SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Endovascular Graft
Device Trade Name:	NEXUS® Aortic Arch Stent Graft System
Procode:	SDZ
Applicant's Name and Address:	Endospan Ltd 4 Maskit St. Herzliya, ISRAEL 4673304
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P250033
Date of FDA Notice of Approval:	April 2, 2026

Breakthrough Device: Granted breakthrough device status on March 27, 2020, because of reasonable expectation that the device can provide more effective treatment of a life-threatening disease, as well as due to lack of approved or cleared endovascular device alternates.

II. INDICATIONS FOR USE

The NEXUS® Aortic Arch Stent Graft System is indicated for the endovascular treatment of chronic dissections involving the aortic arch in patients who are at high risk for open surgical repair and who have appropriate anatomy including:

- Adequate iliac or femoral artery access vessel morphology that is compatible with vascular access techniques, devices, or accessories.
- Proximal/ascending native landing zone aortic anatomy including:
  - 30 mm to 39 mm diameter;
  - ≥ 30mm length
  - Landing zone cannot be aneurysmal, dissected, heavily thrombosed and tortuous
- Proximal/ascending previously implanted surgical graft landing zone including:
  - 26 mm to 39 mm diameter;
  - ≥ 30mm length
- Brachiocephalic trunk native landing zone anatomy including:
  - 12.5mm to 19.5 mm diameter;
  - ≥ 20mm length
  - Landing zone cannot be aneurysmal, dissected, heavily thrombosed and tortuous
- Distal/descending native landing zone aortic anatomy including:
  - 28 mm to 42 mm diameter;

- ≥ 30mm length

III. CONTRAINDICATIONS

- Patient with known sensitivities or allergies to the device materials.
- Patient who has a condition that threatens to infect the graft.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the NEXUS® Aortic Arch Stent Graft System labeling.

V. DEVICE DESCRIPTION

The NEXUS® Aortic Arch Stent Graft System is comprised of two primary implantable stent grafts, and an optional extension. All stent grafts are provided pre-loaded in a disposable 20 French (Fr) delivery system and each is provided sterilized and packaged individually. Each stent graft is introduced and implanted separately into the patient's vascular system. The stent grafts that make up the NEXUS® Aortic Arch Stent Graft System are:

- The **Arch Stent Graft**, whose cranial narrow end is intended to be deployed into the Brachiocephalic artery and whose distal end is to be deployed into the Descending Thoracic Aorta.
- The **Ascending Curved Stent Graft** intended to be deployed in the Ascending Aorta.
- Optional - **Descending Extension** can be used in case the aortic lesion elongates further distally and out of the covered length offered by the Arch Stent Graft. Multiple Descending Extensions can be used if needed to cover the entire length of the lesion.

The pre-loaded stent graft components are sequentially advanced to the diseased location over a guide wire using fluoroscopic guidance. The sequence of delivery and implantation is the Arch Stent Graft System, followed by the Ascending Curved Stent Graft System and if needed the Descending Extension can be implanted overlapping and extending distally. In some cases, it may be decided in advance to implant the Descending Extension Stent Graft in advance of the Arch Stent Graft, in these cases the Arch Stent Graft would be implanted second and extending proximally from the Descending Extension, followed by an Ascending Curved Stent Graft implanted proximal to the Arch Stent Graft. The NEXUS® Stent Graft System is designed to be placed in the native vessel or within a previously implanted surgical graft such that the unconstrained stent graft diameter is larger than the internal diameter of the native vessel/surgical graft landing zone. This "oversizing" at the landing zone helps exclude the lesion from the aortic blood flow and ensures that the stent graft is held in place. The stent graft components are collectively intended to form proximal, distal and brachiocephalic artery (BCA) branch seal zones surrounding the diseased location (follow the shape and size of the true lumen and seal the primary entry tear).

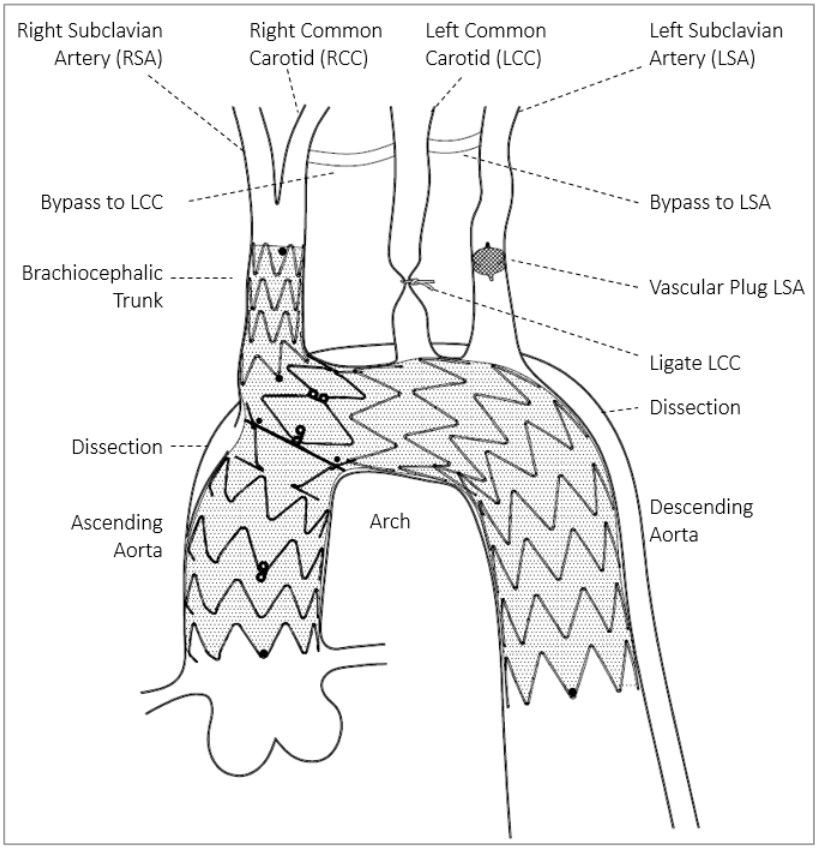

***Figure 1**. Configuration of the NEXUS® Arch & Ascending Curved Stent Grafts within the anatomy*

Each stent graft is made of Nickel-Titanium (Nitinol) alloy stents, sewn to a polyester fabric, using surgical suture material. Each stent graft incorporates radiopaque markers to aid in visualization of the stent graft under fluoroscopy to facilitate accurate placement of the device components relative to each other and in relation to the patient's vascular system. The radiopaque markers consist of tantalum and are described as the B-markers, Dot markers and the Docking radiopaque ring. The B-markers are used to determine rotational alignment, the Dot markers are used to determine axial positioning, and the Docking radiopaque ring, located on the Arch Stent Graft is used for axial alignment with the Locking Stent of the Ascending Curved Arch Stent.

A. Arch Stent Graft (Brachiocephalic Trunk to Descending Aorta)

The Arch Stent Graft is the main base stent graft, implanted from the brachiocephalic trunk (cranially) to the descending aorta (caudally), and is aligned with the aortic arch region (Figure 2). The Arch Stent Grafts are manufactured with equally spaced Nitinol stents which are sewn to the polyester graft using medical grade suture. The shape of the stent graft within the body is a thunderbolt shape which is designed to assist with stability and fixation. This stent graft contains a sleeve named the "Dock" or "Docking Sleeve" with a single fenestration which opens toward the ascending aorta.

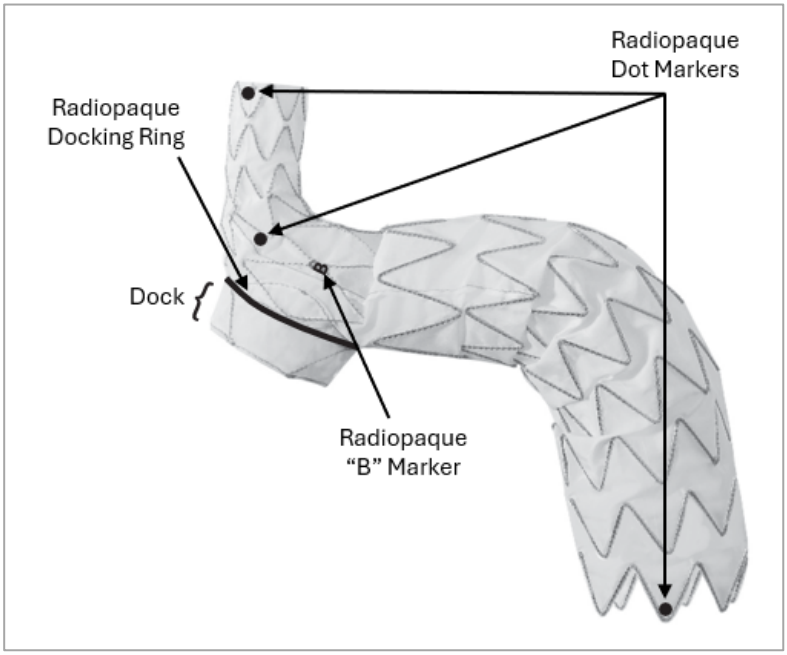

Figure 2. *Arch Stent Graft (Brachiocephalic to Descending Aorta)*

The positioning of the Arch Stent Graft should be such to allow blood flow to the brachiocephalic artery and to the descending aorta. Blood supply to the left carotid artery should flow through a bypass from the distal Brachiocephalic Trunk (BCT) or Right common carotid (RCC) artery. Blood supply to the left subclavian artery (LSA) should be made possible through bypass or it can be sacrificed, according to physician's discretion.

Note: Parallel Stent Grafts are not to be utilized with the NEXUS® System.

The Arch Stent Graft implantation is done over a bracheo-femoral wire (known as "Through & Through" technique) in which a stiff guide wire is placed into the vasculature from the axillary/brachial artery to the iliac-femoral artery of the patient (see **Figure 3**).

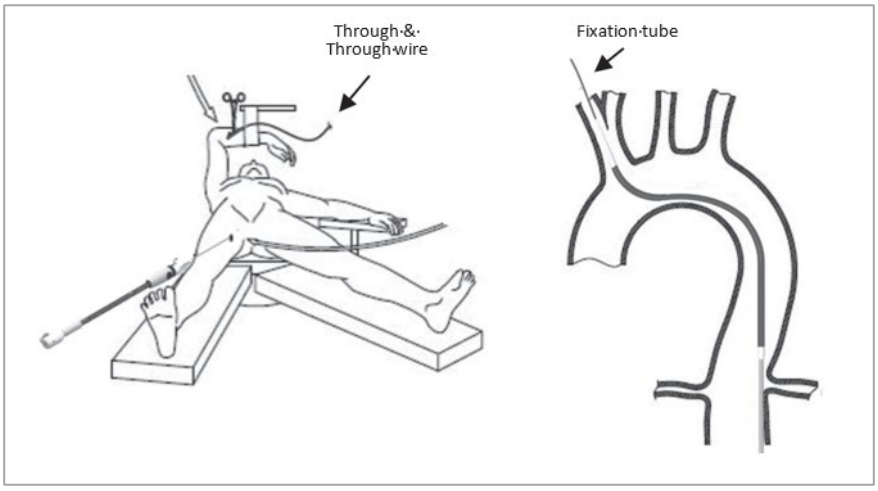

Figure 3. *Through & Through Technique*

B. Ascending Curved Stent Graft

The Ascending Curved Stent Graft is the most proximal stent graft of the stent graft system and is implanted in the ascending aorta. The Ascending Curved Stent Grafts are manufactured with equally spaced Nitinol stents which are sewn to the polyester graft using medical grade suture. The Ascending Curved Stent Graft has additional Compression and Anti-Buckling Springs sewn to the graft material.

The proximal stent of the Ascending Curved Stent Graft is slightly inwardly bent with the intent to prevent damage to the ascending aorta (**Figure 4**). The Ascending Curved Stent Graft is implanted distally to the coronary arteries and the sino-tubular junction, or distal to the most distal take-off of a coronary bypass and extends along the ascending aorta and into the Docking Sleeve of the Arch Stent Graft. The distal stent, called the Lock or Locking Stent is partially exposed and contains non traumatic, triangularly shaped latches. These latches are intermittently proximally and distally oriented, with the intent to provide bidirectional locking of the Ascending Curved Stent Graft inside the Dock of the Arch Stent Graft. The Sealing Stent of the Ascending Curved Stent Graft is located just proximal to the Locking Stent and is designed to seal against the proximal portion of the Arch Stent Graft Docking Sleeve (see **Figure 4**) for the location of the Locking and Sealing Stent).

Note: The Locking and Sealing Stent are the exact same design for all sizes of Ascending Curved Stent Grafts. Once deployed, the Locking and Sealing Stents engage the Dock of the Arch Stent Graft, with the goal of creating a secure connection between the two stent grafts.

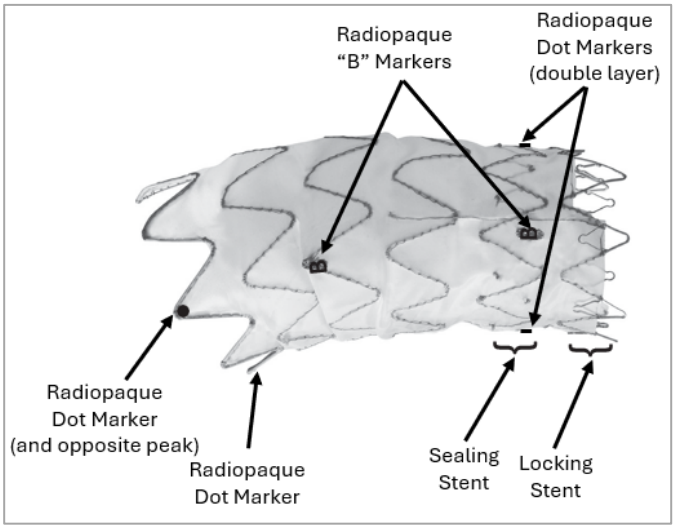

Figure 4. *Ascending Curved Stent Graft*

C. Descending Extension Stent Graft

The Descending Extension (DE) Stent Graft is used only in cases where the aortic lesion elongates further distally and out of the covered length offered by the distal portion of the Arch Stent Graft. The DE Stent Graft can be used in continuation to the Arch Stent Graft to ensure exclusion of the lesion from the blood flow. Multiple DE stent grafts may be utilized depending

on the length of the aortic lesion.

The DE Stent Graft is comprised of equally spaced Nitinol stents which are sewn to the polyester graft using medical grade suture. In addition, tantalum radiopaque markers; two opposite Dot markers indicate both ends of the prosthesis and a "B" shaped marker is positioned distal to the 4th stent and defines the minimum required overlap length. The minimum overlap length is defined by radiographically placing the B marker at the same axial level as the distal Dot marker on the Arch Stent Graft, this results in approximately a 6cm overlap. In all DE stent grafts, at both ends of the prosthesis, the graft follows the end stent's exact circumference to create a crown-like shape. The DE Stent Graft is available in two configurations: Straight and Tapered (**Figure 5**).

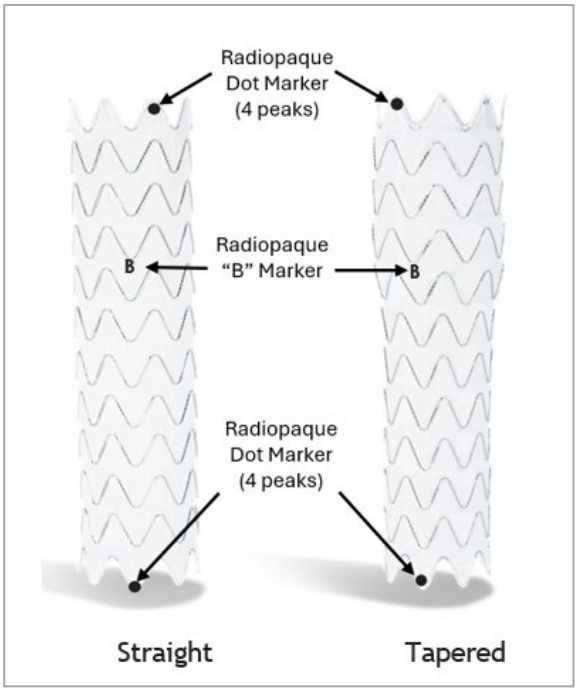

Figure 5. *Descending Extension Stent Graft (Straight and Tapered Configurations)*

D. Delivery System

The NEXUS® Delivery System (DS) is a single-use, disposable catheter-based delivery platform designed to facilitate controlled deployment of the NEXUS® Aortic Arch Stent Graft System components. Both the proximal shaft that contains the Stent Graft and the proximal tip are hydrophilic coated.

The NEXUS® Delivery System has an outer diameter of 20 Fr. for all component sizes, supporting a percutaneous approach. The catheter assembly is flexible and compatible with a 0.035 inch (0.89 mm) guidewire.

The delivery system used for the NEXUS® Arch Stent Graft component is pre-shaped (thunderbolt shape) (**Figure 6**). The delivery system used for the NEXUS® Ascending Curved Stent Graft is pre-curved (**Figure 7**). The delivery system used for the optional NEXUS®

Descending Extension is straight.

