SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Intracranial Coil-Assist Stent
Device Trade Name:	Neuroform Atlas® Stent System
Device Procode:	QCA
Applicant's Name and Address:	Stryker Neurovascular 47900 Bayside Parkway Fremont, California 94538

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number:	P180031
Date of FDA Notice of Approval:	May 16, 2019

II. INDICATIONS FOR USE

The Neuroform Atlas® Stent System is indicated for use with neurovascular embolization coils in the anterior circulation of the neurovasculature for the endovascular treatment of patients ≥ 18 years of age with saccular wide-necked (neck width ≥ 4 mm or a dome-to-neck ratio of < 2) intracranial aneurysms arising from a parent vessel with a diameter of ≥ 2.0 mm and ≤ 4.5 mm.

III. CONTRAINDICATIONS

The Neuroform Atlas® Stent System is contraindicated in the following patients:

- 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 anti-platelet agents prior to stent implantation.
- Patients with an active bacterial infection.
- Patients in whom a pre-existing stent is in place in the parent artery at the target intracranial aneurysm location.
- Patients in whom angiography demonstrates the anatomy is not appropriate for endovascular treatment due to conditions such as:
  - Severe intracranial vessel tortuosity or stenosis;
  - Intracranial vasospasm not responsive to medical therapy.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Neuroform Atlas® Stent System labeling.

V. DEVICE DESCRIPTION

The Neuroform Atlas® Stent System is an intracranial stent intended to be used with neurovascular embolization coils to treat saccular wide-neck intracranial aneurysms. The Neuroform Atlas® Stent System consists of:

- An implantable self-expanding nitinol stent;
- Stent delivery wire;
- Introducer sheath; and
- Accessory pouch with a torque device.

The Neuroform Atlas® Stent System is delivered through a microcatheter. The device is offered in the stent configurations shown in Table 1. The delivery system is available in two tip configurations: with an 8.5 mm distal tip and without a distal tip. All of the devices are compatible with Stryker Neurovascular Excelsior XT-17 and SL-10 Microcatheters.

Table 1. Stent Configurations

Device Diameter	Device Length			
	15 mm	21 mm	24 mm	30 mm
3.0 mm	X	X	X	X
4.0 mm	X	X	X	X
4.5 mm	X	X	X	X

Description of the Stent: The Neuroform Atlas Stent is a self-expanding, open cell, nitinol stent with flared proximal and distal ends. The stent ring is comprised of zig-zag-shaped stent struts joined by interconnects. There are six radiopaque marker bands on the stent, three on each end. The stent is pre-loaded on the stent delivery wire and is constrained by the introducer sheath until transferred into the microcatheter.

Description of the Delivery System: The Neuroform Atlas Stent Delivery System consists of the stent delivery wire and introducer sheath. The stent delivery wire is similar in construction to a guidewire. The delivery wire is a stainless-steel wire with an overall length of 185 cm. The delivery wire has a radiopaque distal tip marker and a fluoro-saver marker on the proximal end. The delivery system is available in two configurations: with a distal tip (8.5 mm) and without a distal tip on the delivery wire. The introducer sheath consists of a clear thin-walled polymer shaft and a distal tapered tip. It has an overall length of 49 cm and inner diameter of 0.0165 inches.

Description of the Accessory Pouch: An accessory pouch containing an optional torque device is also included. The physician may attach the torque device to the proximal end of the stent delivery wire to facilitate handling and stabilization.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of wide-neck intracranial aneurysms including open surgical clipping, endovascular treatment using embolization coils supported with other Premarket Approval (PMA) and Humanitarian Device Exemption (HDE) approved neurovascular coil-assist and flow diverting stents, or balloon catheter assisted coiling of the intracranial aneurysm. One other neurovascular coil-assist stent has been approved via the PMA regulatory pathway from MicroVention, Inc. for the Low-Profile Visualized Intraluminal Support (LVIS) and LVIS Jr. (P170013). Other neurovascular coil-assist stents have been approved through the HDE regulatory pathway including 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 and 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) and Pipeline Flex Embolization Device (PFED) (P100018) and the Stryker Neurovascular Surpass Streamline Flow Diverter (P170024) are the only approved neurovascular flow diverting stents in the United States (US). The PED and PFED are approved with the indications for 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 segments and small and medium wide-necked saccular and fusiform intracranial aneurysms in the ICA up to the terminus. The Surpass Streamline Flow Diverter is indicated for use in the endovascular treatment of unruptured large or giant saccular or fusiform wide-necked intracranial aneurysm in the ICA from the petrous segment to the terminus. Neurovascular flow diverting stents are implanted in the parent vessel and 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 neurovascular flow diverting stent is intended to be used by itself as a stand-alone device.

A similar PMA approved device that is an intrasaccular intracranial aneurysm flow disruption device is the MicroVention, Inc. Woven EndoBridge (WEB) Aneurysm Embolization System (P170032) indicated for use at the middle cerebral artery (MCA) bifurcation, ICA terminus, anterior communicating artery (AComm) complex, or basilar artery apex for the endovascular treatment of saccular, wide-necked, bifurcation intracranial aneurysms with certain aneurysm size dimensions. This device is implanted

within the sac of the intracranial aneurysm and is intended to protect the neck of the intracranial aneurysm to disrupt flow from entering.

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 aneurysms over time. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his or her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Neuroform Atlas Stent System is available in the following countries: Argentina, Australia, Austria, Bahrain, Belgium, Bulgaria, Canada, Canary Islands, Chile, Colombia, Costa Rica, Croatia, Cyprus, Czech Republic, Denmark, Dominican Republic, Ecuador, Egypt, Estonia, Finland, France, Georgia, Germany, Great Britain (UK), Greece, Honduras, Hong Kong, Hungary, Iceland, India, Iran, Ireland, Israel, Italy, Jamaica, Japan, Jordan, Korea, Kuwait, Latvia, Lithuania, Malaysia, Malta, Mexico, Netherlands, New Zealand, Norway, Oman, Peru, Philippines, Poland, Portugal, Qatar, Romania, Russia, Saudi Arabia, Serbia, Singapore, Slovakia, Slovenia, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, Tunisia, Turkey, Vietnam and United Arab Emirates.

The Neuroform Atlas Stent System has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

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.

- Aphasia
- Allergic reaction to nitinol metal and medications
- Aneurysm perforation or rupture, leak or contrast extravasation
- Blindness
- Cardiac arrhythmia
- Coil herniation through stent into parent vessel
- Cranial neuropathy
- Death
- Embolus
- Headache
- Hemiplegia
- Hemorrhage (i.e., intracerebral,
- Reactions to anti-platelet or anti-coagulant agents
- Renal failure
- Seizure
- Stent fracture, migration, embolization, or misplacement
- Stent thrombosis
- Stroke
- Transient ischemic attack
- Vasospasm
- Vessel occlusion or closure including parent vessel or non-target side-branches
- Vessel perforation, dissection, trauma or damage

subarachnoid, retroperitoneal, or in other locations)
- Hydrocephalus
- In-stent stenosis
- Infection
- Ischemia
- Mass effect
- Myocardial infarction
- Neurological deficit or intracranial sequelae
- Pseudoaneurysm
- Reaction to radiation exposure (i.e., alopecia, burns ranging in severity from skin reddening to ulcers, cataracts, delayed neoplasia)
- Vessel thrombosis
- Visual impairment
- Other procedural complications including, but not limited to, anesthetic and contrast media risks, hypotension, hypertension, access site complications including pain, hematoma, local bleeding, local infection, and injury to the artery (i.e., dissection), vein, or adjacent nerves
- Unplanned intervention

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

IX. SUMMARY OF NONCLINICAL STUDIES

The Neuroform Atlas Stent System 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 device has been validated for a 5-year shelf life based on accelerated aging studies. The device is sterilized by ethylene oxide (EO) and has been validated to ensure a sterility assurance level (SAL) of 10^{-6}.

A. Laboratory Studies

The objectives of the laboratory studies were to verify and validate the design of the Neuroform Atlas Stent System and its materials of construction, the biocompatibility of the materials, shelf-life stability, and sterilization.

Design Verification and Validation Testing

The finished and sterile Neuroform Atlas Stent System was evaluated for design verification and validation based on a risk analysis of the device for the proposed intended use. Also, the design verification and validation testing used the FDA guidances titled "*Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*" and "*Select Updates for Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*" as references for the testing. In addition, the design verification and validation testing plan utilized the standards EN ISO 25539-2:2012: "*Cardiovascular Implants – Endovascular Devices – Part 2: Vascular Stents*", ISO 11070:2014: "*Sterile, Single-Use Intravascular Catheter Introducers,*" and EN ISO 10555-1:2013: "*Intravascular Catheters – Sterile and Single-Use Catheters – Part 1: General*

Requirements" for guidance. Table 2 summarizes the design verification and validation testing performed on the Neuroform Atlas Stent System. The results demonstrate that all pre-specified acceptance criteria were met.

