# SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

## I. GENERAL INFORMATION

| | |
|---|---|
| Device Generic Name: | Venous Stent |
| Device Trade Name: | Duo Venous Stent System |
| Device Procode: | QAN |
| Applicant's Name and Address: | Vesper Medical, Inc<br>1285 Drummers Lane, Suite 105<br>Wayne, PA 19087 |
| Date(s) of Panel Recommendation: | None |
| Premarket Approval Application (PMA) Number: | P230021 |
| Date of FDA Notice of Approval: | TBD |

## II. INDICATIONS FOR USE

The Duo Venous Stent System is intended for use in the iliofemoral veins for the treatment of symptomatic venous outflow obstruction. The Duo Hybrid is intended to be used in the iliac vein at the confluence of the inferior vena cava only. The Duo Extend is intended for use in the common iliac and common femoral veins.

## III. CONTRAINDICATIONS

The Duo Venous Stent System is contraindicated for the following:

1. Patients with a known hypersensitivity to nickel-titanium alloy (Nitinol).
2. Patients unable to receive standard medication used for interventional procedures including anticoagulants, contrast agents and antiplatelet therapy.
3. Patients who are judged to have a lesion that prevents complete inflation of a balloon dilation catheter or proper placement of the stent or the stent delivery system.
4. Tortuous vascular anatomy significant enough to prevent safe introduction and passage of the device.
5. Duo Hybrid jugular or contralateral vascular access.

## IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Duo Venous Stent System Instructions for Use.

## V. DEVICE DESCRIPTION

The Duo Venous Stent System consists of a portfolio of self-expanding venous stent configurations mounted on disposable delivery systems designed for improving luminal diameter in symptomatic venous outflow obstructions. The portfolio approach includes delivery systems with either a hybrid venous stent implant (Duo Hybrid Stent) or an extension venous stent implant (Duo Extend Stent), enabling the clinician to customize treatment in the iliofemoral venous anatomy based on disease patterns and severity. The Duo Hybrid Stent is designed with varying mechanical characteristics such as radial force/crush resistance and flexibility along its length to target the variable dynamic loading conditions in the iliofemoral venous system related to the treatment of disease states including non-thrombotic iliac vein compression, May-Thurner syndrome, deep venous thrombosis, and post-thrombotic venous occlusion. The Duo Extend Stent consists of a highly flexible region with inflow reinforcement at both ends. The Duo Hybrid Stent can be used independently or in conjunction with the Duo Extend Stent to personalize the treatment region.

The Duo Hybrid Stent and Duo Extend Stents are loaded in either a Pin/Pull or Triaxial Handle delivery system. **Figure 1** below provides an overview of the Duo Venous Stent System (Pin/Pull).

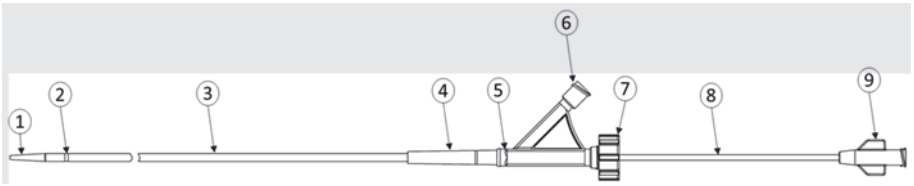


**Figure 1.** ***Duo Venous Stent System (Pin/Pull)***

The delivery catheter has an effective length of either 90cm or 120cm. The Outer Braided Sheath (3), which constrains the Stent implant, is bonded proximally to the Bifurcation Luer (5) within the Transition sleeve (4). The Hemostatic Valve (7) is integrated proximally to the Bifurcation Luer. The Inner Core Shaft (8) slides within the Hemostatic Valve. A soft, tapered Distal Tip (1) is bonded to the distal end of the Inner Core Shaft for ease of advancement in the blood vessel. Constrained within the Outer Braided Sheath the self-expanding Stent implant is positioned on the Inner Core between two radiopaque (RO) Distal Inner Core Markers. A radiopaque Target Band (2) is located on the distal end of the Outer Braided Sheath.

The catheter is flushed prior to the procedure through the side port (6) of the Bifurcation Luer and the Guidewire Port (9). Stent implant positioning is achieved prior to deployment by using the RO Markers on the Stent implant (**Figure 3** and **Figure 4**) and the Target Band on the outer sheath. During Stent implant deployment, the Hemostatic Valve is unlocked by rotating the valve counterclockwise. The Stent implant is unsheathed by pinning the Proximal Inner Core Shaft and pulling back on the outer sheath.

**Figure 2** below provides an overview of the Duo Venous Stent System (Triaxial Handle).

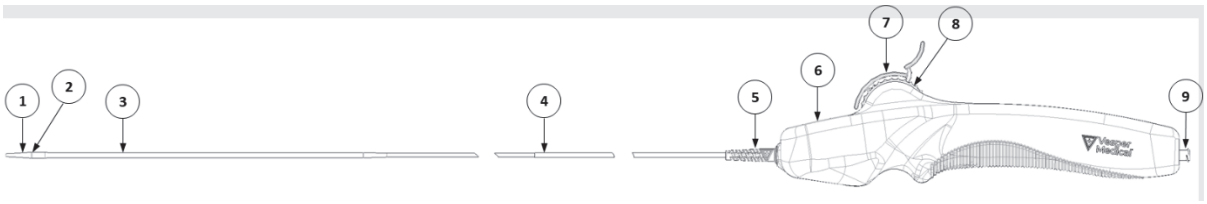


**Figure 2.** ***Duo Venous Stent System (Triaxial Handle)***

The Triaxial, over-the-wire delivery catheter has an effective length of either 90cm or 120cm. The Inner Core Shaft (2) contains the Guidewire Lumen designed for compatibility with a 0.035-inch guidewire which extends through the entire length of the Triaxial Delivery System and is bonded to the Luer hub (9) at the proximal end of the system that is fixed within the Handle Body (6). A soft, tapered Distal Tip (1) is bonded to the distal end of the Inner Core Shaft. The Outer Braided Sheath (3), which constrains the Stent implant, translates over the Inner Core Shaft (2), and is coupled to the deployment Thumbwheel (8) within the Handle body (6). A third Triaxial Sleeve (4) is fixed to the Handle Body (6) via the Strain Relief (5) to prevent unintended movement of the delivery system during Stent Deployment.

Constrained within the Outer Braided Sheath, the self-expanding Stent implant is positioned on the Inner Core between two radiopaque (RO) Distal Inner Core Markers. The catheter is flushed prior to the procedure through the Luer Hub (9). Prior to deployment, the Thumbwheel Safety Lock (7) must be removed and discarded. Stent implant positioning is achieved prior to deployment by using the RO Markers on the Inner Core Shaft and Stent implant (**Figure 3** and **Figure 4**). Deployment of the stent is initiated by rotating the thumbwheel in the proximal direction.

**Figure 3** and **Figure 4** below provide an overview of the Duo Hybrid Stent and Duo Extend Stent, respectively.

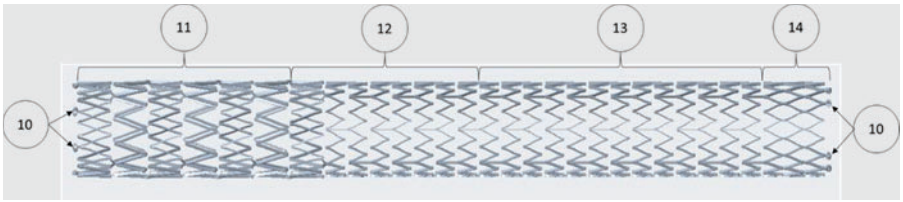


**Figure 3.** ***Duo Hybrid Stent***

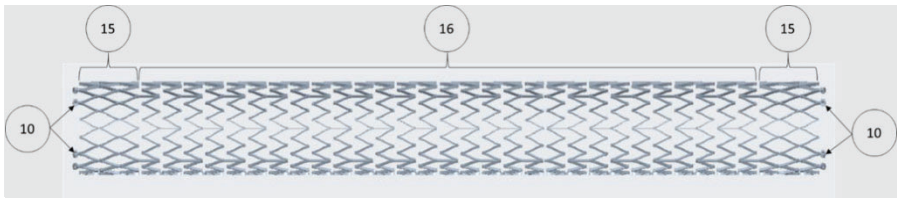


**Figure 4.** ***Duo Extend Stent***

The self-expanding Nitinol (nickel-titanium) Duo Hybrid Stent is designed with a "High Crush Resistance" segment (11) at the cranial end, followed by a "Transition" segment

(12) that transitions into a "Highly Flexible" segment (13). The caudal end of the Duo Hybrid Stent is designed with inflow reinforcement (14). Both the cranial and caudal ends of the Duo Hybrid Stent include four gold radiopaque markers (10) per end.