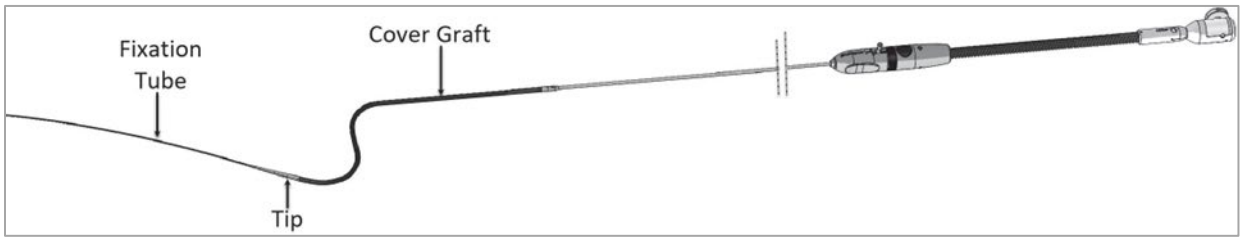

***Figure 6**. NEXUS® Arch Stent Graft Delivery System – Pre-Shaped (thunderbolt shape)*

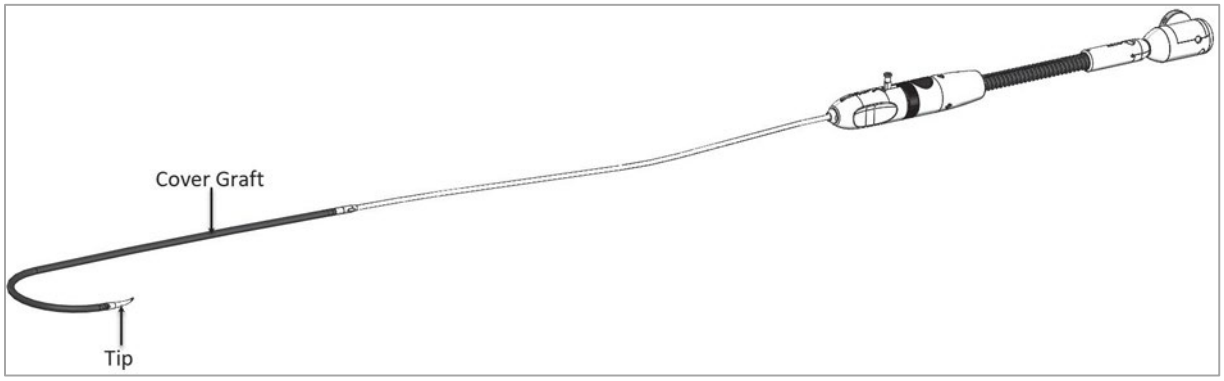

***Figure 7**. NEXUS Ascending Stent Graft Delivery System – Pre-Curved*

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternative treatment options available for patients with chronic dissections involving the aortic arch, including:

- Medical management
- Open surgical repair
- Hybrid Surgery with Thoracic Endovascular Aortic Repair (TEVAR)
- Other commercially available endovascular devices

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with their physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The NEXUS® Aortic Arch Stent Graft System is currently approved in Europe, Serbia, New Zealand, Israel, Argentina, Peru, Chile, and Uruguay. Prior to US commercialization, the NEXUS System was the subject of one recall in Europe during July 2022 that resulted in a correction to ensure continued safe and effective performance of the device. There have been no market withdrawals of the NEXUS System in any geography.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

- Abscess formation
- Acute respiratory distress syndrome (ARDS)
- Adverse foreign body response
- Allergies (including
- Amputation
- Anesthetic complications and subsequent attendant problems
- Aneurysm enlargement or rupture
- Angina
- Aortic damage
- Aortic enlargement
- Aortic regurgitation
- Aortic valve damage and/or functional impairment
- Arrhythmia
- Arteriovenous fistula
- Aortoesophageal fistula
- Bleeding/bleeding complications
- Cardiac complications and subsequent attendant problems
- Claudication (e.g. buttock, lower limb)
- Congestive heart failure
- Contrast toxicity
- Coronary arteries occlusion
- Coronary arteries stenosis
- Death
- Dissection extension
- Dissection of a vessel
- Edema
- Embolization (micro and macro)
- Emergency operation including surgical conversion to open repair
- Endoleak
- Erosion
- Fistula
- Fever
- Genitourinary complications and subsequent attendant problems including erosion
- Hematoma
- Hematuria
- Hemorrhage, requiring blood transfusion
- Hemorrhagic pleural effusion
- Heparin-induced thrombocytopenia (HIT)
- Hepatic Failure
- Lymphatic complications and subsequent attendant problems (lymphocele)
- Multiple organ failure syndrome (MOF)
- Myocardial infarction (MI)
- Myocardial perforation
- Necrosis
- Neurologic complications including lipothymy and encephalopathy
- Obstruction/occlusion
- Pain
- Paralysis including vocal cords and diaphragm
- Paralysis of vocal cords
- Paraparesis
- Paraplegia
- Pericardial tamponade
- Perforation of a vessel wall
- Peritonitis
- Persistent False Lumen
- Pseudoaneurysm
- Pulmonary complications and subsequent attendant problems
- Radiation exposure risks / repetitive radiation sessions
- Renal Insufficiency/failure
- Rupture of a vessel
- Sepsis
- Seroma
- Stenosis
- Stent graft complications: improper component placement; incomplete component deployment; inadequate apposition, “beaking” and subsequent collapse of the component; clinically significant component migration; suture break; stent fracture; graft twisting or kinking; insertion and removal difficulties; graft material wear; dilatation; erosion; puncture and perigraft flow
- Stroke
- Syncope
- Temporary Neurological Deficit (TND)
- Thrombosis
- Transient ischemic attack (TIA)
- Vascular access site complications including lymphocele

- Hypertension
- Hypotension
- Ileus
- Impotence
- Incontinence
- Infarction
- Infection
- Inflammation (localized or general)
- Ischemia transient or permanent
- Ischemic effects to the limbs, genitourinary system including kidneys, myocardium, mesentery, brain and spinal cord
- Vascular spasm or vascular trauma
- Ventricular fibrillation
- Ventricular tachycardia
- Vessel damage
- Wound complications including dehiscence and cellulitis

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

IX. SUMMARY OF NONCLINICAL STUDIES

Nonclinical studies were completed to evaluate the NEXUS® Aortic Arch Stent Graft System including non-clinical bench testing, biocompatibility, sterilization, packaging, shelf-life, and animal studies. These are described in detail in the following sections.

A. Laboratory Studies

In vitro bench testing to support the NEXUS® Aortic Arch Stent Graft System is summarized in **Table 1**. It was developed based on the device risk assessment and is consistent with FDA's Guidance Document *Non-Clinical Tests and Recommended Labeling of Intravascular Stents and Associated Delivery Systems*, April 18, 2010, its addendum, *Select Updates for Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*, August 18, 2015, and ISO 25539-1.

Table 1. In Vitro Engineering Testing Summary

Test	Test Purpose	Acceptance Criteria	Results
Complete System Testing			
Simulated Use*	To evaluate the following attributes of the Nexus Aortic Arch Stent Graft System according to the Instructions for Use: – Compatibility with Accessories – Preparation for Use – Delivery to target location – Push-ability, flexibility, torque-ability, and trackability – Deploy at Target Location, including accuracy of deployment – Conformability – Withdrawal of the Delivery System – Occurrence of Particles	The following criteria were used: • **Packaging:** The packaging must allow for the removal of the loaded delivery system without damage. • **Degassing:** Guidewire lumen can be flushed with slip fit luer syringe and saline should exit at the tip of the catheter. • **Guidewire compatibility:** The guidewire should be able to pass through the guidewire lumen without kinking or damage to the delivery system. • **Sheath compatibility:** The delivery system should be able to pass through the introducer sheath without kinking or damage to the delivery system. • **Accessory Compatibility:** The stent-grafts	**Pass**

Test	Test Purpose	Acceptance Criteria	Results
		shall be compatible with accessory devices (e.g., balloons or pigtail catheters), including insertion, inflation, deflation, and withdrawal, without damage to or displacement of the implanted stent-grafts. • **Deliver to target location:** System can be advanced to the target location with adequate pushability, trackability, and torqueability without buckling or loss of function • **Deployment and accuracy:** Device can be deployed within +/- 5 mm of the target location. • **Conformability:** Stent-graft opposes the vessel wall at intended landing zones and regions of stent graft overlaps. • **Withdrawal:** Delivery system can be withdrawn without causing device migration or damage. • **Migration:** Device migrates ≤ 4 mm from its original implant location. • **Particles:** No clinically significant particle generation observed.	
Delivery System			
Dimensional Verification of the System	Verify the NEXUS Delivery System dimensions meet design specifications.	The measured dimensions shall be compared to the pre-determined specifications (dimension ± accepted tolerance)	**Pass**
Force to Deploy*	Evaluate the maximum force required to deploy the NEXUS Aortic Arch Stent Graft System under simulated use conditions and confirm that deployment forces remain within the mechanical strength limits of the delivery system components.	The maximum deployment force shall remain below the minimum tensile strength of the delivery system structural components to ensure safe deployment without damage or failure of the delivery system.	**Pass**
Stent-Graft Wire Release Force	Characterize and determine the force required to release the stent-graft by retracting the tether wires during deployment of the NEXUS Aortic Arch Stent-Graft System under simulated anatomical conditions.	Wire release torque ≤1.2 Nm	**Pass**
Tubing Tensile Strength*	Determine the longitudinal tensile strength and associated elongation of the NEXUS Delivery System outer tube (shaft) as part of the delivery system.	The tensile strength of the delivery system shaft shall exceed the maximum forces expected during device deployment without impairing system function.	**Pass**
Bond tensile strength*	Determine the bond strength of the joints and/or fixed connections of the delivery system.	Bond strength shall exceed the maximum forces expected during device deployment and use.	**Pass**
Torsional bond strength*	Determine the torsional bond strength of the NEXUS Delivery System.	The torsional strength of the delivery system shall exceed the maximum torque expected during clinical use.	**Pass**
Hemostasis*	Verify that the NEXUS Aortic Arch Stent Graft System provides adequate hemostasis during the implant procedure.	Leakage from the Delivery System shall not exceed the specified limit.	**Pass**
Visibility	Evaluate the ability to visualize the NEXUS system (DS and the implant)	The implant and the delivery system shall be visualized under imaging techniques	**Pass**

Test	Test Purpose	Acceptance Criteria	Results
	using imaging techniques specified in the instructions for use (IFU).	according to the instructions for use, radiopaque components shall be visualized and assessed.	
Implant			
Dimensional Verification of the Prosthesis*	Verify the NEXUS implant dimensions to meet design specifications.	Implant dimensions shall meet pre-determined specifications.	**Pass**
Radial Force*	Evaluate the outward radial force of the NEXUS Stent Graft as a function of diameter.	Radial force shall be within the specified design range to ensure adequate vessel apposition without excessive vessel loading.	**Pass**
Burst Strength*	Determine the pressurized burst strength of the NEXUS Stent-Graft.	The lower expected stent graft burst strength > 75 kPa	**Pass**
Longitudinal tensile strength*	Determine the longitudinal tensile strength of the graft fabric used in the manufacturing of the NEXUS Aortic Arch Stent-Graft System.	Graft tensile strength shall exceed the maximum forces expected during device deployment (i.e., lower tolerance limit of strength measurement ≥ 2.17 N/mm).	**Pass**
Water permeability (textile materials)	Determine the water flow rate through a given area of the NEXUS graft material under a given hydrostatic pressure.	Water permeability shall not exceed the specified maximum flow rate (i.e., upper tolerance limit of flow rate measurement < 600 ml/(min cm^2) under 120mmHg.)	**Pass**
Factory anastomosis – Seam strength	Determine the strength of the graft fabric used in the manufacturing of the NEXUS Aortic Arch Stent-Graft System.	The graft seam strength shall exceed the burst pressure loads expected for the largest diameter NEXUS stent graft configuration.	**Pass**
Strength of Connection Between Stents and Graft Material	Determine the strength of connection between the graft material and the Locking Stent (fixation system)	The connection strength between the Locking Stent and the graft shall exceed the maximum forces expected during device deployment and use. The connection strength between the Dock Stent and the graft shall meet the minimum strength specification.	**Pass**
Integral water leakage	Evaluate the water leakage between modular components of the NEXUS stent-grafts and holes in the graft material resulting from the construction of the endovascular prosthesis.	The water leakage through the entire NEXUS Stent-Graft shall be lower than the pre-determined specified flow rate (600 ml/(min cm^2)) under a pressure of 120[mmHg].	**Pass**
NEXUS Migration resistance and Separation Force of Overlapping Stent Graft Components	Evaluate the resistance of overlapping NEXUS stent graft components to migration and separation under simulated physiological loading conditions representative of clinical use.	Separation Force: The separation force between overlapping stent-graft components shall exceed the minimum specified force required to maintain modular engagement. Migration: Migration shall not exceed clinically acceptable limits.	**Pass**
Implant Resistance to kinking (flexibility)	Determine the radius of curvature required to begin "kinking" the NEXUS Stent-Graft and characterize the minimum BCT angulation of the Arch Stent-Graft	Characterization of the NEXUS Arch Stent-Graft resulted in the determination that the device shall maintain lumen continuity without kinking when subjected to a curvature corresponding to a mandrel diameter of ≥40 mm (radius ≥20 mm). For the branch segment, the device shall maintain lumen continuity at a branch-to-body angulation ≥125°.	**Pass**
Pitting corrosion resistance and	Evaluate the pitting corrosion resistance and nickel release rate from the NEXUS implants over 60-day exposure	If the pre-specified acceptance criteria for pitting corrosion resistance are not met, Nickel release shall not exceed 35 µg/day,	**Pass**

Test	Test Purpose	Acceptance Criteria	Results
Nickel-ion release		consistent with established safety thresholds for nickel exposure.	
Nitinol Austenitic Transitional temperature (Af)	To verify that the austenitic transition temperature (Af) of all Nitinol components is below body temperature to ensure full transition to the austenite phase during clinical use.	The austenitic transition temperature (Af) of all Nitinol components shall meet the specified design requirements to ensure full transition to the austenite phase at physiological temperature.	**Pass**
Magnetic Resonance Imaging (MRI) safety See	Ensure the system is compatible for MRI use. According to applicable standards	• Deflection angle <45° • Magnetically induced torque less than gravitational torque • RF-induced heating ≤2°C • Image artifact characterized	**Pass**
Finite Element Analysis (FEA) modeling of Wire Stents and Laser-Cut Nitinol Components	Finite element modeling of wire stents and laser-cut stents including shape-setting, crimping & deployment, and fatigue at worst-case boundary conditions	Finite element analysis shall demonstrate peak strain amplitudes below the Nitinol fatigue limits reported in literature and internal testing, and a safety factor against fatigue failure ≥1.	**Pass**
Fatigue-to-Failure of Worst-Case Laser-Cut Nitinol Component	Evaluate the fatigue strength of the representative worst-case laser-cut Nitinol component and confirm an adequate margin relative to expected in vivo loading conditions.	The fatigue strength of the component shall exceed the maximum strain expected under worst-case physiological loading conditions.	Pass
Fatigue Resistance of Worst-Case Laser-Cut Nitinol Component	Verify long-term durability of the representative worst-case laser-cut Nitinol component under cyclic loading representative of physiological conditions.	No fatigue fractures shall occur after completion of the defined fatigue cycling test.	**Pass**
Radial Fatigue and Durability of overlapping Arch and Descending Extension Stent Grafts	Evaluate the long-term structural integrity of the overlap region between the stent grafts under cyclic radial loading representative of physiological conditions for a simulated 10-year implant duration.	Test articles shall maintain structural integrity following completion of the durability testing, including no stent fractures, no separation of stents or markers from the graft, and graft integrity maintained within specification.	**Pass**
Radial Fatigue and Durability of Overlapping Bent Stent Grafts	Evaluate the long-term structural integrity of overlapping stent grafts under cyclic radial loading in a fixed bent configuration representative of physiological conditions for a simulated 10-year implant duration.	Test articles shall maintain structural integrity following completion of the durability testing, including no stent fractures, no separation of stents or markers from the graft, and graft integrity maintained within specification.	**Pass**
Axial Durability of Dock-Lock Interface Between the Ascending and Arch Stent Grafts	Evaluate the long-term durability and wear of the Dock-Lock interface between the Ascending and Arch stent grafts under cyclic axial motion representative of physiological cardiac motion for a simulated 10-year implant duration.	Test articles shall maintain structural integrity following completion of the durability testing, including no stent fractures, no separation of stents or markers from the graft, and graft integrity maintained within specification.	**Pass**

* Testing was also completed to support device shelf-life.

B. Animal Studies

The purpose of the GLP animal study was to evaluate the biological safety of the NEXUS® Aortic Arch Stent Graft System in a chronic swine model.

A total of 12 mature swine (Male and Female) were evaluated chronically in this safety study (4 animals in each group – 30-day, 90-day and 180-day). Animals were implanted with the NEXUS Stent Graft and the study implant device was evaluated for biological safety. Study endpoints included assessments through 180 days for overall animal health, local tissue response to the device, and system toxicity. Thrombogenicity was evaluated on the delivery system and implant during the implant procedure, as well as through local (implant site) and downstream tissue evaluation during gross pathology and histopathology. The Good Laboratory Practices (GLP) animal study is summarized in **Table 2**.

Table 2. GLP Animal Study Summary

Study Description and Sample Size	Evaluations	Outcome
30, 90, and 180 Day Safety Evaluation in the Swine Model. 4 animals were evaluated at each time point. One NEXUS Stent Graft* was placed in the thoracic aorta of each of 12 swine.	Acute Assessment: • Success of implantation • Following the dwell time, the delivery system was removed and scored for thrombogenicity • Post implant flow was scored based on the Arterial Flow Assessment (AFA) Flow scale. Chronic Assessments: • Physical examinations, body condition scores, body weights, clinical monitoring and clinical pathology were performed from prior to Day 0 through termination • Evaluation of patency. • Gross pathology. • Evaluation of the structural integrity of the NEXUS Stent Graft at the time of explant. • Evaluation of histology and pathology of explanted test article and surrounding tissue, as well as downstream.	• All animals survived until their scheduled termination time point. • A total of twelve animals were successfully implanted (4 animals per the 30, 90, and 180 day groups). • There was no evidence of thrombus on the delivery system post-implant. • All implanted vessels scored a '3' based on the AFA Flow scale. • All animal health assessments suggested that animals remained in good general health throughout the duration of the study. • There was no evidence of thromboembolism in the downstream organs/tissues in the chronic swine model at any time point. • There was no evidence of adverse systemic toxicity resulting from Test Article implantation in the chronic swine model at any time point. • All study objectives were met for this study. Therefore, the Aortic Arch Stent Graft System is considered safe at 30 days, 90 days, and 180 days following implant.