Table 2. Design Verification and Validation Testing of the Neuroform Atlas Stent System

Tests	Test Description	Results
Stent Dimensional and Functional Attributes		
Corrosion Resistance	The implant shall not exhibit excessive pitting and crevice corrosion after simulated in vivo conditions (10 years).	Pass
Dimensional Verification	The implant shall be suitable for implantation in cerebrovascular vessels of 2.0 mm to 4.5 mm diameter and provide a working length from 15 mm to 30 mm.	Pass
Percent Surface Area	For each stent model, the free surface area in the smallest recommended vessel diameter must be > 75%.	Pass
Foreshortening	The change in stent length from when it is loaded in the recommended 0.0165" to 0.017" microcatheter prior to deployment to post deployment in the largest recommended vessel size for that stent must be less than 20%.	Pass
Stent Integrity	The implant should be free from visual defects, such as broken struts, pits, dents, and bumps, after deployment in the unconstrained state.	Pass
Radial Outward Force	The implant radial force shall be sufficient to provide stent fixation without causing vessel injury	Pass
Stress/Strain Analysis	Worst-case constrained conditions show to be less than yield strength of stent materials.	Pass
Fatigue Analysis	Fatigue stress amplitude shown to be less than endurance limit of stent materials.	Pass
Accelerated Durability Testing	The device shall be suitable for implantation in cerebrovascular arteries without mechanical compromise as a result of being subjected to simulated 10 years of expected pulsatile flow and physiological stress loading.	Pass
Particulate Evaluation	Particulates shall be acceptable following simulated delivery and device deployment.	Pass
Magnetic Resonance Imaging (MRI) Safety and Compatibility	Stent shall be MRI conditional for 1.5 Tesla (T) and 3 T MRI equipment immediately after implantation.	Pass
Radiopacity	Stent shall provide sufficient radiopacity with equally spaced radiopaque markers on each end of the stent for proper stent placement and secondary treatment.	Pass
Kink Resistance	Implant shall conform to the indicated vessel size with a bend radius of 6.5 mm (centerline) without kinking.	Pass
Delivery System Dimensional and Functional Testing		
Dimensional Verification	The stent delivery system, when used with the recommended 0.0165" to 0.017" microcatheter shall reach the intended cerebrovascular anatomical location. It will deliver and deploy implants into vessel diameters of 2.0 mm to 4.5 mm with a working length between 15 mm to 30 mm.	Pass
Delivery, Deployment, and Retraction	The delivery system must be able to safely: deliver the implant to the intended location, deploy the stent accurately, withdrawn from the anatomy post deployment.	Pass

Tests	Test Description	Results
Catheter Bond Strength	The stent delivery system must be able to deliver and deploy the implant to the intended location without damage and be able to be withdrawn safely without damage.	Pass
Tip Pull Test		Pass
Flexibility and Kink Test		Pass
Corrosion Resistance	The delivery wire shall show no visible signs of corrosion after testing.	Pass

Biocompatibility

Biocompatibility testing was conducted on the Neuroform Atlas Stent System and on the previous generation Neuroform stents in accordance with the provisions in EN ISO 10993-1 and Good Laboratory Practice (GLP) regulations specified in 21 CFR 58. Table 3 and Table 4 summarize all of the biocompatibility testing performed on the Neuroform Atlas Stent System. The results demonstrate that the Neuroform Atlas Stent System is biocompatible.

Table 3. Biocompatibility Testing of Neuroform Atlas Stent

Test Performed	Test Description	Results
Cytotoxicity	Minimum Essential Medium (MEM) Elution Test	Pass. No cytotoxicity or cell lysis, Score: 0
Sensitization	Guinea Pig Maximization	Pass. No evidence of sensitization
Irritation	Intracutaneous Study in Rabbits	Pass. Difference between Test – Control is 0.0 for 0.9% Sodium Chloride (SC) and 0.0 for Sesame Oil (SO)
Systemic Toxicity	Systemic Toxicity Study in Mice	Pass. No mortality or evidence of systemic toxicity
	Rabbit Pyrogen Study – Material Mediated	Pass. Nonpyrogenic, maximum temperature rise: 0.2 °C
Systemic Toxicity & Intramuscular Implantation	Implant/Chronic Toxicity 13 Week Systemic Toxicity	Pass. No evidence of systemic toxicity. Test article was classified as a nonirritant. Local macroscopic tissue reaction was not significant as compared to the control article.
Implantation	Muscle Implantation Study in Rabbits (2 & 6 weeks)	Pass. Microscopic reaction was not significant as compared to the negative control article. Test article was classified as a nonirritant as compared to the negative control article.
Genotoxicity	Mouse Peripheral Blood Micronucleus Study	Pass. Test article did not induce micronuclei in mice and is considered non-mutagenic.

Test Performed	Test Description	Results
	Ames Assay	Pass. Non-genotoxic.
	Mouse Lymphoma	Pass. Non-genotoxic.
Hemocompatibility	Hemolysis Direct Contact & Extract Method	Pass. Test article is considered non-hemolytic.
	Complement Activation Assay	Pass. The test article did not induce complement activation.
	In Vitro Hemocompatibility Assay	Pass. Results comparable to negative control; white blood cell (WBC): 124%, red blood cell (RBC): 100%, hemoglobin: 100%, hematocrit: 99%, platelets 125%.
	Partial Thromboplastin Time (PTT)	Pass. Test article average clotting time: 243.0 seconds, 81% of negative control, minimal activator.
	Complement Activation	Pass. The test article did not induce complement activation.
	Preclinical Study Report (GLP Canine Study)	Pass. Results were consistent with a positive safety profile. In addition, there was no evidence of thrombus formation at 30 days or at 180 days.

Table 4. Biocompatibility Testing of Neuroform Atlas Stent Delivery System

Test Performed	Test Description	Result
Cytotoxicity	MEM Elution	Pass. No toxicity or cell lysis. Grade 0
Sensitization	Guinea Pig Maximization	Pass. Sensitization rate: 0
Irritation	Intracutaneous Study in Rabbits	Pass. Difference between Test – Control is 0.0 for SC and 0.2 for SO.
Systemic Toxicity	Systemic Toxicity Study in Mice	Pass. No mortality or evidence of systemic toxicity.
	Rabbit Pyrogen Study - Material Mediated	Pass. Nonpyrogenic, maximum temperature rise: 0.1°C.
Hemocompatibility	Hemolysis – Rabbit Blood	Pass. Hemolytic index: 1.2% (direct contact) and 0.1% (extract)
	SC5b-9 and C3a Complement Activation	Pass. The test article did not induce complement activation.

Shelf-Life Testing

The Neuroform Atlas Stent System was accelerated aged equivalent to 5 years, and then tested for package integrity, sterility, and physical device specification and performance testing. The results support a 5-year expiration date for the Neuroform Atlas Stent System.

Sterilization Validation

The Neuroform Atlas Stent System is sterilized using ethylene oxide (EO). The EO cycle was validated to a sterility assurance level (SAL) of 10^{-6} per EN ISO 11135-1:2014: *Sterilization of Health Care Products – Ethylene Oxide – Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices*. The Neuroform Atlas Stent System was tested and met specifications after 1x and 2x sterilization exposures per ISO 11135:2014. In addition, the entire Neuroform Atlas Stent System was tested for bacterial endotoxins and met the specified endotoxin specification of < 0.06 endotoxin units (EU)/mL or < 2.15 EU/device for devices with potential contact with cerebrospinal fluid (CSF).

B. Animal Studies

The objectives of the GLP animal study were to assess the safety and vascular compatibility of the Neuroform Atlas Stent System when used as intended at approximately 30, 90, and 180 days post-implantation in elastase-induced aneurysms in laprine carotid arteries of New Zealand white rabbits.

The Neuroform Atlas Stent System (test) and the Neuroform EZ Stent System (control) were implanted in 41 New Zealand white rabbits. Animals were sacrificed for analysis at 30 days (10 test and 3 control animals), 90 days (10 test and 5 control animals), and 180 days (10 test and 3 control animals) post-implantation. Excised vessel and organ samples were submitted for gross, histopathology, and morphometric analyses. The findings showed at implant and during in-life there were no deaths related to the Neuroform Atlas Stent System. Vessel stenosis remained below 50% via morphometric analysis for both test and control device treated vessels. Acceptable healing response via histopathology evaluation was observed for Neuroform Atlas Stent System treated vessels. The Neuroform Atlas Stent System also showed no or minimal inflammatory response, which demonstrates local biocompatibility of the implant. At 30, 90, and 180 days, there was absence of clinically relevant stenosis and thrombosis (full patency); near complete or complete endothelialization; and optimal formation of a generally mature and stable neointima with no residual fibrin. Histologically, there were no adverse changes in the test device treated vessels at any time point evaluated. Acute safety during and immediately following implantation of the Neuroform Atlas Stent System showed no vessel spasm, no vessel perforations, and no thrombosis. In conclusion, safety and vascular compatibility of the Neuroform Atlas Stent System was demonstrated at all time points up to 180 days post-implantation.