The self-expanding Nitinol (nickel-titanium) Duo Extend Stent is designed with a "Highly Flexible" (16) body with inflow reinforcement (15) on both ends. Both the cranial and caudal ends of the Duo Extend stent include four gold radiopaque markers (10) per end.

The Duo Venous Stent System device portfolio is provided in **Table 1**.

**Table 1. Duo Venous Stent System Configurations**

| Stent Type | Stent Diameter | Stent Lengths Available | Delivery System/Size |
|---|---|---|---|
| Duo Hybrid Stent | 12mm | 60mm, 80mm, 100mm, 120mm, 140mm, 160mm | 9F Pin/Pull or Triaxial Handle |
| | 14mm | | |
| | 16mm | | 10F Pin/Pull or Triaxial Handle |
| | 18mm | | |
| Duo Extend Stent | 12mm | 40mm, 60mm, 80mm, 100mm, 120mm, 140mm | 9F Pin/Pull or Triaxial Handle |
| | 14mm | | |
| | 16mm | | 10F Pin/Pull or Triaxial Handle |

## VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for treating symptomatic venous outflow obstructions. Some of these options are as listed below:

- Non-invasive Treatment Therapies – compression stockings, pneumatic compression therapy, or direct oral anticoagulation.
- Minimally Invasive Treatment Options – Percutaneous transluminal angioplasty (PTA) and stent placement. Thrombolysis (systemic, catheter directed or pharmaco-mechanical) may also be performed adjunctively.
- Surgical Treatment Options – Endophlebectomy, crossover vein bypass, and surgical bypass with graft, all with or without arteriovenous (A/V) fistula.

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

## VII. MARKETING HISTORY

The Duo Venous Stent System has not been marketed in the United States or any foreign country.

## VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with intravascular stent implantation.

- Access failure or abrupt closure
- Allergic / anaphylactoid reaction to anticoagulant and/or antithrombotic therapy or contrast medium
- Allergic reaction to Nitinol
- Amputation
- Aneurysm
- Angina / coronary ischemia / myocardial infarction
- Arrhythmia
- Arteriovenous fistula
- Death
- Embolism
- Emergent repeat hospital intervention
- Extravasation
- Fever
- Gastrointestinal bleed from anticoagulation / antiplatelet medication
- Hematoma / hemorrhage
- Hypotension / hypertension
- Incorrect positioning of the stent requiring further stenting or surgery
- Intimal Injury / dissection
- Ischemia / infarction of tissue / organ
- Infection / abscess at insertion site
- Inflammation
- Malposition of stent
- Multi-organ failure
- Open surgical repair
- Pain
- Procedure Delay
- Pulmonary Embolism
- Pseudoaneurysm
- Renal insufficiency or failure
- Respiratory distress or failure
- Restenosis
- Septicemia / bacteremia (sepsis)
- Stent implant fracture
- Stent implant migration (device moves over time)

- Trauma to adjacent structures
- Vasospasm
- Venous occlusion/thrombosis, remote from puncture site
- Venous occlusion/thrombosis, near puncture site
- Venous occlusion/restenosis of the treated vessel
- Vessel perforation/rupture

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

## IX. SUMMARY OF NONCLINICAL STUDIES

### A. Biocompatibility

The Duo Venous Stent System biocompatibility testing requirements were determined and conducted based on the nature and duration of patient contact per ISO 10993-1, titled "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing within a risk management process", and the FDA guidance on biocompatibility, titled 'Use of International Standard ISO 10993-1, "Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process'. Per the guidelines of ISO 10993-1, the delivery catheter portion (both Pin/Pull and Triaxial Handle) of the Duo Venous Stent System is classified as an external communicating device with limited contact duration (<24 hours). The Duo Stent portion of the final system is classified as an implant device with permanent contact duration (>30 days).

Biocompatibility testing demonstrates that the Duo Stent and both the Delivery Systems are biocompatible. The tests summarized in **Table 2** were conducted in support of both the Duo Stent and the Delivery System (Pin/Pull and Triaxial Handle) and passed all requirements.

**Table 2. Duo Venous Stent System Biocompatibility Test Summary**

| Biologic Effect | Test Name / Description | Implant | Delivery System | | Results |
|---|---|---|---|---|---|
| | | | Pin/Pull | Triaxial Handle | |
| Cytotoxicity | ISO MEM Elution Assay w/ L-929 Mouse Fibroblast Cells | X | X | X | Non-cytotoxic |
| Sensitization | ISO Guinea Pig Maximization Sensitization | X | X | X | Non-sensitizing |
| Intracutaneous Reactivity | ISO Intracutaneous Reactivity Test | X | X | X | Non-irritating |
| Systemic toxicity (acute) | ISO Acute Systemic Injection Test | X | X | X | Non-toxic |
| Material Mediated Pyrogenicity | USP Rabbit Pyrogen Study, Material Mediated | X | X | X | Non-pyrogenic |

| Biologic Effect | Test Name / Description | Implant | Delivery System | | Results |
|---|---|---|---|---|---|
| | | | Pin/Pull | Triaxial Handle | |
| Genotoxicity | ISO Bacterial Mutagenicity Test – AMES Assay | X | X | N/A | Non-mutagenic |
| | Mouse Lymphoma Assay | X | N/A | X | |
| Implantation | Animal Studies to Evaluate the Duo Venous Stent System in an Ovine Model | X | N/A | N/A | See Section IX.C for additional information |
| Hemocompatibility | ASTM Hemolysis Assay, Direct and Indirect Contact Method | X | X | X | Non-hemolytic |
| | SC5b-9 Complement Activation Assay | X | X | X | Not a complement activator |
| | Thrombogenicity as evaluated in Animal Studies to Evaluate the Duo Venous Stent System in an Ovine Model | X | X | X | Thromboresistant |

## B. Laboratory Studies

In vitro bench testing to assess the safety and effectiveness of the Duo Venous Stent System was conducted based on Vesper Medical's Quality System design control requirements and is consistent with FDA Guidance, Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, April 18, 2010, and Select Updates for Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, August 15, 2015. The relevant in vitro tests outlined in the guidance document and included in support of the Duo Venous Stent System are summarized in **Table 3** and **Table 4**. Unless otherwise specified, all test units were 2x sterilized using a validated Ethylene Oxide sterilization process.