*A cylindrical stent graft (ø31x125mm) representative of the materials and manufacturing process of the NEXUS device

C. Biocompatibility Studies

The NEXUS® Aortic Arch Stent Graft System biological safety was evaluated in accordance with the requirements of International Organization for Standardization (ISO) 10993-1:2018, *Biological evaluation of medical devices – Evaluation and testing*, and the FDA guidance document, *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process."*

The NEXUS® Aortic Arch Stent Graft System consists of two (2) main components, the Stent Graft and the Delivery System. All NEXUS stent grafts are considered implants with long term contact (> 30 days). All the NEXUS delivery systems are considered an external

communicating device, circulating blood with limited exposure (< 24 hours).

All testing performed met the pre-specified acceptance criteria. A summary of the biocompatibility testing can be found in **Table 3**.

Table 3. Biocompatibility Testing Summary

Test Performed	Test Description	Stent	Delivery System	Results
Cytotoxicity	Minimum Essential Medium (MEM) Elution	X	X	Non-cytotoxic
Sensitization	ISO Guinea Pig Maximization Sensitization	X	X	No evidence of causing delayed contact sensitization
Irritation/ Intracutaneous Reactivity	ISO Intracutaneous study in Rabbits	X	X	Non-irritating
Acute Systemic Toxicity	ISO Acute Systemic Toxicity study in Mice	X	X	No evidence of systemic toxicity
Material-Mediated Pyrogenicity	Material Mediated Pyrogenicity Test International Organization for Standardization /United States Pharmacopeia (ISO/USP)	X	X	No evidence of material mediated pyrogenicity
Subacute/ Subchronic Toxicity	ISO Two Week Toxicity Study in the Rat - Repeated Parenteral Administration of Two Extracts	X	N/A	No evidence of systemic toxicity
Genotoxicity	Mouse Lymphoma Assay	X	N/A	Non-mutagenic
Genotoxicity	Bacterial Reverse Mutation Study	X	N/A	Non-mutagenic
Implantation	ISO Muscle Implantation Study in Rabbits, 13-Weeks*	X	N/A	Non- significant tissue contact irritation
Hemocompatibility	ASTM F756 Hemolysis Study	X	X	Non-hemolytic
Hemocompatibility	Soluble C5b-9 (SC5b-9) Complement Activation Assay	X	X	Non-Activator of the Complement System
Hemocompatibility	In Vivo Thrombogenicity*	X	X	The test article average clot time was greater than the vehicle control
Chronic Toxicity	Chemical Characterization/ Toxicological Risk Assessment	X	N/A	Non-toxic
Carcinogenicity	Chemical Characterization/ Toxicological Risk Assessment	X	N/A	No carcinogenic risks

* This was also evaluated as part of the GLP chronic safety animal study

D. Sterilization, Packaging, and Shelf-Life

The NEXUS® Aortic Arch Stent Graft System is sterilized by Ethylene Oxide (EO). Validation of the sterilization method to ensure a Sterility Assurance Level (SAL) of 10^{-6} was conducted in accordance with EN ISO 11135:2014/ A1:2019 *Sterilization of health-care products Ethylene oxide – Requirements for the development, validation and routine control of a sterilization process for medical devices*.

Packaging Validation demonstrated the ability of the packaging to protect the product and maintain a sterile barrier through shipping and shelf life.

A shelf life of one (1) year has been established for the NEXUS® Aortic Arch Stent Graft System based on product performance and package shelf-life testing. The specific

engineering tests completed to support the shelf-life are denoted by an asterisk (*) in **Table 1**.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the NEXUS® Aortic Arch Stent Graft System (NEXUS) for endovascular repair of chronic dissections of the aortic arch in the United States and New Zealand under IDE #G200105. Data from this clinical study were the basis for the Premarket Approval (PMA) approval decision.

A summary of the clinical study is presented below.

A. Study Design

Patients were treated between February 2021 and October 2024. The database for this PMA reflected data collected through November 12, 2025, and included 60 subjects with chronic dissection who were considered high risk for open repair. There were 31 investigational sites: 30 in the United States (US) and one (1) in New Zealand. The clinical study also included enrollment of subjects with aneurysms, penetrating aortic ulcers and intramural hematomas; those lesion types are not within scope of the current PMA.

The TRIOMPHE study was a prospective, multi-center, non-randomized clinical study with comparison to a performance goal. There were two co-primary endpoints: 1) Device Technical Failure and 2) Clinical Failure. These co-primary endpoints were defined as:

- **Device Technical Failure (through 30 days)**:
  - Failure to accurately deliver, track and deploy all required endovascular device components at the intended implantation site and failure to retrieve the device delivery systems without the need for unplanned additional procedures
  - Device occlusion
  - Failed exclusion of primary entry tear
  - Additional unanticipated surgical or interventional procedure related to the device or procedure, to prevent life-threatening or permanent disabling event. Specifically, the below were counted against the endpoint:
    - Surgical conversion
    - Re-intervention to treat migration
    - Re-intervention to treat stenosis or occlusion
    - Re-intervention to treat type Ia, Ib, III, IV endoleaks.
    - Re-intervention for loss of device integrity
- **Clinical Failure (through 30 days)**: Subjects experiencing early mortality or at least one of the following major adverse events (MAEs) through 30-Day of Phase 1 Procedure* and 30-Day of Index procedure:
  - Disabling Stroke
  - Permanent Paralysis/Paraplegia
  - Renal Failure

- Aortic Rupture
- Development of new dissections in the thoracic aorta or brachiocephalic artery

*Phase 1 Procedure was defined as the supra-aortic bypass procedure. If a subject has a supra-aortic bypass however, did not have Index Procedure due to non-device related issues or adverse events (e.g. voluntary withdrawal), the subject was excluded from the primary endpoint analysis. Also, any subjects where the Index Procedure was not initiated due to death after Phase 1 Procedure they were not included in the primary endpoint analysis because the analysis was conducted on subjects where there was an attempt to place the NEXUS device into the subject.

The results of the study were tested against Performance Goals derived from published data on other approved devices and literature reported rates. The hypotheses tested for the co-primary endpoints are presented below:

Device Technical Failure:

- Null Hypothesis (H_0): $P_t \geq 0.30$
- Alternative Hypothesis (H_1): $P_t < 0.30$

Where P_t represents the proportion of subjects experiencing a device failure event.

Clinical Failure:

- Null Hypothesis (H_0): $P_t \geq 0.35$
- Alternative Hypothesis (H_1): $P_t < 0.35$

Where P_t represents the proportion of subjects experiencing a clinical failure event.

The null hypothesis for both endpoints needed to be rejected for the study to be considered a success.

The sample size was based on statistical power calculations for two co-primary endpoints, each evaluated at a one-sided alpha of 0.025, ensuring a minimum desired power of 80%. Sample size calculations were completed based on the exact binomial test calculated via the normal approximation.

- Device Technical Failure Endpoint: With an estimated device technical failure rate of 13%, a sample size of 51 evaluable subjects provided >80% power to test against the 30% performance goal.
- Clinical Failure Endpoint: With an estimated clinical failure rate of 18%, a sample size of 54 evaluable subjects provided ~80% power to test against the 35% performance goal.

A total of 60 subjects were enrolled in the study. The co-primary endpoints were formally evaluated in the “as treated population” which was defined as “any subject where there is an

attempt to place the device into the subject (Index procedure)." Accordingly, any subjects wherein the Index Procedure was not initiated due to adverse events or death after Phase 1 Procedure were not included in the primary endpoint analysis.

Evaluation groups used during the course of the pivotal study are described below:

- During the screening process, all subjects who were assessed by an Investigator to meet all inclusion/exclusion criteria were submitted to Endospan for review and case approval. A Subject Eligibility Committee (SEC) reviewed the pre-treatment Computed Tomography (CT) imaging and made recommendations to Endospan whether the subject should be excluded based on anatomical criteria. The SEC comprised of at least one physician with prior NEXUS experience. Members included an Interventional Radiologist, Vascular Surgeons and Cardiothoracic Surgeons. At the conclusion of the process, the site was notified by Endospan on the subject's eligibility (Accept/Reject).
- An independent Clinical Events Committee (CEC) was established to provide unbiased adjudication. The CEC reviewed and adjudicated device and/or procedure related AEs, SAEs, MAEs, specified clinical endpoints and death data. Members included a Neurologist, Vascular Surgeons and Cardiothoracic Surgeons.
- A Data Safety Monitoring Board (DSMB) was established to provide independent oversight of subject safety and study conduct throughout the TRIOMPHE study. The DSBM was responsible for periodic review of cumulative safety data, including Adverse Events (AEs), Serious Adverse Events (SAEs), Protocol Deviations (PDs), deaths, and device- or procedure-related complications. Members included an independent statistician, Vascular Surgeons and Cardiothoracic Surgeons.
- All imaging data for the TRIOMPHE study were evaluated by an independent core laboratory. The core lab was responsible for evaluations on all CT images submitted by the clinical sites. The Core Lab reported all evaluations to Endospan.

1. <u>Clinical Inclusion and Exclusion Criteria</u>

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

   - Male and female age ≥ 18.
   - Subject with chronic dissections who is considered to be at high risk for open repair, with at least one of the following conditions:
     - An aortic aneurysm with a maximum diameter ≥ 55 mm.
     - Rapidly expanding false lumen (growth of > 0.5 cm/6 months)
     - Compressed true lumen associated with end organ malperfusion
     - Symptomatic
   - Must have appropriate proximal, distal and brachiocephalic landing zone
   - Subject is willing and able to comply with procedures specified in the protocol and is able to return for follow-up visits as specified by the protocol

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

- Acute dissection
- Lesions that can be safely treated with TEVAR landing in zone 2 (with or without LSA vascularization)
- Required emergent treatment (e.g., trauma, rupture)
- Acute vascular injury of the aorta due to trauma
- Aortic rupture
- Received a previous stent or stent graft in the treated area (including planned landing area)
- Any major surgical or interventional procedure 6 weeks before the NEXUS® implantation, exclusive of planned procedures that are needed for the safe and effective placement of the stent graft (e.g. supra-aortic bypass)
- Subject has had a MI or cerebral vascular accident (CVA) within 90 days prior to the planned implantation
- Subjects with severe aortic valvular insufficiency as determined by echocardiography
- Mechanical valve that precludes safe delivery of NEXUS
- Known Connective tissue disease (e.g., Marfan's or Ehler's-Danlos syndromes)
- Subject has an active systemic infection at the time of the procedure documented by pain, fever, drainage, positive culture
- Pregnant
- Life expectancy of less than 2 years
- Unsuitable vascular anatomy
- Subject with hostile groins/axilla (scarring, obesity, or previous failed puncture) unless conduit are used.
- Subjects with severe atherosclerosis, severe calcification or extensive intraluminal thrombus of the aorta or in the brachiocephalic trunk
- Subject with known hypersensitivity or contraindication to anticoagulants, antiplatelets, or contrast media, which is not amenable to pre-treatment
- Subject with known sensitivities or allergies to the device materials
- Subject has history of bleeding diathesis or coagulopathy that may limit the use of dual antiplatelet or anticoagulant therapy by the decision of the investigator
- Acute renal failure; chronic renal failure (excluding dialysis); Creatinine > 2.00 mg/dl

2. Follow-up Schedule

   All patients were scheduled to return for follow-up examinations at 1, 6, 12, 24, 36, 48, and 60 months postoperatively. **Table 4** outlines the required screening evaluations and follow-up visit procedures for subjects. Adverse events and complications were recorded at all visits. The key timepoints are shown below in the tables summarizing safety and effectiveness.

Table 4. Schedule of Events

	Screening/ Baseline	Phase 1 Procedure	Index Procedure	Pre-discharge	30 days	6 Months	1 year	Annual visits: 2-5 years
Physical Exam	X			X	X	X	X	X
Neurological Assessment	X				X	X*	X*	X*
Clinical Laboratory Tests	X				X	X		
CT Angiogram of Chest, Abdomen and Pelvis	X			X	X	X	X	X
CT Angiogram of Head and Neck	X							
Ultrasound	X		X					
Angiography			X					

* Performed only if a neurologic problem occurred, subject has symptoms indicating a neurological issue or if suspected stroke was seen on imaging

3. Clinical Endpoints

With regards to safety and effectiveness, there were two co-primary endpoints: 1) Device Technical Failure and 2) Clinical Failure.

Device Technical Failure was defined as any of the following occurring through 30 days:

- Failure to accurately deliver, track and deploy all required endovascular device components at the intended implantation site and failure to retrieve the device delivery systems without the need for unplanned additional procedures
- Device occlusion
- Failed exclusion of primary entry tear
- Additional unanticipated surgical or interventional procedure related to the device or procedure, to prevent life-threatening or permanent disabling event. Specifically, the below were counted:
    - Surgical conversion
    - Re-intervention to treat migration
    - Re-intervention to treat stenosis or occlusion
    - Re-intervention to treat type Ia, Ib, III, IV endoleaks.
        - Type I: Perigraft blood flow caused by inadequate seal at either the proximal or distal graft end (Type Ia: Proximal; Type Ib: Distal)
        - Type III: Occurs in the midgraft region due to leakage through a defect in the graft fabric or between the segments of multisegmental graft (Type IIIa: Junctional leak or disconnect between devices; Type IIIb: through hole or tear)
        - Type IV: Blush of contrast that is presumed to emanate from

blood diffusion across the porous graft fabric or through small holes in the graft caused by sutures or stent struts.

- Re-intervention for loss of device integrity
  - Stent-Graft Fracture
  - Stent-Graft Kink
  - Stent-Graft Twist
  - Misalignment/Birdbeaking
  - Component Separation
  - Stent-Graft Docking
  - Stent-Graft Dilation
  - Suture Break

The statistical analysis aimed to test the null hypothesis that the device failure rate was greater than or equal to the predefined Performance goal of 30%.

Clinical Failure was defined as the occurrence of any MAEs within 30-Day of Phase 1 Procedure (supra-aortic bypass procedure) and 30-Day of Index Procedure (NEXUS procedure) in subjects where there is an attempt to place the NEXUS device into the subject:

- Early Mortality: a lesion related death or any death that occurs within 30-Days or within initial hospitalization following the Index Procedure, unless there is evidence of accidental or self-inflicted death.
- Disabling Stroke: a stroke with a modified Rankin Scale (mRS) score of two or more at 30 days and an increase in at least one mRS category from an individual's pre-stroke baseline
- Permanent Paralysis/Paraplegia: Spinal Cord Ischemia Scale > 3 (Non-ambulatory and/or wheelchair bound), persisting at least 30 days.
- Renal failure: new onset requiring permanent dialysis
- Aortic rupture: catastrophic rupture or tear of the aorta as confirmed by new hematoma or pericardial effusion based upon CT, MRI or Echocardiographic imaging.
- Development of new dissections in the thoracic aorta or brachiocephalic artery: any great vessel or brachiocephalic artery that clinically requires intervention

The statistical analysis aimed to test the null hypothesis that the clinical failure rate was greater than or equal to the predefined Performance Goal of 35%.

B. <u>Accountability of PMA Cohort</u>

At the time of database lock, 60 subjects were eligible and included for analysis. **Table 5** below provides the disposition and compliance at the time of the database lock.