C. Additional Studies

Magnetic Resonance Imaging (MRI) Compatibility:

The Neuroform Atlas Stent System was evaluated when used as intended for MRI compatibility per ASTM F2503, including magnetically induced displacement force (ASTM F2052), magnetically induced torque (ASTM F2213), heating by radiofrequency fields (ASTM F2182), and image artifact (ASTM F2119). The Neuroform Atlas Stent can be safely scanned under the following conditions:

- Static magnetic field of 1.5 and 3.0 Tesla (T)
- Maximum spatial gradient field up to 2500 Gauss/cm (25 T/m)
- Maximum MR system reported whole body averaged specific absorption rate of 2 W/kg (Normal Operating Mode) and head averaged specific absorption rate of 3.2 W/kg.

Under the scan conditions defined above, the Neuroform Atlas Stent is expected to produce a maximum temperature rise of 4 °C after 15 minutes of continuous scanning. The Neuroform Atlas Stent should not migrate in this MRI environment. In non-clinical testing, the image artifact caused by the device extends approximately 2 mm from the Neuroform Atlas Stent when imaged with a spin echo pulse sequence and 3 T MRI. Magnetic resonance (MR) image quality may be compromised if the area of interest is in the exact same area or relatively close to the position of the Neuroform Atlas Stent. Therefore, optimization of MR imaging parameters to compensate for the presence of this device may be necessary.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness (as defined below) of the endovascular treatment with the Neuroform Atlas Stent System indicated for use with neurovascular embolization coils in the anterior circulation of the neurovasculature in patients ≥ 18 years of age with saccular wide-necked (neck width ≥ 4mm or dome to neck ratio < 2) intracranial aneurysms arising from a parent vessel with a diameter ≥ 2 mm and ≤ 4.5 mm in the US under IDE # G150006. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between July 1, 2015, and October 5, 2016. The database for the anterior-circulation cohort of this PMA reflected data collected through April 17, 2017 and included 201 patients. There were 25 active investigational sites in the US.

The study was a prospective, multi-center, non-randomized, one-arm, unmasked clinical study titled "*Safety and Effectiveness of the Treatment of Wide Neck, Saccular Intracranial Aneurysms with the Neuroform Atlas™ Stent System (ATLAS).*" The pivotal ATLAS study

included follow-up at post-implant, 2 months, 6 months, and 12-months post-procedure to support the current PMA. The pre-specified primary endpoints in the clinical study protocol were:

- Safety: Any major ipsilateral stroke or neurological death within 12 months. A major ipsilateral stroke was defined as an ipsilateral stroke that is associated with an increase of 4 or more points on the National Institutes of Health Stroke Scale (NIHSS) at 24 hours after symptoms onset. An ipsilateral stroke was defined as an acute episode of focal or global neurological dysfunction due to brain or retinal infarction, or due to an intracranial hemorrhage inclusive of subarachnoid, intraventricular or intraparenchymal hemorrhage, occurring in the same hemisphere as the target intracranial aneurysm.

- Effectiveness: Complete intracranial aneurysm occlusion (100% occlusion – Raymond Class 1) of the treated target lesion on 12-month angiography, in the absence of retreatment or significant parent artery stenosis (> 50%) at the target location as evaluated by an independent Core Laboratory. The trial design does not address whether there is decreased disability or decreased incidence of cerebral aneurysm rupture in the long term in patients treated with the device compared to patients treated with a more conservative approach.

The primary endpoint results were compared to performance goals (PGs) developed using published clinical data from endovascular treatments of wide-neck intracranial aneurysms using neurovascular stents for stent-assisted coiling (SAC), balloon-assisted coiling (BAC), and coiling alone. There was no active concurrent control group in the ATLAS study.

A sample size of up to 180 subjects with intracranial aneurysms in the distal anterior circulation was planned to be enrolled into this study in order to provide 153 evaluable subjects at 12 months, with an estimated 15% attrition rate. Assuming a primary effectiveness endpoint response rate of 62% (per the findings of a meta-analysis of Neuroform stent literature as performed by King et al. 2015), the expected lower bound of the exact binomial two-sided 95% confidence interval around the success rate is greater than 50%. Assuming a primary safety endpoint rate of 8%, the expected upper bound of the exact binomial two-sided 95% confidence interval around the success rate is less than 20%. A sample size of 153 evaluable subjects provides 85% power to demonstrate the effectiveness endpoint, and a power of approximately 99% to successfully demonstrate the safety endpoint given the observed rates stated above. The combined probability of the two endpoints is 0.85 x 0.99 = 0.842.

The primary safety and effectiveness endpoint analyses were performed on the modified Intent-to-Treat (mITT) population defined as all subjects who signed the informed consent form for this trial and in whom the Neuroform Atlas Stent System procedure was attempted.

This study included an independent Clinical Events Committee (CEC), Data Safety and Monitoring Board (DSMB), angiographic imaging Core Laboratory (“Core Lab”), and

study monitors who confirmed neurological assessments, adverse events, and study data with source documentation.

1. Clinical Inclusion and Exclusion Criteria

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

   - Subject is between 18 and 80 years of age.
   - Subject has a documented, wide neck (neck ≥ 4 mm or a dome-to-neck ratio < 2), intracranial, saccular aneurysm arising from a parent vessel with a diameter of ≥ 2 mm and ≤ 4.5 mm, which will be treated with bare metal coils.
   - Subject or legal representative is willing and able to provide informed consent.
   - Subject is willing and able to comply with protocol follow-up requirements.

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

   - Subject has known multiple untreated cerebral aneurysms, other than non-target blister aneurysm, infundibulum, or aneurysm measuring < 3 mm for each of three dimensions assessed (height, width, and depth) that will not require treatment during the study period.
   - Subject has a target lesion that is a blister aneurysm, infundibulum, or aneurysm measuring < 3 mm for each of three dimensions assessed (height, width, and depth).
   - Subject has a target aneurysm that will require an investigator to intentionally leave a neck remnant in order to preserve blood flow in a bifurcation or branch.
   - Subject has undergone coiling or stenting of a non-target intracranial aneurysm within 30 days prior to study treatment.
   - Subject has a target aneurysm in the anterior circulation proximal to the superior hypophyseal ICA.
   - Subject has acute target aneurysm rupture less than 14 days prior to study treatment.
   - Subject has a Hunt and Hess score ≥ 3 or a pre-morbid modified Rankin Scale (mRS) score ≥ 4.
   - Subject has an admission platelet count of < 50,000, any known coagulopathy, or an International Normalized Ratio (INR) > 3.0 without oral anticoagulation therapy.
   - Subject has a known absolute contraindication to angiography.
   - Subject has evidence of active cancer, terminal illness, or any condition which, in the opinion of the treating physician, would/could prevent subject from completing the study (e.g., a high risk of embolic stroke, atrial fibrillation, co-morbidities, psychiatric disorders, substance abuse, major surgery ≤ 30 days pre-procedure).
   - Subject has a known absolute contraindication to the use of required study medications or agents (e.g., heparin, aspirin, clopidogrel, and radiographic

contrast agents).

- Subject is female and is pregnant or intends to become pregnant during the study.
- Subject has Moya-Moya disease, arteriovenous malformation(s), arteriovenous fistula(e), intracranial tumor(s), or intracranial hematoma(s) (unrelated to target aneurysm).
- Subject has significant atherosclerotic stenosis, significant vessel tortuosity, vasospasm refractory to medication, unfavorable aneurysm morphology or vessel anatomy, or some other condition(s) that, in the opinion of the treating physician, would/could prevent or interfere with access to the target aneurysm and/or successful deployment of the Neuroform Atlas Stent.
- Subject has had previous treatment (e.g., surgery, stenting) in the parent artery that, in the opinion of the treating physician, would/could prevent or interfere with successful use of the Neuroform Atlas Stent System and/or successful deployment of embolic coils.
- Subject has undergone previous stent-assisted coiling of the target aneurysm.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 2-months, 6-months, and 12-months postoperatively. Preoperatively, the patients underwent a review of their concomitant medications and medical history, neurological examination, completion of neurological rating and grading scales (mRS, NIHSS), laboratory, and angiographic evaluations. Postoperatively, the objective parameters measured during the study included a review of the concomitant medications, neurological, and angiographic evaluations (see Table 5). Adverse events and complications were recorded at all visits.

