transcarotid Stent System.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed a clinical study entitled “INVESTIGATION of FLOW ALTERED, SHORT TRANSCAROTID CAROTID ARTERY STENTING in PATIENTS with SIGNIFICANT CAROTID ARTERY DISEASE with Filter: The ROADSTER Plus Study” (ROADSTER) primarily to support market clearance of the ENROUTE™ Transcarotid Neuroprotection System (ENROUTE Transcarotid NPS, formerly referred to as the MICHIf NPS) used in conjunction with all FDA-approved carotid artery stents under IDE G120143. A sub-study of those subjects, those treated with a combination of the ENROUTE Transcarotid NPS and the Cordis PRECISE stent, was conducted to establish a reasonable assurance of safety and effectiveness of the ENROUTE™ Transcarotid Stent System. The PRECISE stent system was used as a surrogate for the ENROUTE™ Transcarotid Stent System as the only difference is the length of the delivery system with all other components being the same. Data from this clinical sub-study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The ROADSTER study was a prospective, single-arm, multi-center clinical trial of the ENROUTE Transcarotid NPS used in conjunction with all FDA-approved carotid artery stents used for revascularization in patients with carotid disease who are at high risk for complications from carotid endarterectomy (CEA). There was a lead-in phase of up to five (5) patients per investigator to allow investigators to gain experience with the study device prior to pivotal study enrollment. Patients were followed to 30 days post procedure, with additional follow-up (as described below) for patients suspected of having a stroke or cranial nerve injury. Outcomes including major adverse events (stroke, death and myocardial infarction), acute device success, technical success, procedure success, access site complications, and adverse events were tabulated.

The study included patients at high risk for complications from CEA with atherosclerotic extracranial internal carotid stenosis (ICA) with or without involvement of the contiguous common artery (CCA) determined by duplex ultrasound, CT/CTA, MR/MRA or angiography.

Between November 2012 and July 2014, seven hundred five patients (705) were screened for enrollment in the ROADSTER study. Of the screened patients, two hundred and eight (208) subjects at high risk for complications from CEA were enrolled and treated with a combination of the ENROUTE Transcarotid NPS and any FDA-approved carotid stent. Sixty-seven (67) subjects were enrolled in the lead-in phase; 141 subjects were enrolled in the pivotal phase. The subjects enrolled in the

pivotal phase represent the intent-to-treat (ITT) population. Eighteen (18) lead-in and 34 pivotal subjects at high risk for complications from CEA were treated with the PRECISE Stent and are included in the PMA sub-study cohort. The database for this PMA reflected data collected through September 2014. Seventeen (17) sites in the US and one (1) in the European Union enrolled subjects in the ROADSTER study. For the sub-study reported herein, eight (8) centers treated subjects with a PRECISE Stent, all of which were located in the US.

1. Clinical Inclusion and Exclusion Criteria

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

1. Patient must meet one of the following criteria regarding neurological symptom status and degree of stenosis:

Symptomatic: Stenosis must be >50% as determined by angiogram and the patient has a history of stroke (minor or non-disabling), TIA and/or amaurosis fugax within 180 days of the procedure.

OR

Asymptomatic: Stenosis must be >70% as determined by angiogram without any neurological symptoms within the prior 180 days.

2. Target vessel must meet diameter requirements for stent (refer to selected stent IFU for diameter requirements).
3. Patient has a discrete lesion located in the internal carotid artery (ICA) with or without involvement of the contiguous common carotid artery (CCA).
4. Patient is >18 years of age.
5. Patient has no childbearing potential or has a negative pregnancy test within one week prior to the study procedure.
6. Patient understands the nature of the procedure and has provided a signed informed consent using a form that has been reviewed and approved by the Investigational Review Board/Ethics Committee of the respective clinical site prior to the procedure. This will be obtained prior to participation in the study.
7. Patient is willing to comply with the protocol requirements and return to the treatment center for all required clinical evaluations.
8. Patient meets at least one of the surgical high-risk criteria listed below.