Table 5. Follow-Up Compliance

	Subject Follow-Up [2]				Imaging Performed [2]	Imaging Adequate to Assess the Parameter [2] [3]					Subject Status [4]				
Visit [1]	Eligible for follow-up [5]	Visit Performed	No Visit, Still in Window	Missed visit	CT Scan	Size Changes	False Lumen Perfusion	Endoleak	Migration	Fracture	Death	LTFU/ Early Withdrawal	Surgical Conversion	Not due for next visit	One or More Reason for Future Visit Ineligibility [6]
Index Procedure (1-27)	60	100.0% (60/60)	0.0% (0/60)	0.0% (0/60)	100.0% (60/60)	NA	NA	NA	NA	NA	8.3% (5/60)	0.0% (0/60)	1.7% (1/60)	0.0% (0/60)	8.3% (5/60)
30 Days (28-45) [7]	55	100.0% (55/55)	0.0% (0/55)	0.0% (0/55)	100.0% (55/55)	NA	92.7% (51/55)	92.7% (51/55)	NA	100.0% (55/55)	0.0% (0/55)	0.0% (0/55)	0.0% (0/55)	0.0% (0/55)	0.0% (0/55)
6 Months (150-210)	55	83.6% (46/55)	0.0% (0/55)	3.6% (2/55)	83.6% (46/55)	83.6% (46/55)	76.4% (42/55)	78.2% (43/55)	80.0% (44/55)	83.6% (46/55)	10.9% (6/55)	1.8% (1/55)	3.6% (2/55)	0.0% (0/55)	12.7% (7/55)
1 Year (305-425)	48	97.9% (47/48)	0.0% (0/48)	2.1% (1/48)	97.9% (47/48)	97.9% (47/48)	93.8% (45/48)	95.8% (46/48)	93.8% (45/48)	97.9% (47/48)	4.2% (2/48)	2.1% (1/48)	0.0% (0/48)	27.1% (13/48)	33.3% (16/48)
2 Years (670-790)	32	90.6% (29/32)	6.3% (2/32)	0.0% (0/32)	87.5% (28/32)	81.3% (26/32)	75.0% (24/32)	71.9% (23/32)	81.3% (26/32)	87.5% (28/32)	3.1% (1/32)	0.0% (0/32)	0.0% (0/32)	43.8% (14/32)	46.9% (15/32)
3 Years (1035-1155)	17	76.5% (13/17)	11.8% (2/17)	0.0% (0/17)	76.5% (13/17)	76.5% (13/17)	76.5% (13/17)	76.5% (13/17)	76.5% (13/17)	76.5% (13/17)	5.9% (1/17)	5.9% (1/17)	0.0% (0/17)	35.3% (6/17)	47.1% (8/17)
4 Years (1400-1520)	9	66.7% (6/9)	33.3% (3/9)	0.0% (0/9)	66.7% (6/9)	66.7% (6/9)	66.7% (6/9)	66.7% (6/9)	66.7% (6/9)	66.7% (6/9)	0.0% (0/9)	0.0% (0/9)	0.0% (0/9)	100.0% (9/9)	100.0% (9/9)
5 Years (1825-1945)	0	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)

Note: NA – Not Applicable, LTFU – Lost to Follow-Up
Note: Percentages = (Subjects with Adequate Imaging) / (Subjects Eligible)
[1] Windows for visits are as follows: Study period definitions: 30 Days (28-45 days) 6 Months (150-210 days) 1 Year (305-425 days) 2 Years (670-790 days) 3 Years (1035-1155) 4 Years (1400-1520 days) 5 Years (1825-1945 days)
NOTE: When reporting data for subjects with more than one imaging study in a window, all imaging observations should be reported, irrespective of which image is closest to the midpoint of the window.
[2] Denominator is the number of subjects who are eligible.
[3] Not the number of Subjects with these reported events, but rather, the number with adequate imaging as assessed by Core Lab.
[4] These columns reflect subjects that are not eligible at the start of the next visit window due to death, loss to follow-up/ early withdrawal, open surgical conversion, or who are not yet due for the next visit (e.g., the duration between the index procedure and the date of analysis was less than the days for the start of the next window). The last column is necessary to calculate the number of subjects eligible for the subsequent interval, since subjects may experience more than one event (e.g. surgical conversion and death). NOTE: One subject (126001) had a surgical conversion at 6 months but stayed enrolled in the study. They are being included in subsequent visits.
[5] Eligible subjects are those eligible at the prior interval minus those with one or more reason for future ineligibility within the prior visit window.
[6] A subject with multiple reasons for ineligibility is only counted once.
[7] When reporting 1-month endpoint data, the numerator is the number of subjects with an observation between the procedure and the end of the 1-month window. The denominator is includes subjects who did not have adequate imaging within the window but had an observation.

C. Study Population Demographics and Baseline Parameters

1. Demographics

The demographics of the study population are typical for a thoracic endovascular graft study performed in the US on high surgical risk subjects with chronic dissection involving the aortic arch.

A summary of subject demographics can be found in **Table 6**. Across the study population (N=60), the mean age was 65.9 ± 9.61 years (range 41–89). The cohort was predominantly male, with 81.7% (49/60) men, and had a mean Body Mass Index (BMI) of 30.0 ± 7.01 kg/m².

Table 6. Baseline Demographics

Age, years	
Mean ± SD (N)	65.9 ± 9.61 (60)
Median (Q1, Q3)	67.0 (59.0, 74.0)
(Min, Max)	(41.0, 89.0)
Gender	
Male	81.7% (49/60)
Female	18.3% (11/60)
Race	
American Indian/Alaska Native	0.0% (0/60)
Asian	3.3% (2/60)
Black/African American	38.3% (23/60)
Native Hawaiian/Other Pacific Islander	8.3% (5/60)
White	41.7% (25/60)
Other	6.7% (4/60)
Not Answered	1.7% (1/60)
Ethnicity	
Hispanic/Latino	10.0% (6/60)
Not Hispanic/Latino	86.7% (52/60)
Not Answered	3.3% (2/60)
BMI (kg/m2)	
Mean ± SD (N)	30.0 ± 7.01 (60)
Median (Q1, Q3)	28.6 (25.1, 33.7)
(Min, Max)	(18.0, 48.8)
Clinical Presentation of Arch Pathology	
Asymptomatic	88.3% (53/60)
Symptomatic	11.7% (7/60)
NEXUS Proximal Landing Zone	
Native Aorta	38.3% (23/60)
Previously Implanted Surgical Graft	61.7% (37/60)

Note: Subjects may have more than one race indicated

2. Baseline Medical History

Subjects were eligible for enrollment if they were classified as high-risk surgical candidates. Baseline medical history (**Table 8**) and Baseline Risk Factors (**Table 9**) confirmed a substantial burden of comorbidities. Coronary artery disease was present in 40.0% (24/60), significant valvular heart disease in 20.0% (12/60), and 33.3% (20/60) had a history of arrhythmia. A prior history of vascular intervention was reported in 28.3% (17/60). Additionally, 51.7% (31/60) of subjects were either current or former smokers, and 11.7% (7/60) were symptomatic at baseline. Other prevalent comorbidities included

hypertension in 98.3% (59/60), hyperlipidemia in 80.0% (48/60), and chronic obstructive pulmonary disease (COPD) in 18.3% (11/60). Furthermore, 71.7% (43/60) had undergone a previous aortic intervention, and 70.0% (42/60) had a history of prior sternotomy.

All subjects were classified as American Society of Anesthesiologist (ASA) Class IV (severe systemic disease that is a constant threat to life, e.g., unstable angina), or ASA Class III (severe systemic disease with definite functional limitation, e.g., chronic obstructive pulmonary disease), reflecting the high-risk nature of the treated population. Specifically, 55.0% (33/60) were ASA Class IV and 45.0% were ASA Class III (27/60).

Table 7. Subject Baseline Medical History

Chronic Obstructive Pulmonary Disease (COPD)	18.3% (11/60)
Diabetes Mellitus	21.7% (13/60)
Hypertension	98.3% (59/60)
Hyperlipidemia	80.0% (48/60)
Chronic Angina	3.3% (2/60)
Myocardial Infarction	11.7% (7/60)
Coronary Artery Disease (CAD)	40.0% (24/60)
Percutaneous Coronary Intervention (PCI)	10.0% (6/60)
Coronary Artery Bypass Graft	8.3% (5/60)
Congestive Heart Failure (CHF)	15.0% (9/60)
Transient Ischemic Attack	8.3% (5/60)
Cerebrovascular Accident	16.7% (10/60)
Peripheral Vascular Disease	20.0% (12/60)
Valvular Heart Disease	20.0% (12/60)
Arrhythmia	33.3% (20/60)
Carotid Arterial Disease	10.0% (6/60)
History of Malignancy	20.0% (12/60)
Previous Vascular Intervention	28.3% (17/60)
Previous Aortic Intervention	71.7% (43/60)
Previous Sternotomy	70.0% (42/60)
Previous Thoracotomy	3.3% (2/60)
Renal Insufficiency	38.3% (23/60)
Connective Tissue Disorder	0.0% (0/60)
Family History of Aortic Disease	6.7% (4/60)
Aortic Dissection	91.7% (55/60)
Paraplegia/Paraparesis	1.7% (1/60)

Table 8. Baseline Risk Factors

Smoking Status	
Current (within 30 days)	8.3% (5/60)
Former (>30 days)	43.3% (26/60)
Never smoked	48.3% (29/60)
Incomplete Circle of Willis [1]	12.1% (7/58)

ASA Classification	
I – Healthy subject	0.0% (0/60)
II – Mild systemic disease – no functional limitation	0.0% (0/60)
III – Severe systemic disease – definite functional limitation	45.0% (27/60)
IV – Severe systemic disease that is constant threat to life	55.0% (33/60)
V – Moribund subject unlikely to survive 24 hours with or without operation	0.0% (0/60)
New York Heart Association (NYHA) Classification	
I – Cardiac disease, physical activity not limited	46.7% (28/60)
II – Cardiac disease, physical activity slightly limited	36.7% (22/60)
III – Cardiac disease, physical activity markedly limited	0.0% (0/60)
IV – Cardiac disease, physical activity very limited	0.0% (0/60)
Not Applicable [2]	16.7% (10/60)

[1] Restricted to those with information known

[2] The Electronic Data Capture (EDC) allows you to indicate the NYHA classification as Not Applicable; however, a follow-up question asks "If Not Applicable, please confirm for eligibility that the subject does not have NYHA Classification of III of IV. Currently 15 patients have indicated they are not applicable and confirm the subject met the NYHA eligibility.

Common reasons investigators deemed the subject as high surgical risk are listed in **Table 9**. Other reasons are refusal of open repair or general frailty; however, this information was not captured in the study.

Table 9. Reasons For High Risk in Open Repair

ASA Score III or IV	100% (60/60)
Current or Former Smoker	51.7% (31/60)
Prior Sternotomy	70.0% (42/60)
Advanced Age (>75)	18.3% (11/60)
COPD	18.3% (11/60)
BMI (>30)	43.3% (26/60)
Female	18.3% (11/60)
Arrythmia	33.3% (20/60)
Prior Cerebrovascular Event	25.0% (15/60)
Inadequate Cardiac Function	
MI	11.7% (7/60)
PCI	10.0% (6/60)
CHF	15.0% (9/60)
Valvular Heart Disease	20.0% (12/60)
CAD	40.0% (24/60)

3. Lesion Characteristics

Table 10 presents core lab–reported baseline characteristics describing the extent of the aortic disease. Sixty percent (60.0%, 36/60) had proximal disease involvement beginning in Zone 0, and 80.4% (45/56) had distal disease extending to Zone 9 or beyond. All subjects in the TRIOMPHE study required a Zone 0 landing zone.

Table 10. Core Lab Reported Disease Extension

Proximal End of Disease	
Zone 0	36/60 (60.0%)
Zone 1	6/60 (10.0%)
Zone 2	9/60 (15.0%)
Zone 3	9/60 (15.0%)
Other	-
Distal End of Disease	
Zone 0	-

Zone 1	-
Zone 2	-
Zone 3	1/56 (1.8%)
Zone 4	2/56 (3.6%)
Zone 5	3/56 (5.4%)
Zone 6	1/56 (1.8%)
Zone 7	2/56 (3.6%)
Zone 8	1/56 (1.8%)
Zone 9	7/56 (12.5%)
Zone 10 - Right	4/56 (7.1%)
Zone 10 - Left	10/56 (17.9%)
Zone 11 - Right	12/56 (21.4%)
Zone 11 - Left	12/56 (21.4%)
Other	1/56 (1.8%)

Note: For subjects with the proximal extent of disease in Zone 2 or Zone 3, an adequate proximal landing zone was not available; therefore, device implantation required a proximal landing in Zone 0.

4. Device Usage

Table 11 provides a summary of the Stent Graft configurations implanted in subjects during the Index Procedure. Arch Stent Grafts implanted in subjects are summarized in **Table 12** Ascending Stent Grafts in **Table 13**, and optional Descending Extension Stent Grafts in **Table 14**.

Table 11. Stent Graft Configurations Implanted During Index Procedure

	# implanted
Arch Stent Graft and 1 Ascending Stent Graft	26.7% (16/60)
Arch Stent Graft and 2 Ascending Stent Grafts	0.0% (0/60)
Arch Stent Graft, 1 Ascending Stent Graft, and 1 Descending Extension	58.3% (35/60)
Arch Stent Graft, 1 Ascending Stent Graft, and 2 Descending Extensions	10.0% (6/60)
Arch Stent Graft, 2 Ascending Stent Grafts, and 1 Descending Extension	3.3% (2/60)
Arch Stent Graft, 2 Ascending Stent Grafts, and 2 Descending Extensions	1.7% (1/60)

Table 12. Arch Stent Graft Implanted

Branch Diameter	Branch Length	Descending Aorta Diameter	Descending Aorta Length	# Implanted
14	20	32	180	1.7% (1/60)
14	20	36	180	0.0% (0/60)
14	20	40	180	0.0% (0/60)
14	30	32	180	20.0% (12/60)
14	30	36	180	8.3% (5/60)
17	20	32	180	5.0% (3/60)

Branch Diameter	Branch Length	Descending Aorta Diameter	Descending Aorta Length	# Implanted
17	20	36	180	1.7% (1/60)
17	30	32	180	21.7% (13/60)
17	30	36	180	10.0% (6/60)
17	30	40	180	1.7% (1/60)
17	40	32	180	1.7% (1/60)
17	40	36	180	5.0% (3/60)
20	20	32	180	1.7% (1/60)
20	20	36	180	5.0% (3/60)
20	30	32	180	8.3% (5/60)
20	30	36	180	1.7% (1/60)
20	30	40	180	1.7% (1/60)
20	40	32	180	5.0% (3/60)
20	40	36	180	0.0% (0/60)

Table 13. Ascending Stent Graft Sizes Implanted

Ascending Diameter	Length	Configuration	# Implanted
36	40	Curved	12.7% (8/63)
36	55	Curved	20.6% (13/63)
36	70	Curved	3.2% (2/63)
40	40	Curved	7.9% (5/63)
40	55	Curved	25.4% (16/63)
40	70	Curved	12.7% (8/63)
43	55	Curved	9.5% (6/63)
43	70	Curved	7.9% (5/63)

Note: Denominators are based on the number of Ascending Stent Grafts used

Table 14. Descending Extension Stent Graft Sizes Implanted

Tapered			
Proximal Diameter	**Length**	**Distal Diameter**	**#Implanted**
36	125	31	7.1% (3/42)
36	157	31	19.0% (8/42)
36	189	31	38.1% (16/42)
36	189	36	4.8% (2/42)
40	125	36	2.4% (1/42)
40	157	36	4.8% (2/42)
40	157	40	2.4% (1/42)
40	189	36	11.9% (5/42)
40	189	40	7.1% (3/42)
43	162	40	2.4% (1/42)
43	194	40	0.0% (0/42)

Straight			
Diameter	**Length**		
31	189		0.0% (0/9)
36	125		11.1% (1/9)
36	157		0.0% (0/9)
36	189		22.2% (2/9)
40	157		11.1% (1/9)
40	189		33.3% (3/9)
43	166		11.1% (1/9)
43	200		11.1% (1/9)

Note: Denominators are based on the number of Descending Extension Stent Grafts used

5. Procedure Characteristics

Supra-aortic bypass (Phase 1)

Phase 1 Procedure was defined as the supra-aortic bypass procedure. Phase 1 Procedural information is provided in **Table 15**.

Table 15. Phase 1 Parameters

Length of Surgical Procedure (min)	
Mean ± SD (N)	230.9 ± 84.71 (60)
Median (Q1, Q3)	220.5 (178.5, 273.0)
(Min, Max)	(73.0, 455.0)
Intubation Time (min)	
Mean ± SD (N)	286.5 ± 80.07 (57)
Median (Q1, Q3)	287.0 (223.0, 324.0)
(Min, Max)	(141.0, 466.0)
Estimated Blood Loss (ml)	
Mean ± SD (N)	299.7 ± 307.38 (59)
Median (Q1, Q3)	200.0 (100.0, 350.0)
(Min, Max)	(25.0, 1500.0)
Transfusion Required	8.3% (5/60)
Transfusion Amount (ml)	
Mean ± SD (N)	535.8 ± 292.47 (4)
Median (Q1, Q3)	535.0 (285.0, 786.5)
(Min, Max)	(250.0, 823.0)
RCC-Left Common Carotid (LCC)	
Native	2.5% (1/40)
Graft	97.5% (39/40)
Diameter	
Mean ± SD (N)	7.9 ± 0.27 (39)
Median (Q1, Q3)	8.0 (8.0, 8.0)
(Min, Max)	(7.0, 8.0)
LCC-LSA	
Native	11.1% (4/36)
Graft	88.9% (32/36)
Diameter	
Mean ± SD (N)	7.8 ± 0.45 (32)
Median (Q1, Q3)	8.0 (8.0, 8.0)
(Min, Max)	(6.0, 8.0)
RCC-LSA	
Native	0.0% (0/20)

Graft	100.0% (20/20)
Diameter	
Mean ± SD (N)	7.9 ± 0.72 (20)
Median (Q1, Q3)	8.0 (8.0, 8.0)
(Min, Max)	(6.0, 10.0)
Other Anatomic Locations	
Native	50.0% (10/20)
Graft	50.0% (10/20)
Diameter	
Mean ± SD (N)	8.0 ± 0.00 (10)
Median (Q1, Q3)	8.0 (8.0, 8.0)
(Min, Max)	(8.0, 8.0)
Was Mini Sternotomy Performed?	
Yes	6.7% (4/60)
No	93.3% (56/60)
Retropharyngeal bypass performed?	
Yes	76.7% (46/60)
No	23.3% (14/60)
Bypass Patent at End	100.0% (60/60)

Note: Information in this table is limited to study subjects who proceeded to the index procedure.

One subject was initially enrolled for treatment with NEXUS. This subject completed the Phase 1 Procedure, in preparation for the Index Procedure, it was noticed the subject no longer met anatomical eligibility. The subject was withdrawn from the study and was treated with NEXUS under expanded access/compassionate use. Data from this subject is not included in the analysis. All other subjects who underwent the Phase 1 procedure proceeded to the index procedure.

Index Procedure (NEXUS Procedure)

The mean time from insertion of the first stent graft delivery system to withdrawal of the final delivery system (Ascending, or Descending, if applicable) was 85 minutes overall. Use of the optional descending stent graft was implanted in 73.3% (44/60). Rapid pacing, performed at three predefined time points during the procedure, had an overall mean cumulative duration of 102.9 seconds.

In 61.7% (37/60) the proximal landing zone was within a surgical graft. Conversely, the native aorta served as the proximal landing zone in 38.3% (23/60) of subjects (**Table 16**).