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

Table 5. ATLAS Study Required Evaluations from Baseline through 12-Month Follow-Up Visit

	Pre-Implant	**Implant /Procedural**	**Post-Implant†**	**2 ± 1 Month**	**6 ± 1 Month**	**12 ± 2 Months**
Medical History	✓					
Neurological Exam*	✓					✓
mRS*	✓		✓	✓	✓	✓
NIHSS*/**	✓			+/-**	+/-**	✓
Hunt and Hess*/***	✓		✓			✓

	Pre-Implant	Implant /Procedural	Post-Implant†	2 ± 1 Month	6 ± 1 Month	12 ± 2 Months
Angiography****	✓**** (MRA, CTA or DSA)	✓ (DSA)		+/-**** (MRA or DSA, per institution standards)	+/-**** (MRA or DSA, per institution standards)	✓ (DSA)
Adverse Event Assessment	✓	✓	✓	✓	✓	✓
Antiplatelet Medication	✓		✓	✓	✓	✓
Quality of Life Assessment	✓					✓

† Assessments must be performed within 72 hours after implant procedures, and prior to hospital discharge.
* At each site, a non-treating physician or an appropriately trained/qualified designee will be responsible for performing neurological examinations and/or performing assessments using neurologic rating/grading scales (mRS, NIHSS, Hunt and Hess). In addition to the assessment schedule outlined in tabular form above, a neurological examination and/or an assessment using a neurologic rating/grading scale may be performed at any point in time if it is appropriate to do so, or in the case of a new neurological event.
** The NIHSS is required at baseline and at 12 months of follow-up. In addition, the NIHSS is required at the 2- and 6-month follow-up visit and at any unscheduled visit if the subject's mRS score is > 0 in association with an adverse neurological event.
*** Hunt and Hess scoring will be performed as outlined in tabular form above only when evaluating subjects who have evidence of subarachnoid hemorrhage.
**** Pre-implant angiography (magnetic resonance angiography (MRA), computed tomography angiography (CTA), or digital subtraction angiography (DSA)) may be performed up to 6 months prior to treatment. In addition to the post-implant and 12-month angiographic studies outlined in tabular form above, it is recommended that an imaging study be performed within 24 hours of the onset of symptoms in any treated subject suspected of having a stroke. Although not required, if it is standard of care to do so at a given site, imaging (MRA or DSA) may be performed at the 2- or 6-month follow-up visit.

3. Clinical Endpoints

With regards to safety, the percentage of patients who had a major ipsilateral stroke 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 parent artery stenosis (> 50%) or target intracranial aneurysm re-treatment within 12-months post-procedure was used to analyze the clinical study results.

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 ATLAS trial using alternative treatment modalities such as neurovascular stents used for SAC, BAC, or coiling embolization alone. The primary endpoints were analyzed using the modified intent-to-treat (mITT) population and Fisher's Exact Binomial test. 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 Neuroform Atlas Stent System. For effectiveness, a one-sided p-value < 0.025 results in rejecting the null hypothesis that the primary effectiveness endpoint is ≤ 50% in favor of the alternative hypothesis that treatment with the subject device has a likelihood of success in > 50% of patients.

B. Accountability of PMA Cohort

At the time of database lock, of 201 patients enrolled in the PMA study, 90.5% (182/201) of patients comprised the mITT population and are available for analysis at the completion of the study, the 12-month post-operative visit (see Figure 1).

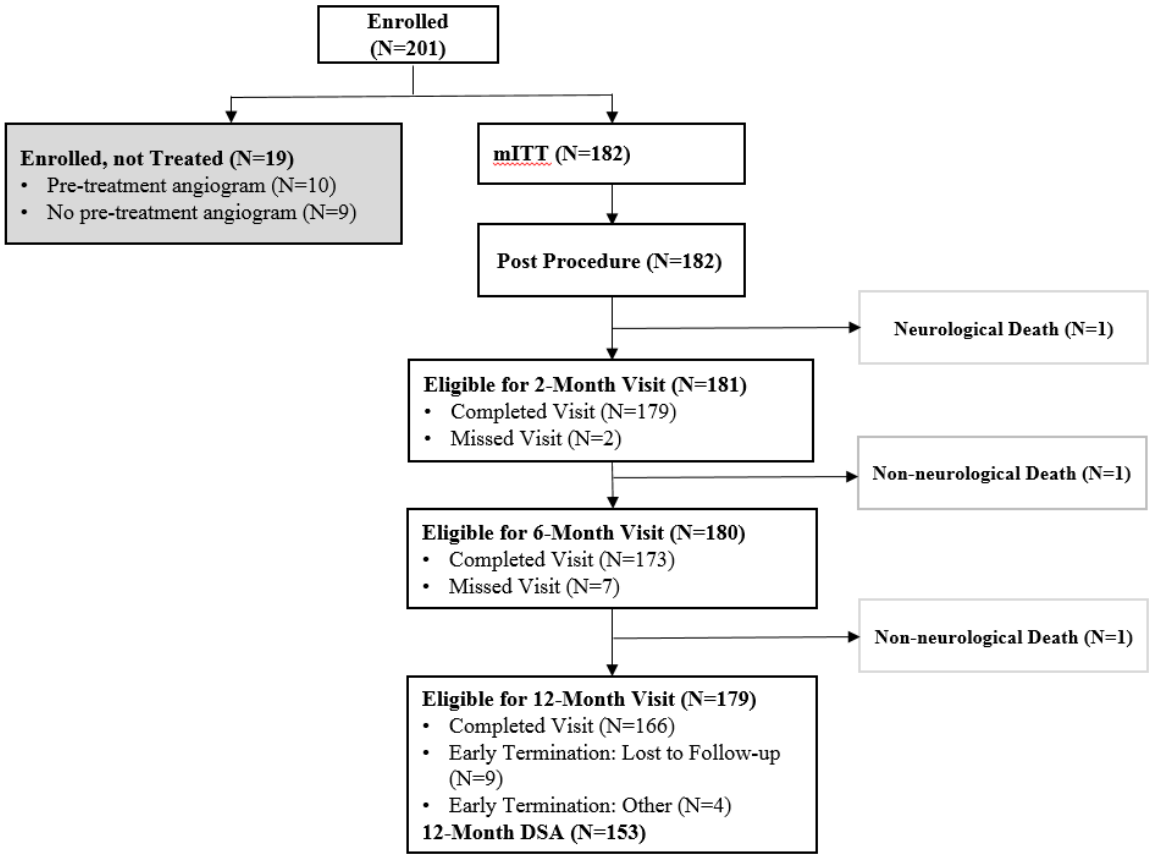

Figure 1. Subject Accountability Flowchart

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 ATLAS trial (see Table 6). Table 7, Table 8, and Table 9 present the location, measurement characteristics, and rupture status of the intracranial aneurysms treated in the ATLAS trial based on the baseline (pre-procedure) site-reported results of digital subtraction angiography (DSA) exams.

Table 6. Demographic and Baseline Characteristics – mITT Population

Characteristic	mITT Population (N=182)
Age (yrs)	
Mean ± Standard Deviation (SD) (N)	60.3 ± 11.4 (182)
Median (Q1 - Q3)	61.0 (53.0 - 69.0)
Minimum (Min) – Maximum (Max)	23.0 - 80.0
Height (cm)	
Mean ± SD (N)	166.2 ± 9.9 (182)
Median (Q1 - Q3)	165.1 (160.0 - 171.0)
Min – Max	138.0 - 195.6
Weight (kg)	
Mean ± SD (N)	79.8 ± 19.2 (182)
Median (Q1 - Q3)	79.4 (65.8 - 91.0)
Min – Max	36.3 - 157.0
Body Mass Index (BMI) (kg/m²)	
Mean ± SD (N)	28.8 ± 6.2 (182)
Median (Q1 - Q3)	28.2 (24.5 - 32.3)
Min – Max	16.2 - 55.0
Gender	
Female	73.1% (133/182)
Male	26.9% (49/182)
Race	
White	80.8% (147/182)
Black or African American	13.7% (25/182)
Asian	2.7% (5/182)
Native Hawaiian or other Pacific Islander	0.5% (1/182)
American Indian or Alaskan Native	0.0% (0/182)
Other [1]	2.2% (4/182)
Ethnicity	
Not Hispanic or Latino	93.4% (170/182)
Hispanic or Latino	6.6% (12/182)
[1] Specified as Arabic (n=1), Portuguese (n=1), Hispanic (n=1), and mixed race (n=1).	

Table 7. Target Intracranial Aneurysm Location – mITT Population

Target Aneurysm Location	mITT Population (N=182)
Anterior Cerebral Artery	2.2% (4/182)
Anterior Communicating Artery	35.2% (64/182)
Middle Cerebral Artery Bifurcation	14.8% (27/182)
Middle Cerebral Artery-M1	2.7% (5/182)
Middle Cerebral Artery-M2	1.6% (3/182)
Internal Carotid Artery-Ophthalmic	15.9% (29/182)
Internal Carotid Artery-Anterior Choroidal Artery	0.5% (1/182)
Internal Carotid Artery-Posterior Communicating Artery	13.2% (24/182)
ICA Bifurcation/Terminus	4.9% (9/182)
Supraclinoid Carotid Artery	3.3% (6/182)
Superior Hypophyseal	3.3% (6/182)
Other [1]	2.2% (4/182)
[1] ICA paraclinoid (n = 1), para-ophthalmic ICA (n = 1), and fetal posterior communicating artery (PCA) origin (n = 2).	

