SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Intracranial Aneurysm Flow Diverter
Device Trade Name:	Surpass Streamline Flow Diverter
Device Procode:	OUT
Applicant's Name and Address:	Stryker Neurovascular 47900 Bayside Parkway Fremont, CA 94538
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P170024
Date of FDA Notice of Approval:	July 13, 2018

II. INDICATIONS FOR USE

The Surpass Streamline Flow Diverter is indicated for use in the endovascular treatment of patients (18 years of age and older) with unruptured large or giant saccular wide-neck (neck width ≥ 4 mm or dome-to-neck ratio < 2) or fusiform intracranial aneurysms in the internal carotid artery from the petrous segment to the terminus arising from a parent vessel with a diameter ≥ 2.5 mm and ≤ 5.3 mm.

III. CONTRAINDICATIONS

The Surpass Streamline Flow Diverter is contraindicated in the following patient types:

- Patients in whom the parent vessel size does not fall within the indicated range.
- Patients in whom antiplatelet and/or anticoagulation therapy (e.g., aspirin and clopidogrel) is contraindicated.
- Patients who have not received dual anti-platelet agents prior to the procedure.
- Patients with an active bacterial infection.
- Patients in whom the angiography demonstrates the anatomy is not appropriate for endovascular treatment due to conditions such as:
  - Severe intracranial vessel tortuosity or stenosis; and/or
  - Intracranial vasospasm not responsive to medical therapy.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Surpass Streamline Flow Diverter labeling.

V. DEVICE DESCRIPTION

The Surpass Streamline Flow Diverter is a self-expandable braided device preloaded into a delivery system. Each device is shipped sterile and labeled for single use only. The device consists of the following major components (Figure 1):

- Surpass Flow Diverter (Implant)
- Delivery Catheter
- Pusher

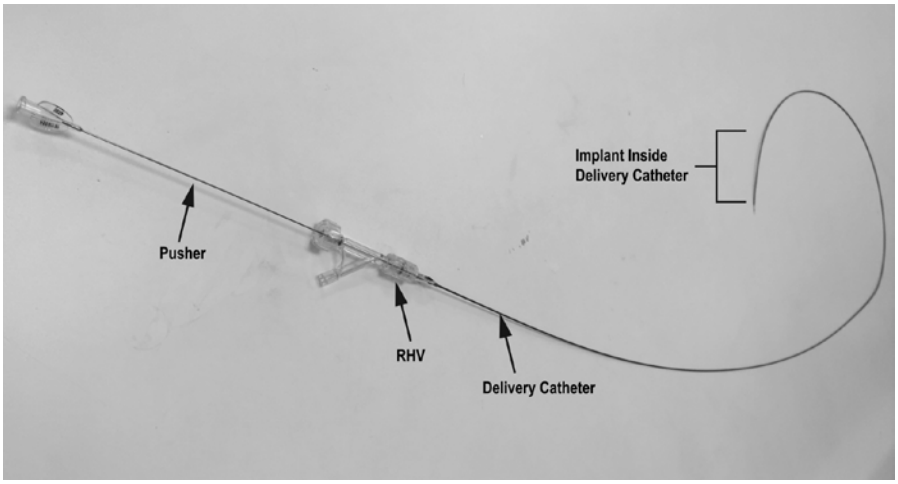


Figure 1. Product Components

A. Surpass Flow Diverter (Implant)

The braided Surpass Flow Diverter is the implant portion of the device. It is shipped preloaded within the delivery system. The device comes in different diameter and length combinations ranging from 3 mm to 5 mm in diameter and from 15 mm to 50 mm in length (Table 1). Interwoven within the Surpass Flow Diverter cobalt chromium braids are platinum tungsten wires for visualization under fluoroscopy. Once released from the constraint of the delivery system into the vessel, the Implant expands to the vessel lumen diameter. The Surpass Flow Diverter (Implant) is intended to divert blood flow from entering into the sac of the intracranial aneurysm.

Table 1. Implant Sizes

Device Diameter (mm)	Device Length (mm)	Unconstrained Implant Outer Diameter (OD) (mm)	Maximum Vessel Diameter (mm)	Recommended Minimum Vessel Diameter (mm)
3.0	15, 20, 25	> 3.5	3.5	2.5
4.0	15, 20, 25, 30, 40, 50	> 4.4	4.4	3.4
5.0	20, 25, 30, 40, 50	> 5.3	5.3	4.3

B. Delivery Catheter

The Delivery Catheter functions in housing and protecting the Implant during its passage through the vasculature for implantation across the intracranial aneurysm neck. The Delivery Catheter is constructed with polytetrafluoroethylene (PTFE) on the inner lumen for lubricity, nitinol wire reinforcement within the wall for pushability, torque transmission and strength, and polymer materials along the length of the catheter for support and flexibility. The distal section has a hydrophilic coating approximately 80 cm in length to improve device tracking in tortuous vessels. The Delivery Catheter has one radiopaque marker located at the distal tip.

C. Pusher

The Pusher is a second catheter that resides within the Delivery Catheter. It pushes the Implant out of the Delivery Catheter and into the parent artery across the intracranial aneurysm neck. It also functions to stabilize the Implant while inside the Delivery Catheter. The Pusher is comprised of two segments: 1) a proximal shaft with PTFE on the inner lumen for lubricity, stainless steel braid reinforcement for pushability and strength, polymer materials outside the braid for support and flexibility, and 2) a stainless steel hypotube for pushability and support during Implant deployment and a distal shaft comprised of several bonded polymeric segments for flexibility and support of the Implant during deployment. The distal segment of the Pusher has two radiopaque markers, one at the tip and one at a variable position (depending on length of the Implant) proximal to the tip, to aid visualization under fluoroscopy. The Implant is loaded between the proximal and tip radiopaque markers of the Pusher. A stainless steel recapture feature is located on the Pusher shaft under the loaded Implant, near the proximal marker of the Pusher, as shown in Figure 2 below.

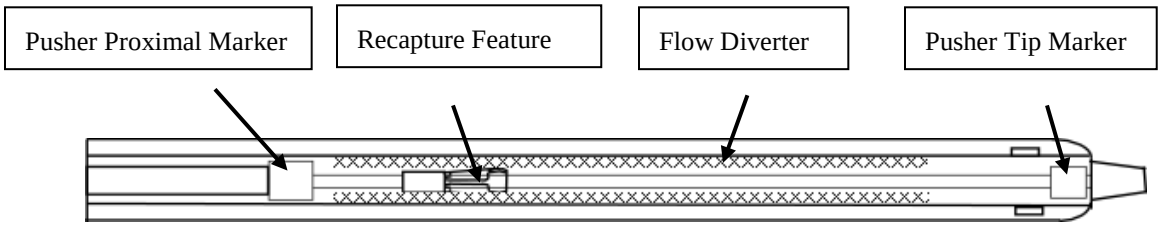


Figure 2. Distal Segment of Pusher with Recapture Feature

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of wide-neck intracranial aneurysms including open surgical clipping, endovascular stent-assisted coiling treatment using neurovascular stents to support embolization coils in the intracranial aneurysm sac or balloon catheter assisted coiling of the intracranial aneurysm, and flow diverters. The neurovascular stents available in the United States (US) for stent-assisted coiling of wide-neck intracranial aneurysms were approved through the premarket approval (PMA) regulatory pathway (i.e., MicroVention, Inc. Low-Profile Visualized Intraluminal Support (LVIS) and LVIS Jr. (P170013)) and the Humanitarian Device Exemption (HDE) regulatory pathway, which include the Stryker Neurovascular Neuroform EZ, 3,

and Atlas Stent Systems (H020002) and the Codman & Shurtleff, Inc. Enterprise Vascular Reconstruction Device and Delivery System (H060001). A similar HDE approved device that is indicated to support neurovascular embolization coils specifically for the treatment of unruptured wide-necked intracranial aneurysms originating on or near a vessel bifurcation of the basilar tip or carotid terminus is the Pulsar Vascular, Inc. PulseRider Aneurysm Neck Reconstruction Device (H160002).

The Micro Therapeutics, Inc. d/b/a ev3 Neurovascular Pipeline Embolization Device (PED) (P100018) is an approved flow diverter in the US and was approved with the intended use of endovascular treatment of large or giant wide-necked intracranial aneurysms in the internal carotid artery (ICA) from the petrous to the superior hypophyseal segment. The flow diverter is implanted in the parent vessel and is placed across the neck of the intracranial aneurysm. Its mechanism of action is to divert the blood flow from entering the intracranial aneurysm sac and endothelialization will occur on the implant over time to further promote complete intracranial aneurysm occlusion. The flow diverter is intended to be used by itself as a stand-alone device. The subject Surpass Streamline Flow Diverter has the same mechanism of action as the approved Pipeline Embolization Device.

In addition to these alternative treatments, certain intracranial aneurysms may be managed medically or by observation only with no treatment but with regular imaging follow-up examinations to ensure there are no morphological changes in the intracranial aneurysm(s) over time. 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 Surpass Streamline Flow Diverter is approved for marketing in the following countries: Australia, Austria, Bahrain, Bangladesh, Belgium, Bulgaria, Canada, Chile, Cyprus, Denmark, Dominican Republic, Estonia, Finland, France, Germany, Hong Kong, Hungary, Iceland, India, Indonesia, Ireland, Italy, Jamaica, Jordon, Korea, Kuwait, Latvia, Lebanon, Libya, Liechtenstein, Lithuania, Luxembourg, Malaysia, Malta, Netherlands, New Zealand, Norway, Oman, Philippines, Poland, Qatar, Romania, Singapore, Slovakia, Slovenia, South Africa, Spain, Sweden, Switzerland, Thailand, Tunisia, Turkey, United Arab Emirates, United Kingdom, and Vietnam.

The Surpass Streamline Flow Diverter has not been withdrawn from the market outside of the US for safety or effectiveness reasons.

VIII. PROBABLE ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the probable adverse effects (e.g., complications) associated with the use of the device.