Anatomic High Risk Inclusion Criteria:

- A. Contralateral carotid artery occlusion
- B. Tandem stenoses >70%
- C. High cervical carotid artery stenosis
- D. Restenosis after carotid endarterectomy

- E. Bilateral carotid artery stenosis requiring treatment (Treatment of the contralateral vessel must be scheduled at least 30 days post index procedure).
- F. Hostile Necks which the Investigator deems safe for transcervical access including but not limited to:
 - I. Prior neck irradiation
 - II. Radical neck dissection
 - III. Cervical spine immobility

Clinical High Risk Inclusion Criteria:

- G. Patient is ≥ 75 years of age
- H. Patient has > 2 -vessel coronary artery disease and history of angina of any severity
- I. Patient has a history of angina
 - Canadian Cardiovascular Society (CCS) angina class 3 or 4
 - Or
 - unstable angina
- J. Patient has congestive heart failure (CHF) - New York Heart Association (NYHA)
 - Functional Class III or IV
- K. Patient has known severe left ventricular dysfunction
 - LVEF $< 30\%$.
- L. Patient has had a myocardial infarction > 72 hours and < 6 weeks prior to procedure.
- M. Patient has severe pulmonary disease (COPD) with either:
 - FEV1 $< 50\%$ predicted or
 - chronic oxygen therapy or
 - resting PO2 of ≤ 60 mmHg (room air)
- N. Patient has permanent contralateral cranial nerve injury
- O. Patient has chronic renal insufficiency (serum creatinine > 2.5 mg/dL).

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

1. Patient has chronic atrial fibrillation.
2. Patient has had any episode of paroxysmal atrial fibrillation within the past 6 months, or history of paroxysmal atrial fibrillation requiring chronic anticoagulation.
3. Patient has an evolving stroke.
4. Patient has severe dementia.
5. Patient has a history of spontaneous intracranial hemorrhage within the past 12 months.

6. Patient has had a recent (<7 days) stroke of sufficient size (on CT or MRI) to place him or her at risk of hemorrhagic conversion during the procedure.
7. Patient had hemorrhagic transformation of an ischemic stroke within the past 60 days.
8. Patient has active bleeding diathesis or coagulopathy or will refuse blood transfusion.
9. Patient had or will have CABG, endovascular stent procedure, valve intervention or vascular surgery within 30 days before or after the intervention.
10. Patient has had a recent GI bleed that would interfere with antiplatelet therapy.
11. Life expectancy of < 12 months post procedure.
12. Patient has history of intolerance or allergic reaction to any of the study medications or stent materials (refer to stent IFU), including aspirin (ASA), ticlopidine, clopidogrel, prasugrel, statin or contrast media (that can't be pre medicated). Patients must be able to tolerate statins and a combination of ASA and ticlopidine, ASA and clopidogrel or ASA and prasugrel.
13. Myocardial Infarction within 72 hours prior to the intervention.
14. Presence of a previous placed intravascular stent in target vessel or the planned arteriotomy site.
15. Patient has had neurologic illnesses within the past two years characterized by fleeting or fixed neurologic deficit which cannot be distinguished from TIA or stroke (e.g. partial or secondarily generalized seizures, complicated or classic migraine, tumor or other space-occupying brain lesions, subdural hematoma, cerebral contusion or other post-traumatic lesions, intracranial infection, demyelinating disease, moderate to severe dementia, or intracranial hemorrhage).
16. Patient with a history of major stroke (CVA or retinal embolus) with major neurological deficit likely to confound study endpoints within 1 month of index procedure.
17. Patient has Hgb <10 g/dl, platelet count <125,000/ μ l, uncorrected INR >1.5, bleeding time >1 minute beyond upper limit normal, or heparin-associated thrombocytopenia.
18. Patient has an intracranial tumor.
19. Patient is actively participating in another drug or device trial (IND or IDE) that has not completed the required protocol follow-up period.
20. Patient has inability to understand and cooperate with study procedures or provide informed consent.