Table 8. Pre-implant Target Intracranial Aneurysm Characteristics (Site-reported) – mITT Population

	mITT Subjects (N=182)
Subjects with Number of Target Aneurysms	
1	100.0% (182/182)
Type of imaging used	
1.DSA	83.5% (152/182)
2.CTA/MRA/Other [1]	16.5% (30/182)
Aneurysm height (mm) (superior inferior on anteroposterior (AP) or lateral)	
Mean ± SD (N)	5.4 ± 2.2 (182)
Median (Q1 - Q3)	5.1 (4.0 - 6.1)
Min - Max	1.8 - 16.3
Aneurysm width (mm) (horizontal on AP)	
Mean ± SD (N)	5.2 ± 2.0 (182)
Median (Q1 - Q3)	5.0 (4.0 - 6.1)
Min - Max	1.9 - 19.0
Aneurysm depth (mm) (AP or lateral)	
Mean ± SD (N)	5.0 ± 1.8 (182)
Median (Q1 - Q3)	4.9 (3.9 - 6.0)
Min - Max	1.5 - 12.8
Aneurysm neck width (mm)	
Mean ± SD (N)	4.1 ± 1.2 (182)
Median (Q1 - Q3)	4.0 (3.3 - 4.7)
Min - Max	1.6 - 8.7
Aneurysm Size (mm) [2]	
Mean ± SD (N)	6.1 ± 2.2 (182)
Median (Q1 - Q3)	6.0 (4.8 - 7.0)
Min - Max	2.3 - 19.0
Dome/Neck Ratio [3]	

	mITT Subjects (N=182)
Mean ± SD (N)	1.2 ± 0.3 (182)
Median (Q1 - Q3)	1.1 (1.0 - 1.3)
Min - Max	0.4 - 2.1
Parent vessel diameter proximal to the aneurysm neck (mm)	
Mean ± SD (N)	3.0 ± 0.7 (182)
Median (Q1 - Q3)	2.9 (2.4 - 3.6)
Min - Max	2.0 - 4.5
Parent vessel diameter distal to the aneurysm neck (mm)	
Mean ± SD (N)	2.7 ± 0.7 (182)
Median (Q1 - Q3)	2.5 (2.1 - 3.2)
Min - Max	1.6 - 4.4
Parent vessel stenosis pre-implant	
No	96.7% (176/182)
Yes	3.3% (6/182)
% stenosis:	
25% or less	83.3% (5/6)
26% - 50%	16.7% (1/6)

[1] CTA only (n=19), MRA only (n=10), and "Other" defined as CTA+MRA+MRI (n=1).
[2] The aneurysm size is defined as the maximum of three dimensions (AP plane, lateral plane, height).
[3] The dome size is defined as the minimum of two widths (AP plane, lateral plane).

Table 9. Target Intracranial Aneurysm Rupture Status at Baseline and Prior Target Aneurysm Treatment - mITT Population

	mITT Population (N=182)		
Measure	**Ruptured**	**Unruptured**	**Total**
Previous target aneurysm rupture	12.1% (22/182)	87.9% (160/182)	100.0% (182/182)
Days from last rupture to index procedure			
Mean ± SD (N)	642.6 ± 1352.8 (19)		
Median (Q1 - Q3)	274.0 (105.0 - 530.0)		
Min - Max	23.0 - 6128.0		
Prior Treatment/Intervention			
Coiling only	72.7% (16/22)	3.8% (6/160)	12.1% (22/182)
Balloon assisted coiling	4.5% (1/22)	0.0% (0/160)	0.5% (1/182)
Other [1]	22.7% (5/22)	1.9% (3/160)	4.4% (8/182)

[1] Five subjects with previously ruptured target intracranial aneurysms underwent clipping (n = 4) or partial embolization (n = 1). All 3 subjects with unruptured target intracranial aneurysms who received prior treatment underwent clipping.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the mITT cohort of 182 patients available for the 12-month evaluation. The key safety outcomes for this study are presented below in Table 12. Adverse effects are reported in Tables 10 and 11.

Adverse effects that occurred in the PMA clinical study:

Table 10 reports serious adverse events (SAEs) and non-SAEs that occurred with an overall frequency greater than 1% through one-year follow-up in the ATLAS trial.

Table 10. Adverse Events (AEs) with > 1% Overall Frequency through 12-Months Post-Procedure by Medical Dictionary for Regulatory Activities (MedDRA) Codes – mITT Population

MedDRA System Organ Class/Preferred Term	mITT Population (N = 182)					
	SAEs		Non-serious AEs		All AEs	
	Events	Subjects with Events (%)	Events	Subjects with Events (%)	Events	Subjects with Events (%)
Any Adverse Event (AE)	81	51 (28.0%)	377	128 (70.3%)	458	141 (77.5%)
Blood and lymphatic system disorders						
Anemia	0	0	3	3 (1.6%)	3	3 (1.6%)
Increased tendency to bruise	0	0	2	2 (1.1%)	2	2 (1.1%)
Cardiac disorders						
Arrhythmia	0	0	2	2 (1.1%)	2	2 (1.1%)
Cardiomyopathy	1	1 (0.5%)	1	1 (0.5%)	2	2 (1.1%)
Eye disorders						
Diplopia	1	1 (0.5%)	1	1 (0.5%)	2	2 (1.1%)
Photophobia	0	0	4	4 (2.2%)	4	4 (2.2%)
Vision blurred	1	1 (0.5%)	5	5 (2.7%)	6	6 (3.3%)
Vitreous floaters	0	0	2	2 (1.1%)	2	2 (1.1%)
Gastrointestinal disorders						
Abdominal pain	1	1 (0.5%)	1	1 (0.5%)	2	2 (1.1%)
Constipation	1	1 (0.5%)	1	1 (0.5%)	2	2 (1.1%)
Diarrhea	1	1 (0.5%)	1	1 (0.5%)	2	2 (1.1%)
Dysphagia	0	0	2	2 (1.1%)	2	2 (1.1%)
Nausea	0	0	10	8 (4.4%)	10	8 (4.4%)
Vomiting	0	0	2	2 (1.1%)	2	2 (1.1%)
General disorders and administration site conditions						
Administration site pain	0	0	2	2 (1.1%)	2	2 (1.1%)
Application site hematoma	1	1 (0.5%)	5	5 (2.7%)	6	6 (3.3%)
Asthenia	0	0	3	3 (1.6%)	3	3 (1.6%)
Catheter site haemorrhage	0	0	2	2 (1.1%)	2	2 (1.1%)
Chest pain	1	1 (0.5%)	3	3 (1.6%)	4	4 (2.2%)
Fatigue	0	0	3	3 (1.6%)	3	3 (1.6%)
Local swelling	0	0	2	2 (1.1%)	2	2 (1.1%)
Wound secretion	0	0	6	6 (3.3%)	6	6 (3.3%)
Immune system disorders						
Hypersensitivity	0	0	2	2 (1.1%)	2	2 (1.1%)
Infections and infestations						
Acute sinusitis	0	0	3	3 (1.6%)	3	3 (1.6%)
Bronchitis	0	0	2	2 (1.1%)	2	2 (1.1%)

MedDRA System Organ Class/Preferred Term	mITT Population (N = 182)					
	SAEs		Non-serious AEs		All AEs	
	Events	Subjects with Events (%)	Events	Subjects with Events (%)	Events	Subjects with Events (%)
Herpes zoster	0	0	2	2 (1.1%)	2	2 (1.1%)
Sinusitis	0	0	3	3 (1.6%)	3	3 (1.6%)
Urinary tract infection	1	1 (0.5%)	9	9 (4.9%)	10	10 (5.5%)
Injury, poisoning and procedural complications						
Fall	0	0	3	2 (1.1%)	3	2 (1.1%)
Metabolism and nutrition disorders						
Hypokalemia	0	0	5	5 (2.7%)	5	5 (2.7%)
Musculoskeletal and connective tissue disorders						
Arthralgia	0	0	3	3 (1.6%)	3	3 (1.6%)
Back pain	0	0	6	6 (3.3%)	6	6 (3.3%)
Musculoskeletal pain	0	0	2	2 (1.1%)	2	2 (1.1%)
Neck pain	0	0	3	3 (1.6%)	3	3 (1.6%)
Pain in extremity	0	0	4	4 (2.2%)	4	4 (2.2%)
Nervous system disorders						
Amnesia	0	0	2	2 (1.1%)	2	2 (1.1%)
Aphasia	0	0	2	2 (1.1%)	2	2 (1.1%)
Balance disorder	0	0	3	3 (1.6%)	3	3 (1.6%)
Cerebral infarction	0	0	3	3 (1.6%)	3	3 (1.6%)
Cerebral vasoconstriction	0	0	14	14 (7.7%)	14	14 (7.7%)
Cognitive disorder	0	0	2	2 (1.1%)	2	2 (1.1%)
Convulsion	2	2 (1.1%)	2	2 (1.1%)	4	4 (2.2%)
Dizziness	0	0	9	9 (4.9%)	9	9 (4.9%)
Headache	1	1 (0.5%)	57	48 (26.4%)	58	49 (26.9%)
Hypoesthesia	0	0	8	7 (3.8%)	8	7 (3.8%)
Ischemic stroke	8	8 (4.4%)	1	1 (0.5%)	9	9 (4.9%)
Migraine	0	0	2	2 (1.1%)	2	2 (1.1%)
Muscular weakness	0	0	2	2 (1.1%)	2	2 (1.1%)
Paresthesia	0	0	3	3 (1.6%)	3	3 (1.6%)
Presyncope	1	1 (0.5%)	1	1 (0.5%)	2	2 (1.1%)
Ruptured cerebral aneurysm	2	2 (1.1%)	0	0	2	2 (1.1%)
Subarachnoid hemorrhage	3	3 (1.6%)	0	0	3	3 (1.6%)
Syncope	2	2 (1.1%)	1	1 (0.5%)	3	3 (1.6%)
Transient ischemic attack	3	2 (1.1%)	3	3 (1.6%)	6	4 (2.2%)
Psychiatric disorders						
Anxiety	0	0	2	2 (1.1%)	2	2 (1.1%)
Delirium	1	1 (0.5%)	1	1 (0.5%)	2	2 (1.1%)
Depression	0	0	2	2 (1.1%)	2	2 (1.1%)
Renal and urinary disorders						
Hematuria	0	0	2	2 (1.1%)	2	2 (1.1%)