**Table 3. Duo Venous Stent System - Bench Testing**

| Test | Purpose | Acceptance Criteria | Results/Conclusion |
|---|---|---|---|
| **Material Characterization** | | | |
| Material Composition (Duo Stent) | To verify that the Duo Stent materials conform to the chemical composition requirements of ASTM F2063 (nitinol), and ASTM B562 (gold) | The Duo Stent materials (nitinol and gold) must meet ASTM F2063 and ASTM B562 specifications | Pass |
| Material Composition (Delivery System – Pin/Pull & Triaxial Handle) | To verify the material composition of the delivery system | All materials and components must meet specifications | Pass |
| Shape Memory & Elasticity | To verify the transition temperature of the nitinol | Duo Stents shall have an active Austenite finish temperature in the range of 19°C ± 5°C | Pass |
| Corrosion Resistance | To evaluate the susceptibility of the Duo Stent material to corrosion, including pitting and crevice, fretting for overlapped Duo Stents implants. | Fretting Corrosion<br>Nickel release from the Nitinol Duo Stent less than the Permitted Daily Dose (PDD) derived from the ICH Guideline Q3D: Guideline for Elemental Impurities | Pass |
| | | Pitting and Crevice Corrosion<br>The implant shall have a breakdown potential ≥ 600mV. | Pass |
| **Implant Dimensional and Functional Attributes** | | | |
| Diameter & Length Verification | To verify the Duo stent dimensions post-deployment | The diameter and length should meet the labeled specifications. | The acceptance criteria were met. |
| Percent Surface Area of the Implant | To determine the Duo Stent surface area that contacts the vessel | The percent surface area was calculated for characterization only. | Percent Surface area was between 11.6% – 25.1%. |
| Foreshortening | To characterize foreshortening of the Duo Stents. | The implant shall not foreshorten more than 10% from the crimped diameter to the unconstrained diameter. | All test articles passed the pre-defined acceptance criteria for percent foreshortening of ≤ 10% |
| Stent Integrity | To report any defects on the deployed Duo Stents. | Duo Stent should be free from unacceptable scratches, fractures, and permanent set, following deployment in a simulated use model and exposure to external test deformations | Pass |

| Test | Purpose | Acceptance Criteria | Results/Conclusion |
|---|---|---|---|
| Radial Outward Force | To characterize the radial outward force of self-expanding stents | Duo Stents should meet requirements of radial outward force for each treatment diameter.<br>• Chronic outward force ≥ 0.25 N/mm for intended treatment range<br>• Radial resistive force ≤ 2.0N/mm for intended treatment range<br>• Implant recovers to original shape and size after application of radial force loads | Pass |
| Mechanical Properties | To characterize the mechanical properties of stent raw materials as inputs to stress/strain analysis. | N/A - characterization only | N/A - characterization only |
| Stress/strain and Fatigue Analysis | To characterize the stress/strains that the Duo Stent will experience within the intended vasculature to support fatigue analysis. To evaluate the device durability based on results of the stress and strain analysis | The safety factor determined by the fatigue analysis must be equal to or greater than 1.0 for all fatigue loads. | The acceptance criterion was met |
| Accelerated Durability Testing | To evaluate Duo Stent structural durability under physiologically relevant loading conditions | No strut fractures of Type III, IV, or V at 1-year and 10 years of simulated use. | The acceptance criterion was met |
| MRI Safety and Compatibility | To evaluate the MRI safety and compatibility of the Duo Stent | For characterization purposes only, the conditions under which the device can be safely scanned are provided in the product labeling. | The implanted single and overlapped Duo Stents are "MR Conditional" to 1.5 and 3 Tesla. |
| Radiopacity | To evaluate the radiopacity of the Duo Stent | The Duo Stent must be visible under fluoroscopy. | The radiopaque design features of the Duo Stent were adequate for base-line delivery, deployment, and identification under fluoroscopy |
| Crush Resistance | To demonstrate the ability of the Duo Stent to recover its desired size and shape after application and removal of external loads, deformations, or both. | Following an acute crush event and load release, the implant diameter must meet diametrical specification. | The acceptance criterion was met. |

| Test | Purpose | Acceptance Criteria | Results/Conclusion |
|---|---|---|---|
| Kink Resistance | To evaluate the potential for kink and/or permanent deformation of the Duo Stent when exposed to bending deformations. | Test samples should meet following pre-defined acceptance criteria:<br>• Stent does not kink when subjected to a 180° bend around a radius equal to 70mm for the "High Crush Segment" and 30mm for the "Flexible Segment.".<br>• Implant should recover to its original shape and size after testing. | The acceptance criterion was met. |

**Table 4. Duo Venous Stent System - Delivery System Bench Testing**

<table>
<tr><th rowspan="2">Test</th><th rowspan="2">Purpose</th><th rowspan="2">Acceptance Criteria</th><th colspan="2">Results/Conclusions</th></tr>
<tr><th>Pin/Pull Delivery System</th><th>Triaxial Handle Delivery System</th></tr>
<tr><td>Dimensional Verification</td><td>To verify the key dimensions of each delivery system</td><td>The delivery system must meet the relevant design specifications:<br><br>Pin/Pull and Triaxial Handle System<br>• Delivery catheter effective length: 47.24" ± 0.39" (120cm ± 1cm) or 35.43" ± 0.39" (90cm ± 1cm)<br><br>• Delivery Catheter minimum inner diameter of 0.0365" (.94mm) and compatible with a standard 0.035" guidewire.<br><br>• Maximum outer diameter of 0.122" (3.09mm) and compatible with a standard 9Fr introducer sheath or 0.136" (3.46mm) and compatible with a standard 10Fr introducer sheath.</td><td>Pass</td><td>Pass</td></tr>
<tr><td>Delivery, Deployment and Retraction</td><td>To demonstrate that the delivery systems can safely and reliably deliver the Duo Stent to the intended location</td><td>The Duo Stents must be able to be delivered to the target zone with no anomalies or damage upon deployment and delivery system withdrawal.<br><br><table><tr><th>Deployment:</th><th>Force</th><th>Accuracy</th></tr><tr><td>Pin/Pull</td><td><8lbf</td><td>±4mm</td></tr><tr><td>Triaxial</td><td><6lbf</td><td>±3mm</td></tr></table></td><td>Pass</td><td>Pass</td></tr>
<tr><td>Catheter Bond Strength</td><td>To verify the bond strength of the delivery system bond joints for the intended use.</td><td>Pin/Pull System<br><table><tr><th>Bond</th><th>Acceptance Criteria</th></tr><tr><td>RO Pusher</td><td></td></tr></table></td><td>Pass</td><td>Pass</td></tr>
</table>

<table>
<tr><th rowspan="2">Test</th><th rowspan="2">Purpose</th><th rowspan="2">Acceptance Criteria</th><th colspan="2">Results/Conclusions</th></tr>
<tr><th>Pin/Pull Delivery System</th><th>Triaxial Handle Delivery System</th></tr>
<tr><td></td><td></td><td>
<table>
<tr><td>Braided Shaft to Y-Connector</td><td>≥8.8lbf (39.2N)</td></tr>
<tr><td>SS Shaft to Inner Core & Luer Fitting</td><td></td></tr>
</table>
Triaxial Handle System
<table>
<tr><th>Bond</th><th>Acceptance Criteria</th></tr>
<tr><td>RO Pusher</td><td rowspan="6">≥7.25lbf (32.2N)</td></tr>
<tr><td>Anchor Cleat to Outer Sheath</td></tr>
<tr><td>Snap Connector to Drive Belt and Outer Sheath</td></tr>
<tr><td>SS Shaft to Luer Fitting</td></tr>
<tr><td>Inner Core to SS Shaft</td></tr>
<tr><td>Thumbwheel</td></tr>
<tr><td>PEEK to Strain Relief</td><td>≥5lbf (22.2N)</td></tr>
</table>
</td><td></td><td></td></tr>
<tr><td>Tip Pull Test</td><td>To determine the tensile force that will separate the distal tip from the catheter.</td><td>Bond Strength ≥ 5lbf (22.2N).</td><td>Pass</td><td>Pass</td></tr>
<tr><td>Flexibility and Kink Test</td><td>To verify that the Duo Stent delivery system will not kink at a worst-case bend radius that is appropriate for the intended anatomy</td><td>• Delivery catheter shall not kink, suffer any structural damage and successfully deploy implants when subject to a minimum bend radius of 0.98” (25mm) in a simulated anatomical model.<br><br>• The Distal Tip shall not damage the mock vessel in any way.</td><td>Pass</td><td>Pass</td></tr>
<tr><td>Torque Strength</td><td>To evaluate the torque strength of the delivery systems when the distal tip is not free to rotate.</td><td>Delivery system must withstand any physical or mechanical damage and successfully deploy the implant when the proximal end is subject to one full twist rotation (360°) about its center axis, in either the clockwise or counterclockwise direction with the distal end restrained.</td><td>Pass</td><td>Pass</td></tr>
</table>

## C. Animal Studies

Two GLP animal studies were performed to evaluate the safety of the Duo Venous Stent System in non-diseased ovine, femoral, and iliac veins. This includes a 180-day study

focused on Duo Venous Stent System (Pin/Pull) safety and performance and an acute study of the Duo Venous Stent System (Triaxial Handle). These animal studies are summarized in **Table 5**.