21. Occlusion or [Thrombolysis In Myocardial Infarction Trial (TIMI 0)] “string sign” >1cm of the ipsilateral common or internal carotid artery.
22. Patient has vertebrobasilar insufficiency symptoms only, without clearly identifiable symptoms referable to the study carotid artery.
23. Knowledge of cardiac sources of emboli.e.g. left ventricular aneurysm, intracardiac filling defect, cardiomyopathy, aortic or mitral prosthetic heart valve, calcific aortic stenosis, endocarditis, mitral stenosis, atrial septal defect, atrial septal aneurysm, or left atrial myxoma).
24. Recently (<60 days) implanted heart valve (either surgically or endovascularly), which is a known source of emboli as confirmed on echocardiogram.
25. Ostium of Common Carotid Artery (CCA) requires revascularization.
26. Presence of extensive or diffuse atherosclerotic disease involving the proximal common carotid artery that would preclude the safe introduction of the study device.
27. The patient has less than 5cm between the clavicle and bifurcation, as assessed by duplex Doppler ultrasound.
28. Bilateral carotid stenosis if intervention is planned within 37 days of the index procedure.
29. An intraluminal filling defect (defined as an endoluminal lucency surrounded by contrast, seen in multiple angiographic projections, in the absence of angiographic evidence of calcification) that is not associated with an ulcerated target lesion.
30. Abnormal angiographic findings: ipsilateral intracranial or extracranial arterial stenosis greater in severity than the lesion to be treated, cerebral aneurysm > 5 mm, AVM (arteriovenous malformation) of the cerebral vasculature, or other abnormal angiographic findings.
31. Patient has had a previous intervention in the ipsilateral proximal CCA.
32. Patient has had a TIA or amaurosis fugax within 48 hours prior to the procedure.
33. Patient has contralateral lateral recurrent, laryngeal or vagus nerve injury.
34. Patient is otherwise unsuitable for intervention in the opinion of the investigator.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30 days (+7 days) postoperatively. In addition, patients suspected of having a stroke were followed at 3 months (± 14 days) and patients suspected of having a cranial nerve injury were followed at 6 months (± 30 days).

Table 3 below list all pre-procedure and post-procedure evaluations performed in relation to the index procedure.

Table 3: ROADSTER Study - Schedule of Events

PROCEDURE/TEST	Pre-Procedure (within # of days)				Procedure	Post-Procedure					Follow-up Visits		
	60 days	30 days	7 days	24 hrs		6-9 hrs	12-16 hrs	20-24 hrs	Within 24 hrs	Prior to Discharge	30-days (+7 days)	3-month (±14 days)	6-month (±30 days)
Patient Informed Consent	X	X	X	X									
Neurological Examinations¹													
NIH Stroke Scale Barthel ADL Index Modified Rankin Scale Cranial Nerve Injury Evaluation			X						X		X	X ²	X ³
Lab Assessments													
RBC, Hemoglobin, Hematocrit, Platelet count, Creatinine		X								X			
WBC, Fasting Glucose, PT, PTT (must include INR), Pregnancy test 4		X											
CK, CKMB, Troponin				X		X	X	X					
Imaging													
Carotid Angiogram ⁵					X								
Duplex Ultrasound ⁶	X									X ⁷	X		
CT Angiogram / Angiogram (optional)	X												
Other Assessments													
Medical History		X											
Physical Examination		X								X			
12 lead ECG ⁸				X						X	X		
Medications	X	X	X	X	X	X	X	X	X	X	X		
Adverse events					X	X	X	X	X	X	X		

Adverse events were recorded at the timepoints indicated in the table above.

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

1 Must be performed by a Neurologist or NIHSS-certified personnel
2 3 month visit is only required for patients suspected of having a stroke
3 6 month visit is only required for patients suspected of having a cranial nerve palsy
4 For women of childbearing potential only
5 Must be labeled and submitted to the Angiographic Core Laboratory
6 Must be labeled and submitted to the Ultrasound Core Laboratory
7 Submitted to Sponsor
8 Must be labeled and submitted to ECG Core Laboratory

3. Clinical Endpoints

The safety and effectiveness of the Cordis PRECISE stent was established through a randomized clinical trial, Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE), supporting PMA approval for that device (P030047) and further supported through large, multi-center, post-market registries. Therefore, the ROADSTER sub-study was intended to evaluate the safety and effectiveness of transcarotid delivery of the PRECISE stent that will then be extrapolated to the Silk Road Medical ENROUTE™ Transcarotid Stent System because it differs only in the length of the delivery system.