MedDRA System Organ Class/Preferred Term	mITT Population (N = 182)					
	SAEs		Non-serious AEs		All AEs	
	Events	Subjects with Events (%)	Events	Subjects with Events (%)	Events	Subjects with Events (%)
Respiratory, thoracic and mediastinal disorders						
Cough	0	0	2	2 (1.1%)	2	2 (1.1%)
Epistaxis	0	0	6	6 (3.3%)	6	6 (3.3%)
Hemoptysis	0	0	3	3 (1.6%)	3	3 (1.6%)
Pneumonia aspiration	1	1 (0.5%)	1	1 (0.5%)	2	2 (1.1%)
Pulmonary edema	0	0	2	2 (1.1%)	2	2 (1.1%)
Skin and subcutaneous tissue disorders						
Rash	0	0	4	4 (2.2%)	4	4 (2.2%)
Surgical and medical procedures						
Intra-cerebral aneurysm operation	9	7 (3.8%)	0	0	9	7 (3.8%)
Vascular disorders						
Contusion	0	0	3	3 (1.6%)	3	3 (1.6%)
Hypertension	1	1 (0.5%)	2	2 (1.1%)	3	3 (1.6%)
Hypotension	0	0	6	5 (2.7%)	6	5 (2.7%)
Thrombosis in device	1	1 (0.5%)	2	2 (1.1%)	3	3 (1.6%)

The incidence of all CEC adjudicated ischemic or hemorrhagic adverse events (i.e., ischemic and hemorrhagic, ipsilateral and contralateral, of all severities, at all times after enrollment, and of any duration, including transient ischemic attacks (TIAs)) that occurred in the study was 11.3% (18/160) and 9.1% (2/22) in the mITT population with unruptured and ruptured intracranial aneurysms, respectively (Table 11). For all subjects in the mITT population, the overall cerebrovascular adverse event rate was 11.0% (20/182) with a 95% unadjusted confidence interval of 6.8%-16.5%.

Table 11. mITT Subjects with Cerebrovascular Events within 12-Months Follow-up

		Unruptured			Ruptured		
CEC-adjudicated Categories [1]	MedDRA Preferred Term [2]	# of Events	# of Subjects	% Subjects (n/N)	# of Events	# of Subjects	% Subjects (n/N)
Stroke, minor		**8**	**8**	**5.0% (8/160)**	**0**	**0**	**0.0% (0/22)**
	Aphasia	1	1	0.6% (1/160)	0	0	0.0% (0/22)
	Ischemic stroke	2	2	1.3% (2/160)	0	0	0.0% (0/22)
	Muscular weakness	1	1	0.6% (1/160)	0	0	0.0% (0/22)
	SAH	1	1	0.6% (1/160)	0	0	0.0% (0/22)
	Ruptured cerebral aneurysm	1	1	0.6% (1/160)	0	0	0.0% (0/22)
	TIA	2	2	1.3% (2/160)	0	0	0.0% (0/22)
Ischemic stroke, major		**6**	**6**	**3.8% (6/160)**	**2**	**2**	**9.1% (2/22)**
	Confusional state	1	1	0.6% (1/160)	0	0	0.0% (0/22)
	Ischemic stroke	4	4	2.5% (4/160)	2	2	9.1% (2/22)

CEC-adjudicated Categories [1]	MedDRA Preferred Term [2]	Unruptured # of Events	Unruptured # of Subjects	Unruptured % Subjects (n/N)	Ruptured # of Events	Ruptured # of Subjects	Ruptured % Subjects (n/N)
	TIA	1	1	0.6% (1/160)	0	0	0.0% (0/22)
SAH or SAH/aneurysm rupture		**7**	**7**	**4.4% (7/160)**	**0**	**0**	**0.0% (0/22)**
	ICH	1	1	0.6% (1/160)	0	0	0.0% (0/22)
	SAH	3	3	1.9% (3/160)	0	0	0.0% (0/22)
	Ruptured cerebral aneurysm	2	2	1.3% (2/160)	0	0	0.0% (0/22)
	Vessel perforation	1	1	0.6% (1/160)	0	0	0.0% (0/22)
Not a stroke/ SAH/aneurysm rupture		**3**	**2**	**1.3% (2/160)**	**0**	**0**	**0.0% (0/22)**
	TIA	3	2	1.3% (2/160)	0	0	0.0% (0/22)
Overall		**22**	**18**	**11.3% (18/160)**	**2**	**2**	**9.1% (2/22)**

[1] AEs could be adjudicated into more than one CEC category; therefore, event/subject counts across CEC categories are not additive. A total of 24 separate AEs occurred in 20 subjects.
[2] ICH: intracranial hemorrhage; SAH: subarachnoid hemorrhage; TIA: transient ischemic attack.

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 or neurological death) in the mITT population was 4.4% (8/182) (see Table 12). One of the 8 subjects who experienced a major ipsilateral stroke subsequently experienced neurological death (1/182 (0.5%)).

Table 10. Pre-specified Primary Safety Endpoint at 12-Month Follow-up – mITT Population

Endpoint	**mITT Population (N=182)**		
	% of Subjects with Events (n/N)	**95% CI [1]**	**P-value [2]**
Any Major Ipsilateral Stroke or Neurologic Death	4.4% (8/182)	[1.9%, 8.5%]	< 0.001
Major Ipsilateral Stroke [3]	4.4% (8/182)	[1.9%, 8.5%]	
Neurologic Death [3]	0.5% (1/182)	[0.0%, 3.0%]	
Multiple Imputation [4]	4.6%	[1.1%, 8.1%]	< 0.001
Worst Case Analysis [5]	8.2% (15/182)	[4.7%, 13.2%]	

[1] Clopper-Pearson exact confidence interval (CI).
[2] One-sided Fisher's Exact test of success against the performance goal of < 0.20 at 12 months (α=0.025).
[3] One subject experienced both major ipsilateral stroke and neurological death.
[4] Seven subjects with missing endpoint data were imputed using logistic regression models.
[5] Seven subjects with missing endpoint data were imputed as primary safety endpoint failure.

There were 8 subjects in the ATLAS trial who experienced a minor stroke, defined as a stroke associated with an increase in NIHSS score ≤ 3 as adjudicated by the CEC (4.4%;8/182). Five of these 8 minor stroke events were site-reported as serious and

were MedDRA-coded as ischemic stroke (n = 2), TIA (n = 1), ruptured cerebral aneurysm (n = 1), and SAH (n = 1). Three events were site-reported as non-serious, and were MedDRA-coded as muscular weakness, TIA, and aphasia. All 8 events resolved with no residual effects.

In the primary safety endpoint analysis (Table 12), 10 subjects had unknown primary safety outcomes due to loss-to-follow-up (n=9) or study discontinuation (n=1). Retrospectively collected data on these missing data subjects after 1-year follow-up demonstrated there were no primary safety endpoint events that occurred in 3 of the 10 subjects. Therefore, Table 12 also shows the primary safety endpoint analyses using a multiple imputation analysis performed in accordance with the National Research Council Guidelines on Prevention and Treatment of Missing Data in Clinical Trials using the assumption that the 12-month data were missing at random. In addition, a *post hoc* sensitivity analysis was performed that included a worst-case scenario where 7 of the 10 subjects were counted as primary safety endpoint failures (Table 12). The results of this analysis demonstrated that, in the worst-case scenario, the primary safety endpoint was still met and the upper 95% confidence interval of 13.2% remained below the pre-specified safety threshold of 20%.

Baseline and 12-month modified Rankin Scale (mRS) scores were obtained in the ATLAS study and recorded by a certified assessor, who was not the neurointerventionalist that performed the surgical procedure. It cannot be confirmed that the mRS assessor was truly independent and free from frequent contact with the study investigators in the ATLAS study. The shifts in numerical mRS scores from baseline to the 12-month follow-up visit were analyzed on a per subject basis. The results for subject cohorts with unruptured intracranial aneurysms and ruptured intracranial aneurysms in the mITT population are shown in Table 13 and Table 14, respectively.