Table 16. Procedural Parameters

Device Deployment Time (min) [1]	
Mean ± SD (N)	85.0 ± 41.68 (59)
Median (Q1, Q3)	75.0 (57.0, 103.0)
(Min, Max)	(21.0, 250.0)
Rapid Pace Time (Sec)	
Mean ± SD (N)	102.9 ± 70.25 (60)
Median (Q1, Q3)	90.0 (63.0, 130.0)
(Min, Max)	(12.0, 420.0)
Length of Procedure (min) [2]	
Mean ± SD (N)	229.8 ± 69.61 (60)
Median (Q1, Q3)	213.0 (179.5, 263.0)

(Min, Max)	(131.0, 470.0)
Intubation Time (min)	
Mean ± SD (N)	333.5 ± 194.73 (55)
Median (Q1, Q3)	305.0 (254.0, 352.0)
(Min, Max)	(153.0, 1583.0)
Fluoroscopy Time (min)	
Mean ± SD (N)	50.1 ± 18.97 (59)
Median (Q1, Q3)	46.0 (36.0, 64.0)
(Min, Max)	(1.0, 96.0)
Volume of Contrast (ml)	
Mean ± SD (N)	150.1 ± 68.70 (60)
Median (Q1, Q3)	135.0 (100.0, 190.0)
(Min, Max)	(33.0, 337.0)
Estimated Blood Loss (ml)	
Mean ± SD (N)	214.8 ± 185.88 (58)
Median (Q1, Q3)	200.0 (100.0, 300.0)
(Min, Max)	(0.0, 900.0)
Transfusion Required	23.3% (14/60)
Transfusion Amount (ml)	
Mean ± SD (N)	1214.6 ± 1994.16 (13)
Median (Q1, Q3)	620.0 (350.0, 1000.0)
(Min, Max)	(340.0, 7750.0)
Anesthesia	
General	100.0% (60/60)
Local	0.0% (0/60)
Main Access Method	
Cutdown	95.0% (57/60)
Percutaneous	5.0% (3/60)
Main Access Vessel	
Right Femoral	85.0% (51/60)
Left Femoral	15.0% (9/60)
Additional Access Sites	
Right Femoral	15.3% (9/59)
Left Femoral	84.7% (50/59)
Axillary Access Method	
Cutdown	33.9% (19/56)
Percutaneous	66.1% (37/56)
Axillary Access Sites	
Right	94.5% (52/55)
Left	5.5% (3/55)
Additional Access Used?	60.0% (36/60)
Proximal Landing Zone	
Within Surgical Graft	61.7% (37/60)
Within Native Aorta	38.3% (23/60)
Distal Extension Used?	
Yes	73.3% (44/60)
No	26.7% (16/60)
Surgical Conversion [3]	0.0% (0/60)

[1] First insertion of Arch Stent Graft delivery to withdrawal of Ascending Stent graft delivery system. If Descending stent is being used, then withdrawal of Descending Stent graft delivery.
[2] Skin to skin time.
[3] At time of Index Procedure.
[4] Extended procedure time due to non-device related adverse events, estimated blood loss was 250 mL, Hemoglobin decreased from 13.0 g/dL to a nadir of 10.5 g/dL.

Table 17 presents the hospitalization period. The median hospital stay after Index Procedure was 8.0 days (5.0, 12.0), with a median ICU stay of 3.0 days (1.0, 4.5).

Table 17. Hospitalization Period

Number of Days between Phase 1 and Index Procedures	
Mean ± SD (N)	11.6 ± 27.92 (60)
Median (Q1, Q3)	4.5 (3.0, 9.0)
(Min, Max)	(2.0, 212.0)
Phase 1 Procedure	
Length of ICU Stay (days)	
Mean ± SD (N)	3.6 ± 5.04 (60)
Median (Q1, Q3)	2.0 (1.0, 4.0)
(Min, Max)	(0.0, 23.0)
Phase 1 and Index procedure in same admission?	
Yes	73.3% (44/60)
No	26.7% (16/60)
Index Procedure	
Length of Intensive Care Unit (ICU) Stay (days) [1]	
Mean ± SD (N)	3.8 ± 3.82 (56)
Median (Q1, Q3)	3.0 (1.0, 4.5)
(Min, Max)	(0.0, 22.0)
Length of Hospital Stay (days) [1]	
Mean ± SD (N)	9.4 ± 7.00 (56)
Median (Q1, Q3)	8.0 (5.0, 12.0)
(Min, Max)	(1.0, 40.0)
[1] Subjects who experienced early mortality are not included in the length of ICU or hospital stay	

Table 18 Lists the unanticipated and anticipated adjunctive procedures that occurred during the Phase 1 Procedure (5.0%, 3/60) or during the Index Procedure (15.0%, 9/60).

Table 18. Adjunctive Procedures by Subject

	Time Point	Event (n)	Anticipated	Intervention
110003	Phase 1	Clamp injury	Yes	Stent
120011	Phase 1	Dissection flap seen on imaging of the right carotid artery	Yes	Patch angioplasty of right carotid artery
124011	Phase 1	Acute pulmonary oedema	Yes	Reintubation
102008	Index Procedure	Femoral artery access was high	Yes	Stent across the access site via a contralateral approach
103002	Index Procedure	Right brachial occlusion	Yes	Graft repair
103005	Index Procedure	Right brachial dissection	Yes	Repair sutures and bovine patch
103013	Index Procedure	Commercial catheter breakage	Yes	Retrieval
103020	Index Procedure	Bend at the NEXUS BCT origin	Yes	Stent in BCT[1]
105001	Index Procedure	Left renal artery occlusion	Yes	Stent
111016	Index Procedure	Cardiac perforation	Yes	Pericardial window, cardiopulmonary bypass

	Time Point	Event (n)	Anticipated	Intervention
115012	Index Procedure	1) Acute compartment syndrome; 2) CVA	1) No 2) Yes	1)Forearm fasciotomy and decompression with carpel tunnel release 2) Reintubation
124011	Index Procedure	Transient Paraparesis	Yes	Lumbar Drain Placed

[1]Subject also met device technical failure, site does not consider this an adverse event

D. Safety and Effectiveness Results

This study (CIP009) had two co-primary endpoints: 1) Device Technical Failure and 2) Clinical Failure through 30 days. These capture both safety and effectiveness.

1. Safety and Effectiveness Results

   The analysis of safety and effectiveness was based on the chronic dissection cohort of 60 subjects available for the 30-day evaluation. The co-primary endpoint results are presented below in **Table 19** with details of each endpoint event in **Table 20**.

   Device Technical Failure (through 30-Day):

   - Failure to accurately deliver, track and deploy all required endovascular device components at the intended implantation site and failure to retrieve the delivery systems without the need for unplanned additional procedures
     - Including the placement of a commercial stent in the BCT
   - Device occlusion (complete absence of blood flow at any point)
   - Failed exclusion of primary entry tear
   - Additional unanticipated surgical or interventional procedure related to the device or procedure, to prevent life-threatening or permanent disabling event.
     - Surgical Conversion
     - Re-Intervention to treat migration (movement greater than 10mm)
     - Re-Intervention to treat stenosis (>50% narrowing) or occlusion (complete absence of blood flow at any point)
     - Re-Intervention to treat Type Ia, Ib, III, IV Endoleaks
     - Re-Intervention to treat for loss of device integrity

   Clinical Failure: Subjects experiencing at least one of the following MAEs through 30-Day of Phase 1 Procedure and 30-Day of Index Procedure:

   - Early Mortality
   - Disabling Stroke
   - Permanent Paralysis/Paraplegia
   - Renal failure
   - Aortic rupture
   - Development of new dissections in the thoracic aorta or brachiocephalic artery

The null hypothesis was rejected for both co-primary endpoints.

Freedom from device technical failure, was met in 95.0% (57/60) of subjects, with a failure rate of 5.0% (3/60; 95% CI: 1.04–13.92; p<0.001 versus the 30% performance goal). Technical failure events included failure to deliver/track/deploy system (3.3%, 2/60), additional unanticipated procedures: surgical conversion (1.7%, 1/60).

Freedom from clinical failure, was met in 85.0% (51/60) of subjects, with a clinical failure rate of 15.0% (9/60; 95% CI: 7.10–26.57; p<0.001 versus the 35% performance goal). Contributing events included death (10.0%, 6/60), disabling stroke (8.3%, 5/60), and development of new dissection (1.7%, 1/60). Two strokes and the dissection resulted in fatalities. No cases of permanent paralysis/paraplegia, renal failure, or aortic rupture were reported.

There were no occurrences of device occlusion, failed exclusion of the primary entry tear, or reinterventions for type I, III or IV endoleak, stenosis, migration, or loss of device integrity through 30 days. Of the two deployment-related failures, one involved intraoperative placement of a stent in the BCT following NEXUS deployment. In the second case, the device failed to deploy and was removed, and a new device was successfully implanted, all without any associated complications or adverse events.

The Co-Primary Endpoints (30 Days) are provided in **Table 19**. The components of the primary endpoints over time are provided in **Table 22**.

Table 19. Co-Primary Endpoints (30 Days)

	% (n/N)	95% CI	p-value
Device Technical Failure [1]	5.0% (3/60)	1.04, 13.92	<0.001
Failure to deliver/track/deploy components or retrieve delivery system	3.3% (2/60)	0.41, 11.53	
Device Occlusion	0.0% (0/60)	0.00, 5.96	
Failed Exclusion of Primary Entry Tear	0.0% (0/60)	0.00, 5.96	
Additional Unanticipated Procedure	1.7% (1/60)	0.04, 8.94	
Surgical Conversion	1.7% (1/60)	0.04, 8.94	
Re-intervention for Migration	0.0% (0/60)	0.00, 5.96	
Re-intervention for Stenosis or Occlusion	0.0% (0/60)	0.00, 5.96	
Re-intervention for Type Ia, Ib, III, IV Endoleaks	0.0% (0/60)	0.00, 5.96	
Re-intervention for Loss of Device Integrity	0.0% (0/60)	0.00, 5.96	
Clinical Failure [2], [3]	15.0% (9/60)	7.10, 26.57	<0.001
Death	10.0% (6/60)	3.76, 20.51	
Disabling Stroke	8.3% (5/60)	2.76, 18.39	
Permanent Paralysis/Paraplegia	0.0% (0/60)	0.00, 5.96	
Renal Failure	0.0% (0/60)	0.00, 5.96	
Aortic Rupture	0.0% (0/60)	0.00, 5.96	
Development of New Dissection	1.7% (1/60)	0.04, 8.94	

[1] p-value is derived from a one sample, one-sided exact binomial test against a reference safety goal of 30%.
[2] p-value is derived from a one sample, one-sided exact binomial test against a reference safety goal of 35%
[3] The clinical failure events include any MAE occurring through 30 days of the Phase 1 (supra-aortic bypass) procedure and though 30 days of Index (NEXUS) procedure. One MAE (disabling stroke) occurred following the Phase 1 Procedure. All other MAEs occurred following the Index procedure.

Table 20 provides a description of the events considered device technical or clinical failure. **Table 22** Provides the primary endpoint components through 12 months.

Table 20. Event Descriptions for Subjects Who Met Endpoint

Subject #	Device Technical Failure	Clinical Failure	Description of Event
103002	Yes – Surgical Conversion	Yes - Development of a New Dissection Requiring Treatment (Surgical Conversion) and Early Mortality (Anoxic Brain Injury)	Uneventful Phase 1 and Index Procedure. On Post Operative Day (POD) 1, Computed Tomography Angiography (CTA) demonstrated an acute Type A aortic dissection requiring surgical repair. The subject expired on POD 14 due to anoxic brain injury.
103020	Yes - Failure to Deliver/Track/Deploy Components or Retrieve Delivery System (including placement of a commercial stent in the BCT)	No	Uneventful Phase 1 Procedure. During Index Procedure, imaging suggested a bend at the NEXUS BCT origin; a commercial stent was placed in the BCT without complication. Post-placement imaging showed good flow. No adverse events occurred.
110012	No	Yes -Disabling Stroke	Uneventful Phase 1 and Index Procedure. On POD 2, CT demonstrated new hypodense foci in the right cerebellar hemisphere and left frontal lobe. mRS went from 1 to 3.
110018	No	Yes – Disabling Stroke Resulting in Early Mortality	Uneventful Phase 1 and Index Procedure. On POD 3, a seizure occurred and imaging demonstrated a right temporoparietal intraparenchymal hemorrhage. Hemicraniectomy and hematoma evacuation were performed. Subject expired on POD 55 without hospital discharge. Note: After the Index Procedure and prior to death the subject was diagnosed with cerebral amyloid angiopathy, a condition associated with increased risk of intracerebral bleeding.
111014	No	Yes - Early Mortality (Hypertension)	Uneventful Phase 1 and Index Procedure. Subject was discharged to home on POD 3 following uneventful hospital course. Subject expired on POD 11. Site was notified of the death through the electronic medical records system. Cause of death was indicated as hypertension.
112011	Yes - Failure to Deliver/Track/Deploy Components or Retrieve Delivery System	No	Uneventful Phase 1 Procedure. During the Index Procedure, the initial arch device did not deploy and was removed without complication. A new arch device was implanted without issue. No adverse events occurred.
115012	No	Yes -Disabling Stroke (after phase 1 prior to Index Procedure)	Uneventful Phase 1 Procedure. Later that day, CT demonstrated an acute right parietal stroke. mRS increased from 0 to 4. Over time, mRS improved and the Index Procedure was successfully performed 211 days later.
120013	No	Yes - Disabling Stroke	Uneventful Phase 1 and Index Procedure. On POD 6, seizure-like activity occurred and CT demonstrated a trace acute left frontal subarachnoid hemorrhage without large vessel occlusion. Baseline mRS was 0;

Subject #	Device Technical Failure	Clinical Failure	Description of Event
			no post-event mRS was recorded.
122010	No	Yes - Early Mortality (Bradycardia)	Uneventful Phase 1 Procedure. The subject had a prolonged recovery from the Phase 1 Procedure and remained intubated and on inotropic support on POD 3 when the Index Procedure was performed. Following the Index Procedure, the subject experienced respiratory and hemodynamic instability. The family elected to withdraw care on POD 14 and the subject expired.
126002	No	Yes – Disabling Stroke and Early Mortality (Hemorrhage Intracranial)	Uneventful Phase 1 and Index Procedure. On POD 4, the subject experienced a disabling hemorrhagic stroke. The subject expired on POD 6 due to left lobar intracranial hemorrhage.
130012	No	Yes - Early Mortality (Cardiac Failure)	Uneventful Phase 1 Procedure, though technically challenging due to prior cervical fusion and limited neck mobility. Postoperatively, the subject required inotropic support and experienced airway swelling. Recovery was complicated by reduced cardiac function. The Index Procedure was performed on POD 2 with difficult intubation but was otherwise uneventful. The subject subsequently developed progressive heart failure and multi-organ failure. The family elected withdrawal of life support and the subject expired on POD 18 due to cardiac failure.

Sensitivity Analysis

A sensitivity analysis was conducted to assess the potential impact of missing data on the co-primary endpoint of 'device technical failure'. The only subjects who did not complete 30 days of follow-up were those who experienced early mortality and were therefore counted as events for the co-primary endpoint of 'clinical failure'. Among these subjects, one had already experienced a device technical failure and one died on Day 55 during the index hospitalization and was classified as early mortality, leaving four subjects who could potentially be considered as having missing 'device technical failure' endpoint data. As described in the table below, even assuming all four subjects experienced device technical failure, the upper bound of the 95% confidence interval remained below the prespecified performance goal of 30%.

Table 21. Device Technical Failure Tipping Point Analysis

	% (n/N)	95% CI	p-value [1]
No Imputation	5.0% (3/60)	1.04, 13.92	<0.001
Impute 1 Failure	6.7% (4/60)	1.85, 16.20	<0.001
Impute 2 Failures	8.3% (5/60)	2.76, 18.39	<0.001
Impute 3 Failures	10.0% (6/60)	3.76, 20.51	<0.001
Impute 4 Failures	11.7% (7/60)	4.82, 22.57	<0.001

[1]p-value is derived from a one sample, one-sided exact binomial test against a reference safety goal of 30%.
Note: A total of 4 subjects had potential missing data for device technical failure.

2. Primary Endpoint Component Event Results through 12-Months

The device technical failure rate was 5.0% (3/60) at 30 days and 8.3% (5/60) at 12 months. The two additional events observed after 30 days were surgical conversions

occurring on POD 67 and POD 92. No subjects experienced device occlusion, failure to exclude the primary entry tear per Core Laboratory assessment, or reinterventions for migration, stenosis or occlusion, loss of device integrity, or Type Ia, Ib, III, or IV endoleaks.

The 30-day clinical failure rate was 15.0% (9/60). By 12 months, six additional subjects experienced a clinical failure, including one disabling stroke, one new dissection, and five deaths. The disabling stroke and all deaths were adjudicated by the CEC as not related to the investigational device. No subjects experienced permanent paralysis/paraplegia, renal failure requiring permanent dialysis, or aortic rupture.