With regards to safety, the primary endpoint for the ROADSTER sub-study was major adverse events (defined as a composite of any stroke, myocardial infarction and death) during a 30-day post-procedural period. Additional information related to adverse events and access site complications were also collected.

With regards to effectiveness, the primary effectiveness outcomes for the ROADSTER sub-study were acute device success, technical success, and procedural success. Acute device success was defined as the ability to insert the NPS device, establish flow reversal, and remove the device. Technical success was defined as acute device success plus the ability to deliver interventional tools. Procedural success was defined as technical success in the absence of a Major Adverse Event (MAE defined as death, stroke, or MI).

B. Accountability of PMA Cohort

At the time of database lock, of 52 patients enrolled in the PMA sub-study, 100% (52) patients were available for analysis at the completion of the study. All subjects in the sub-study population (those treated with a PRECISE Stent) completed their 30-day follow-up visit. When applicable, all subjects in the sub-study experiencing a stroke during the 30-day follow-up period (1/52) returned for the 90-day follow-up visit. No patients in the sub-study were suspected of experiencing a cranial nerve injury requiring 6-month follow-up.

Table 4: ROADSTER Sub-study - Patient Follow-up and Accountability

30-Day Follow-Up		90-Day Follow-Up ¹		6-Month Follow-Up ²	
N	%	N	%	N	%
52/52	100%	1/1	100%	N/A	N/A

¹ For only those subjects suspected of having a stroke.

² For only those patients suspected of having a Cranial Nerve Injury (CNI)

C. Study Population Demographics and Baseline Parameters

The demographics of the sub-study population are typical for a high surgical risk carotid artery stenting study performed in the US. Please see Tables 5 and 6 below for additional details.

Table 5: ROADSTER Sub-study – Patient Demographics

Observation	All PRECISE Stent Patients in ROADSTER (N=52)
Age (Years)	73.0 ± 9.07
Symptomatic	23.1%
Male	57.7%
Diabetes	34.6%
Hypertension	94.2%
History of Peripheral Artery Disease	34.6%
History of Coronary Artery Disease	48.1%
History of Angina	19.2%
Congestive Heart Failure	11.5%
Recent MI	1.9%
Severe Pulmonary Disease	9.6%
Dyslipidemia	88.5%
History of Stroke	15.4%
History of TIA	21.2%
History of Amaurosis Fugax	13.5%
Current Nicotine Use	25.0%
Age >75 Years	51.9%
Age >80 Years	23.1%
Contralateral Carotid Occlusion	9.6%
High Cervical Carotid Stenosis	15.4%
Restenosis after CEA	28.8%
Bilateral Stenosis Requiring Treatment	32.7%
Hostile Neck	15.4%
>2 Vessel Coronary Disease	7.7%
Chronic Renal Insufficiency	1.9%

Table 6: ROADSTER Sub-study - Summary of Baseline Vessel and Lesion Characteristics

Observation	All PRECISE Stent Subjects (N=52)
Target Lesion Location	
Left	27 (51.9%)
Right	25 (48.1%)
Vessel to be Treated	
ICA	37 (71.2%)
ICA + CCA	15 (28.8%)
Distance between clavicle and bifurcation (cm)	
N	52
Mean	6.6
Standard Deviation	1.21
Median	6.5
Minimum, Maximum	5, 10
95% Confidence Interval	(6.3, 6.9)
Target Vessel Calcification	
Normal	26 (50.0%)
Mild	17 (32.7%)
Moderate	6 (11.5%)
Severe	1 (1.9%)
Unknown / NA	2 (3.8%)
Target Vessel Tortuosity	
Normal	10 (19.2%)