**Table 5. Duo Venous Stent System Animal Study Summary**

| | |
|---|---|
| **Study** | A GLP 180-day Animal Study to Evaluate the Duo Venous Stent System in an ovine model |
| **Purpose** | To evaluate the performance and safety of the Duo Venous Stent System (Pin/Pull) in the iliofemoral veins of an Ovine model. |
| **Methods** | • 18 sheep (ovis aries) implanted with Duo stents<br>• Equally divided in three cohorts: 30-Day, 90-Day, and 180-Day.<br>• On Day 0, venography with QVA and IVUS to assess the vasculature sizing.<br>• Bilateral implantation with Test Articles (Duo Hybrid Stent, Duo-Extend Stent and/or Duo Hybrid Stent + Duo Extend stents) in the right and left iliofemoral vein.<br>• Prior to termination, venography with QVA and IVUS were performed according to the cohort-assigned schedule.<br>• Following euthanasia, full necropsy was performed with target, and non-target organs harvested for histopathologic analysis. |
| **Results** | • All devices were successfully implanted with no device-related adverse events such as dissection and perforation, mortality, noted morbidity or thrombosis during or immediately after the stent deployments.<br>• No thrombi were noted on the blood-contacting surfaces of the delivery systems post-implantation.<br>• 23/24 devices passed all acute handling and performance criteria. 1/24 devices moved forward/cranially during deployment (this device passed all other criteria)<br>• All treated vessels were patent at all time points via fluoroscopy and IVUS imaging.<br>• Stented segments at all time points were widely patent with no evidence of vessel lacerations, hematoma, or obstructive thrombi.<br>• Overall, the histopathological results up to 180-days using the Duo Venous Stent System did not raise any significant safety issues for clinical use in humans. |
| | |
| **Study** | A GLP Acute Animal Study for Deployment Performance Evaluation of the Duo Venous Stent System (Triaxial Handle) |
| **Purpose** | To conduct an acute deployment performance evaluation of the Duo Venous Stent System (Triaxial Handle) in the iliofemoral veins of an ovine model. |
| **Methods** | • Three sheep (ovies aries) implanted with Duo stents.<br>• Venography with QVA and IVUS were performed prior to implantation to assess the vasculature sizing at baseline.<br>• Bilateral implantation with overlapped Test Article configurations (Duo Hybrid Stent and Duo Extend Stent, 12 mm x 80 mm) via peripheral access approach (femoral vein) in 1 of the iliofemoral veins and then via jugular vein access approach in the contralateral iliofemoral vein, for a total of 2 sets of stents in overlapped configurations per animal.<br>• Clinical pathology analyses (hematology, serum chemistry and coagulation testing) were performed prior to implant (baseline).<br>• Venography with QVA and IVUS were performed following the Test Article implantations. |
| **Results** | • All objectives of this study to conduct an acute deployment performance evaluation of the Duo Venous Stent System (Triaxial Handle) in the iliofemoral veins of a healthy Ovine model were successfully met.<br>• All Test Articles were successfully implanted in overlapped configuration with no significant vessel dissections or perforations during or immediately after the stent deployments. |

| | |
|---|---|
| | • No thrombi were noted on the blood-contacting surfaces of the delivery systems post-implantation.<br>• All Test Articles met the success criteria for compatibility with accessory products, delivery system navigation (flexibility and trackability), visualization, deployment performance (accuracy), functionality (ease of operation and deployment force), and system withdrawal following stent deployment as assessed by the Interventionalists who performed the stent deployments in the study. |

### D. Sterilization Testing

The Duo Venous Stent System is a single-use device. The device is sterilized in accordance with AAMI/ANSI/ISO 11135, "Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation and routine control of a sterilization process for medical devices." The test results from the sterilization testing confirmed that the product can be adequately sterilized to the desired level of sterility assurance of $10^{-6}$. Additionally, routine testing of biological indicators is performed to confirm that the sterilization process is effective in eradicating viable microorganisms.

### E. Packaging and Shelf Life

Packaging qualification testing (visual inspection, package integrity (bubble leak/dye penetration), and seal strength testing) demonstrated the ability of the packaging to protect the product and maintain a sterile barrier through shipping and shelf life. The Duo Venous Stent System packaging consists of a backer card to secure the system and a single pouch (sterile barrier) which is placed in a shelf carton. A shelf life of two years has been established for the Duo Venous Stent System (Pin/Pull) based on product and package shelf-life testing. A shelf life of one year has been established for the Duo Venous Stent System (Triaxial Handle) based on product and package shelf-life testing.

## X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study (VIVID Study) to establish a reasonable assurance of safety and effectiveness of the Duo Venous Stent System for treating symptomatic iliofemoral venous outflow obstructions under IDE G190030. Data from this clinical study is the basis for this PMA approval decision. A summary of the clinical study is presented below.

### A. Study Design

The VIVID study is a prospective, multi-center, single-arm, non-blinded clinical trial designed to investigate the safety and effectiveness of the Duo Venous Stent System as compared to a pre-defined performance goal (PG) established from published, peer reviewed scientific literature related to stenting of iliofemoral venous outflow obstructions.

Patients were treated between November 30, 2020 and December 6, 2021. The database for this PMA reflected data collected through June 15, 2023. The study enrolled 162 subjects at 30 clinical sites in the United States and European Union.

The study enrolled subjects with nonmalignant iliofemoral venous outflow obstruction presenting with non-thrombotic (NT), acute thrombotic (AT) or chronic post-thrombotic

(CPT) disease pathogenesis. Any subject that received one or more Duo Stents had follow-up at 30-days, 6 months, 12 months, 24 months, and 36 months.

An independent Clinical Events Committee consisting of a team of clinical experts with experience in the conduct of clinical trials was formed to review clinical events reported by the investigators that had potential to be classified as Major Adverse Events. A medical monitor was employed to provide a first review of all Adverse Events to review unanticipated adverse device effects (UADE) potential, seriousness, severity, causality, and effectiveness. Additionally, an independent board of multi-disciplinary physicians and subject matter experts was convened to serve as the Data Safety and Monitoring Board (DSMB) for the study. The DSMB served as an independent body conducting a review and oversight of all key safety events to monitor the rate of occurrence (both site-reported and CEC-adjudicated events) as part of their mission to protect the rights and safety of research subjects.

1. Clinical Inclusion and Exclusion Criteria

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

*General Inclusion criteria:*

1. Males or non-pregnant, non-breastfeeding females ≥18 years of age at the time of consent.
2. Subject is able and willing to provide written informed consent prior to receiving any non-standard of care, protocol specific procedures.
3. Female subjects of childbearing potential must have a negative pregnancy test within 7 days prior to treatment and must use some form of contraception (abstinence is acceptable) throughout the time of clinical trial exit.
4. Willing and capable of complying with all required follow-up visits.
5. Estimated life expectancy ≥1 year
6. Subject is ambulatory (use of assistive walking device such as a cane or walker is acceptable)
7. Body mass index (BMI) <45
8. Clinically significant symptomatic venous outflow obstruction in one iliofemoral venous segment (one limb) per subject, is indicated for venoplasty and stenting, and meets at least one of the following clinical indicators:
    a. CEAP score ≥3
    b. VCSS (Venous Clinical Severity Score) pain score ≥2
    c. Suspected deep vein thrombosis (DVT) with symptoms occurring prior to receiving a Duo Stent
9. Subject is willing and able to comply with principle investigator (PI) recommendation for compression therapy, if required.
10. Presence of unilateral, non-malignant venous obstruction of the common femoral vein (CFV), external iliac vein (EIV), common iliac vein (CIV), or any

combination thereof, defined as a ≥50% reduction in target vessel lumen diameter and confirmed by venographic or intravenous ultrasound (IVUS) imaging. The cranial point of the obstruction may extend to the iliac vein confluence of the inferior vena cava (IVC) and the caudal point may be 2mm above either the inflow of the deep femoral (or profunda) or the lesser trochanter, whichever is most cranial.