- Allergic reaction

- Adverse reaction to anesthesia, contrast or antiplatelet/anticoagulation agents
- Aphasia
- Cardiac arrhythmia
- Cranial neuropathy
- Confusion, coma, change in mental status
- Death
- Device migration, fracture, misplacement
- Dissection or perforation of the parent artery
- Embolism (air, clots, device fragments)
- Groin injury (bleeding, pain, vessel/nerve damage)
- Headache
- Hemiplegia
- Hydrocephalus
- Implant or parent vessel stenosis
- Implant thrombosis/occlusion
- Infection
- Intracerebral bleeding
- Mass effect
- Myocardial infarction
- Neurological deficits
- Perforation or rupture of aneurysm
- Progressive neurologic symptoms related to intracranial aneurysm (IA)
- Pseudoaneurysm formation
- Reaction to radiation exposure (i.e., alopecia, burns ranging in severity from skin reddening to ulcers, cataracts, delayed neoplasia)
- Renal failure
- Retroperitoneal hematoma
- Seizure
- Stroke
- Subarachnoid hemorrhage
- Thromboembolism from device
- Thrombosis of parent artery or branch vessel
- Transient ischemic attack (TIA)
- Vasospasm

Risks that are eye related with the use of the Surpass Streamline Flow Diverter may include:

- Amaurosis fugax/transient blindness
- Blindness
- Diplopia
- Reduced visual acuity/field
- Retinal artery occlusion
- Retinal ischemia

- Retinal infarction
- Vision impairment

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

IX. SUMMARY OF NONCLINICAL STUDIES

The Surpass Streamline Flow Diverter underwent mechanical, functional, biocompatibility, and animal testing to evaluate its safety and design verification and validation as a long-term implant for the proposed indicated use. The physical device stability has been validated for a labeling claim of 1-year shelf life based on accelerating aging studies. The device packaging and sterility has been demonstrated to maintain stability with a shelf-life of 3 years based on accelerated aged test samples. Therefore, the final device will be labeled with an initial 1-year shelf-life until further shelf-life studies can be conducted on the physical device to ensure the performance attributes are not affected by aging beyond 1-year shelf-life. The device is sterilized by ethylene oxide (EO) and has been validated to ensure a sterility assurance level (SAL) of 10^{-6}. Tables 2, 3A, 3B, 4, and 5 present the results of device nonclinical testing.

A. Laboratory Studies

Table 2. Surpass Streamline Flow Diverter Design Verification and Validation Studies

Test	Acceptance Criteria	Result
Flow Diverter Implant Dimensional and Functional Attributes		
Dimensional Verification	The device shall have acceptable expanded diameters and lengths to maintain parent vessel patency and resist migration.	Pass
Percent Surface Area of the Stent (Implant)	The device shall have adequate surface area.	Pass
Foreshortening	The percent foreshortening of the Implant from compressed length in the Delivery Catheter to expanded length in the maximum recommended vessel (measured via bench testing) shall be reported as a percentage of the compressed length in the Delivery Catheter.	Pass
Stent Integrity	The Implant should be free from visual defects after deployment in the unconstrained state. Device shall also be free from kinks and bends, meet pore density and porosity, and picks per inch (PPI) criteria.	Pass
Radial Outward Force	The device shall have acceptable radial outward forces to maintain parent vessel patency and resist migration.	Pass
Stress/Strain analysis	Worst-case load conditions shown to be less than yield strength of Implant materials.	Pass
Fatigue Analysis	Fatigue stress amplitude shown to be less than endurance limit of Implant materials.	Pass

Test	Acceptance Criteria	Result
Accelerated Durability Testing	The device shall not exhibit broken wires, excessive wear, crack (fretting corrosion), or permanent set as a result of being subjected to simulated 10 years of expected physiological stress loading.	Pass
Particulate Evaluation	Particulates shall be acceptable following simulated delivery and device deployment.	Pass
Magnetic Resonance Imaging (MRI) Safety and Compatibility	The device must be confirmed to be "MR Conditional."	Pass
Radiopacity	The device shall be visible under fluoroscopy.	Pass
Delivery System Dimensional and Functional Attributes		
Dimensional Verification	The delivery system shall be suitable for access to the intended cerebrovascular anatomical location and delivery and deployment of Implants of 2.5 mm to 5.3 mm diameter, and usable length from 15 mm to 50 mm.	Pass
Delivery, Deployment, and Retraction	The delivery system must be able to safely: deliver the Implant to the intended location, deploy the Implant accurately, and be withdrawn from the anatomy post deployment.	Pass
Catheter Bond Strength	The delivery system must be sufficiently robust to safely: deliver the Implant to the intended location; deploy the Implant accurately, and be withdrawn from the anatomy post deployment without failure.	Pass
Tip Pull Test		Pass
Flexibility and Kink Test		Pass
Torque Strength		Pass
Coating Integrity		Pass
Implant Detachment Reliability		Pass

Table 3A. Biocompatibility (Implant Only)

Test Performed / Applicable EN ISO 10993 Part Number	Result
Minimum Essential Media (MEM) Elution Cytotoxicity / Part 5	Pass No cytotoxicity or cell lysis, Score: 0.
Guinea Pig Maximization Sensitization / Part 10	Pass No evidence of sensitization.
Intracutaneous Reactivity / Part 10	Pass Difference between Test and Control is 0.0 for sodium chloride (SC) and 0.2 for sesame oil (SO).
Acute Systemic Injection / Part 11	Pass No mortality or evidence of systemic toxicity.
Rabbit Pyrogen / Part 11	Pass Nonpyrogenic, max rise: 0.1°C.
Ames Mutagenicity / Part 3	Pass Test article is considered to be non-mutagenic.
Micronucleus Assay / Part 3	Pass

Test Performed / Applicable EN ISO 10993 Part Number	Result
	Test article is considered non-clastogenic.
Chromosomal Aberration Assay / Part 3	Pass Test article is considered non-clastogenic after prolonged exposure.
Hemolysis Direct Contact Method / Part 4	Pass Test article is considered non-hemolytic.
Partial Thromboplastin / Part 4	Pass Average clotting time: 252.4 seconds, 83% of negative control, minimal activator.
Thrombogenicity Study in Dogs / Part 4	Pass The amount of thrombosis was not considered significant.
Complement Activation / Part 4	Pass The test article did not induce complement activation.
Sub-Chronic/Implant – 2 week / Part 3	Pass Test article is considered as a non-irritant.
Sub-Chronic/Implant – 13 weeks / Part 3	Pass No evidence of system toxicity, non-irritant.

Table 3B. Biocompatibility (Finished Device)

Test Performed / Applicable EN ISO 10993 Part No.	Result
MEM Elution Cytotoxicity / Part 5	Pass Grade 0
Guinea Pig Maximization Sensitization / Part 10	Pass Sensitization rate: 0
Intracutaneous Reactivity / Part 10	Pass Score 0.0
Acute Systemic Injection / Part 11	Pass No mortality or evidence of systemic toxicity.
Materials Mediated Rabbit Pyrogen / Part 11	Pass No single animal showed a rise 0.5 °C or more above its baseline temperature, the extract is judged nonpyrogenic.
Hemolysis Direct Contact and Extract Method / Part 4	Pass Hemolytic index: 0.0% (direct contact) and 0.1% (extract).
Partial Thromboplastin Time / Part 4	Pass Results indicate the clotting time of the test article is 96% of the negative control. This test article is considered as a minimal activator.
In Vitro Hemocompatibility Assay / Part 4	Pass All biomaterials have the potential to affect the make-up of the various components of the blood. At this time, there are no ranges or levels that have been established as

Test Performed / Applicable EN ISO 10993 Part No.	Result
	acceptable. All counts of the test sample are found to not be significantly different from the reference material and negative control. Results comparable to Reference Control: • White Blood Cell (WBC): 93% • Red Blood Cell (RBC): 93% • Hemoglobin: 93% • Hematocrit: 92% • Platelet: 87%
Complement Activation (SC5b-9) / Part 4	Pass Concentration of SC5b-9 in the test article was not statistically higher than the negative control. Test article is not considered to be a potential activator of the complement system.
Complement Activation (C3a) / Part 4	Pass Concentration of C3a in the test article was not statistically higher than the negative control. Test article is not considered to be a potential activator of the complement system.
United States Pharmacopeia (USP) Physicochemical <661> / Part 18	Pass Non-volatile residue: 1 mg Residue on ignition: $\leq$ 1 mg Heavy metal: < 1 ppm Buffering capacity: < 1.0 ml
Fourier Transform Infrared Spectroscopy (FTIR) / Part 18	Scan was conducted to establish device baseline.
Natural Rubber Latex Enzyme-Linked Immunosorbent Assay (ELISA) for Antigenic Protein, ASTM D6499-12	Below level of detection.

B. Animal Studies

Table 4. Animal Studies

Test	Purpose	Result
Chronic Implant Study for Feasibility in Rabbits with Elastase Induced Aneurysms	The purpose of this study was to compare the performance of three Implant configurations (B, C and E). Each of the three device configurations have varying porosities and pore densities and were assessed at 21, 90 and 180 days.	The overall composite score results suggest that Configuration E had the best performance with a relative effectiveness of 100%, and that Configuration C was about 86% as effective as Configuration E, and that Configuration B was about 79% as effective as Configuration E.

Test	Purpose	Result
Acute Delivery in Swine Model	The purpose of this *in vivo* test was to ensure the Surpass system meets the product specifications and clinical needs addressed in the risk management regarding deliverability to the neuro anatomy.	The objectives and user needs were met for this study.
Chronic Implant Study in Rabbit Aorta	This study aimed to demonstrate the vascular compatibility of the Surpass flow diverter (Implant) in a rabbit aorta model.	After 7, 28, 90, 180, and 365 days implantation of the Implant in the rabbit aorta model, angiographic evaluation showed percent stenosis was minimal and the Implant had no impact on the involved lumbar arteries. Histopathological assessment demonstrated favorable tissue responses. Results of this study demonstrate that following 7, 28, 90, 180, and 365 days of implantation in rabbit aortas, the Implant showed acceptable vascular healing and produced a minimal tissue response.
Acute Delivery in Porcine Model	This was a design validation user evaluation study to assess whether the intended customer needs met the pre-defined user specifications for performance of the delivery system. The test article was compared against a control device (a previous device iteration) and were evaluated by qualified users.	The test device was found to have results that were the same as or better than the control device in terms of pushability, resheathability, ease of deployment and withdrawal. The results of the physician device evaluation showed that the test device met intended user needs.