Observation	All PRECISE Stent Subjects (N=52)
Mild	26 (50.0%)
Moderate	10 (19.2%)
Severe	2 (3.8%)
Unknown / NA	4 (7.7%)
Pre-Procedure Vessel Diameter (mm)	
N	52
Mean	6.7
Standard Deviation	1.78
Median	6.8
Minimum, Maximum	4, 11
95% Confidence Interval	(6.2, 7.2)
Target Lesion Length (mm)	
N	52
Mean	18.7
Standard Deviation	8.05
Median	17.6
Minimum, Maximum	5, 39
95% Confidence Interval	(16.4, 20.9)
Pre-Procedure Percent Stenosis (%)	
N	52
Mean	86.1
Standard Deviation	9.01
Median	90.0
Minimum, Maximum	60, 99
95% Confidence Interval	(83.6, 88.6)

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the sub-study cohort of 52 patients receiving the PRECISE Stent available for the 30-day evaluation. The key outcomes for this study are presented below in Table 7. Adverse effects are reported in Tables 8 and 9. No formal statistical analysis was planned or conducted; therefore, only descriptive outcomes are presented.

Table 7: ROADSTER Sub-study – Primary and Secondary Endpoints

Observations (at 30 days)	All PRECISE Stent Patients in ROADSTER (N=52)
PRIMARY ENDPOINTS	
Safety:	
30 Day MAE (Stroke, Death, or MI)	1 (1.9%)
Effectiveness:	
Acute Device Success	52 (100%)
Technical Success	52 (100%)
Procedural Success	51 (98.1%)
SECONDARY ENDPOINTS	
All Death (non-hierarchical)	0 (0.0%)
All Stroke (non-hierarchical)	1 (1.9%)
All Myocardial Infarction (non-hierarchical)	0 (0.0%)
All Cardiac Death (non-hierarchical)	0 (0.0%)
Ipsilateral Stroke (non-hierarchical)	1 (1.9%)

Observations (at 30 days)	All PRECISE Stent Patients in ROADSTER (N=52)
Access Site Complications	
Oozing	0 (0.0%)
Limited Surgical Wound Hematoma	0 (0.0%)
Surgical Wound Hematoma	0 (0.0%)
Arterial Access Site Hematoma	0 (0.0%)
Femoral Vein Access Site Hematoma	0 (0.0%)
Re-bleeding	1 (1.9%)
Contrast Usage (cc)	
N	47
Mean	66.1
Standard Deviation	42.14
Median	55.0
Minimum, Maximum	12, 220

Adverse effects that occurred in the PMA clinical study:

Table 8 below summarizes all adverse events reported for the sub-study population. This table includes all adverse events including those deemed to be Serious Adverse Events by the protocol definition. Twenty-one (21) subjects experienced one or more adverse events (40.4%). A separate tabulation of Serious Adverse Events follows in Table 9.

Table 8: Summary of All Adverse Events (Sub-study Subjects)

System Organ Class Preferred Term	All PRECISE Stent Subjects (N=52)
Number (%) of Subjects with one or more Adverse Events	21 (40.4%)
Blood And Lymphatic System Disorders	2 (3.8%)
Anaemia	2 (3.8%)
Cardiac Disorders	1 (1.9%)
Atrial Fibrillation	1 (1.9%)
Cardiac Failure Congestive	1 (1.9%)
Gastrointestinal Disorders	6 (11.5%)
Nausea	5 (9.6%)
Vomiting	3 (5.8%)
General Disorders And Administration Site Conditions	5 (9.6%)
Pain	5 (9.6%)
Infections And Infestations	3 (5.8%)
Adenoviral Upper Respiratory Infection	1 (1.9%)
Infection	1 (1.9%)
Urinary Tract Infection	1 (1.9%)
Injury, Poisoning And Procedural Complications	1 (1.9%)
Post Procedural Haemorrhage	1 (1.9%) ⁹
Investigations	3 (5.8%)
Blood Creatine Phosphokinase Increased	1 (1.9%)
Oxygen Saturation Decreased	1 (1.9%)
Troponin Increased	1 (1.9%)
Metabolism And Nutrition Disorders	1 (1.9%)

⁹ One subject was noted to have post-operative bleeding from the incision site. The subject received two (2) units of blood post-operatively. This event is also tabulated as an access site complication.