11. Obstructive lesion(s) able to be treated with continuous stent coverage.
12. Adequate inflow to the target lesion(s) involving at least a patent femoral or deep femoral vein and a landing zone in the CFV free from significant disease requiring treatment.
13. Reference vessel diameter is of adequate size to accommodate the appropriate size stent as measured by IVUS.
14. All vessels from insertion site through target vessel can accommodate a 9F or 10F sheath, depending on the stent size used.
15. Ability to cross interventional devices through target lesion(s).
16. In DVT subjects, successful treatment of acute thrombus must have occurred prior to receiving any Duo Stents for an underlying obstructive lesion. Successful treatment of acute thrombus is defined as reestablishment of antegrade flow with ≤30% residual thrombus confirmed by venogram or IVUS) and freedom from bleeding and symptomatic pulmonary embolism (confirmed by imaging). After successful treatment of thrombus is confirmed, eligible obstructive lesion(s) can be treated with a Duo Stent during the same procedure.
17. All subjects must undergo a SARS-CoV-2 test and have a negative test result within 8 days prior to the index procedure. If a SARS-CoV-2 test is unavailable due to institution policy, a test shortage, or if there is a delay in test results, the subject must complete the COVID-19 questionnaire and must have answered NO to all questions to be eligible for enrollment. A SARS-CoV-2 test will not be required for enrollment if a subject has received a complete cycle of an authorized COVID-19 vaccine or has documented evidence of a positive COVID- 19 antibody test and is asymptomatic and has no long-lasting effects (per PI discretion) from a prior COVID-19 infection.
18. A measured temperature less than 99.5°F (37.5°C) on the day of the index procedure and no history of fever or feeling feverish within 14 days of the index procedure.
19. No prior history, within 60 days of the index procedure of a SARS-CoV-2 positive test, or COVID-19 symptoms.

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

*General exclusion criteria:*

1. Target limb symptoms caused by peripheral arterial disease.
2. Presence of unresolved significant pulmonary emboli prior to use of the Duo

Venous Stent System confirmed by chest computed tomography (CT). If subject has documented history of significant pulmonary embolism within the last 6 months, a chest CT is required to confirm significant pulmonary embolism is not currently present.

3. Presence of IVC obstruction or target venous obstruction that extends into the IVC.
4. Presence of acute DVT located outside target limb.
5. Contralateral venous occlusive disease of the CFV, EIV, and/or CIV, with planned treatment ≤390 days after the index procedure.
6. Uncontrolled or active coagulopathy or known, uncorrectable bleeding diathesis.
7. Coagulopathy causing INR >2 which is not amenable to medical treatment.
8. Platelet count <50,000 cells/$mm^3$ or >1,000,000 cells/$mm^3$ and/or White blood cell (WBC) <3,000 cells/$mm^3$ or >12,500 cells/$mm^3$
9. Uncorrected hemoglobin of ≤9 g/dL.
10. Subject is on dialysis or has an estimated glomerular filtration rate (eGFR) <30 mL/min. In subjects with diabetes mellitus, eGFR <45 mL/min.
11. History of Heparin Induced Thrombocytopenia.
12. Presence of known aggressive clotting disorders such as Lupus Anticoagulant Disorder, Antiphospholipid antibody syndrome, homozygous gene Factor V Leiden or Prothrombin gene abnormalities, Protein C and S deficiency or Antithrombin deficiency.
13. Known hypersensitivity or contraindication to antiplatelet therapy or anticoagulation, nickel, or titanium.
14. Contrast agent allergy that cannot be managed adequately with pre-medication.
15. Intended concurrent adjuvant procedure (except for venoplasty) such as creation of temporary arteriovenous fistula, femoral endovenectomy, or saphenous vein ablation and/or saphenous vein stripping during the index procedure.
16. Subjects who have had any prior surgical or endovascular procedures to the target vessel. Note that subjects who have had successful catheter-directed or mechanical thrombolysis in the target vessel for DVT at least 90 days prior to the index procedure may be included.
17. Planned surgical or interventional procedures of the target limb (except thrombolysis and/or thrombectomy in preparation for the procedure or vena cava filter placement prior to stent implantation in subjects at high risk for pulmonary embolism) within 30 days prior to or 30 days after the index procedure.
18. Planned surgical or interventional procedures for other medical conditions (i.e., not associated with the target limb) 30 days prior to or 30 days after the index procedure.

19. Previous venous stenting of the target limb, the IVC, or contralateral limb if stents extend into the IVC.
20. Iliofemoral venous segment unsuitable for treatment with available sizes of Duo Stent implants.
21. Lesions with intended treatment lengths extending into the IVC.
22. No safe landing zone at or above the profunda femoral confluence
23. Participating in another investigational study in which the subject has not completed the primary endpoint(s).
24. Has other comorbidities that, in the opinion of the PI, would preclude them from receiving this treatment and/or participating in study-required follow-up assessments.

2. Follow-up Schedule

After hospital discharge, subjects were required to return to the study center for clinical assessments on Day 30 (-2 days / +14 days), 12 months ± 30 days, 24 months ± 30 days and 36 months ± 30 days. A time and events schedule for all assessments is provided in **Table 6**.

**Table 6. Time and Events Schedule**

| Assessment | Baseline[1] | Index Procedure | Post-Procedure/ Pre-Discharge[2] | 30 days (-2 days/+14 Days) | 6 Month (±30 Days) | 12 Month (± 30 Days) | 24 Month (± 30 Days) | 36 Month (± 30 Days) |
|---|---|---|---|---|---|---|---|---|
| Informed Consent | X[3] | | | | | | | |
| Inclusion/Exclusion Criteria | X | X | | | | | | |
| SARS-CoV-2 Test/COVID-19 Questionnaire[5] | X[4] | | | X | X | X | X | X |
| Demographics, Medical History and Risk Factors | X | | | | | | | |
| Brief Physical Exam (Height, Weight, Temp) | X | | | | | | | |
| Serum Creatinine, eGFR, White Blood Count, Platelet Count, Hemoglobin | X | | | | | | | |
| Prothrombin Time (PT)/ International Normalized Ratio (INR)[6] | X | | X | | | | | |
| Activated Partial Thromboplastin time (aPTT)[7] | X | | X | | | | | |
| Urine or Blood Pregnancy Test[8] | X | | | | | | | |
| Venous Ulcer Assessment | X | | | X | X | X | X | X |
| CEAP Classification | X | | | | X | X | X | X |

| Assessment | Baseline[1] | Index Procedure | Post-Procedure/ Pre-Discharge[2] | 30 days (-2 days/+14 Days) | 6 Month (±30 Days) | 12 Month (± 30 Days) | 24 Month (± 30 Days) | 36 Month (± 30 Days) |
|---|---|---|---|---|---|---|---|---|
| Villalta Score | X | | | | X | X | X | X |
| VCSS Pain Score | X | | | | X | X | X | X |
| VEINES-QOL/Sym Questionnaire | X | | | | X | X | X | X |
| EQ-5D-3L Questionnaire | X | | | | X | X | X | X |
| Concomitant Medications | X | X | X | X | X | X | X | X |
| Duplex Ultrasound (DUS)[9] | | | | X | X | X | X | X |
| Venogram[10] | | X | | | | X[11] | X | X |
| Intravascular Ultrasound (IVUS)[10] | | X | | | | X[11] | X | X |
| X-ray of Implanted Stent[10] | | | | | | X | X | X |
| Adverse Event (AE) Assessment | | X | X | X | X | X | X | X |

[1] Assessments may be done up to 30 days prior to the index procedure, except for a pregnancy test and SARS-CoV-2 test.
[2] Assessments are to be completed post-index procedure and prior to the subject being discharged from the hospital/clinic.
[3] Informed Consent may be obtained up to 30 days prior to index procedure.
[4] All subjects must undergo a SARS-CoV-2 test and have a negative result within 8 days of the Index Procedure to be eligible for study inclusion.
[5] If a SARS-CoV-2 test is unavailable due to institution policy, a test shortage, or if there is a delay in test results, the subject must complete the COVID-19 questionnaire and answer NO to all questions to be eligible for study treatment.
[6] PT/INR to be obtained only if a subject is on chronic warfarin therapy.
[7] aPTT to be obtained only if a subject is on chronic heparin therapy.
[8] Negative urine or blood pregnancy test is required for female subjects of childbearing potential within 7 days of the index procedure.
[9] All scheduled DUS exams should be performed per the protocol established by the core laboratory. If a DUS is non-diagnostic (per the imaging protocol), the site should make every effort to obtain a repeat exam within the visit window.
[10] All imaging of the target limb acquired during scheduled visits or an interventional procedure to the target limb (such as venogram, IVUS, DUS, or X-ray) should be submitted to the respective core laboratory within 3 business days.
[11] Required if DUS suggests >50% stenosis or occlusion of the stented segment, or if the DUS is non-diagnostic or sub-optimal (i.e., due to obesity).