Table 22. Primary Endpoint Component Events through 12-Months

Primary Endpoint Analysis	Phase 1	Index Procedure (1)	Pre-Discharge	30 Days (2-30)	6 Months (31-180)	12 Months (181-365)	Total (Through 12 Months)
Number of Enrolled Subjects	60	60	60	60	55	48	60
Number of Subject with Imaging	-	-	49	55	46	47	58
Subjects with Device Technical Failure Co-Primary Endpoint	-	3.3% (2/60)	-	1.7% (1/60)	3.6% (2/55)	0.0% (0/48)	8.3% (5/60)
Subject with Clinical Failure Co-Primary Endpoint	-	0.0% (0/60)	-	13.3% (8/60)	14.5% (8/55)	4.2% (2/48)	26.7% (16/60)
Device Technical Failure	-	3.3% (2/60)	-	1.7% (1/60)	3.6% (2/55)	0.0% (0/48)	8.3% (5/60)
Failure to Deliver/Track/Deploy Components or Retrieve Delivery System	-	3.3% (2/60)	-	-	-	-	3.3% (2/60)
Device Occlusion	-	0.0% (0/60)	-	0.0% (0/60)	0.0% (0/55)	0.0% (0/48)	0.0% (0/60)
Failed Exclusion of Primary Entry Tear	-	0.0% (0/60)	-	0.0% (0/60)	0.0% (0/55)	0.0% (0/48)	0.0% (0/60)
Additional Unanticipated Procedure	-	0.0% (0/60)	-	1.7% (1/60)	3.6% (2/55)	0.0% (0/48)	5.0% (3/60)
Surgical Conversion	-	0.0% (0/60)	-	1.7% (1/60)	3.6% (2/55)	0.0% (0/48)	5.0% (3/60)
Re-intervention for Migration	-	0.0% (0/60)	-	0.0% (0/60)	0.0% (0/55)	0.0% (0/48)	0.0% (0/60)
Re-intervention for Stenosis or Occlusion	-	0.0% (0/60)	-	0.0% (0/60)	0.0% (0/55)	0.0% (0/48)	0.0% (0/60)
Re-intervention for Type Ia, Ib, III, IV Endoleaks [2]	-	0.0% (0/60)	-	0.0% (0/60)	3.6% (2/55)	2.1% (1/48)	5.0% (3/60)
Re-intervention for Loss of Device Integrity	-	0.0% (0/60)	-	0.0% (0/60)	0.0% (0/55)	0.0% (0/48)	0.0% (0/60)
Clinical Failure	1.7% (1/60)	0.0% (0/60)	-	13.3% (8/60)	14.5% (8/55)	4.2% (2/48)	28.3% (17/60)
Death [1]	0.0% (0/60)	0.0% (0/60)	-	8.3% (5/60)	10.9% (6/55)	4.2% (2/48)	21.7% (13/60)
Disabling Stroke	1.7% (1/60)	0.0% (0/60)	-	6.7% (4/60)	1.8% (1/55)	0.0% (0/48)	10.0% (6/60)
Permanent Paralysis/Paraplegia	0.0% (0/60)	0.0% (0/60)	-	0.0% (0/60)	0.0% (0/55)	0.0% (0/48)	0.0% (0/60)
Renal Failure	0.0% (0/60)	0.0% (0/60)	-	0.0% (0/60)	0.0% (0/55)	0.0% (0/48)	0.0% (0/60)
Aortic Rupture	0.0% (0/60)	0.0% (0/60)	-	0.0% (0/60)	0.0% (0/55)	0.0% (0/48)	0.0% (0/60)
Development of New Dissection	0.0% (0/60)	0.0% (0/60)	-	1.7% (1/60)	1.8% (1/55)	0.0% (0/48)	3.3% (2/60)

[1] One subject expired on POD55; however, was never discharged. Thus, this subject counts towards the 30-day Clinical Endpoint.

[2] Endoleak Assessment by Site. Core laboratory reported these subjects as having Type II endoleaks; however, site assessments in these subjects raised concern for Type III endoleaks and led to reintervention. Specifically:115034: The PI attributed the endoleak to the carotid artery, false lumen of the LSA, and partially the vertebral artery; however, the relative contribution of each source was uncertain. Based on this assessment, a reintervention was performed, which resolved the endoleak. The core laboratory reported this as a Type II endoleak with inflow from intercostal/lumbar vessels.116011: The site initially assessed the endoleak as Type II; however, subsequent concern for a possible Type III endoleak led to endovascular intervention. The endoleak remained unchanged following reintervention. The core laboratory reported this as a Type II endoleak with the LSA as the source.100004: The site initially reported an unknown endoleak and later determined a possible Type III endoleak, prompting endovascular intervention. The core laboratory reported this as a Type II endoleak with the LSA as the source.

3. Intraprocedural and Post Procedural Adverse Events

Nine subjects (15.0%, 9/60) experienced a site reported complication during the Phase 1 Procedure resulting in an adverse event related to the bypass procedure. These included neck hematoma requiring evacuation or exploration (n=3), clamp-related injury to the left subclavian artery requiring stenting (n=1), dysphagia requiring airway monitoring (n=1), acute pulmonary edema requiring reintubation (n=1), coagulopathy requiring transfusion (n=1), acute kidney injury (n=1), and one disabling stroke (n=1).

Eight subjects (13.3%, 8/60) experienced a site reported complication occurring during the Index Procedure resulting in an adverse event. These included ventricular fibrillation requiring defibrillation and chest compressions and blood loss anemia requiring transfusion and medical management, in addition to the events listed in Table 18 (Adjunctive Procedures).

None of the Intra-Index Procedure complications described above were classified as device-related.

Separately, five SAEs were adjudicated by the CEC as related (n=4) or possibly related (n=1) to the NEXUS device. The related events included two aortic dissections that resulted in surgical conversion and two Type II endoleaks requiring reintervention. The event was adjudicated as possibly related was a non-disabling stroke that occurred on POD 11 and resolved without intervention.

4. Additional Outcomes

In addition to the Primary Endpoints noted above, secondary endpoints were evaluated through 30 days. No events of prolonged intubation, extension of a dissection, distal device-related thromboembolic events requiring reintervention or a surgery, MI, life threatening bleeding, fistula formation or false lumen perfusion through the primary entry tear, false lumen perfusion through an aortic arch branch vessel without distal entry tear were reported within 30 days, as assessed by the site or core laboratory, as applicable. **Table 23** provides a summary of secondary endpoints with observed occurrences.

Table 23. Secondary Endpoints: Proportion of Subjects Free from Event At 30 Days

	% (n/N)
Renal dysfunction or volume overload requiring ultrafiltration	98.3% (59/60)
Laryngeal or Phrenic Nerve injury post Index Procedure	95.0% (57/60)
Severe Heart Failure/Hypertension	95.0% (57/60)
Type II endoleaks from supraortic arch vessels	95.0% (57/60)

The following endpoints were evaluated through 30 days and all subsequent intervals:

Table 24. CEC Adjudicated and Core Lab Reported Secondary Endpoints Over Time

	Index Procedure (1)	30 Days (2-30)	6 Months (31-180)	1 Year (181-365)	2 Years (366-730)	3 Years (731-1095)	4 Years (1096-1460)	Total [1]
	% (n/N)	% (n/N)	% (n/N)	% (n/N)	% (n/N)	% (n/N)	% (n/N)	% (n/N)
All-cause mortality	- (0/60)	8.3% (5/60)	10.9% (6/55)	4.2% (2/48)	2.2% (1/46)	3.2% (1/31)	- (0/14)	25.0% (15/60)
Lesion related mortality	- (0/60)	6.7% (4/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	6.7% (4/60)
Rupture within or adjacent to the treated segment	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)
Any neurological event	- (0/60)	13.3% (8/60)	3.6% (2/55)	2.1% (1/48)	4.3% (2/46)	3.2% (1/31)	- (0/14)	18.3% (11/60)
Any paralysis/paraplegia	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)
Renal failure [2]	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)
Development of new dissection proximal or distal to the treatment zone	3.3% (2/60)	1.7% (1/60)	1.8% (1/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	6.7% (4/60)
Unintentional rupture of the dissection septum	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)
Endoleaks	- (0/60)	11.7% (7/60)	7.3% (4/55)	2.1% (1/48)	6.5% (3/46)	- (0/31)	7.1% (1/14)	18.3% (11/60)
Type Ia	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)
Type Ib	- (0/60)	- (0/60)	- (0/55)	- (0/48)	2.2% (1/46)	- (0/31)	- (0/14)	1.7% (1/60)
Type II	- (0/60)	6.7% (4/60)	5.5% (3/55)	2.1% (1/48)	2.2% (1/46)	- (0/31)	- (0/14)	8.3% (5/60)
Type IIIa	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	7.1% (1/14)	1.7% (1/60)
Type IIIb	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)
Type IV	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)
Type V	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)
Type Undetermined	- (0/60)	5.0% (3/60)	1.8% (1/55)	- (0/48)	2.2% (1/46)	- (0/31)	- (0/14)	6.7% (4/60)
Migration [3]	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)
Patency-related events	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)
Conversion to open repair	- (0/60)	1.7% (1/60)	3.6% (2/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	5.0% (3/60)
Secondary procedures in the treatment area/treatment branches [4]	- (0/60)	3.3% (2/60)	7.3% (4/55)	2.1% (1/48)	- (0/46)	3.2% (1/31)	- (0/14)	11.7% (7/60)
Fistula formation	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)
Loss of stent graft integrity [5]	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)
New ischemia	- (0/60)	- (0/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/60)

[1] Event percentages in this column may be an underestimation as 5-year follow-up is not complete, [2] New onset requiring permanent dialysis. [3] Greater than 10 mm or clinically significant migration, [4] Includes reintervention to treat endoleaks, stenosis, or occlusion of the investigational device, does not include reintervention for planned staged treatment of LSA or DE
Note: Core lab data is summarized per assigned visit, not study day.
Note: Subjects are included in the denominator if they reached the opening of the visit window.

5. Key Events: Information presented below is inclusive of key events reported after Phase 1 procedure and the index procedure:

Neurological Events

All reported neurological events were reviewed and adjudicated by the independent CEC which includes a neurologist. Five subjects (8.3%, 5/60) experienced a disabling stroke within 30-days of the Phase 1 Procedure or Index Procedure. One subject (1.7%, 1/60) had

a disabling stroke after 30 days post the Index Procedure. Five subjects (8.3%, 5/60) experienced a non-disabling neurological event within 1 year of the Index Procedure.

Table 25 shows the CEC adjudicated neurological events across all timepoints.

Table 25. CEC Adjudication Details: Neurological Events

Subject	AE Description	Onset POD Index Procedure	Status (days to resolution)	Phase I Procedure Related	Device Related	Index Procedure Related	Disabling
103005	Subarachnoid Hemorrhage	987	Death	Not Related	Not Related	Not Related	N
103005	Acute/Early Subacute Embolic Infarcts in the Cerebrum and Cerebellum	35	Recovered/Resolved with Sequelae (44)	Possibly	Not Related	Possibly	Y
103007	Acute Cerebellar Embolic Infarcts	365	Recovered/Resolved (4)	Not Related	Not Related	Not Related	N
105008	Stroke	11	Recovered/Resolved (5)	Possibly	Possibly	Related	N
110012	Stroke	3	Recovered/Resolved with Sequelae (5)	Probably	Not Related	Not Related	Y
110015	Stroke	7	Recovered/Resolved (193)	Probably	Not Related	Probably	N
110018	Ischemic Stroke with Hemorrhagic Conversion	3	Death	Probably	Not Related	Probably	Y
111016	Stroke	9	Recovered/Resolved with Sequelae (45)	Not Related	Not Related	Related	N
111016	General Brain Infarctions	53	Recovered/Resolved with Sequelae (1)	Not Related	Not Related	Probably	N
115012	Post Phase 1 CVA	-211[1]	Recovered/Resolved with Sequelae (398)	Related	Not Applicable	Not Applicable	Y
116006	Basilar Artery Occlusion	530	Death	Not Related	Not Related	Not Related	N
120013	Left frontal Subarachnoid Hemorrhage	7	Recovered/Resolved with Sequelae (42)	Probably	Not Related	Probably	Y
126002	Intracranial Hemorrhage, Intraparenchymal, Large Acute	5	Death	Possibly	Not Related	Related	Y
130012	Watershed Stroke	16	Recovered/Resolved (2)	Probably	Not Related	Probably	N
[1] Occurred day of Phase 1 Procedure, subject completed Index Procedure 211 days after the disabling stroke							

New Dissections, Extension of Dissection

Four subjects had a new dissection event as described below:

- Two (3.3%, 2/60) were Retrograde Type A requiring conversion to open surgery within 92 days of the NEXUS procedure.
- The third (1.7%, 1/60) was a dSINE occurring 2-years after implantation with NEXUS and was treated with a TEVAR.
- One subject had a new dissection in the BCT identified by the core lab on the discharge CT. No reintervention was performed; subject remains stable at the 2-year follow-up visit.

Core lab identified one subject with proximal extension of the original dissection first observed at the 1-year follow-up (1.7%, 1/60). The extension remains stable at the 2-year follow-up. No reintervention was performed. No subjects experienced distal extension.

Open Conversions

Three Subjects had open conversions as described below:

- Two (3.3%, 2/60) were Retrograde Type A requiring conversion to open

surgery within 92 days of the NEXUS procedure.

- One (1.7%, 3/60) was an Endoleak (Type II – intercostal/lumbar endoleak) treated with a surgical conversion.

Additional information on these three occurrences can be found in **Table 31.**

Mortality Over Time

Subjects enrolled in the study were considered high risk for open surgical repair, and the mortality reflects a clinically complex and medically fragile population. **Table 26** summarizes all-cause mortality over time. Most subjects who died were classified as ASA Class IV, indicating severe systemic disease posing a constant threat to life. The most common causes of death were cardiac arrest or cardiac failure (10.0%, 6/60), followed by stroke (6.7%, 4/60).

All-cause mortality by follow-up period is shown below in **Table 26**. The CEC adjudicated relatedness and cause of death per Medical Dictionary for Regulatory Activities (MedDRA) coding are also provided (**Table 27**).

Table 26. Mortality

	Index Procedure (1)	30 Days (2-30)	6 Months (31-180)	1 Year (181-365)	2 Years (366-730)	3 Years (731-1095)	4 Years (1096-1460)	5 Years (>1460)	Total [1]
All-Cause Death	- (0/60)	8.3% (5/60) [2]	10.9% (6/55)	4.2% (2/48)	2.2% (1/46)	3.2% (1/31)	- (0/14)	- (0/9)	25.0% (15/60)
Lesion Related Mortality	- (0/60)	6.7% (4/60)	- (0/55)	- (0/48)	- (0/46)	- (0/31)	- (0/14)	- (0/9)	6.7% (4/60)

[1] Event percentages in this column may be an underestimation as 5-year follow-up is not complete

[2] One subject died post 30 days of Index Procedure but death was during original index hospitalization. It is included in the 6 Months window but is considered a primary endpoint event.

Table 27. All-Cause Mortality Over Time with CEC Adjudication

Subject ID	# Days Post-Index Procedure Death Occurred	Cause of Death	CEC Adjudicated Lesion Related Mortality (LRM)	CEC Adjudicated Phase 1 Relatedness	CEC Adjudicated Device Relatedness	CEC Adjudicated Procedure Relatedness
103002	14	Brain Injury	Yes	Not Related	Not Related	Related
103005	1056	Subarachnoid Hemorrhage	No	Not Related	Not Related	Not Related
103020	317	Cardiac Arrest	Unable to assess [1]	Not Related	Not Related	Not Related
105012	104	Cardiac Arrest	Unable to Assess	Not Related	Not Related	Not Related
110018	55	Ischemic Stroke	No	Probably	Not Related	Probably
111014	11	Hypertension	Yes	Not Related	Not Related	Related
111016	54	Cardiac Failure	No	Not Related	Not Related	Related
112011	310	Cardiac Arrest	No	Not Related	Not Related	Not Related
116006	531	Basilar Artery Occlusion	No	Not Related	Not Related	Not Related
116011	81	Unknown Cause	No	Not Related	Not Related	Not Related

Subject ID	# Days Post-Index Procedure Death Occurred	Cause of Death	CEC Adjudicated Lesion Related Mortality (LRM)	CEC Adjudicated Phase 1 Relatedness	CEC Adjudicated Device Relatedness	CEC Adjudicated Procedure Relatedness
120013	49	Cardiac Arrest	Unable to assess	Probably	Not Related	Probably
122010	14	Bradycardia	Yes	Probably	Not Related	Probably
124002	74	Unknown Cause	Unable to assess	Not Related	Not Related	Not Related
126002	6	Hemorrhage Intracranial	No	Possibly	Not Related	Related
130012	18	Cardiac Failure	Yes	Probably	Not Related	Probably

[1]The CEC adjudicated this event as "unable to assess" for LRM. An Independent Consulting Physician conducted a comprehensive review of all available imaging and source documentation. As stated in the death report, "In conclusion, the NEXUS device successfully sealed the proximal and distal extents of the aortic segment it was intended to treat. The false lumen subsequently recanalized, leading to re-pressurization and rupture. This event should not be classified as lesion-related mortality, as the source of rupture occurred outside the treatment zone of the NEXUS system."

Additional details on subjects with undetermined cause of death or where the lesion related mortality is adjudicated as "unable to assess" by the CEC are presented below:

- **Subject 103020:** The subject underwent an uneventful Phase 1 and Index Procedure apart from an additional BCT stent that was placed, and the subject was subsequently discharged. Follow-up CT scan on postoperative day 312 showed an occluded false lumen. On POD 317, the subject experienced acute left flank pain, and CT imaging revealed acute false lumen reperfusion from an entry in the peri-visceral aorta, beyond the aorta treated with the stent. The subject died rapidly from cardiac arrest.

- **Subject 105012:** The subject had a medical history significant for COPD, atrial fibrillation, first-degree heart block, chronic kidney disease stage 3, left ventricular ejection fraction of 32%, abnormal right ventricular function, and severe global hypokinesis of the left ventricle. The subject was discharged home after Index Procedure but presented acutely to the hospital on POD 87 with chest pain, which subsequently settled. Imaging at that time revealed expansion of the distal descending aorta, and a branched repair was planned. The subject died prior to this planned procedure on POD105, which was reported as a myocardial infarction.