Hypomagnesaemia	1 (1.9%)
Hypophosphataemia	1 (1.9%)
Nervous System Disorders	4 (7.7%)
Cerebrovascular Accident	1 (1.9%) ¹⁰
Headache	3 (5.8%)
Psychiatric Disorders	1 (1.9%)
Hallucination, Visual	1 (1.9%)
Respiratory, Thoracic And Mediastinal Disorders	3 (5.8%)
Atelectasis	1 (1.9%)
Rales	1 (1.9%)
Rhinorrhoea	1 (1.9%)
Wheezing	1 (1.9%)
Vascular Disorders	8 (15.4%)
Artery Dissection	1 (1.9%) ¹¹
Hypotension	6 (11.5%)
Orthostatic Hypotension	1 (1.9%)

Table 9: ROADSTER Sub-study – Summary of all Serious Adverse Events

System Organ Class Preferred Term	All PRECISE Stent Subjects in ROADSTER (N=52)
Number (%) of Subjects with one or more Serious Adverse Events	7 (13.5%)
Blood And Lymphatic System Disorders	1 (1.9%)
Anemia	1 (1.9%)
Cardiac Disorders	1 (1.9%)
Cardiac Failure Congestive	1 (1.9%)
Injury, Poisoning And Procedural Complications	1 (1.9%)
Post Procedural Hemorrhage	1 (1.9%)
Nervous System Disorders	1 (1.9%)
Cerebrovascular Accident	1 (1.9%)
Respiratory, Thoracic And Mediastinal Disorders	1 (1.9%)
Atelectasis	1 (1.9%)
Vascular Disorders	2 (3.8%)
Artery Dissection	1 (1.9%)
Hypotension	1 (1.9%)

It should be noted that the safety of the device for transcarotid delivery was not based on this sample alone, but rather on all the data available for the device to date, including data from the PRECISE stent. Please see Section XI below for a summary of supplemental clinical information.

2. Effectiveness Results

The analysis of effectiveness was based on the 52 evaluable subjects at the 30-day time point. Effectiveness outcomes are presented Table 10.

¹⁰ One subject had a minor ipsilateral stroke during the 30-day follow-up period.

¹¹ An arterial dissection was noted for Subject 324-502 following Transcarotid Arterial Sheath placement. A 0.014" wire was used to traverse the dissection in the true lumen. A PRECISE Stent was placed to treat the index lesion and a second PRECISE Stent was placed to tack down the dissection flap. There were no clinical sequelae related to the dissection or placement of a second stent (confirmed by ultrasound).

Table 10: ROADSTER Sub-study - Acute Device, Technical and Procedural Success

Observations	All PRECISE Stent Subjects (N=52)
Acute Device Success	52 (100%)
Technical Success	52 (100%)
Procedural Success	51 (98.1%)

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 45 of which 0 were full-time or part-time employees 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: 1
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 1

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

The Silk Road Medical Embolic **Protection** System: **First In Man Study (PROOF)** was a prospective, single arm first-in-man study that collected procedural data from 75 patients in Germany using an early design of the ENROUTE Transcarotid NPS. A subset of patients in the PROOF study (n=13) was treated with a combination of PRECISE and the ENROUTE Transcarotid NPS.

The primary endpoint was a composite of any major stroke, myocardial infarction, and death during the 30-day post-procedural period. The three secondary endpoints included:

- Acute Device Success, defined as the ability to establish a reverse flow circuit as demonstrated by blood flow (arterial to vein) through the shunt circuit before and after stent implantation,
- Procedural Success, defined as the ability to deliver therapeutic devices (balloons, stents, etc.) through the arterial sheath and the ability to provide embolic protection

throughout the procedure with the freedom from device related Major Adverse Events (major stroke, myocardial infarction, or death) at 30 days, and

- Tolerance To Reverse Flow, where intolerance to reverse flow was defined as the inability to complete the procedure with the reverse flow circuit in either the high flow or low flow setting due to intolerance by the patient.