3. Clinical Endpoints

*Primary Safety Endpoint*

The primary safety endpoint was to demonstrate freedom from major adverse events (MAEs) at 30 days post index procedure, as adjudicated by the Clinical Events Committee (CEC) or Core Laboratory, including:

- Device or procedure-related death
- Device or procedure-related bleed at the target vessel and/or the target lesion or at the access site requiring surgical or endovascular intervention or blood transfusion of ≥2 units
- Device or procedure-related venous injury occurring in the target vessel and/or the target lesion or at the access site requiring surgical or endovascular intervention

- Major amputation of the target limb
- Clinically significant pulmonary embolism (PE), confirmed by CT angiography
- Stent embolization outside of the target vessel
- Presence of new thrombus within the stented segment requiring surgical or endovascular intervention

Disease specific PG was calculated from the point estimates for major bleeding, pulmonary embolism and peri-procedural mortality from Razavi et al (2015) converted to freedom from estimates and application of a 10% delta. The resulting PGs were 89%, 87% and 88% for the non-thrombotic, acute thrombotic and chronic post-thrombotic, respectively. Given the similarity of the disease-state specific PGs, it was determined that a disease state specific goal was not necessary. A PG of 89% was adopted for the study in both the SARS-CoV-2 negative subset and overall.

Statistical hypothesis testing was performed as follows:

$H_0$: Proportion of subjects with freedom from MAE (pMAE) is less than or equal to the (PG) at 30 days, pMAE $\leq$89%

$H_1$: Proportion of subjects with freedom from MAE is greater than the (PG) at 30 days, pMAE >89%

The primary statistical analysis was conducted in the full-analysis set (FAS) subset for the primary safety endpoint overall and in the SARS-CoV-2 negative subset. A subject was defined as an Intent-To-Treat (ITT) patient once the subject had the Duo Venous Stent System advanced through the introducer sheath. A subject is defined as full-analysis set (FAS) if they meet the ITT definition and have data evaluable for the primary endpoints. The Per-Protocol (PP) population was defined as ITT subjects with evaluable data that met the definition for Device Success and did not have any major protocol deviations. The primary statistical method is a one-sample exact test comparing the proportion of subjects free from a MAE to the PG using a one-sided $\alpha$=0.025. The exact two-sided 95% confidence interval for the proportion of subjects free from MAE was calculated.

*Primary Effectiveness Endpoint*

The primary effectiveness endpoint is primary patency of stented segment at 12 months defined as freedom from:

- Duplex Ultrasound (DUS) core laboratory adjudicated stenosis or occlusion >50% within the stented segment. If DUS shows >50% stenosis or occlusion, confirmation by diagnostic intravascular ultrasound (IVUS) is required.
- CEC adjudicated clinically driven target lesion reintervention (CD-TLR) defined as endovascular or surgical procedure for new, recurrent, or worsening symptoms and core lab adjudicated >50% stenosis or occlusion within the stented segment confirmed by diagnostic IVUS.

The PG for primary effectiveness was set when all enrolled subjects completed the

index procedure and was based upon the proportions of ITT subjects in each of the disease states, (i.e., non-thrombotic, acute thrombotic and chronic post-thrombotic). The disease specific PGs were adopted as suggested in Razavi et al (2015) with the lower 95% confidence limit minus 10%. The PGs were 83%, 70% and 66% for non-thrombotic, acute thrombotic and chronic post-thrombotic subjects respectively. The PG for the VIVID study is a weighted combination of these disease state specific PGs, where the weights are the proportion of subjects in each disease state in the ITT sample. Therefore, the performance goal (PG) was defined as follows:

PG = (0.642)*0.83 + (0.099)*0.70 + (0.259)*0.66 = 77.3%

Statistical hypothesis testing was performed as follows:

$H_0$: Proportion of subjects with primary patency (pp_pat) is less than or equal to performance goal (PG) at 12 months, pp_pat ≤PG

$H_1$: Proportion of subjects with primary patency is greater than the performance goal at 12 months, pp_pat >PG

The study device was considered to have met the effectiveness endpoint if the one-sided p-value from hypothesis testing, comparing the proportion of subjects in the FAS with primary patency to the PG using a one-sample Z-test, was less than 0.025.

*Secondary Endpoints*

The following secondary endpoints were evaluated through 12 months:

- Subject symptom relief via VCSS pain score at 12 months
- Primary assisted patency at 12 months
  - Defined as freedom from DUS core laboratory adjudicated occlusion or stenosis >50% within the stented segment following a clinically driven target lesion reintervention due to a >50% but <100% stenosis. If DUS shows >50% stenosis or occlusion, confirmation by diagnostic IVUS was required.
- Secondary patency at 12 months
  - Defined as freedom from DUS core laboratory adjudicated occlusion or stenosis >50% within the stented segment following a clinically driven target lesion reintervention. If DUS shows >50% stenosis or occlusion, confirmation by diagnostic IVUS was required.

*Observational Endpoints*

- Device Success defined as:
  - Successful deployment of the Duo Stent(s) at the intended target site, AND
  - Successful withdrawal of the delivery catheter(s) from the introducer sheath, AND
  - The Duo Stent remaining at the intended deployment location through completion of the index procedure as determined by the Principal

Investigator (PI)

- Lesion success defined as target lesion patency of ≤50% residual diameter or area stenosis of the stented segment at the completion of the procedure*
- Procedural success defined as lesion success without the occurrence of CEC adjudicated major adverse events (MAEs) from the time start of the index procedure through discharge.
- Stent fracture via X-ray through 36 months*
- Stent migration via X-ray through 36 months*
- Stent embolization via X-ray or venogram through 36 months*
- Primary patency of the stented segment via DUS at 24 and 36 months. If DUS shows >50% stenosis or occlusion, confirmation by diagnostic IVUS may be required.*
- Primary assisted patency of the stented segment via DUS at 24 and 36 months. If DUS shows >50% stenosis or occlusion, confirmation by diagnostic IVUS may be required.*
- Secondary patency of the stented segment via DUS at 24 and 36 months. If DUS shows 50% stenosis or occlusion confirmation by diagnostic IVUS may be required.*
- Change in the CEAP classification through 36 months.
- Changes in the EQ-5D-3L through 36 months.
- Changes in the Villalta Score through 36 months.
- Changes in the VCSS Pain Score at 24 and 36 months.
- Changes in the VEINES QOL/Sym Score through 36 months.
- CEC adjudicated MAEs post 30 days through 36 months.
- CEC adjudicated CD-TLR through 36 months.
- CEC adjudicated CD-TVR through 36 months.
- Venous Ulcer Assessment through 36 months.

** Core Laboratory Adjudicated*

## B. Accountability of PMA Cohort

Of the 270 subjects consented for the VIVID study, 162 patients were enrolled and represent the Intent-to-Treat (ITT) population. The Per Protocol (PP) population includes 158 subjects and excludes three subjects that did not meet the criteria for device success and one subject that did not meet Inclusion Criteria #10. The Full-Analysis Set (FAS) is subjects who meet the ITT definition and have data evaluable for the primary endpoints. Of the 162 enrolled subjects, 155 completed 30-day follow-up or telemedicine/phone visit and 140 completed 12-month follow-up or telemedicine/phone visit per **Figure 5**.