C. Additional Studies

Table 5. Additional Studies

Test	Acceptance Criteria	Result
Shelf Life		
Device Performance	Device meets performance specifications following 1 year accelerated aging.	Pass (variable and attribute data analysis)
Packaging Integrity	Packaging integrity is maintained following 3 year accelerated aging.	Pass (variable and attribute data analysis)
Sterilization		

Test	Acceptance Criteria	Result
Sterilization	Device is 100% EO sterilized with a minimum SAL of 10^{-6}.	Pass (variable and attribute data analysis)

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the Surpass Streamline Flow Diverter for the endovascular treatment of patients (18 years of age and older) with unruptured large or giant saccular wide-neck (neck width ≥ 4 mm or dome-to-neck ratio < 2) or fusiform intracranial aneurysms in the internal carotid artery from the petrous segment to the terminus arising from a parent vessel with a diameter ≥ 2.5 mm and ≤ 5.3 mm in the US and Netherlands under IDE #G110229. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between October 25, 2012 and November 18, 2015. The database for this PMA reflected data collected through March 20, 2017 and included 236 patients. There were 25 active investigational sites in the US and 1 investigational site in the Netherlands.

The study, titled "*Surpass Intracranial Aneurysm Embolization System Pivotal Trial to Treat Large or Giant Wide Neck Aneurysms (SCENT),*" was a multi-center, prospective, non-randomized clinical study. The pivotal study included follow-up at discharge, 30 days, 6 months, and 12-months post-procedure. The pre-specified primary endpoints in the clinical study protocol were:

- Safety: Percent of subjects experiencing neurologic death or major ipsilateral stroke through 12-months post-procedure, as adjudicated by an independent Clinical Events Committee (CEC).
- Effectiveness: Percent of subjects with complete (100%) occlusion (Raymond-Roy Class I) of the treated intracranial aneurysm without clinically significant stenosis (clinically significant stenosis defined as > 50% stenosis) of the parent artery based on independent Core Laboratory ("Core Lab") evaluation of the 12 month follow up angiogram and without any subsequent treatment at the target intracranial aneurysm at the 12-month follow-up visit.

The primary endpoint results were compared to performance goals (PGs) developed using prior published data from the Pipeline Embolization Device (P100018) and the "Pipeline for Uncoilable or Failed Aneurysms (PUFS)" study. In addition, the PGs were also developed using published clinical data from endovascular treatments of wide-neck intracranial aneurysms using neurovascular stents for stent assisted coiling (SAC), such as the Neuroform Stent Systems (H020002), LVIS (P170013, H130005), and the Enterprise Vascular Reconstruction Device (H060001).

Sample size calculations demonstrated 150 evaluable subjects provided sufficient power for both the primary safety and effectiveness endpoints. If the true rate of primary safety events was 11%, a sample of 150 treated subjects with evaluable 12-month data would provide 90.1% power in rejecting the null hypothesis that the true rate is 20%. If the true primary effectiveness success rate was 62%, the same sample of 150 treated subjects with evaluable 12-month data would provide 89.6% power in rejecting the null hypothesis that the true rate is 50%. With the two primary endpoints combined, this equates to a study-wide power level of just over 80%.
The enrollment ceiling, which included the maximum sample size of evaluable treated subjects (n = 150) with an additional 20% to account for loss to follow-up (n = 30), was set at 180 evaluable treated subjects. An additional 45 "Roll-In" subjects were permitted in the original approved clinical protocol, which was updated to allow for up to 70 "Roll-In" and "Enrolled but Not Treated" subjects such that the maximum total approved enrollment limit for the SCENT trial was set at 250 subjects.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the SCENT trial was limited to patients who met the following inclusion criteria:

   - Age 19 to 80 years
   - Subject or legal representative is willing and able to give informed consent
   - Subject has a single targeted intracranial aneurysm that:
     - Is located in the internal carotid artery (ICA) distribution up to the terminus
     - Is able to be crossed with a standard 0.014" guide wire
     - Has a neck ≥ 4 mm or no discernible neck and an aneurysm size ≥ 10 mm (including saccular, fusiform and dissecting configuration)
     - Has a vessel diameter between 2.5 mm and 5.3 mm at both the proximal and distal segments where the implant will be placed
   - Subject agrees to return to the treating Investigator for all scheduled follow up visits and is capable of returning to the hospital for follow up

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

   - Known allergy or contraindication to aspirin, clopidogrel/Plavix, heparin, local or general anesthesia
   - Subject has documented resistance to clopidogrel/Plavix
   - Platelet count < 100 x 10^3 cells/mm^3 or known platelet dysfunction
   - Subject has a history of bleeding diathesis or coagulopathy, international normalized ratio (INR) greater than 1.5, or will refuse blood transfusions
   - Subject has a need for long-term use of anticoagulants (i.e., Warfarin, Dabigatran)
   - Known history of life threatening allergy to contrast dye

- Known allergy to nickel, chromium cobalt, tungsten or platinum
- Major surgery within previous 30 days or planned in the next 120 days after enrollment date
- Previous intracranial implant associated with the symptomatic distribution within the past 12 weeks prior to treatment date
- Stenting, angioplasty, or endarterectomy of an extracranial (carotid or vertebral artery) or intracranial artery within 30 days prior to treatment date
- Any previous stenting of parent artery at or proximal to the aneurysm where it would interfere with the placement and proper apposition of the device
- Any previous coiling where it would interfere with the placement and proper apposition of the device
- More than one intracranial aneurysm (IA) that requires treatment within 12-months
- Asymptomatic extradural aneurysms requiring treatment
- Contraindication to computed tomography (CT) scan or MRI
- Severe neurological deficit that renders the subject incapable of living independently
- Unstable neurological deficit (i.e., worsening of clinical condition in the last 30 days)
- Evidence of active infection at the time of treatment
- Dementia or psychiatric problem that prevents the subject from completing required follow-up
- Co-morbid conditions that may limit survival to less than 24 months
- Serum creatinine $\geq$ 2.5 mg/dL
- Female subjects who are pregnant or planning to become pregnant within the study period (all females of child bearing age must take a pregnancy test within 24 hours of treatment) and who are unwilling or unable to take adequate method of contraception for at least until the 12-months study follow-up
- Subject with anatomy not appropriate for endovascular treatment due to severe intracranial vessel tortuosity or stenosis
- Extra-cranial stenosis or parent vessel with stenosis > 50% in the area proximal to the aneurysm
- Other known serious concurrent medical conditions such as heart disease (e.g., atrial fibrillation/pacemaker, recent myocardial infarction, symptomatic congestive heart failure, or carotid stenosis), pulmonary disease, uncontrolled diabetes, progressive neurologic disorders, vasculitis, or subjects using immunosuppressants including corticosteroids
- History of intracranial vasospasm not responsive to medical therapy
- Subject with an intracranial mass (tumor, except meningioma, abscess, or other infection), or is undergoing radiation therapy for carcinoma or sarcoma of the head or neck region
- Subject had a subarachnoid hemorrhage within 30 days prior to the enrollment date

- Subject has a non-treated arterio-venous malformation (AVM) in the territory of the target aneurysm
- Inability to understand the study or a history of non-compliance with medical advice
- Current use of illicit substance
- Enrollment in another trial involving an investigational product

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 1 month, 6 months, and 12-months postoperatively. Preoperatively, the patients underwent a review of their concomitant medications, medical history, physical, clinical, neurological, laboratory, and angiographic evaluations. Postoperatively, the objective parameters measured during the study included a review of the concomitant medications, medical, physical, clinical, neurological, and angiographic evaluations (see Table 6). Adverse events and complications were recorded at all visits.

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

Table 6. Study Required Evaluations from Baseline through 12-Month Follow-Up Visit

	Screening/ Baseline	Intra-Procedure	Post-Procedure Through Discharge	1-Month (± 14 Days)	6-Month (± 30 Days)	12-Month (± 30 Days)
Consent[1,2]	X	--	--	--	--	--
Inclusion/Exclusion	X	--	--	--	--	--
Clopidogrel/Plavix Resistance Testing	X[12]	--	--	--	--	--
Pregnancy Test[6]	X	--	--	--	--	--
Physical Assessment/Vital Signs/Medical History	X[9]	--	--	--	--	--
Neurological Evaluations (Neurologic Exam, Cranial Nerve Exam, National Institute of Health Stroke Scale (NIHSS), modified Rankin Scale (mRS))[11]	X	--	X (at 24 ± 12 hrs post-procedure)	X[10]	X[10]	X[10]
Concomitant Medications	X	--	X (update with any daily changes)	X	X	X
Clinical Laboratory Tests[3]	X	--	--	--	--	--

	Screening/ Baseline	Intra-Procedure	Post-Procedure Through Discharge	1-Month (± 14 Days)	6-Month (± 30 Days)	12-Month (± 30 Days)
Surpass Flow Diverter Procedure	--	X	--	--	--	--
Procedural Medications[4]	--	X	--	--	--	--
Angiogram	Within 6 months prior to procedure (computed tomography angiography (CTA)/magnetic resonance angiography (MRA) acceptable)	X[8]	--	--	X	X
Visual Exam[7]	X	--	--	--	X	X
Adverse Event Evaluation[5]	X	X	X (assess daily after procedure)	X	X	X

X = Required Evaluations

1. The informed consent MUST be signed BEFORE any study specific procedures are performed.
2. Inform Sponsor and study monitor.
3. RBC, WBC, hematocrit, platelet count, Prothrombin Time and Partial Thromboplastin Time (PT/PTT), INR and serum creatinine (within 7 days of device procedure).
4. Antithrombotic, antiplatelet, anticoagulant, inhibitor of adenosine diphosphate (ADP)-induced platelet aggregation, IIb-IIIa inhibitor and vasoactive medications.
5. If serious adverse event (SAE), scan and email to Sponsor/Contract Research Organization (CRO) and study monitor within 24 hours of knowledge of event or as early as feasible.
6. All females of child bearing age required to take a pregnancy test within 24 hours of treatment.
7. Visual exam is required only if the aneurysm is located on the ophthalmic artery.
8. Angiogram images will be taken pre-treatment and post-treatment of the aneurysm.
9. Medical history completed at the baseline evaluation. Physical assessment and vital signs completed pre-procedure.
10. NIHSS done only if needed.
11. Neurological exam and cranial nerve exam by independent neurologist, mRS and NIHSS by independent certified personnel.
12. Within 7 days of procedure.