- **Subject 120013:** The subject underwent an uneventful Phase 1 and Index Procedure. On postoperative day 7, the subject developed urinary retention and required catheterization. This was followed by Klebsiella sepsis complicated by pulseless electrical activity arrest and subsequent anoxic brain injury. The subject was discharged to long-term care on POD 26, experienced gradual deterioration, and received palliative care before dying on POD 49.

- **Subject 124002:** The subject was a 64-year-old female with a previously implanted surgical graft due to history of type A aortic dissection in November

2012, hypertension, deep vein thrombosis, asthma, and active smoking with a 50 pack-year history. Subject underwent an uneventful Index Procedure completed in 96 minutes and was discharged on POD 3. Subject was readmitted on POD 10 with a chest infection and again on postoperative day 29 with ground-glass lung changes on CT, along with multi-chamber cardiomegaly and pulmonary hypertension. Follow-up aortic CT on POD 38 was unremarkable. The subject death on POD 74 was reported with no further details available.

- **Subject 116011:** This subject was a 56-year-old male subject with an extensive medical history including peripheral vascular disease, a right axillary-femoral bypass that was subsequently explanted due to infection with residual sections remaining in place, an arteriovenous fistula, prior sternotomy for thoracic aortic dissection, end-stage renal disease on hemodialysis before receiving a renal transplant (requiring immunosuppression), and a history of mesenteric ischemia. The subject underwent an uneventful Index Procedure but developed urinary retention on POD 5, necessitating urinary catheter insertion, and was discharged on POD 6. He was readmitted on POD 11; CTA revealed a Type 2 endoleak originating from the left subclavian artery. On POD 28, the subject underwent left subclavian artery occlusion but subsequently developed esophagitis and gastritis. The subject required one additional treatment for the Type 2 endoleak, followed by a third intervention for what was suspected to be a Type III endoleak, though the Core Lab classified it as a Type 2 endoleak with the left subclavian artery as the source. On POD67, he was readmitted and was noted to have lost notable weight over the preceding six months. The subject died in a skilled nursing facility on POD 80, and no post-mortem examination was performed. Possible causes of death include chronic sepsis masked by immunosuppression, upper gastrointestinal bleeding, or aortic complications, though the latter seems less likely given the prolonged clinical deterioration.

Endoleaks

Table 28 provides the endoleaks by timepoint evaluated by the core lab. The most common endoleak was Type II and it was seen in five subjects (8.3%, 5/60). Six subjects had non-type II endoleaks (10.0%, 6/60). Two subjects (3.3%, 2/60) had Type 1b endoleaks involving thoracic aortic locations which were planned as a staged procedure to reduce the risk of Spinal Cord Ischemia (SCI). The majority of endoleaks were seen at the discharge or 30-day visit with many resolving spontaneously.

Table 29 provides the endoleaks by timepoint as assessed by the site. Site-reported endoleak rates were higher than those reported by the Core Laboratory. Site investigators were instructed to report endoleaks conservatively; if there was uncertainty regarding the presence of an endoleak, it was reported as an endoleak to ensure subject safety and close monitoring. In contrast, the Core Laboratory performed independent centralized image review using a predefined, standardized, and blinded adjudication process conducted by

experienced reviewers. These differences in reporting approach likely contributed to the higher rate of site-reported endoleaks compared with Core Laboratory assessments.

A total of 11 subjects (18.3%, 11/60) experienced core lab reported endoleaks over time . Of these 5.0% (3/60) resolved without intervention, and 3.3% (2/60) subjects expired with ongoing endoleaks, neither death was assessed as related to the endoleak.

Two subjects (103013, 124012) had reported endoleak with reintervention and aortic enlargement. Additional information can be found in the Aortic Enlargement section and **Table 31**.

A total of 30 subjects (50%) experience site reported endoleak across all timepoints. Out of these, 11.7% (7/60) underwent reintervention for a site reported endoleak, of which 85.7% (6/7) were performed using an endovascular approach. Within the first year, 5.0% (3/60) of subjects (115034, 116011, 100004) required reintervention for an endoleak.

Beyond the first year, the next reintervention for an endoleak occurred on POD806 due to a dSINE, which the core laboratory classified as a Type Ib endoleak. Additionally, two subjects underwent TEVAR reinterventions at approximately 3 and 4 years of follow-up, respectively. The reintervention at 4-years was performed to address an endoleak involving commercial (not NEXUS) stent grafts. These cases are summarized in **Table 31.** Additional Procedures Post Phase 1 Procedure and Reinterventions Post Index Procedure.

Table 28. Core Lab Reported Endoleaks

	Pre-Discharge	30-Day	6-Month	1-Year	2-Year	3-Year	4-Year	Total (Subjects) [1]
Subjects with Adequate Imaging	43	51	43	46	23	13	6	60
Subjects with Endoleak Ongoing in Window	11.6% (5/43)	13.7% (7/51)	11.6% (5/43)	2.2% (1/46)	13.0% (3/23)	0	16.7% (1/6)	18.3% (11/60)
New	11.6% (5/43)	5.9% (3/51)	2.3% (1/43)	0	4.3% (1/23)	0	16.7% (1/6)	-
Persistent	-	7.8% (4/51)	9.3% (4/43)	2.2% (1/46)	4.3% (1/23)	0	0	-
Type I	2.3% (1/43)	0	0	0	4.3% (1/23)	0	0	3.3% (2/60)
New	2.3% (1/43)	0	0	0	4.3% (1/23)	0	0	-
Type Ia	0	0	0	0	0	0	0	-
Type Ib	2.3% (1/43)	0	0	0	4.3% (1/23)	0	0	-
Persistent	-	0	0	0	0	0	0	-
Type II	7.0% (3/43)	7.8% (4/51)	9.3% (4/43)	2.2% (1/46)	4.3% (1/23)	0	0	8.3% (5/60)
New	7.0% (3/43)	2.0% (1/51)	2.3% (1/43)	0	0	0	0	-
Persistent	-	5.9% (3/51)	7.0% (3/43)	2.2% (1/46)	4.3% (1/23)	0	0	-

	Pre-Discharge	30-Day	6-Month	1-Year	2-Year	3-Year	4-Year	Total (Subjects) [1]
Type III	0	0	0	0	0	0	16.7% (1/6)	1.7% (1/60)
New	0	0	0	0	0	0	16.7% (1/6)	-
Type IIIa	0	0	0	0	0	0	16.7% (1/6)	-
Type IIIb	0	0	0	0	0	0	0	-
Persistent	-	0	0	0	0	0	0	-
Type IV	0	0	0	0	0	0	0	0
New	0	0	0	0	0	0	0	-
Type V	0	0	0	0	0	0	0	0
New	0	0	0	0	0	0	0	-
Undetermined	2.3% (1/43)	5.9% (3/51)	2.3% (1/43)	0	0	0	0	5.0% (3/60)
New	2.3% (1/43)	3.9% (2/51)	0	0	0	0	0	-
Persistent	-	2.0% (1/51)	2.3% (1/43)	0	0	0	0	-
Subjects with no Endoleak Ongoing in Window	88.3% (38/43)	86.3% (44/51)	88.4% (38/43)	97.6% (41/42)	86.9% (20/23)	100% (13/13))	83.3% (5/6)	81.6% (49/60)
[1] Event percentages in this column may be an underestimation as 5-year follow-up is not complete								

Table 29. Site Reported Endoleaks

	Pre-Discharge	30 Days	6 Months	1 Year	2 Years	3 Years	4 Years	Total [1]
Subjects with Adequate Imaging	45	55	45	43	23	11	3	60
Subjects with Endoleak Ongoing in Window	37.8% (17/45)	30.9% (17/55)	17.8% (8/45)	25.6% (11/43)	13.0% (3/23)	18.2% (2/11)	33.3% (1/3)	50.0% (30/60)
New	37.8% (17/45)	14.5% (8/55)	2.2% (1/45)	7.0% (3/43)	0	9.1% (1/11)	-0	-
Persistent	-	16.4% (9/55)	15.6% (7/45)	18.6% (8/43)	13.0% (3/23)	9.1% (1/11)	33.3% (1/3)	-
Type I	17.8% (8/45)	18.2% (10/55)	6.7% (3/45)	7.0% (3/43)	4.3% (1/23)	9.1% (1/11)	0	26.7% (16/60)
New	17.8% (8/45)	10.9% (6/55)	- (0/45)	4.7% (2/43)	0	0	0	-
Persistent	-	7.3% (4/55)	6.7% (3/45)	2.3% (1/43)	4.3% (1/23)	9.1% (1/11)	0	-
Type Ia	6.7% (3/45)	7.3% (4/55)	2.2% (1/45)	2.3% (1/43)	0	0	0	-
Type Ib	11.1% (5/45)	10.9% (6/55)	4.4% (2/45)	4.7% (2/43)	4.3% (1/23)	9.1% (1/11)	0	-
Type II	13.3% (6/45)	5.5% (3/55)	6.7% (3/45)	9.3% (4/43)	4.3% (1/23)	9.1% (1/11)	0	23.3% (14/60)
New	13.3% (6/45)	1.8% (1/55)	6.7% (3/45)	6.7% (3/45)	0	9.1% (1/11)	0	-
Persistent	-	3.6% (2/55)	0	0	4.3% (1/23)	0	0	-
Type III	4.4% (2/45)	5.5% (3/55)	0	2.3% (1/43)	0	0	33.3% (1/3)	8.3% (5/60)
New	4.4% (2/45)	3.6% (2/55)	0	0	0	0	33.3% (1/3)	-
Persistent	-	1.8% (1/55)	0	2.3% (1/43)	0	0	0	-
Type IIIa	4.4% (2/45)	5.5% (3/55)	0	2.3% (1/43)	0	0	33.3% (1/3)	-
Type IIIb	0	0	0	0	0	0	0	-
Type IV	0	0	0	0	0	0	0	0

	Pre-Discharge	30 Days	6 Months	1 Year	2 Years	3 Years	4 Years	Total [1]
New	0	0	0	0	0	0	0	-
Persistent	-	0	-0	0	0	0	0	-
Type Undetermined	2.2% (1/45)	1.8% (1/55)	4.4% (2/45)	4.7% (2/43)	4.3% (1/23)	0	0)	5.0% (3/60)
New	2.2% (1/45)	1.8% (1/55)	2.2% (1/45)	0	0	0	0	-
Persistent	-	0	2.2% (1/45)	4.7% (2/43)	4.3% (1/23)	0	0	-
Subjects with no Endoleak Ongoing in Window	62.2% (28/45)	69.1% (38/55)	82.2% (37/45)	74.4% (32/43)	87.0% (20/23)	81.8% (9/11)	66.7% (2/3)	43.3% (26/60)

[1] Event percentages in this column may be an underestimation as 5-year follow-up is not complete
Note: Site reported data is summarized per assigned visit, not study day.
Note: Subjects are included in the denominator if they had imaging available.
Note: Type V Endoleak was not an option for the site to select.

False Lumen Perfusion

Table 30 provides a summary of false lumen perfusion and false lumen status by follow-up period, as reported by the core lab. No cases of perfusion from the primary intimal tear were identified. At 30 days, three subjects (3/33; 9.1%) demonstrated FLP attributed to an aortic arch branch vessel. Among these subjects, one subject had perfusion from the LCC, two had perfusion from both the LCC and LSA. All three subjects also had concurrent perfusion from a distal entry tear.

Most subjects at 1-year (80.0%, 36/45) demonstrated FLP through a distal entry tear. This finding is consistent with baseline anatomy, as 80.4% of subjects (45/56) presented with dissections extending distally to Zone 9 or beyond, outside the treated segment, thereby providing a persistent potential source for false lumen perfusion.

By the 1-year follow-up window, all subjects demonstrated either partial thrombosis (57.8%, 26/45), complete thrombosis (40.0%, 18/45), or no longer had a visible false lumen (2.2%, 1/45) within the treated segment, yielding 100% (45/45) with favorable remodeling.

In the untreated distal aorta at 1-year 15.6% (7/45) of subjects exhibited a patent false lumen, consistent with expectations for chronic dissections extending beyond the treated segment.

It is important to note subjects may demonstrate FLP even when the perfused false lumen is located beyond the distal extent of the NEXUS stent graft. The NEXUS system is designed to seal the primary entry tear and protect the aortic arch wall; persistent perfusion in the distal descending thoracic aorta reflects underlying disease outside the treated segment.

Table 30. Core Lab Reported False Lumen Perfusion and Patency Over Time

	Pre-Discharge	30-Day	6-Month	1-Year	2-Year	3-Year	4-Year	Total [1]
Number of Subjects with Adequate Imaging	44	51	42	45	24	13	6	60
False Lumen Perfusion through Primary Intimal Tear	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
False Lumen Perfusion Proximal Aorta	1 (2.3%)	1 (2.0%)	-	1 (2.2%)	-	-	-	2
False Lumen Perfusion through a Distal Entry Tear	40 (90.9%)	35 (68.6%)	37 (88.1%)	33 (73.3%)	21 (87.5%)	10 (76.9%)	4 (66.7%)	50
False Lumen Perfusion through an Aortic Branch Vessel	39 (88.6%)	33 (64.7%)	35 (83.3%)	36 (80.0%)	19 (79.2%)	10 (76.9%)	4 (66.7%)	51
Through Aortic Arch Branch Vessel Only (Without Distal Entry Tear)[2]	0	0	0	0	0	0	0	0
Through Aortic Arch Branch Vessel and Distal Entry Tear[2]	11 (28.2%)	3 (9.1%)	2 (5.7%)	3 (8.3%)	3 (15.8%)	1 (10.0%)	0 (0.0%)	15
LSA		0	0	0	1	1	-	
LCC		1	1	1	1	0	-	
LCC + LSA		2	0	1	1	0	-	
Undetermined		0	1	1	0	0	-	
Through Non-Arch Aortic Branch Vessel[2]	23 (59.0%)	20 (60.6%)	20 (57.1%)	23 (63.9%)	11 (57.9%)	7 (70.0%)	3 (75.0%)	38
False Lumen Perfusion Undetermined	-	1 (2.0%)	-	-	-	-	-	1
False Lumen Status: Treated Segment								
No False Lumen	-	-	-	1 (2.2%)	1 (4.2%)	-	-	1
Patent	-	-	-	-	-	-	-	0
Partially Thrombosed	38 (86.4%)	36 (70.6%)	25 (59.5%)	26 (57.8%)	16 (66.7%)	8 (61.5%)	3 (50.0%)	49
Completely Thrombosed[3]	6 (13.6%)	15 (29.4%)	17 (40.5%)	18 (40.0%)	6 (25.0%)	5 (38.5%)	3 (50.0%)	34
False Lumen Status: Untreated Distal Aorta								
No False Lumen	1 (2.3%)	1 (2.0%)	2 (4.8%)	3 (6.7%)	1 (4.2%)	-	-	4
Patent	15 (34.1%)	13 (25.5%)	9 (21.4%)	7 (15.6%)	6 (25.0%)	4 (30.8%)	1 (16.7%)	23
Partially Thrombosed	27 (61.4%)	33 (64.7%)	29 (69.0%)	31 (68.9%)	14 (58.3%)	6 (46.2%)	5 (83.3%)	47
Completely Thrombosed	-	2 (3.9%)	2 (4.8%)	3 (6.7%)	-	2 (15.4%)	-	6
False Lumen Perfusion (New + Persistent)								
New	1 (2.3%)	1 (2.0%)	2 (4.8%)	6 (13.3%)	2 (8.3%)	2 (15.4%)	0 (0.0%)	13
Persistent	43 (97.7%)	39 (76.5%)	38 (90.5%)	37 (82.2%)	21 (87.5%)	10 (76.9%)	4 (66.7%)	51
New+Persistent	43 (97.7%)	39 (76.5%)	38 (90.5%)	37 (82.2%)	21 (87.5%)	10 (76.9%)	4 (66.7%)	51

[1] Event percentages in this column may be an underestimation as 5-year follow-up is not complete
Note: USFU images were reviewed by core lab and are reflected in the number of subjects with adequate imaging

Aortic Enlargement

Across all timepoints 11.7% (7/60) of subjects treated with NEXUS demonstrated aortic

diameter enlargement (more than 5 mm compared to 30-day) as assessed by the core lab. Four subjects (105001, 112011, 124012, 126001) had re-interventions for aortic enlargement within the first year (6.7%, 4/60). Six of the seven subjects with enlarging aortas had distal false lumen perfusion present (FLP). No aortic ruptures or unexplained sudden deaths were reported among these subjects. Additional details on these subjects are as follows:

- Subject 103007 (distal end of disease: Zone 9) had aortic enlargement observed at 1-year follow-up with distal FLP. On POD614 the subject had false lumen embolization using shape memory and ruby coils and Impede-FX embolization plug. Aortic enlargement continues at most recent 4-year follow-up.
- Subject 103013 (distal end of disease: Zone 11) had aortic enlargement observed at 2-year follow-up with distal FLP and unknown type endoleak per core lab. On POD 957 TEVAR (C-TAG) was placed. The next follow-up visit post endovascular reintervention has not yet happened.
- Subject 105001 (distal end of disease: Zone 9) had aortic enlargement observed at 6 months with distal FLP. On POD173 a TEVAR (NEXUS) was placed, POD419 a custom Fenestrated Endovascular Aortic Repair (FEVAR) was placed to extend, on POD706 Endovascular Aneurysm Repair (EVAR) to extend further and left renal and celiac stent extensions were performed. On POD1156 relining of left renal and celiac extensions, right iliac limb extension and embolization was performed. Next follow-up visit post recent reintervention has not yet happened.
- Subject 110003 (distal end of disease: Zone 11) had aortic enlargement observed at 2-years with distal FLP and distal stent graft-induced new entry (dSINE). TEVAR (C-TAG) placed and at the 4-year follow-up the aorta remains stable without further expansion.
- Subject 112011 (distal end of disease: Zone 11) had aortic enlargement observed at 1-year follow-up due to distal FLP. Prior to the 1-year follow-up the subject had a TAA repair with four-vessel branched endograft (TAMBE). At the time of the data cut, the 2-year visit had not yet occurred.
- Subject 124012 (distal end of disease: Zone 11) had a Type II endoleak reported at 6 months and aortic enlargement observed at 1 year follow-up. Prior to this visit, the subject had False Lumen (FL) embolization for Type II intercostal sources. The 2-year visit showed a continued increase in the aortic enlargement but no further action was taken.
- Subject 126001 (distal end of disease: Right Iliac) had aortic enlargement observed at 6 months. On POD 92 subject had a surgical conversion from a delayed retrograde type A. The 3-year scan showed a decrease in the aortic diameter compared to the 2-year scan.