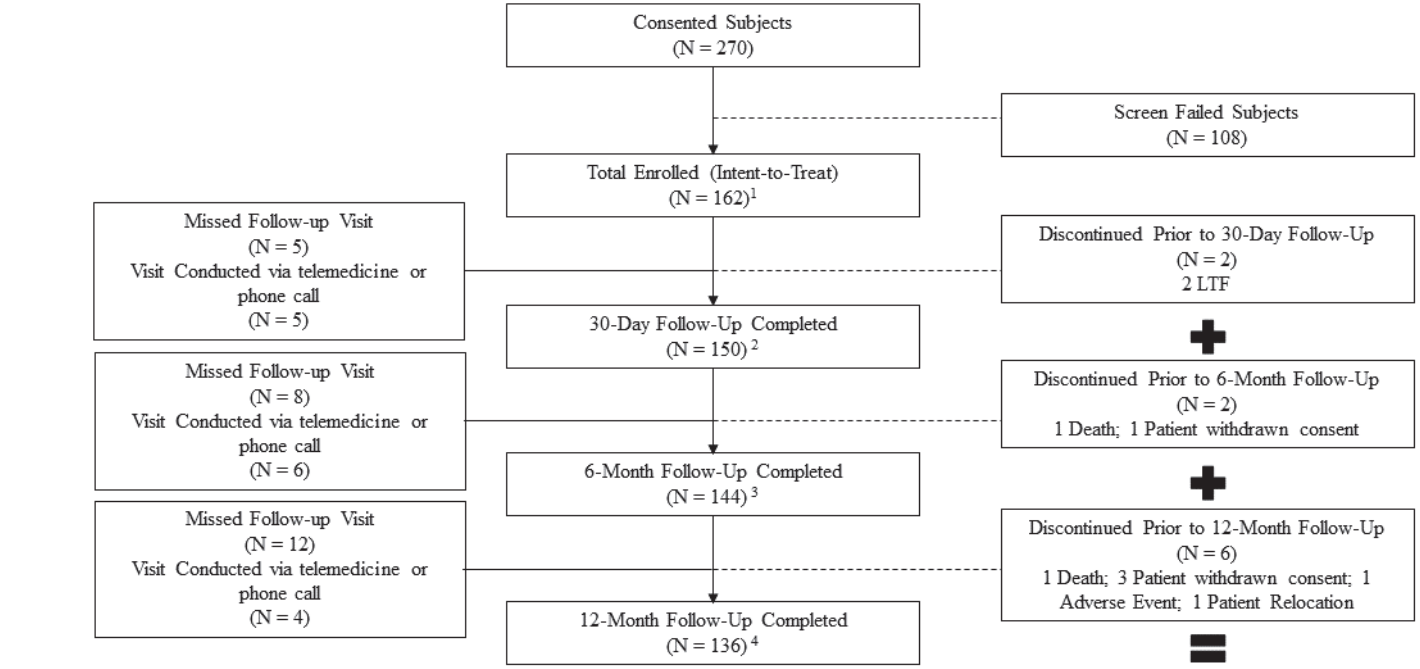


**Figure 5: VIVID Study Subject Enrollment**

## C. Study Population Demographics and Baseline Parameters

Baseline demographics and clinical characteristics for subjects treated in the trial are summarized in **Table 7**. The mean age was 59.4 ± 15.8 years and males comprised 63.0% of the ITT population. CEAP clinical assessment category C3 (edema) comprised 66.0% of the subjects and an additional 20.5% were in category C4 (changes in skin and subcutaneous tissue secondary to venous disease). Most subjects reported pain rated as moderate (52.5%) or severe (25.6%) on the VCSS pain scale.

**Table 7. VIVID Subject Demographics**

| | ITT Subjects |
|---|---|
| **SARS-CoV-2 Status at Enrollment** | |
| Positive | 8.0% (13/162) |
| Negative | 92.0% (149/162) |
| **Age at consent (years)** | 59.4 ± 15.8 (162)<br>(19.0, 61.0, 90.0) |
| **Biological Gender** | |
| Female | 37.0% (60/162) |
| Male | 63.0% (102/162) |
| **Ethnicity** | |
| Hispanic or Latino | 12.3% (20/162) |
| Not Hispanic or Latino | 84.0% (136/162) |
| Unknown | 3.7% (6/162) |
| **Race (Check all that apply)** | |
| American Indian or Alaska Native | 0.0% (0/162) |
| Asian | 0.6% (1/162) |
| Black | 9.3% (15/162) |
| Native Hawaiian or Pacific Islander | 0.0% (0/162) |
| Caucasian | 82.7% (134/162) |
| Other | 1.9% (3/162) |
| Decline to Answer | 1.9% (3/162) |
| Unknown | 3.7% (6/162) |
| **BMI** | 30.1 ± 5.7 (162)<br>(18.4, 29.2, 43.7) |
| **CEAP Clinical Assessment** | |
| C0 | 1.2% (2/162) |
| C1 | 0.6% (1/162) |
| C2 | 0.6% (1/162) |
| C2r | 0.0% (0/162) |
| C3 | 66.0% (107/162) |
| C4 | 5.6% (9/162) |
| C4a | 13.0% (21/162) |
| C4b | 1.9% (3/162) |
| C4c | 0.0% (0/162) |
| C5 | 4.9% (8/162) |
| C6 | 5.6% (9/162) |
| C6r | 0.6% (1/162) |
| **VCSS Pain** | |
| 0 - none | 6.9% (11/160) |
| 1 - mild | 15.0% (24/160) |
| 2 - moderate | 52.5% (84/160) |
| 3 - severe | 25.6% (41/160) |

*Data presented as Mean ± SD (N) (Min, Median, Max) or % (#/#)*

The risk factors for developing venous disease are summarized in **Table 8.** The most common include hyperlipidemia (48.8%) and hypertension (44.4%).

**Table 8. VIVID Subject Risk Factors**

| | ITT Subjects |
|---|---|
| **Smoking** | |
| Current | 9.3% (15/162) |
| Former | 29.6% (48/162) |
| Never | 61.1% (99/162) |
| **Diabetes Mellitus** | 19.1% (31/162) |
| Type I | 2.5% (4/162) |
| Type II | 16.7% (27/162) |
| **Hypertension** | 44.4% (72/162) |
| **Hyperlipidemia** | 48.8% (79/162) |
| **Mobility** | |
| Able to ambulate without assistance | 90.1% (146/162) |
| Able to walk with walking device | 9.9% (16/162) |
| Not ambulatory | 0.0% (0/162) |
| Other | 0.0% (0/162) |
| **Knee replacement** | 9.3% (15/162) |
| Right | 3.1% (5/162) |
| Left | 3.1% (5/162) |
| Both | 3.1% (5/162) |
| **Hip replacement** | 4.9% (8/162) |
| Right | 1.2% (2/162) |
| Left | 2.5% (4/162) |
| Both | 1.2% (2/162) |
| **Family history of venous disease** | |
| Yes | 16.7% (27/162) |
| No | 34.0% (55/162) |
| Unknown | 49.4% (80/162) |

*Data presented as % (#/#)*

A summary of the medical history for all subjects is provided in **Table 9**. As would be expected for this subject population, 66.0% and 31.5% have a history of May-Thurner Syndrome and varicosis, respectively. Previous diagnosis and resolution of DVT in the target limb was reported by 14.8% of subjects and 14.2% had a previous superficial venous ablation to the target limb.