3. Clinical Endpoints

With regards to safety, the percentage of patients who had a disabling stroke (defined as mRS score ≥ 3 assessed at a minimum of 90 days post-stroke event) or neurological death within 12-months post-procedure was used to analyze the clinical study results.

With regards to effectiveness, the percentage of patients who had complete (100%) occlusion (equivalent to Raymond-Roy Class I) of the target intracranial aneurysm

without clinically significant in-stent stenosis (> 50%) or target intracranial aneurysm re-treatment within 12-months post-procedure was used to analyze the clinical study results.

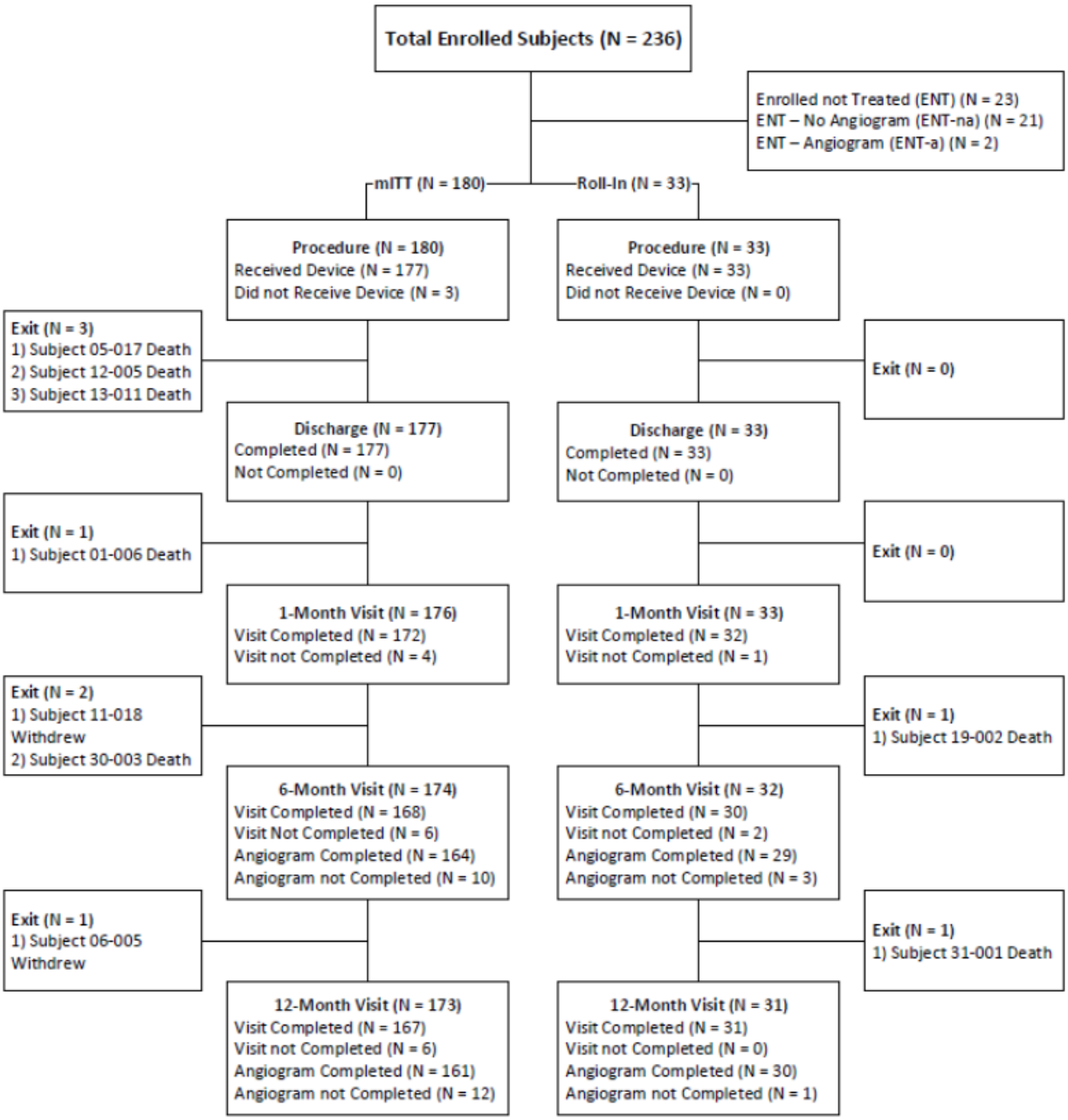
These primary safety and effectiveness endpoints were determined to be most clinically meaningful for evaluating the safety and performance of the Surpass Streamline Flow Diverter, and are consistent with the recommendations from a March 1, 2018 general issues meeting of the Neurological Devices Panel of the Medical Devices Advisory Committee to discuss the evaluation of benefits vs. risks of new endovascular medical devices intended to treat intracranial aneurysms. The pre-specified primary endpoints for the SCENT trial are described in Section X (A. Study Design).

With regard to success/failure criteria, the primary endpoints were compared to PGs developed from the published literature based on a similar patient population as those treated in the SCENT trial using alternative treatment modalities (endovascular treatment or open surgery). The primary endpoints were analyzed using the modified intent-to-treat (mITT) population and Fisher's Exact Binomial test. The mITT population was defined in the clinical protocol as all enrolled subjects for whom the investigational device entered the body, regardless of whether or not the device was successfully implanted. For safety, a one-sided p-value < 0.025 results in rejecting the null hypothesis that the primary safety endpoint is 20% or higher when treated with the Surpass Streamline Flow Diverter. For effectiveness, a one-sided p-value < 0.025 results in rejecting the null hypothesis that the likelihood of effective treatment with the subject device based on the primary effectiveness endpoint definition is ≤ 50% in favor of the alternative hypothesis that effective treatment with the subject device has a likelihood of success in > 50% of patients. As part of the decision-making process for the subject PMA, the FDA did not consider the safety PG of 20% to be acceptable and evaluated the safety profile of the Surpass Streamline Flow Diverter based on the actual rate of primary safety endpoint events observed in the SCENT trial.

B. Accountability of PMA Cohort

At the time of database lock, of 236 patients enrolled in the PMA study, 76.3% (180) patients are available for primary analysis at the completion of the study, the 12-months post-operative visit (i.e., mITT population) (see Figure 3).

Figure 3. Subject Disposition in SCENT Trial



C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an intracranial aneurysm treatment study performed in the US. This disease predominantly affects more women than men, and most patients are Caucasian, similar to the demographic and baseline characteristics of the patient population in the SCENT trial (see Table 7). Table 8 presents the characteristics of the intracranial aneurysms treated in the SCENT trial based on the baseline (pre-procedure) digital subtraction angiogram (DSA) that is site-reported.

Table 7. Demographic and Baseline Characteristics - mITT and Roll-In Subjects in SCENT Trial

Variable	mITT (N=180)	Roll-In (N=33)	Total (N=213)
Age (years)			
Mean ± Standard Deviation (SD)	61.0 ± 9.9	62.4 ± 11.1	61.2 ± 10.1
Median (Minimum, Maximum)	61.5 (38.0, 80.0)	65.0 (39.0, 79.0)	62.0 (38.0, 80.0)
Sex, % (n/N)			
Male	8.3% (15/180)	12.1% (4/33)	8.9% (19/213)
Female	91.7% (165/180)	87.9% (29/33)	91.1% (194/213)
Race, % (n/N) [1]			
American Indian/Alaska Native	1.1% (2/180)	0.0% (0/33)	0.9% (2/213)
Asian	3.3% (6/180)	6.1% (2/33)	3.8% (8/213)
Black or African American	14.4% (26/180)	21.2% (7/33)	15.5% (33/213)
Native Hawaiian or Other Pacific Islander	0.0% (0/180)	0.0% (0/33)	0.0% (0/213)
White	77.8% (140/180)	66.7% (22/33)	76/1% (162/213)
Other	1.1% (2/180)	6/1% (2/33)	1.9% (4/213)
Not Reported	3.3% (6/180)	3.0% (1/33)	3.3% (7/213)
Ethnicity, % (n/N)			
Hispanic or Latino	7.8% (14/180)	12.1% (4/33)	8.5% (18/213)
Not Hispanic or Latino	87.8% (158/180)	87.9% (29/33)	87.8% (187/213)
Unknown	3.3% (6/180)	0.0% (0/33)	2.8% (6/213)
Not Reported	1.1% (2/180)	0.0% (0/33)	0.9% (2/213)
Height (inches (in))			
Mean ± SD	64.8 ± 3.2	64.3 ± 3.6	64.7 ± 3.3
Median (Minimum, Maximum)	65.0 (52.0, 75.0)	64.2 (59.1, 72.0)	65.0 (52.0, 75.0)
Weight (pounds (lbs))			
Mean ± SD	166.0 ± 40.2	154.5 ± 31.6	164.2 ± 39.1
Median (Minimum, Maximum)	158.4 (83.6, 281.6)	149.6 (95.0, 215.6)	158.4 (83.6, 281.6)
Body Mass Index (BMI) (lbs/in^2)			
Mean ± SD	27.8 ± 6.1	26.3 ± 4.5	27.5 ± 5.9
Median (Minimum, Maximum)	27.0 (16.0, 49.0)	26.0 (18.0, 35.0)	27.0 (16.0, 49.0)
Smoking Status/Alcohol Use, % (n/N) [2]			
Current Smoker	20.0% (36/180)	30.3% (10/33)	21.6% (46/213)
Past Smoker	43.9% (79/180)	33.3% (11/33)	42.3% (90/213)
Current Consumer of Alcohol	50.6% (91/180)	36.4% (12/33)	48.4% (103/213)

[1] Patients may contribute toward more than one criterion for race. The total count may exceed the number of study patients in each study cohort.
[2] Patients may contribute toward more than one criterion for smoking status.