Reinterventions

Through 12 months, 25% (15/60) of subjects underwent reintervention, of which 10% (6/60) were planned.

- 3 subjects (5.0%, 3/60) had a reintervention after the Phase 1 Procedure and prior to the Index Procedure. All involved neck exploration.
- 3 subjects (5.0%) had a reintervention for endoleaks
- 4 subjects (6.7%) had a reintervention for aortic enlargement
- 2 subjects (3.3%) had surgical conversions
- 6 (10%) subjects had planned re-interventions after being discharged from the Index Procedure. These include staged exclusion of the LSA or DE.

Reinterventions reported for the study subjects through all timepoints are described in **Table 31**.

Table 31. Additional Procedures Post Phase 1 Procedure and Reinterventions Post Index Procedure

Event	Subject ID	POD from Index Procedure	Comment
Acute Respiratory Distress Post Phase 1 Procedure	105027	-9 [1]	Acute respiratory distress post Phase 1 Procedure, emergent neck exploration performed. Index procedure occurred nine days later.
Left Neck Hematoma Post Phase 1 Procedure	103002	-5 [1]	Bilateral neck exploration and hematoma evacuation due to neck swelling and complaints of difficulty with swallowing and breathing. Index Procedure was performed five days later.
Left Neck Hematoma Post Phase 1 Procedure	122010	-3 [1]	Exploration of neck wounds of bypass surgery which didn't show evidence of active bleeding. Index Procedure was performed 3 days later.
Type A Retrograde Dissection	103002	2	Acute type A aortic dissection, underwent a surgical conversion with an aortic root and valve replacement, a two-vessel coronary artery bypass graft (left anterior descending & ramus intermedius) and ligation of the proximal LSA.
Planned Occlusion LSA	132002	13	LSA was not occluded at time of Phase 1 or Index Procedure as recommended by protocol. Principal Investigator (PI) preferred to stage placement of plug in LSA.
Endoleak	116011	15	LSA was not occluded at time of Phase 1 or Index Procedure as recommended by protocol.
		29	CTA taken two weeks later on showed continued endoleak coils were added to the LSA.
		39	Endoleak persisted 10 days later, site became concerned was possible Type III Endoleak instead of Type II endoleak. The site used a commercial graft to reline the NEXUS (TBE and C-TAG). Endoleak remained. Core Lab reported Endoleak as Type II with LSA as source.
Planned DE Extension	108006	43	PI preferred to stage the NEXUS distal extension from the index procedure.
Planned Occlusion LSA	129001	47	LSA was not occluded at time of Phase 1 or Index Procedure as recommended by protocol. PI preferred to stage coiling of LSA.
Planned DE Extension	122006	50	PI preferred to stage the NEXUS distal extension with knickerbocker from the index procedure.
Endoleak	115034	67	PI assessed a Type III endoleak and noted flow involving the carotid artery, false lumen of the LSA, and partially the vertebral artery; however, the relative contribution of each source was uncertain. Based on this assessment, a surgical conversion was

Event	Subject ID	POD from Index Procedure	Comment
			performed, which resolved the endoleak. The core laboratory reported this as a Type II endoleak with inflow from intercostal/lumbar vessels.
Planned DE Extension	130008	86	PI preferred to stage the NEXUS distal extension with knickerbocker from the index procedure.
Surgical Conversion	126001	92	Developed a subacute type A aortic dissection, underwent a surgical conversion with a 28mm Gelweave graft, continues in the study.
Aortic Enlargement		499	Left heart bypass and elective surgical repair of thoracoabdominal aortic aneurysm (TAA)
Aortic Enlargement	112011	99	Repair of thoracoabdominal aortic aneurysm using 4 vessel branched endograft (TAMBE)
Persistent FLP	116006	170	TEVAR (Valiant) placed due to false lumen perfusion not from primary entry tear and coil embolization in LSA. Site Reported event as resolved.
Aortic Enlargement	124012	172	Candy Plug used to embolize FL. Due to persistent FL perfusion with aneurysm growth.
Planned DE Extension, Aortic Enlargement and Commercial Graft Type IIIa Endoleak	105001	174	Planned TEVAR (NEXUS) Extension to treat ongoing thoracoabdominal aortic dissection
		419	Treat ongoing thoracoabdominal aortic dissection with custom four vessel FEVAR
		706	EVAR extension, left renal stent extension, celiac stent extension
		1156	Treat lumbar vessel Type II Endoleak and continued enlargement. Relining left renal, celiac extension, right iliac limb extension, right iliac limb coil embolization in the descending thoracic aorta
		1506	Type IIIa Endoleak of commercial (not NEXUS) device and Left Gastric Artery Aneurysm
Endoleak	100004	197	PI initially reported an unknown endoleak and later determined a possible Type III endoleak, prompting endovascular intervention (ballooning). The core laboratory reported a Type II endoleak with the LSA as the source.
Descending Thoracic Aorta – Enlargement	120012	301	Extension TEVAR (NEXUS) performed for descending thoracic aortic diameter measuring 5.1 cm. Site reported event as resolved.
Aortic Enlargement	103007	614	Persistent FL filling via multiple fenestrations with increased diameter of descending thoracic aorta. FL embolization using shape memory and ruby coils and Impede- FX embolization plug.
dSINE with Aortic Enlargement	110003	806	Stent graft induced tear in flap at the distal portion of treatment area with growth of the descending thoracic. Asymptomatic at this time. Re-intervention of an endograft extension (C-TAG) was completed. Note: Core Lab reported this as a Type Ib endoleak.
Endoleak with Aortic Enlargement	103013	957	CT showed unknown type endoleak and enlargement of the aortic arch. The patient underwent TEVAR (C-TAG) with retrograde plug placement into false lumen. Post-op CTA showed successful endoleak occlusion, stable residual dissection.
[1] Occurred after Phase 1 Procedure and Prior to Index Procedure			

6. Subgroup Analyses

Subgroup analyses of the co-primary device technical failure and clinical failure endpoints

were performed for the following subgroups: gender, subjects with an existing graft, and subjects receiving an extension device. Neither co-primary endpoint differed notably between any of the subgroups.

7. Pediatric Extrapolation
   Existing clinical data was not leveraged to support approval of a pediatric subject population in this premarket application.

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 118 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c) and (f). The information provided does not raise any questions about the reliability of the data.

XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

NEXUS is CE Marked and has been evaluated in a comprehensive European clinical program encompassing prospective feasibility studies and compassionate use, with follow-up extending to 5 years. A total of 28 subjects (17 aneurysms, 6 chronic dissections, 4 mixed etiology, 1 penetrating aortic ulcers (PAU)) with complex aortic arch pathology were included. Imaging follow-up compliance was approximately 80% at 30 days and 100% at 1 year in the feasibility study with robust follow-up maintained through 5 years. The clinical study included CT imaging assessed by an independent reviewer acting as a core lab, adverse event adjudication by an independent CEC, and monitoring to ensure data accuracy. The results for 28 subjects demonstrated 100% technical success, a 30-day mortality rate of 7.1% and a single additional death between 30 days and 1 year bringing the overall 1-year mortality rate to 10.7%. Rate of unplanned reintervention within the first year was 7.1%, and rate of disabling stroke, non-disabling stroke, conversion to open surgery, and device migration was 3.6% respectively. There were no reported cases of aneurysm rupture, stent graft occlusion, stent graft fracture or deformity, renal failure requiring dialysis, paraplegia, myocardial infarction, or new aortic dissection.

In addition, there is an ongoing post-market clinical study to collect standard of care clinical data of subjects treated with the NEXUS and the NEXUS Multi-Branch devices. The study includes 16 NEXUS subjects, 12 of whom have completed at least one year of follow-up. Clinical data is generated through CT imaging and assessed by an independent reviewer acting as a core lab, adverse event adjudication by an independent CEC, and monitoring to ensure data accuracy. The results demonstrated 100% technical success, no events of early mortality, and one subject experienced disabling stroke. In addition, no events of conversion to open surgery and no unanticipated surgical or interventional procedure to treat endoleak, occlusion, migration or loss of device integrity. There was one event of spinal cord ischemia (SCI). There were no reported

cases of aneurysm rupture, stent graft occlusion, stent graft fracture or deformity and renal failure requiring dialysis.

Finally, the NEXUS device remains under IDE investigation for use in treatment of high surgical risk subjects with aneurysms, PAUs and intramural hematomas. A total of 34 subjects have been treated (27 aneurysms and 7 PAUs) as of November 2025. Out of these, 100% (16/16) of the eligible aneurysm subjects and 100% of the eligible PAU subjects (4/4) have completed their 1-year visit. Analysis of the baseline characteristics (age, comorbidities, BMI etc.) indicate that the aneurysm cohort exhibited a distinctly higher-risk clinical profile, which may contribute to increased mortality observed in this group. Targeted risk mitigations have been identified and implemented in the clinical study protocol and training materials. In terms of outcomes available to date, a total of 7 subjects (6 aneurysms and 1 PAU) reported device technical failure at the end of index procedure. These events were primarily associated with need for unplanned BCT stenting with a commercial device (n=5). In terms of clinical events reported within 30 days of Phase 1 procedure and within 30-days of index procedure, 7 all cause mortalities (6 aneurysms and 1 PAU) were reported, out of which 2 were adjudicated by the CEC as lesion related mortalities (1 aneurysm and 1 PAU). Additionally, 2 disabling strokes (1 aneurysm and 1 PAU) and 1 new dissection event (aneurysm subject) have been reported within 30 days of index procedure. No cases of renal failure, aortic rupture, device occlusion, failed exclusion of the primary entry tear, or reintervention for device-related issues were reported through 30 days.

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

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

XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety and Effectiveness Conclusions

The study was successful in meeting the Performance Goals for both co-primary endpoints, device technical failure and clinical failure through 30 days (i.e., PGs of 30% and 35%, respectively). The device technical failure rate through 30 days was 5.0% (3/60), and contributing events included failure to deliver, track, or deploy (3.3%, 2/60), and one surgical conversion (1.7%). The clinical failure rate through 30 days was 15.0% (9/60), and contributing events included death (10.0%, 6/60), disabling stroke (8.3%, 5/60; including two fatal hemorrhagic events), and one case of a new fatal retrograde Type A aortic dissection (1.7%, 1/60). No subjects experienced permanent paralysis, renal failure, or aortic rupture. No reinterventions were performed for site or core lab reported Type I, Type III, or Type IV endoleaks, device integrity concerns, or migration through 30 days.

Through the 1-year analysis window, no additional mortalities occurred that were definitively adjudicated as "lesion related" by the CEC. However, there were four additional mortalities

reported beyond 30 days, which resulted in an overall rate of 21.7% (13/60) mortality through 1 year. There was one disabling stroke (10.0%, 6/60), and one new dissection observed after 30 days which brings the total rate of these events to 10% (6/60) and 3.3% (2/60), respectively, through 1 year. There were two additional surgical conversions, resulting in a 1-year surgical conversion rate of 5.0% (3/60). Additionally, there were 3 subjects who underwent reintervention for site reported Type I and III endoleaks beyond 30 days, bringing the overall rate of reinterventions for Type I, III and IV endoleaks to 5% through 1 year. There were no reinterventions for device occlusion, migration, stenosis, and no cases of failed exclusion of the primary entry tear.

Based on the outcomes presented above, there is reasonable assurance of the safety and effectiveness of the NEXUS Aortic Arch Stent Graft System when used for treatment of chronic dissection subjects who are at high risk of open repair.

B. 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 study was successful in meeting its performance goal for the co-primary endpoints. After an initial surgical debranching procedure, NEXUS facilitates endovascular repair of chronic dissections while maintaining blood flow to the brachiocephalic artery. The study demonstrated ability of the device to exclude the primary entry tear in 100% of the subjects with no reports of patency loss, migration, aortic rupture and low rates of new dissection events and core lab reported endoleaks through 1 year.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. These risks include all cause and lesion related mortality (21.7% and 6.4%; through 1 year), disabling stroke (10%; through 1 year), and unplanned reintervention (overall rate of 21.7% (13/60) through 1 year). There were also risks identified relating to the Phase 1 procedure which include adverse events such as death in 1.7% (1/60) subjects as well as disabling stroke in 1.7% (1/60) subjects. There were important learnings from the clinical study that have resulted in risk mitigation recommendations implemented in the labeling and physician training (e.g., the importance of confirming BCT length post phase 1, allowing adequate recovery time between Phase 1 and the Index Procedure).

Additional factors to be considered in determining probable risks and benefits for the NEXUS® Aortic Arch Stent Graft System included:

- absence of full 5-year subject follow-up data

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

In conclusion, given the available information above, the data support that for endovascular repair of chronic dissections in high-risk surgical candidates, the probable benefits outweigh the probable risks.

C. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the device when used in accordance with the indications for use.

The clinical study met the pre-specified performance goal for safety and effectiveness. Therefore, it is reasonable to conclude that the benefits of use of the device for the indicated population outweigh the risk of illness or injury when used as indicated in accordance with the IFU.

XV. CDRH DECISION

CDRH issued an approval order on April 2, 2026. The final clinical conditions of approval cited in the approval order are described below.

1. **Clinical Update**: Endospan has agreed to provide a Clinical Update to physician users at least annually. At a minimum, this update will include, for the IDE and Post-Approval studies, respectively, a summary of the number of patients for whom data are available, with the rates of mortality (device-and lesion-related), stroke, paraplegia / paraparesis, aortic enlargement in the region encompassed by the initial lesion, aortic rupture, endoleaks, new dissections, loss of device integrity, device migration, loss of aortic / aortic branch patency, reinterventions, and technical success. Any adverse events associated with the Phase 1 procedure are also to be reported separately. Reasons for secondary interventions and conversion to open surgery as well as causes of lesion-related death and rupture are to be described. Additional relevant information from the training program and commercial experience within and outside the United States is also to be included. A summary of any explant analysis findings is to be included. The clinical update for physician users and the information supporting the updates must be provided in the Annual Report.

2. **Continued Follow-up of the IDE Study Subjects**: This study is a non-randomized, multicenter, prospective study that consists of continued follow-up of all chronic dissection subjects from the IDE Pivotal Study. A total of 60 subjects were enrolled in the Primary Arm and eligible for analysis in the pivotal study. The remaining subjects will be followed annually for 5 years. Clinical endpoints include assessment of the following events through all follow-up intervals: all-cause mortality, lesion related mortality, rupture within or adjacent to the treated segment, neurological events, paralysis/paraplegia, renal failure, development of new dissections proximal or distal to the treatment zone (unintentional rupture of the dissection septum, false lumen patency and false lumen perfusion source), aortic enlargement,

endoleaks, migration, patency related events, conversion to open repair, secondary procedures in the treated aorta and branch vessels, fistula formation, loss of stent graft integrity and new ischemia. These endpoints will be analyzed descriptively.

3. **NEXUS New Enrollment Post Approval Study**: This is a prospective, multi-center, single-arm post-market study. The objective of the study is to evaluate long-term real-world safety and effectiveness of the Nexus device and to assess adequacy of the training program. The study will prospectively enroll a minimum of 135 subjects treated with NEXUS device at up to 60 sites globally. A minimum of 30 US sites will participate in the study and a minimum of 100 subjects will be enrolled in the US sites. A minimum of 100 chronic dissection high surgical risk subjects will be enrolled, with at least 60 subjects evaluable at 5 years post-implantation. A minimum of 20 new US sites will participate in the study and enroll a minimum of 40 US subjects. Follow-up will occur at 1 month, 6 months, 1 year, and yearly thereafter through 10 years from the index procedure. Two co-primary endpoints will be evaluated in the study 1) Device Technical Failure, evaluated through 30 days, is a composite of the following events: failure to accurately deliver, track and deploy all required endovascular device components at the intended implantation site and failure to retrieve the device delivery systems without the need for unplanned additional procedures, device occlusion, failed exclusion of primary entry tear, additional unanticipated surgical or interventional procedures related to the device or procedure, to prevent life threatening or permanent disabling events and 2) Clinical Failure which is a composite of the following MAEs (evaluated through 30-Day of Phase 1 Procedure and 30-Day of Index Procedure): lesion related mortality, disabling stoke, permanent paralysis/paraplegia, renal failure, aortic rupture and development of new dissection. Individual elements of the co-primary endpoints and all device and procedure related serious adverse events will be evaluated at all subsequent follow-up intervals. Other endpoints such as all-cause mortality, neurological events, new dissections, as defined in the protocol, will be collected and reported at each follow-up time point. Outcomes will be reported using descriptive statistics. Core lab, Clinical Events Committee, and Data Safety Monitoring Board will be utilized in the study, at least through 5 years. A subset analysis of select outcomes will be conducted to assess whether the training program is adequate to support the safe use of Nexus in the real-world. The results of this subgroup analysis, as well as learnings and any resulting modifications to the training program will be included in the post approval study reports.

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

XVI. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.