Among those subjects with unruptured intracranial aneurysms who had 12-month mRS data available, the majority (90.5%; 133/147) had unchanged or improved functional outcomes compared to baseline (Table 13). A total of 109 subjects (74.1%) had unchanged mRS scores and 24 subjects (16.3%) had improved mRS scores at 12 months compared to their baseline mRS. There were 14 subjects with worsened mRS scores (14/147; 9.9%) at 12-months post-operative. For 13 subjects, the mRS assessment was not performed due to loss-to-follow-up (n = 8), study discontinuation (n = 4), and protocol deviation (n = 1).

Table 13. Change in mRS Score through 12-month Follow-up Compared to Baseline – mITT Population with Previously Unruptured Aneurysm

	Score at 12 Month Follow-up Visit*								
Score at Baseline	**No Data (ND)**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**Total**
0	8	86	7	0	0	0	1	2	104

Score at Baseline	Score at 12 Month Follow-up Visit*								
	No Data (ND)	0	1	2	3	4	5	6	Total
1	3	19	21	1	2	0	0	0	46
2	2	2	1	1	0	0	0	0	6
3	0	0	1	1	1	0	0	1	4
Total	**13**	**107**	**30**	**3**	**3**	**0**	**1**	**3**	**160**

*Grey = no change

Similarly, among those subjects with ruptured intracranial aneurysms who had 12-month mRS data available, the majority (78.9%; 15/19) had unchanged or improved functional outcomes compared to baseline (Table 14). Nine subjects (47.4%) had unchanged mRS scores and 6 subjects (31.6%) had improved mRS scores at 12 months compared to their baseline mRS. Four subjects had worsened mRS scores (4/19; 21.1%). For 3 subjects, the mRS assessment was not performed due to loss-to-follow-up (n = 1) or protocol deviation (n = 2).

Table 14. Change in mRS Score through 12-month Follow-up Compared to Baseline – mITT Population with Previously Ruptured Intracranial Aneurysm

Score at Baseline	Score at 12 Month Follow-up Visit*								
	No Data (ND)	0	1	2	3	4	5	6	Total
0	0	3	2	0	1	0	0	0	6
1	1	3	5	1	0	0	0	0	10
2	0	0	2	0	0	0	0	0	2
3	2	0	0	1	1	0	0	0	4
Total	**3**	**6**	**9**	**2**	**2**	**0**	**0**	**0**	**22**

*Grey = no change

A key safety consideration is to assess the patient's risk of intracranial aneurysm rupture in their expected life time prior to device treatment to justify that the benefit of treatment to potentially reduce the risk of intracranial aneurysm rupture outweighs the risks associated with device treatment and having a permanent implant for the patient's remaining life time. Therefore, a life time intracranial aneurysm rupture risk estimate analysis was performed for all subjects with unruptured intracranial aneurysms in the ATLAS study utilizing the *Population-Hypertension-Age-Size of Aneurysms-Earlier SAH from Another Aneurysm-Site of Aneurysm* (PHASES) model. The intracranial aneurysm rupture risk was stratified into categories of ≤ 5%, > 5 to ≤ 10%, and > 10%, and the numbers of subjects that had primary safety endpoint events or did not return for their 12-month safety follow-up evaluation within each stratum were calculated (Table 15**)**. Based on the PHASES model, the majority of subjects with no prior history of intracranial aneurysm rupture had a life time rupture risk of > 5% to ≤ 10% (46.9%; 75/160) or > 10% (15.6%; 25/160).

Table 15. Lifetime Intracranial Aneurysm Rupture Risk Estimated by PHASES

	% of Subjects (n/N)	Subjects with Primary Safety Endpoint Events (n)	Subjects Lost to Follow-up (n)
No history of intracranial aneurysm rupture			
PHASES lifetime rupture risk ≤ 5%	37.5% (60/160)	1	3
PHASES lifetime rupture risk > 5% to ≤ 10%	46.9% (75/160)	3	4
PHASES lifetime rupture risk > 10%	15.6% (25/160)	2	3
History of intracranial aneurysm rupture	12.1% (22/182)	2	0

2. Effectiveness Results

The analysis of effectiveness was based on the182 evaluable patients in the mITT population at the 12-month time point. Key effectiveness outcomes are presented in Table 16.

The primary effectiveness endpoint in the ATLAS trial was defined as a composite of the percent of subjects with 100% occlusion (Raymond-Roy Class 1) of the treated target lesion in the absence of retreatment or significant parent artery stenosis (> 50%) at the target vessel location at 12 months as adjudicated by an independent Core Laboratory. The pre-specified primary effectiveness endpoint analysis was performed on the mITT population using regression methods to impute missing data. Subjects who suffered neurological death prior to 1-year follow-up were imputed as Raymond-Roy Class 3 (the worst-case) and regression methods were used to impute other missing data. Five separate imputed data sets were constructed and inferences were completed using pooled estimates across the five data sets. In the event that no predictor variables were found for the regression models, missing data were imputed by a random draw from observed data for patients with similar baseline characteristics (e.g., gender, intracranial aneurysm location, race) as those with the missing data. As summarized in Table 16, the primary effectiveness endpoint composite success rate in the mITT population with regression imputation was 84.7% (95% CI: 78.6, 90.9).

Table 11. Primary Effectiveness at 12-month Follow-up – mITT Population

Primary Effectiveness Composite Success	%(n/N) [95% CI] [4]	p-value [5]
Primary Effectiveness Analysis		
mITT Population with Regression Imputation [1]	84.7% [78.6%, 90.9%]	< 0.001
Additional Analyses of Primary Effectiveness Endpoint		

Primary Effectiveness Composite Success	%(n/N) [95% CI] [4]	p-value [5]
"Completed Endpoint Cohort" Analysis [2]	84.5% (131/155) [77.8%, 89.8%]	< 0.001
Worst-Case Analysis [3]	72.0% (131/182) [64.9%, 78.4%]	< 0.001

[1] Missing endpoint data was imputed using regression methods. The five separate imputed data sets were constructed. One subject who suffered neurological death was imputed as a failure.
[2] Subgroup of mITT subjects who had DSA results available at 12 months (n = 153), had a known retreatment at 12 months without DSA data (n = 1), or experienced neurological death (n = 1) imputed as a failure.
[3] All missing endpoint data (n=13) imputed as failure.
[4] Clopper-Pearson exact confidence interval (CI).
[5] One-sided Fisher's Exact test of success against the performance goal of > 0.50 at 12 months (α=0.025).

3. Subgroup Analyses

Subgroup analysis of safety and effectiveness outcomes in the Per Protocol (PP) population (N=151) was pre-specified in the ATLAS study protocol. As summarized in Table 17, the incidence of primary safety endpoint failure in the PP population was 2.6% (4/151) with the incidence of major ipsilateral stroke as 2.6% (4/151) and the incidence of neurological death was 0.7% (1/151) that was caused by a major ipsilateral stroke. The primary effectiveness endpoint composite success rate in the PP population was 86.6% (129/149).

Table 12. Safety and Effectiveness Outcomes through 12-month Follow-up – PP Population

	Per Protocol Population (N=151)*		
	% of Subjects (n/N))	95% CI [1]	P-value [2]
Safety Failure Rate			
Any major ipsilateral stroke or neurologic death	2.6% (4/151)	[0.7%, 6.6%]	< 0.001
Major ipsilateral stroke [3]	2.6% (4/151)	[0.7%, 6.6%]	
Neurologic death [3]	0.7% (1/151)	[0.0%, 3.6%]	
Effectiveness Success Rate			
PP Population without Imputation [4]	86.6% (129/149) [5]	[80.0%, 91.6%]	< 0.001

*Primary reasons for exclusion of 31 subjects from the PP analysis included failure to complete 12-month digital subtraction angiography (DSA) due to missed visits or subject refusal (n = 25), violation of study entry criteria (n = 3), and intraprocedural protocol violations (i.e., staged procedure [n = 2]; no coil placement [n = 1]).
[1] Clopper-Pearson exact confidence interval (CI).
[2] One-sided Fisher's Exact test of safety failure rate against the performance goal of < 0.20 at 12 months (α=0.025).
[3] One subject experienced both major ipsilateral stroke and neurological death.
[4] Primary effectiveness endpoint defined as Raymond-Roy Class 1 in the absence of retreatment or significant parent artery stenosis (> 50%) at the target location. One subject who suffered neurological death was imputed as failure.
[5] Two subjects who expired due to non-neurologic causes (gallbladder cancer [post-operative day (POD) 76], acute fentanyl intoxication [POD 344]) were excluded from the effectiveness analysis.

4. Pediatric Extrapolation

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

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 82 investigators and sub-investigators of which none were full-time or part-time employees of the sponsor and 15 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: 15 investigators.
- Proprietary interest in the product tested held by the investigator: 0.
- Significant equity interest held by investigator in sponsor of covered study: 0.

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

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

FDA did convene a general issues, non-voting, 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, primarily to assess safety and effectiveness of the subject device as described within the SSED in Section X. 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 in the ATLAS trial was defined as a composite of the percent of subjects with 100% occlusion (Raymond-Roy Class 1) of the treated target lesion on 12-month angiography in the absence of retreatment or significant parent artery stenosis (> 50%) at the target vessel location. The results of the primary effectiveness endpoint analysis showed the composite success rate in the mITT population with regression imputation was 84.7% (95% CI: 78.6%, 90.9%). In addition, the procedural technical success demonstrated that 100% (182/182) of subjects had successful delivery, deployment, and placement of the Neuroform Atlas Stent at the target location. The re-treatment rate within 1-year post-operative in the mITT population was 3.8% (7/182). Because the Neuroform Atlas Stent System 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.