Table 8. Site Reported Pre-Procedure Intracranial Aneurysm Measurements/Characteristics - mITT and Roll-In Subjects in SCENT Trial

Measurement/Characteristic	mITT (N=180)	Roll-In (N=33)	Total (N=213)
Number Assessed [1]	100.0% (180/180)	100.0% (33/33)	100.0% (213/213)

Measurement/Characteristic	mITT (N=180)	Roll-In (N=33)	Total (N=213)
Parent Vessel Diameter (millimeters (mm))			
Proximal to Aneurysm Neck			
Mean ± SD (n)	3.9 ± 0.6 (180)	4.1 ± 0.5 (33)	3.9 ± 0.6 (213)
Median (Minimum, Maximum)	4.0 (2.6, 5.3)	4.0 (3.4, 5.3)	4.0 (2.6, 5.3)
Distal to Aneurysm Neck			
Mean ± SD (n)	3.4 ± 0.6 (180)	3.4 ± 0.6 (33)	3.4 ± 0.6 (213)
Median (Minimum, Maximum)	3.4 (2.5, 5.1)	3.3 (2.5, 4.5)	3.4 (2.5, 5.1)
Aneurysm Sac Size (mm)			
Dome Height			
Mean ± SD (n)	13.4 ± 5.7 (178)	13.5 ± 5.9 (33)	13.4 ± 5.8 (211)
Median (Minimum, Maximum)	11.8 (1.3, 43.0)	11.4 (4.0, 28.9)	11.7 (1.3, 43.0)
Dome Width			
Mean ± SD (n)	12.3 ± 5.7 (179)	14.1 ± 6.4 (33)	12.6 ± 5.8 (212)
Median (Minimum, Maximum)	10.8 (1.3, 33.0)	12.8 (4.5, 28.6)	11.1 (1.3, 33.0)
Dome Depth (If Not Spherical)			
Mean ± SD (n)	11.6 ± 6.4 (151)	11.4 ± 5.7 (27)	11.1 ± 6.3 (178)
Median (Minimum, Maximum)	10.8 (0.0, 26.2)	11.0 (0.0, 24.7)	10.9 (0.0, 26.2)
Neck Width			
Mean ± SD (n)	6.7 ± 2.8 (169)	7.5 ± 2.5 (32)	6.9 ± 2.8 (201)
Median (Minimum, Maximum)	6.0 (0.0, 27.1)	7.0 (4.1, 14.6)	6.2 (0.0, 27.1)
Aneurysm Size (mm)			
< 10 mm	0.0% (0/180)	0.0% (0/33)	0.0% (0/213)
10 to < 25 mm	92.8% (167/180)	90.0% (30/33)	92.5% (197/213)
25 mm or larger	7.2% (13/180)	9.1% (3/33)	7.5% (16/213)
Aneurysm Type			
Saccular	70.0% (126/180)	78.8% (26/33)	71.4% (152/213)
Fusiform	18.3% (33/180)	12.1% (4/33)	17.4% (37/213)
Blister	0.0% (0/180)	0.0% (0/33)	0.0% (0/213)
Segmental	5.0% (9/180)	3.0% (1/33)	4.7% (10/213)
Focal	0.0% (0/180)	0.0% (0/33)	0.0% (0/213)
Dissecting	0.6% (1/180)	0.0% (0/33)	0.5% (1/213)
Dysplastic	6.1% (11/180)	6.1% (2/33)	6/1% (13/213)
Aneurysm Location			
Petrous Segment	2.2% (4/180)	3.0% (1/33)	2.3% (5/213)
Cavernous Segment	23.3% (42/180)	36.4% (12/33)	25.4% (54/213)
Carotid Cavernous Artery	1.1% (2/180)	0.0% (0/33)	0.9% (2/213)
Carotid-Ophthalmic	31.1% (56/180)	21.2% (7/33)	29.6% (63/213)
Superior Hypophyseal Artery	5.0% (9/180)	6.1% (2/33)	5.2% (11/213)
Supraclinoid Carotid Artery	25.0% (45/180)	24.2% (8/33)	24.9% (53/213)
Cerebral Segment (Not Otherwise Specified)	1.1% (2/180)	0.0% (0/33)	0.9% (2/213)
Anterior Choroidal Artery	0.6% (1/180)	0.0% (0/33)	0.5% (1/213)
Other	10.6% (19/180)	9.1% (3/33)	10.3% (22/213)
Aneurysm Side			
Right	45.6% (82/180)	63.6% (21/33)	48.4% (103/213)
Left	54.4% (98/180)	36.4% (12/33)	51.6% (110/213)
[1] Includes subjects with a completed angiogram.			

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the mITT cohort of 180 patients available for the 12-month evaluation. The key safety outcomes for this study are presented below in Tables 9 and 10. Adverse effects are reported in Table 13.

Based on the pre-specified primary safety endpoint definition, the primary safety endpoint was met in the mITT population and the null hypothesis was rejected ($p < 0.001$). The incidence of primary safety endpoint failure (major ipsilateral stroke defined as an increase in the NIHSS score from baseline by ≥ 4 points during stroke event or neurological death) in the mITT population was 10.6% (19/180). All of the subjects that comprised the composite primary safety endpoint failure rate experienced a major ipsilateral stroke, 19/180 (10.6%), and of these 19 subjects that experienced a major ipsilateral stroke, 5 subjects died from their stroke (5/180 (2.8%)).

Table 9. Pre-Specified Primary Safety Endpoint Events through 12 Month Follow-Up – mITT Population (N=180)

Event Type [1]	% of Patients with Observations (n/N) (95% Confidence Interval (CI)) [2]	p-value [3]
Major Ipsilateral Stroke [4]	10.6% (19/180) (6.5, 16.0)	
Neurological Death [4]	2.8% (5/180) (0.9, 6.4)	
Primary Safety Endpoint Failure (Major Ipsilateral Stroke or Neurological Death)	10.6% (19/180) (6.5, 16.0)	< 0.001

[1] Occurrence from enrollment date through 365 days post-procedure.
[2] Clopper-Pearson exact confidence interval.
[3] One-sided Fisher's Exact test of success against the performance goal of < 0.20 at 12 months (α=0.025).
[4] Individual subjects may have experienced both major ipsilateral stroke and neurological death. The overall primary safety endpoint failure rate includes 15 major ipsilateral strokes as adjudicated by the CEC and 4 strokes that were determined to meet the definition of primary safety endpoint failure post-CEC review.

An additional post-hoc analysis was performed wherein the mITT population was analyzed using a composite primary safety endpoint definition of disabling stroke (mRS score of ≥ 3 at a minimum of 90-days post-stroke event) or neurological death within 12-months post-procedure based on the recommendations of the Advisory Committee of the Neurological Devices Panel at the March 1, 2018 general issues meeting. Using this modified primary safety endpoint definition, the primary safety failure rate within 12-months post-treatment with the Surpass Streamline Flow Diverter was 6.1% (11/180).

Table 10: *Post-Hoc* Primary Safety Endpoint of Disabling Stroke or Neurologic Death through 12 Month Follow-Up – mITT Population (N=180)

Event [1]	% of Patients with Observations (n/N) 95% CI [2]
Disabling Stroke or Neurologic Death	6.1% (11/180) (3.1, 10.7)
Neurologic Death [3]	2.8% (5/180) (0.9, 6.4)
Disabling Stroke [3]	6.1% (11/180) (3.1, 10.7)

[1] Disabling stroke defined as mRS of 3 or higher measured at least 90 days after stroke event.
[2] Unadjusted Clopper-Pearson exact confidence interval. The confidence intervals are calculated without multiplicity adjustment. As such, the confidence intervals are provided to show the variability only and should not be used to draw any statistical conclusions.
[3] Individual subjects may have experienced both disabling stroke and neurological death.

Table 11 presents the baseline and 12-month mRS scores on all subjects in the mITT population (N=180) to evaluate long-term clinical outcome. The majority of subjects (82.2%; 148/180) had unchanged or improved functional outcomes compared to baseline. A total of 107 out of 180 subjects (59.4%) had unchanged mRS scores, and 41 of the 180 subjects in the mITT population (22.8%) had improved mRS scores at 12-months compared to their baseline mRS. There were 23 subjects with worsened mRS scores (23/180; 12.8%). For 9 subjects, the mRS assessment was not performance due to confirmed missed visits (6), subject withdrawal (2), and protocol deviation (1).

Table 11. Change in Modified Rankin Scale Score through 12 Month Follow-Up Compared to Baseline – mITT Population (N=180)

	Score at 12 Month Follow-Up Visit [1]								
Score at Baseline	**ND [2]**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**Total**
0	7	86	12	3	0	0	1	3	**112**
1	0	22	16	1	1	0	0	2	**42**
2	1	11	4	3	0	0	0	0	**19**
3	1	0	1	2	0	0	0	0	**4**
4	0	1	0	0	0	1	0	0	**2**
5	0	0	0	0	0	0	1	0	**1**
Total	9	120	33	9	1	1	2	5	**180**

[1] Each cell indicates score frequency at 12 month follow-up relative to baseline score frequency. Gray-shaded cells show subjects who worsened.
[2] mRS exams were not done (ND) on 9 subjects at the 12-month follow-up visit for the following reasons: confirmed missed visit (6), subject withdrawal (2), and protocol deviation (1).

Table 12 shows the percentage of subjects in the mITT population in the SCENT trial who experienced a minor stroke, defined as a stroke associated with an increase in NIHSS score ≤ 3, adjudicated by the CEC. The minor stroke rates in the mITT and roll-in populations were 6.7% (12/180) and 3.0% (1/33), respectively.

Table 12. CEC Adjudicated Rate of Minor Strokes through 12 Month Follow-Up (mITT and Roll-In Subjects)

Outcome	mITT Population N=180		Roll-In Population N=33	
	% (n/N) of Subjects with Outcome	[95% CI] [2]	% (n/N) of Subjects with Outcome	[95% CI] [2]
Minor Stroke [1]	6.7% (12/180)	[3.5, 11.4]	3.0% (1/33)	[0.1, 15.8]

[1] Minor strokes in the first 12 months, as adjudicated by the CEC.
[2] The confidence intervals are calculated without multiplicity adjustment. As such, the confidence intervals are provided to show the variability only and should not be used to draw any statistical conclusions.

Adverse effects that occurred in the PMA clinical study:

Table 13 reports serious adverse events (SAEs) and non-SAEs through one year follow-up in the SCENT trial.