Tables 11-13 below summarize the outcomes from the PROOF sub-study of patients where a combination of the earlier generation ENROUTE Transcarotid NPS and PRECISE stent were used.

Table 11: PROOF Sub-study – Patient Demographics and Baseline Parameters

Parameters and Statistics	PROOF population with PRECISE Stent (N=13)
Male Gender	7 (53.8%)
Caucasian Race	13 (100.0%)
Symptomatic Neurological Status	3
Median Height in cm	170
Median Age in years	67.16
Median weight in kg	86

Table 12: PROOF Sub-study – Results

Parameters and Statistics	PROOF population with PRECISE Stent (N=13)
Number of Patients who experienced an MAE	0 (0%)
Number of Patients who died within 30 days of the Index Procedure	0 (0%)
Number of Patients who had a major stroke within 30 days of the Index Procedure	0 (0%)
Number of Patients who had an MI within 30 days of the Index Procedure	0 (0%)
Acute Device Success	13 (100.0%)
Procedural Success	13 (100.0%)
Tolerance to Reverse Flow	13 (100.0%)

Table 13: PROOF Sub-study – Observed Adverse Events

System Organ Class and Severity	PROOF population with PRECISE Stent (N=13)
Number (%) of Subjects \geq 1 Treatment Emergent Adverse Events	13
Cardiac Disorders	2 (15.4)
Gastrointestinal Disorders	2 (15.4)
General Disorders and Administration Site Conditions	1 (7.7)
Infections and Infestations	1 (7.7)
Investigations	2 (15.4)
Nervous System Disorders	7 (53.8)
Respiratory, Thoracic, and Mediastinal Disorders	1 (7.7)
Skin and Subcutaneous Tissue Disorders	2 (15.4)
Surgical and Medical Procedures	1 (7.7)
Vascular Disorders	7 (53.8)

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 Systems 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

A. Safety and Effectiveness Conclusions

The clinical testing conducted demonstrated that the product provides a reasonable assurance of safety and effectiveness when used as indicated in accordance with the Instructions for Use.

The ROADSTER study was a prospective, single-arm, multi-center clinical trial of the ENROUTE Transcarotid NPS used in conjunction with all FDA-approved carotid artery stents used for revascularization in patients with carotid disease who are at high risk for complications from carotid endarterectomy (CEA). The ROADSTER sub-study included those patients who received the Cordis PRECISE stent. The ENROUTE™ Transcarotid Stent System differs from the approved Cordis PRECISE Stent System only in the length of the delivery system, shortened to accommodate the transcarotid delivery approach.

The primary safety endpoint for the Roadster sub-study was major adverse events (defined as a composite of any stroke, myocardial infarction and death) during a 30-day post-procedural period. The 30-day major adverse event rate was 1.9% (one out of 52 subjects experienced an ipsilateral stroke within the 30-day post-procedure period).

The primary effectiveness endpoints for the Roadster sub-study were acute device success (100%), technical success (100%), and procedural success (98.1% due to one subject experiencing a major adverse event).

The PROOF first-in-man study provided additional supporting evidence that the PRECISE stent system can be used in conjunction with the ENROUTE Transcarotid NPS during transcarotid carotid artery stenting procedures. The 30-day major adverse event rate was 0% (none of the 13 patients experienced a major adverse event), and acute device success, technical success, and procedural success were all 100%. In addition, there were no reports of unanticipated adverse device effects (UADEs) in the ROADSTER or PROOF sub-studies relating to either the stent or the ENROUTE Transcarotid NPS.

Results of the non-clinical and clinical studies were appropriately leveraged from the Cordis P030047 PMA to support the longer term (3 year) safety and performance of the device.

The risks of the device are based on non-clinical laboratory and/or animal studies as well as data collected in clinical studies conducted to support PMA approval as described above.

The *in vitro* engineering testing conducted on the delivery system demonstrates that the ENROUTE™ Transcarotid Stent System performance characteristics met appropriate safety and performance specifications.

B. Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in clinical studies conducted to support PMA approval as described above. The ENROUTE™ Transcarotid Stent System used in conjunction with the ENROUTE Transcarotid Neuroprotection System (NPS) offers similar benefits that traditional stenting via the femoral approach offers over alternative treatments to stenting. In addition, the transcarotid access approach of the ENROUTE™ Transcarotid Stent System offers an alternative option for physicians performing carotid stent procedures that does not involve navigating the aortic arch, thus avoiding risks associated with endovascular aortic arch navigation.

Additional factors to be considered in determining probable risks and benefits for the ENROUTE™ Transcarotid Stent System included:

- The benefits and risks of the ENROUTE™ Transcarotid Stent System device are similar to those for other marketed carotid stents with the exception of risks associated with the cut-down procedure for transcarotid access (e.g., cranial nerve injury).
- Since complication rates in carotid stenting procedures are known to correlate with the experience of the operator, the sponsor plans training to mitigate these risks and also plans to perform a post-approval study that will assess success using the shorter delivery catheter length and outcomes as a function of physician experience.
- The pre-market data support reasonable assurance of safety and effectiveness. However, post-market data will also add information regarding: (1) clinical confirmatory data regarding the use of the shorter delivery catheter; and (2) more extensive assessment of outcomes related to physician experience.

In conclusion, given the available information above, the data support that for the treatment of patients at high risk for adverse events from carotid endarterectomy who require carotid revascularization, the probable benefits of the ENROUTE™

Transcarotid Stent System used in conjunction with the ENROUTE Transcarotid Neuroprotection System (NPS) outweigh the probable risks.

C. 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 novelty of the device is related to the transcarotid delivery of the stent, which will offer an alternative approach to treat carotid disease that does not involve navigating the aortic arch.

XIV. CDRH DECISION

CDRH issued an approval order on May 18, 2015. The final conditions of approval cited in the approval order are described below.

The sponsor agreed to conduct a study as follows:

The purpose of this study is to further establish the safety and effectiveness of the ENROUTE Transcarotid Stent when used with the ENROUTE Transcarotid Neuroprotection System (NPS) by physicians of varying experience with the transcarotid technique.

This is an open label, single-arm, multi-center, new enrollment study of the treatment of patients at high risk for adverse events from carotid endarterectomy who require carotid revascularization and who are eligible for treatment with a combination of the ENROUTE Transcarotid Stent System and the ENROUTE Transcarotid NPS. Eligible patients will be enrolled sequentially and followed through 30 days post stent implant.

Site participation will be limited to institutions with current CMS carotid stent certification and with access to a validated electronic data management system. A minimum of 30 institutions will be included in the study, up to a maximum of 100 institutions. No more than 30% of the sites will be sites that previously enrolled in the ROADSTER study and no more than 30 patients from the same physician will contribute to the minimum sample size.

The primary endpoint is the 30-day incidence proportion of procedural success following index procedure defined as the absence of hierarchical stroke, death or myocardial infarction.

Secondary endpoints include the following 30-day incidence proportions following the index procedure:

- acute device success (defined as the ability to insert the device, establish flow reversal, and remove the device);

- technical success (defined as acute device success plus the ability to deliver interventional tools);
- rate of cranial nerve injury;
- rate of hierarchical stroke, death or myocardial infarction;
- rate of hierarchical stroke, death or myocardial infarction by symptom status;
- acute device, technical and procedural success by physician experience;
- acute device, technical and procedural success by physician training level;
- acute device, technical and procedural success by enrollment quartile.

The observed 30-day incidence of procedural success in this study will be compared to an a priori threshold of 85% derived from the ROADSTER study. A minimum of 600 patients will be enrolled.

Suspected neurologic events and suspected cranial nerve injuries will be adjudicated by an independent Clinical Events Committee. Patients will be evaluated at discharge and 30 days (+7 days) after the index procedure.

Progress reports will be provided to FDA every six (6) months. A final report will be provided no later than 3 months following the final 30-day follow-up for the last patient enrolled.

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

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.