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 comprised the rate of major ipsilateral stroke defined as an increase in the NIHSS score from baseline by ≥ 4 points or neurological death in the mITT population and was analyzed to be 4.4% (8/182) in the ATLAS study. The incidence of major ipsilateral stroke was 4.4% (8/182) and the incidence of neurological death was 0.5% (1/182) that resulted from a major ipsilateral stroke. There were 7 missing data subjects that did not have a neurological examination at 12-months post-operative. In a worst-case analysis if these 7 missing data subjects were imputed as failures for the primary safety endpoint as having the adverse events of interest, the primary safety endpoint is 8.2% (15/182) with a 95% unadjusted confidence interval of 4.7% to 13.2%. The incidence of all CEC adjudicated ischemic or hemorrhagic adverse events (i.e., ischemic and hemorrhagic, ipsilateral and contralateral, of all severities, at all times after enrollment, and of any duration, including TIAs) that occurred in the study was 11.3% (18/160) and 9.1% (2/22) in the subject cohorts with unruptured and ruptured intracranial aneurysms, respectively. For all mITT subjects, the overall ischemic or hemorrhagic adverse event rate was 11.0% (20/182) with an unadjusted 95% confidence interval of 6.8%-16.5%. The primary safety endpoint rates observed in the ATLAS trial with the Neuroform Atlas Stent System is within the safety rates published in the scientific literature for stent-assisted coiling of wide-neck intracranial aneurysms and the study met the a priori study success criteria with statistical significance.

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 primary effectiveness endpoint in the ATLAS trial was defined as a composite of the percent of subjects with

100% occlusion (Raymond-Roy Class 1) of the treated target lesion on 12-month angiography in the absence of retreatment or significant parent artery stenosis (> 50%) at the target vessel location. The results of the primary effectiveness endpoint analysis showed the composite success rate in the mITT population with regression imputation was 84.7% (95% CI: 78.6%, 90.9%). Because the Neuroform Atlas Stent System 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 and the effectiveness of treatment to reduce the risk of intracranial aneurysm rupture in the patient's life time are 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 comprised the rate of major ipsilateral stroke defined as an increase in the NIHSS score from baseline by ≥ 4 points or neurological death in the mITT population and was analyzed to be 4.4% (8/182) in the ATLAS study. The incidence of major ipsilateral stroke was 4.4% (8/182) and the incidence of neurological death was 0.5% (1/182) that resulted from a major ipsilateral stroke. The incidence of all CEC adjudicated ischemic or hemorrhagic adverse events (i.e., ischemic and hemorrhagic, ipsilateral and contralateral, of all severities, at all times after enrollment, and of any duration, including TIAs) that occurred in the study was 11.3% (18/160) and 9.1% (2/22) in the subject cohorts with unruptured and ruptured intracranial aneurysms, respectively. For all mITT subjects, the overall ischemic or hemorrhagic adverse event rate was 11.0% (20/182) with an unadjusted 95% confidence interval of 6.8%-16.5%. The overall AEs reported in the ATLAS study is provided in Table 10. The study met the *a priori* study success criteria (performance goals) with statistical significance.

Additional factors to be considered in determining probable risks and benefits for the Neuroform Atlas Stent System included weighing the benefits and risks of device treatment with the patient's risk of intracranial aneurysm rupture during their expected life time. The risk of rupture of an untreated unruptured intracranial aneurysm is dependent on multiple factors including, but not limited to, intracranial aneurysm size, shape, morphology, and location; patient history of smoking; age; family history; and the patient co-morbidities such as hypertension, presence of multiple intracranial aneurysms, or 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). The annual risk of rupture of an intact intracranial aneurysm is estimated to be approximately 1.9% (Rinkel et al. 1998). The effect of intracranial aneurysm rupture is extremely severe, resulting in subarachnoid hemorrhage, which is associated with a high level of neurological disability and mortality. Therefore, if the patient may have a high risk of intracranial aneurysm rupture within their expected life time, then the probable benefit of treatment with the subject device may outweigh the risks of device use with consideration of the seriousness of the adverse effects if the intracranial aneurysm ruptures.

One additional factor to be considered in determining probable risks and benefits for the Neuroform Atlas Stent System is the assessment of uncertainty in the ATLAS study, which was a non-randomized, open-label clinical study. Although the ATLAS trial was conducted in accordance with all applicable US federal regulations (including 21 CFR Parts 11, 50, 54, 56 and 812), the Declaration of Helsinki, Good Clinical Practices, ISO 14155, all conditions of approval from participating Institutional Review Boards (IRBs), the requirements of all other governing regulatory authorities, there is always bias in subject selection in a single-arm study design, regardless of whether the study results were 100% monitored with safety oversight delegated to an independent Clinical Events Committee (CEC) and Data Safety Management Board (DSMB) and the primary effectiveness endpoint adjudicated by an independent Core Lab. Also, although it was stated the neurological examinations (NIHSS and mRS) were performed by an independent certified assessor, it is unclear if the assessor was truly independent and free from any contact or relationships with the site investigators. Therefore, based on these uncertainties in the conduct of the ATLAS study, the results obtained should be viewed on a best-case scenario and use of the device in clinical practice may result in worse clinical outcomes.

1. Patient Perspectives

   Patient perspectives considered during the review included a quality of life assessment that was performed at baseline and the 12-month follow-up visits using the EQ-5D-3L™ to measure general health status (King et al. 2009). The mean EQ-5D index score increased minimally from 0.83 ± 0.16 at baseline to 0.85 ± 0.18 at 12-months post-operative. The mean EQ visual analog scale (VAS) score also increased from 71.9 ± 22.6 at baseline to 76.2 ± 19.0 at 12-months post-operative.

In conclusion, given the available information above, the data support that the Neuroform Atlas Stent System for the indicated use with neurovascular embolization coils in the anterior circulation of the neurovasculature for the endovascular treatment of patients ≥ 18 years of age with saccular wide-necked (neck width ≥ 4 mm or dome-to-neck ratio < 2) intracranial aneurysms arising from a parent vessel with a diameter of ≥ 2.0 mm and ≤ 4.5 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. As previously specified, the primary effectiveness endpoint analysis resulted in 84.7% (95% CI: 78.6%, 90.9%) of patients obtaining complete (100%) intracranial aneurysm occlusion (Raymond-Roy Class 1) at 12-months post-operative without any re-treatment or significant parent artery stenosis (> 50%) at the target vessel location. Safety results through 12-month follow-up demonstrated a 4.4% (8/182) rate of primary safety endpoint events of neurological death or major ipsilateral stroke. The overall ischemic or hemorrhagic adverse event rate was 11.0% (20/182) in the ATLAS study with an unadjusted 95% confidence interval of 6.8%-16.5%.

XIV. CDRH DECISION

CDRH issued an approval order on May 16, 2019. The final conditions of approval cited in the approval order are described below.

PMA Post-Approval Study - "Safety and Effectiveness of the Treatment of Wide Neck, Saccular Intracranial Aneurysms with the Neuroform Atlas™ Stent System (ATLAS)": The Office of Neurological and Physical Medicine Devices (Office of Health Technology (OHT) 5) will have the lead for this study initiated prior to device approval. The ATLAS study was conducted under investigational device exemption (IDE) G150006 and patients were consented to be followed for up to three (3) years post-operative. The 1-year follow-up data from the ATLAS study was used to support the approval of the subject PMA P180031. As part of the PMA post-approval study, the long-term follow-up from the ATLAS study can provide safety and effectiveness information on the durability and safety of treatment using the Neuroform Atlas Stent System up to 3 years post-operative. The pre-specified safety endpoint is the incidence of patients who experienced a major ipsilateral stroke or neurological death. The pre-specified effectiveness endpoint is the incidence of patients who had complete (100%) intracranial aneurysm occlusion (Raymond-Roy Class 1) without significant in-stent stenosis (> 50%) or retreatment of the target aneurysm. The incidence of all ischemic or hemorrhagic adverse events (i.e., ischemic and hemorrhagic, ipsilateral and contralateral, of all severities, at all times after enrollment, and of any duration, including transient ischemic attacks (TIAs)) should also be reported as part of the long-term safety analysis. Patients will be assessed at 2- and 3-years (within ± 6 months) post-operative with neurological exams conducted in person per the G150006 clinical study protocol. In addition, all new and ongoing adverse events will be recorded and adjudicated by the Clinical Events Committee per the approved G150006 clinical study protocol. Imaging assessment of intracranial aneurysm occlusion and in-stent stenosis will be performed after 1-year post-operative if imaging assessments will be performed as part of usual care.

Be advised that failure to comply with any post-approval requirement, including the requirements to meet the enrollment, treatment and completion dates outlined above, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c).

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

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