Table 13. Adverse Events with > 1% Overall Frequency Through 12 Months Post-Procedure by Medical Dictionary for Regulatory Activities (MedDRA) Codes – mITT Population (N=180)

MedDRA Classification		Serious Adverse Events		Non-Serious Adverse Events		All Adverse Events	
System/Organ Class	Preferred Term	Total Events (Patients)	Rate of Patients with Event (N=180)	Total Events (Patients)	Rate of Patients with Event (N=180)	Total Events (Patients)	Rate of Patients with Event (N=180)
Blood and Lymphatic System Disorders	Anemia	1 (1)	0.6%	1 (1)	0.6%	2 (2)	1.1%
Cardiac Disorders	Arrhythmia	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Atrial Fibrillation	1 (1)	0.6%	1 (1)	0.6%	2 (2)	1.1%
	Cardiac Arrest	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
Ear and Labyrinth Disorders	Tinnitus	0 (0)	0.0%	3 (2)	1.1%	3 (2)	1.1%
	Ear Pain	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
Eye Disorders	Visual Impairment	2 (2)	1.1%	15 (14)	7.8%	17 (16)	8.9%
	Diplopia	2 (2)	1.1%	7 (7)	3.9%	9 (9)	5.0%
	Eye Pain	0 (0)	0.0%	8 (8)	4.4%	8 (8)	4.4%
	Vision Blurred	0 (0)	0.0%	7 (7)	3.9%	7 (7)	3.9%
	Vitreous Floaters	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Blepharitis	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Cataract	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Dry Eye	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Eye Pruritus	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Photophobia	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Retinal Artery Occlusion	1 (1)	0.6%	1 (1)	0.6%	2 (2)	1.1%

MedDRA Classification		Serious Adverse Events		Non-Serious Adverse Events		All Adverse Events	
System/Organ Class	Preferred Term	Total Events (Patients)	Rate of Patients with Event (N=180)	Total Events (Patients)	Rate of Patients with Event (N=180)	Total Events (Patients)	Rate of Patients with Event (N=180)
	Retinal Hemorrhage	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Retinal Infarction	2 (2)	1.1%	0 (0)	0.0%	2 (2)	1.1%
Gastrointestinal Disorders	Nausea	0 (0)	0.0%	10 (10)	5.6%	10 (10)	5.6%
	Constipation	0 (0)	0.0%	6 (6)	3.3%	6 (6)	3.3%
	Gastrointestinal Hemorrhage	6 (5)	2.8%	0 (0)	0.0%	6 (5)	2.8%
	Vomiting	0 (0)	0.0%	6 (6)	3.3%	6 (6)	3.3%
	Dysphagia	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Mouth Hemorrhage	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Rectal Hemorrhage	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Abdominal Pain	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Dyspepsia	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Hematochezia	1 (1)	0.6%	1 (1)	0.6%	2 (2)	1.1%
	Retroperitoneal Hematoma	1 (1)	0.6%	1 (1)	0.6%	2 (2)	1.1%
General Disorders and Administration Site Conditions	Fatigue	0 (0)	0.0%	11 (10)	5.6%	11 (10)	5.6%
	Thrombosis in Device	4 (4)	2.2%	2 (2)	1.1%	6 (6)	3.3%
	Catheter Site Hemorrhage	0 (0)	0.0%	4 (4)	2.2%	4 (4)	2.2%
	Chest Pain	3 (3)	1.7%	1 (1)	0.6%	4 (4)	2.2%
	Oedema Peripheral	0 (0)	0.0%	4 (4)	2.2%	4 (4)	2.2%
	Gait Disturbance	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Implant Site Pain	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
Infections and Infestations	Urinary Tract Infection	0 (0)	0.0%	11 (10)	5.6%	11 (10)	5.6%
	Pneumonia	1 (1)	0.6%	3 (3)	1.7%	4 (4)	2.2%
	Sinusitis	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Bronchitis	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
Injury, Poisoning and Procedural Complications	Contusion	0 (0)	0.0%	9 (9)	5.0%	9 (9)	5.0%
	Fall	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Traumatic Hematoma	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Vascular Injury	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Vascular Pseudo-Aneurysm	1 (1)	0.6%	1 (1)	0.6%	2 (2)	1.1%
Investigations	Neurological Examination Abnormal	0 (0)	0.0%	4 (4)	2.2%	4 (4)	2.2%
	Carotid Bruit	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
Metabolism and Nutrition Disorders	Hyponatremia	1 (1)	0.6%	2 (2)	1.1%	3 (3)	1.7%
	Decreased Appetite	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%

MedDRA Classification		Serious Adverse Events		Non-Serious Adverse Events		All Adverse Events	
System/Organ Class	Preferred Term	Total Events (Patients)	Rate of Patients with Event (N=180)	Total Events (Patients)	Rate of Patients with Event (N=180)	Total Events (Patients)	Rate of Patients with Event (N=180)
Musculoskeletal and Connective Tissue Disorders	Pain in Extremity	0 (0)	0.0%	7 (6)	3.3%	7 (6)	3.3%
	Back Pain	0 (0)	0.0%	6 (6)	3.3%	6 (6)	3.3%
	Neck Pain	0 (0)	0.0%	4 (4)	2.2%	4 (4)	2.2%
	Arthralgia	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Groin Pain	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Muscular Weakness	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Plantar Fasciitis	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
Nervous System Disorders	Headache	3 (3)	1.7%	57 (52)	28.9%	60 (54*)	30.0%
	Dizziness	1 (1)	0.6%	13 (12)	6.7%	14 (13)	7.2%
	Reversible Ischemic Neurological Deficit	0 (0)	0.0%	12 (12)	6.7%	12 (12)	6.7%
	Ischemic Stroke	11 (11)	6.1%	0 (0)	0.0%	11 (11)	6.1%
	Hypoesthesia	0 (0)	0.0%	9 (7)	3.9%	9 (7)	3.9%
	Transient Ischemic Attack	3 (3)	1.7%	4 (3)	1.7%	7 (6)	3.3%
	Subarachnoid Hemorrhage	5 (5)	2.8%	0 (0)	0.0%	5 (5)	2.8%
	Amnesia	1 (1)	0.6%	3 (3)	1.7%	4 (4)	2.2%
	Embolic Stroke	3 (3)	1.7%	1 (1)	0.6%	4 (4)	2.2%
	Hemorrhagic Stroke	4 (4)	2.2%	0 (0)	0.0%	4 (4)	2.2%
	Memory Impairment	0 (0)	0.0%	4 (4)	2.2%	4 (4)	2.2%
	Migraine	0 (0)	0.0%	4 (4)	2.2%	4 (4)	2.2%
	Syncope	4 (4)	2.2%	0 (0)	0.0%	4 (4)	2.2%
	Aphasia	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Presyncope	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Ataxia	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Carotid Artery Occlusion	1 (1)	0.6%	1 (1)	0.6%	2 (2)	1.1%
	Hemiparesis	1 (1)	0.6%	1 (1)	0.6%	2 (2)	1.1%
	Hydrocephalus	1 (1)	0.6%	1 (1)	0.6%	2 (2)	1.1%
	Third Nerve Paralysis	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Paresthesia	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Restless Legs Syndrome	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Tremor	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
Psychiatric Disorders	Anxiety	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Confusional State	1 (1)	0.6%	2 (2)	1.1%	3 (3)	1.7%
	Depression	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Insomnia	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Mental Status Changes	1 (1)	0.6%	1 (1)	0.6%	2 (2)	1.1%
Renal and Urinary Disorders	Urinary Retention	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%

MedDRA Classification		Serious Adverse Events		Non-Serious Adverse Events		All Adverse Events	
System/Organ Class	Preferred Term	Total Events (Patients)	Rate of Patients with Event (N=180)	Total Events (Patients)	Rate of Patients with Event (N=180)	Total Events (Patients)	Rate of Patients with Event (N=180)
Respiratory, Thoracic and Mediastinal Disorders	Epistaxis	1 (1)	0.6%	5 (5)	2.8%	6 (6)	3.3%
	Cough	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Dyspnea	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Hemoptysis	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
	Respiratory Failure	2 (2)	1.1%	0 (0)	0.0%	2 (2)	1.1%
	Sleep Apnea Syndrome	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
Skin and Subcutaneous Tissue Disorders	Ecchymosis	0 (0)	0.0%	3 (3)	1.7%	3 (3)	1.7%
	Rash	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
Surgical and Medical Procedures	Intra-Cerebral Aneurysm Operation	3 (3)	1.7%	0 (0)	0.0%	3 (3)	1.7%
Vascular Disorders	Hypotension	0 (0)	0.0%	12 (10)	5.6%	12 (10)	5.6%
	Hematoma	1 (1)	0.6%	7 (7)	3.9%	8 (8)	4.4%
	Vasospasm	0 (0)	0.0%	7 (6)	3.3%	7 (6)	3.3%
	Hemorrhage	2 (2)	1.1%	3 (3)	1.7%	5 (5)	2.8%
	Hypertension	1 (1)	0.6%	4 (4)	2.2%	5 (5)	2.8%
	Deep Vein Thrombosis	1 (1)	0.6%	1 (1)	0.6%	2 (2)	1.1%
	Embolism	2 (2)	1.1%	0 (0)	0.0%	2 (2)	1.1%
	Orthostatic Hypotension	0 (0)	0.0%	2 (2)	1.1%	2 (2)	1.1%
*One patient had a serious adverse event and a non-serious adverse event.							

2. Effectiveness Results

The analysis of effectiveness was based on the 180 evaluable patients at the 12-month time point. Key effectiveness outcomes are presented in Table 14.

The primary effectiveness endpoint in the SCENT trial was defined as the percent of subjects in the mITT population with 100% occlusion (Raymond-Roy Class I) without clinically significant stenosis (clinically significant stenosis defined as > 50% stenosis) of the parent artery based on Core Lab evaluation of the 12-month follow-up angiogram and without any subsequent retreatment of the target intracranial aneurysm through the 12-month follow-up visit. As summarized in Table 14, the primary effectiveness composite success rate in the mITT population was 62.8% (113/180).

Table 14. Primary Effectiveness Endpoint through 12 Month Follow-Up – mITT Population (N=180)

	% (n/N) (95% CI) [3]	p-value [4]
Primary Effectiveness Endpoint Composite Success [1, 2]	62.8% (113/180) (55.3, 69.9)	< 0.001
Parent Artery Stenosis > 50%	3.3% (6/180) (1.2, 7.1) [5]	
Retreatment of Target Intracranial Aneurysm	0.6% (1/180) (0.0, 3.1) [5]	

[1] Primary effectiveness endpoint success defined as Raymond-Roy Class I (100% occlusion) without clinically significant stenosis of the parent artery or retreatment of the target intracranial aneurysm, adjudicated by the Core Lab.
[2] mITT patients missing 12 month follow-up data (n=11) were imputed as failures.
[3] Clopper-Pearson Exact confidence interval.
[4] One-sided Fisher's Exact test of success against the PG of > 0.50 (α=0.025).
[5] The confidence intervals are calculated without multiplicity adjustment. As such, the confidence intervals are provided to show the variability only and should not be used to draw any statistical conclusions.

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes: intracranial aneurysm size (large vs. giant), anatomical location, age, subject baseline characteristics. Subgroup analyses of the primary safety endpoint events did not show statistically significant differences based on intracranial aneurysm size (large vs. giant), age, anatomical location of the treated intracranial aneurysm, or subject baseline characteristics due to the low rate of safety events. Therefore, no statistical conclusions can be made for safety of the device and treatment from these subgroup analyses.

For effectiveness, Table 15 shows the predictive variables that were assessed to determine whether they can affect the primary effectiveness endpoint success in the mITT population. In addition, Tables 16-18 shows the primary effectiveness endpoint rates based on the subgroups of age (< 65 years old vs. ≥ 65 years old), anatomical location of the intracranial aneurysm treated, and intracranial aneurysm size (large vs. giant). The subgroup analysis based on age (Table 16) does show that there is a statistically significant difference in the primary effectiveness endpoint success rate that favors effectiveness of the subject device and treatment in patients < 65 years old [70.2% (80/114)] as compared to patients ≥ 65 years old [50.0% (33/66)] in the mITT population in the SCENT trial. This decreased effectiveness result in patients ≥ 65 years old may be caused by delayed healing and endothelialization on the device over time in those patients who have advanced aged, which is required for successful treatment with flow diversion stents such as the subject Surpass Streamline Flow Diverter. A warning is added to the device labeling to inform clinical users of the decreased device effectiveness in older patients and to consider alternative treatment options based on the patient's advanced age.

Table 15. Full Multivariate Model for Primary Effectiveness Endpoint Success in the mITT Population

Predictive Variable	Odds Ratio (95% CI) [1]	Wald Chi-Square	Pr > Chi-Square [2]
Intercept	--	15.269	<.001
Aneurysm Location (compared to Carotid-ophthalmic Segment)			
Superior Hypophyseal Artery	7.56 (0.59-96.4)	2.423	0.120
Petrous Segment	3.41 (0.20-58.0)	0.719	0.396
Supraclinoid Carotid Artery	0.61 (0.19-1.96)	0.688	0.407
Posterior Communicating Artery	1.34 (0.51-3.54)	0.350	0.554
Cavernous Segment	1.29 (0.52-3.21)	0.294	0.588
Age 65 and Older vs. Under Age 65	0.30 (0.15-0.61)	10.785	0.001
History of Stroke	0.14 (0.04-0.46)	10.294	0.001
History of Aneurysm	0.25 (0.08-0.80)	5.411	0.020
Aneurysm Size (mm)	0.94 (0.89-1.00)	4.038	0.044
Black or African-American	0.58 (0.22-1.54)	1.186	0.276

[1] The confidence intervals are calculated without multiplicity adjustment. As such, the confidence intervals are provided to show the variability only and should not be used to draw any statistical conclusions.
[2] Pr = Probability.

Table 16. Subgroup Analysis of Primary Effectiveness Endpoint Based on Subject Age ≥ 65 Years versus < 65 Years in mITT Population

	Under Age 65 N=114		Age 65 and Older N=66	
Outcomes	**% (n/N)**	**95% CI***	**% (n/N)**	**95% CI***
Primary Effectiveness Endpoint	70.2% (80/114)	(60.9, 78.4)	50.0% (33/66)	(37.4, 62.6)

*The confidence intervals are calculated without multiplicity adjustment. As such, the confidence intervals are provided to show the variability only and should not be used to draw any statistical conclusions.

Table 17 shows the subgroup analysis for the primary effectiveness endpoint based on intracranial aneurysm location. There does not appear to be a statistically significant difference in device effectiveness based on the intracranial aneurysm location treated. Table 18 shows the subgroup analysis of the primary effectiveness endpoint based on giant vs. large intracranial aneurysms treated in the mITT population. The results show that there is decreased effectiveness with the subject device and treatment in giant intracranial aneurysms [46.2% (6/13)] compared to large intracranial aneurysms [64.1% (107/167)] but the difference is not statistically significant.

Finally, the secondary effectiveness endpoints of Raymond-Roy intracranial aneurysm occlusion classifications at 12-months follow-up were compared in subgroups of patients who had full apposition of the device to the vessel wall and those who did not, per Core Lab imaging findings (Table 19). The rate of complete intracranial aneurysm occlusion (Raymond-Roy Class I) at 12-months post-procedure was statistically significantly higher among patients who had full device apposition (79.2%; 99/125) compared to those who did not (50.0%; 17/34).

This may be due to increased endothelialization on the device over time for devices that are completely apposed to the vessel walls.

Table 17. Primary Effectiveness Endpoint Success Based on Intracranial Aneurysm Location – mITT Population

Aneurysm Location	Aneurysm Size (mm) (CORE LAB) Mean (SD) (min, max)		Primary Effectiveness Success % (n/N)	95% CI [1]
Petrous Segment	14.2 (4.8) (8.3,20.1)		75.0% (3/4)	[19.4, 99.4]
Cavernous Segment	17.6 (7.4) (4.9,41.7)		59.6% (31/52)	[45.1, 73.0]
Carotid-Ophthalmic	13.1 (5.2) (3.9,28.3)		63.3% (38/60)	[49.9, 75.4]
Posterior Communicating Artery	12.2 (5.0) (3.4,27.0)		65.8% (25/38)	[48.6, 80.4]
Supraclinoid Carotid Artery	13.5 (4.4) (6.7,25.1)		55.0% (11/20)	[31.5, 76.9]
Superior Hypophyseal Artery	10.5 (3.1) (5.5,13.9)		83.3% (5/6)	[35.9, 99.6]

[1] The confidence intervals are calculated without multiplicity adjustment. As such, the confidence intervals are provided to show the variability only and should not be used to draw any statistical conclusions.

Table 18. CEC Adjudicated Primary Effectiveness Endpoint Outcomes for Giant and Non-Giant (Large) Intracranial Aneurysms through 12 Month Follow-Up – mITT Population (N=180)

	All Intracranial Aneurysm Sizes Except Giant N=167		Giant Intracranial Aneurysms N=13	
Outcome	**% (n/N) of Patients with Outcome**	**[95% CI]***	**% (n/N) of Patients with Outcome**	**[95% CI]***
Primary Effectiveness Success	64.1% (107/167)	[56.3, 71.3]	46.2% (6/13)	[19.2, 74.9]

*The confidence intervals are calculated without multiplicity adjustment. As such, the confidence intervals are provided to show the variability only and should not be used to draw any statistical conclusions.

Table 19. Raymond-Roy Score per Core Lab Assessment Based on Device Apposition at 12 Months Post-Procedure – mITT Population

	Device Not Fully Apposed to Vessel Wall at 12 Months N=34		Device Fully Apposed to Vessel Wall at 12 Months N=125	
Adjudicated Raymond-Roy Score at 12 Months [1]	**% (n/N)**	**[95% CI]***	**% (n/N)**	**[95% CI]***
Raymond-Roy I	50.0% (17/34)	[32.4, 67.6]	79.2% (99/125)	[71.0, 85.9]
Raymond-Roy II	8.8% (3/34)	[1.9, 23.7]	11.2% (14/125)	[6.3, 18.1]
Raymond-Roy III	41.2% (14/34)	[24.6, 59.3]	9.6% (12/125)	[5.1, 16.2]
[1] Complete 12-month angiographic data not available for 21 mITT subjects. *The confidence intervals are calculated without multiplicity adjustment. As such, the confidence intervals are provided to show the variability only and should not be used to draw any statistical conclusions.				

4. Pediatric Extrapolation

In this premarket application, existing clinical data was leveraged to support the reasonable assurance of safety and effectiveness of the proposed device in the adolescent pediatric sub-population between 18 years of age through 21 years of age. The inclusion/exclusion criteria in the SCENT trial used to support the PMA approval of the Surpass Streamline Flow Diverter included subjects 19-80 years of age. Because patients with intracranial aneurysms indicated for treatment with the subject device that are 18 years of age are no different from the subjects that are aged 19-80 years old studied in the SCENT trial from a human development and anatomy perspective, for the purposes of the final indications for use (IFU) of the subject Surpass Streamline Flow Diverter, the age limit specified can include subjects 18 years of age and older.

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 95 investigators of which none were full-time or part-time employees of the sponsor and 32 investigators 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: 30
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 2

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine

whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Not applicable.

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

During the review of this PMA, the FDA convened a general issues meeting on March 1, 2018 of the Neurological Devices Panel of the Medical Devices Advisory Committee regarding factors to consider in the evaluation of benefits and risks when reviewing clinical evidence of new endovascular medical devices intended to treat intracranial aneurysms. Feedback from the Neurological Devices Panel at the March 1, 2018 meeting was considered during the review of this PMA (see clinical study results described in Section X of the SSED). The background and meeting materials for the March 1, 2018 general issues meeting can be accessed at the following link: https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/NeurologicalDevicesPanel/ucm598450.htm.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The primary effectiveness endpoint was analyzed for the number of patients in the mITT population who had complete (100%) occlusion (equivalent to Raymond-Roy I intracranial aneurysm occlusion classification) of the target intracranial aneurysm without clinically significant in-stent stenosis (clinically significant stenosis defined as > 50%) or target intracranial aneurysm re-treatment within 12-months post-procedure. The results show that 62.8% (113/180) of mITT patients in the SCENT trial met the primary effectiveness endpoint. Therefore, the pivotal study met the primary effectiveness endpoint success criteria at one year, and the majority of the patients in the clinical trial exhibited a good effectiveness outcome. This primary effectiveness endpoint rate is slightly lower than the primary effectiveness endpoint observed in the PUFS trial to support PMA approval of the Pipeline Embolization Device (P100018). The PUFS trial had a primary effectiveness endpoint rate of 70.8% (75/106) at 1-year post-procedure based on the same primary effectiveness endpoint definition as the SCENT trial. The small difference in the primary effectiveness endpoint rate between the PUFS and the subject SCENT trial may be due to the number of devices implanted. In the SCENT trial, a mean of 1.1 and 1.3 devices were implanted per subject in the mITT and roll-in populations, respectively (see Table 20). Whereas, in the PUFS trial, a mean of 3.1 Pipeline Embolization Devices were implanted per subject.

Table 20. Number of Surpass Streamline Flow Diverters Implanted per Subject in SCENT Trial – mITT and Roll-In Populations

# of Devices Implanted	mITT N=180 n (%)	Roll-in N=33 n (%)	Total N=213 n (%)
None	3 (1.7%)	0	3 (1.4%)
One	156 (86.7%)	25 (75.8%)	181 (85.0%)
Two	21 (11.7%)	7 (21.2%)	28 (13.1%)
>2	0	1 (3.0%)	1 (0.5%)
Mean (range)	1.1 (0 - 2)	1.3 (1 - 3)	1.1 (0 - 3)

Subgroup analyses showed that effectiveness, using the primary effectiveness endpoint definition, may be impacted by subject age, with subject over the age of 65 performing worse than the younger subjects. The subgroup analysis also showed that effectiveness may be lower for device treatment in giant intracranial aneurysms but the results are not conclusive because there were only 13 out of 180 patients with intracranial aneurysms > 25 mm in the SCENT study. Even with the potential for decreased effectiveness with the device and treatment in giant wide-neck intracranial aneurysms, these aneurysms have a greater risk for rupture (Wiebers 1998 and Ishibashi et al. 2009) and must be treated because the overall mortality rate can be as high as 66% observed in the ISUIA trial if the intracranial aneurysm ruptures (Wiebers 1998).

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in a clinical study conducted to support PMA approval as described above. The primary safety endpoint was analyzed based on the mITT population for the rate of patients who exhibited a disabling stroke (ischemic or hemorrhagic) or neurological death within 12-months post-procedure. These two (2) primary safety events are the most significant adverse events to assess the device safety for the treatment of wide-neck intracranial aneurysms because these events are the most debilitating, can result in permanent disability, or expiration of the patient. The primary safety endpoint rate observed in the SCENT trial was 6.1% (11/180), with six (6) of the eleven (11) primary safety endpoint events being a disabling stroke without suffering neurological death (3.3% (6/180)) and the remaining five (5) primary safety events being neurological deaths caused by a significant stroke (2.8% (5/180)). There was a total of 31 stroke events (17.2% (31/180)) in the mITT population that occurred in the SCENT trial observed through 12-months post-procedure of which five (5) resulted in death, six (6) were categorized as disabling strokes, and twenty-five (25) were categorized as non-disabling strokes. The mRS scores (measurement of patient disability) was also assessed to determine the rate of patients who had a worsening mRS score 12-months post-procedure compared to their baseline mRS prior to device treatment. Of the 180 patients in the mITT population in the SCENT trial, 12.8% (23/180) had a worsening of the mRS at 12-months post-procedure compared to their baseline mRS.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The effectiveness results show that 62.8% (113/180) of patients in the SCENT trial had complete (100%) intracranial aneurysm occlusion (Raymond-Roy Class I) without clinically significant in-stent stenosis or retreatment of the target intracranial aneurysm within 12 months post-procedure. Because the Surpass Streamline Flow Diverter is a permanent implant and the pivotal study with 1-year follow-up data was used to support the PMA, the long-term durability of treatment after 1-year post-procedure is currently unknown.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The primary safety endpoint rate observed in the SCENT trial based on the rate of disabling strokes (ischemic and hemorrhagic) or neurological death was 6.1% (11/180), with six (6) of the eleven (11) primary safety endpoint events being a disabling stroke without suffering neurological death (3.3% (6/180)) and the remaining five (5) primary safety events being neurological deaths caused by a significant stroke (2.8% (5/180)). The pre-specified primary safety endpoint defined using major ipsilateral stroke (increase in NIHSS score by ≥ 4 points during the stroke event) or neurological deaths was 10.6% (19/180), with 14 of the nineteen (19) primary safety endpoint events being a major stroke (7.8% (14/180)) and the five (5) primary safety events being neurological deaths caused by a major stroke (2.8% (5/180)). The primary safety endpoint rates observed in the SCENT trial with the Surpass Streamline Flow Diverter is within the safety rates published in the scientific literature for flow diversion stent treatment of wide-neck intracranial aneurysms and the prior PUFS study for the Pipeline Embolization Device to support approval of PMA P100018. The primary safety event rate in the PUFS trial was 5.6% (6/107; 95% posterior credible interval is 2.6-11.7%) (PMA P100018 Summary of Safety and Effectiveness Data). The PUFS trial may have had a slightly lower primary safety endpoint rate because the intracranial aneurysms treated were located in the internal carotid artery (ICA) from the petrous to the superior hypophyseal segments, and the subject SCENT trial included more distal intracranial aneurysms in the ICA from the petrous segment to the terminus, which may have contributed to the slightly higher stroke rate.

Additional factors to be considered in determining probable risks and benefits for the Surpass Streamline device included: weighing the benefits and risks of device treatment with the patient's risk of intracranial aneurysm rupture. The risk of rupture of an untreated unruptured intracranial aneurysm is dependent on multiple factors including aneurysm size, shape, and morphology, and the patient co-morbidities (e.g., high blood pressure, family history, multiple aneurysms, diabetes). Based on natural history, it has been suggested that intracranial aneurysms have an average rupture rate of around 1% per year in patients with a diagnosed intracranial aneurysm, although that number can vary based on the study (Ishibashi et al. 2009; Juvela et al. 2013). Size and location of the cerebral aneurysm in the neurovasculature can also affect the

risk of rupture. In the article by Wiebers (2003), intracranial aneurysms in the ICA, anterior communicating artery (AComm), anterior cerebral artery (ACA), or middle cerebral artery (MCA) that were < 7 mm, 7-12 mm, 13-24 mm, and > 25 mm had rupture rates of 0%, 2.6%, 14.5%, and 40%, respectively, at 5 years. Larger aneurysms are at a greater risk for rupture (i.e., the rupture rate for aneurysms > 25 mm have a reported 6% rupture rate in the first year (Wiebers 1998) with other studies reporting an annual rupture rate as high as 43.1% (Ishibashi et al. 2009)).

One additional factor to be considered in determining probable risks and benefits for the Surpass Streamline device include some uncertainty based on the single arm pivotal trial design that may introduce some bias in patient selection for treatment because there was no blinding or randomized concurrent control group. Since there was no active control arm in the pivotal study, there are uncertainties of whether the subject device treatment may be more or less beneficial or more or less safe than alternative treatment modalities for the proposed patient population. In addition, it is unclear whether there may have been some bias in subject selection for treatment with the Surpass Streamline Flow Diverter to result in better clinical outcomes.

1. Patient Perspectives

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

In conclusion, given the available information above, the data support that for use of the Surpass Streamline Flow Diverter in the endovascular treatment of patients (18 years of age and older) with unruptured large or giant saccular wide-neck (neck width ≥ 4 mm or dome-to-neck ratio < 2) or fusiform intracranial aneurysms in the internal carotid artery from the petrous segment to the terminus arising from a parent vessel with a diameter ≥ 2.5 mm and ≤ 5.3 mm, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The study population of large or giant wide-neck saccular and fusiform intracranial aneurysms carries a high risk for intracranial aneurysm rupture during the patient's life time. The primary safety and effectiveness endpoints were met and demonstrate that the Surpass Streamline Flow Diverter can be a reasonably safe and effectiveness treatment based on the indications for use and the benefits outweigh the risks of treatment with the subject device given the higher risk of intracranial aneurysm rupture of large or giant intracranial aneurysms.

XIV. CDRH DECISION

CDRH issued an approval order on July 13, 2018. The final conditions of approval cited in the approval order are described below.

ODE Lead PMA Post-Approval Study – "Surpass Intracranial Aneurysm Embolization System Pivotal Trial to Treat Large or Giant Wide Neck Aneurysms (SCENT)": The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. The SCENT study is a prospective, multi-center, non-randomized pivotal study that was conducted under IDE G110229. The study subjects were consented to be followed for up to five (5) years post index procedure. The 1-year follow-up data from the SCENT study was used to support the approval of the subject PMA P170024. As part of the PMA post-approval study, the long-term follow-up from the SCENT study can provide safety and effectiveness information on the durability and safety of treatment using the Surpass Streamline Flow Diverter up to 5 years post-procedure. The primary safety and effectiveness endpoints are the rate of disabling strokes or neurological deaths and the rate of patients who had complete (100%) Raymond-Roy Class I intracranial aneurysm occlusion without clinically significant in-stent stenosis or retreatment of the target aneurysm. Patients will be followed at 2 years, 3 years, 4 years, and 5 years post-procedure with imaging assessment of intracranial aneurysm occlusion and in-stent stenosis performed at 3 and 5 years using the approved IDE G110229 clinical study protocol. In addition, all new and ongoing adverse events will be recorded and adjudicated by the CEC per the approved G110229 clinical study protocol.

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.

XVI. REFERENCES

Ishibashi, T., et al. Unruptured Intracranial Aneurysms Incidence of Rupture and Risk Factors. Stroke 2009; 40(1):313-16.

Juvela, S., et al. Natural History of Unruptured Intracranial Aneurysms: A Long-Term Follow-Up Study. Stroke 2013; 44(9):2414-21.

Pipeline Embolization Device (P100018), Micro Therapeutics, Inc. d/b/a ev3 Neurovascular (Medtronic Neurovascular), "Summary of Safety and Effectiveness Data (SSED)," https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100018B.pdf.

Wiebers, D.O. Unruptured Intracranial Aneurysms – Risk of Rupture and Risks of Surgical Intervention. New England Journal of Medicine 1998; 339(24):1725-33.

Wiebers, D.O. Unruptured Intracranial Aneurysms: Natural History, Clinical Outcome, and Risks of Surgical and Endovascular Treatment. The Lancet 2003; 362(9378):103-10.