**Table 9. VIVID Subject Medical History**

| | ITT Subjects |
|---|---|
| Stroke | 2.5% (4/162) |
| Transient Ischemic Attack (TIA) | 4.3% (7/162) |
| Angina | 8.0% (13/162) |
| Myocardial Infarction | 5.6% (9/162) |
| Congestive Heart Failure | 6.8% (11/162) |
| Coronary Artery Disease | 14.2% (23/162) |
| Vascular Heart Disease | 4.9% (8/162) |
| Cardiomyopathy | 2.5% (4/162) |
| Venous Valve Disease | 13.0% (21/162) |

| | ITT Subjects |
|---|---|
| Atrial Fibrillation | 10.5% (17/162) |
| Arrythmia (Other than atrial fibrillation) | 3.7% (6/162) |
| May-Thurner Syndrome | 66.0% (107/162) |
| Peripheral Arterial Disease | 10.5% (17/162) |
| Varicosis | 31.5% (51/162) |
| Chronic Renal Insufficiency | 3.1% (5/162) |
| Uremia | 0.0% (0/162) |
| Uncontrolled or active coagulopathy or known uncorrectable bleeding diathesis | 0.0% (0/162) |
| Clinically Significant Pulmonary Emboli | 3.7% (6/162) |
| Cancer | 14.8% (24/162) |
| Gastrointestinal Disease | 17.3% (28/162) |
| Genitourinary Disorder | 3.1% (5/162) |
| Respiratory Disorder | 9.3% (15/162) |
| Liver Disease | 1.2% (2/162) |
| Allergic reaction sensitivity or intolerance to nickel or titanium | 0.0% (0/162) |
| Allergic reaction sensitivity or intolerance to contrast media antiplatelet anticoagulant or thrombolytic medications | 1.9% (3/162) |
| Superficial venous ablation to the target limb | 14.2% (23/162) |
| Previously diagnosed and resolved DVT in target limb | 14.8% (24/162) |
| Previously diagnosed and resolved DVT in non-target limb | 5.6% (9/162) |
| Contralateral venous occlusive disease | 5.6% (9/162) |
| Onset of symptoms that led to venous stenting intervention | |
| ≤14 days | 15.4% (25/162) |
| >14 days | 84.6% (137/162) |

*Data presented as % (#/#)*

Core laboratory reported assessments of the target lesion are summarized in **Table 10**. The median lesion length was 43.3 mm but ranged widely from a minimum of 6.3 mm to a maximum of 295.0 mm. As such, the overall stented length also varied widely from the median of 110.0 mm from a minimum of 26.5 mm to 274.0 mm. The median pre- and post-procedure stenosis was 74% and 1%, respectively.

**Table 10. VIVID Core Laboratory Reported Target Lesion Details**

| | ITT Subjects |
|---|---|
| **Most Cranial Lesion Location[1]** | |
| IVC | 2.0% (3/150) |
| Common Iliac Vein - Cranial | 79.3% (119/150) |
| Common Iliac Vein - Mid | 6.7% (10/150) |
| Common Iliac Vein - Caudal | 5.3% (8/150) |
| External Iliac Vein - Cranial | 6.0% (9/150) |
| External Iliac Vein - Mid | 0.0% (0/150) |
| External Iliac Vein - Caudal | 0.0% (0/150) |

| | ITT Subjects |
|---|---|
| Common Femoral Vein | 0.7% (1/150) |
| **Most Caudal Lesion Location**[1] | |
| IVC | 0.0% (0/150) |
| Common Iliac Vein - Cranial | 2.0% (3/150) |
| Common Iliac Vein - Mid | 10.0% (15/150) |
| Common Iliac Vein - Caudal | 23.3% (35/150) |
| External Iliac Vein - Cranial | 9.3% (14/150) |
| External Iliac Vein - Mid | 13.3% (20/150) |
| External Iliac Vein - Caudal | 23.3% (35/150) |
| Common Femoral Vein | 18.7% (28/150) |
| **Reference Lumen Diameter (mm)** [1] | 14.0 ± 4.0 (143)<br>(3.6, 13.9, 28.5) |
| **Lesion Length (mm)** [1] | 55.2 ± 44.6 (145)<br>(6.3, 43.3, 295.0)[3] |
| **Pre-Intervention Stenosis (%)**[2] | 71.2 ± 15.0 (162)<br>(23.0, 74.0, 95.0) |
| **Pre-Intervention Occlusion (%)**[2] | 0.0% (0/162) |
| **Post Stent Placement Stenosis (%)**[2] | 6.7 ± 9.6 (162)<br>(0.0, 1.0, 41.0) |
| **Overall Stented Length (mm)** [1] | 126.4 ± 46.9 (147)<br>(26.5, 110.0, 274.0) |
| **Minimum Lumen Diameter In-Stent (mm)** [1] | 13.9 ± 3.7 (144)<br>(6.4, 13.5, 44.0) |

*Data presented as Mean ±SD (N) (Min, Median, Max) or % (#/#)*

*[1] Measured by venogram*

*[2] Measured by both IVUS and venogram. IVUS was preferred, and venogram was used only when IVUS was not available*

A summary of the index procedure is provided in **Table 11**. The final disease state classification of the ITT subjects was primarily non-thrombotic (64.2%). Chronic post-thrombotic and acute thrombotic accounted for 25.9% and 9.9% of the subjects, respectively.

**Table 11. VIVID Index Procedure Details**

| | ITT Subjects |
|---|---|
| **Target Limb** | |
| Left | 79.6% (129/162) |
| Right | 20.4% (33/162) |
| **Index Procedure Location** | |
| Ambulatory surgical center | 2.5% (4/162) |
| Hospital | 59.3% (96/162) |
| Office base labs | 38.3% (62/162) |
| **Sedation Type** | |
| General | 17.3% (28/162) |
| IV Sedation | 82.7% (134/162) |
| **PI Reported Pre-Intervention Stenosis (%)** | 77.6 ± 15.2 (162)<br>(38.9, 79.2, 100.0) |
| **Procedure Length (min)** | 56.9 ± 32.2 (162)<br>(8.0, 50.0, 245.0) |
| **Total Fluoroscopy Time (min)** | 13.4 ± 13.9 (159)<br>(0.0, 9.8, 139.0) |

| | ITT Subjects |
|---|---|
| **Total amount of contrast used (mL)** | 80.8 ± 53.0 (160)<br>(0.0, 70.0, 426.0) |
| **Final Disease State Classification** | |
| Acute thrombotic | 9.9% (16/162) |
| Chronic post-thrombotic | 25.9% (42/162) |
| Non-thrombotic | 64.2% (104/162) |

*Data presented as Mean ± SD (N) (Min, Median, Max) or % (#/#)*

Stent placement details are provided in **Table 12**. Of the 162 patients enrolled, 112 (69.1%) received the Duo Hybrid Stent only while 50 (30.9%) received both the Duo Hybrid Stent and Duo Extend Stent to extend treatment. Overall, 166 Duo Hybrid Stents and 53 Duo Extend Stents were implanted.

**Table 12. VIVID Stent Placement Details**

| | ITT Subjects |
|---|---|
| **Per Subject** | |
| **Stent Treatment** | |
| Duo Hybrid Stent Alone | 69.1% (112/162) |
| Duo Hybrid + Duo Extend Stent(s) | 30.9% (50/162) |
| **Number of Duo Stents per subject** | |
| 1 | 67.3% (109/162) |
| 2 | 30.2% (49/162) |
| 3 | 2.5% (4/162) |
| **Number of Duo Hybrid Stents per subject** | |
| 1 | 97.5% (158/162) |
| 2 | 2.5% (4/162) |
| 3 | 0.0% (0/162) |
| **Number of Duo Extend Stents per subject** | |
| 0 | 69.1% (112/162) |
| 1 | 29.0% (47/162) |
| 2 | 1.9% (3/162) |
| **Per Stent** | |
| **Stent Type** | |
| Duo Hybrid | 75.8% (166/219) |
| Duo Extend | 24.2% (53/219) |
| **Stent Length** | 105.5 ± 29.8 (219)<br>(40.0, 100.0, 160.0) |
| **Stent Diameter** | 15.5 ± 1.5 (219)<br>(12.0, 16.0, 18.0) |
| **Approach for study device introduction** | |
| Ipsilateral Antegrade | 99.5% (218/219) |
| Contralateral Retrograde/Crossover | 0.5% (1/219) |
| **Access site location for study device introduction** | |
| Femoral | 63.0% (138/219) |
| Popliteal | 28.8% (63/219) |
| Jugular | 0.5% (1/219) |
| Other | 7.8% (17/219) |
| **Successful introduction of the device through the introducer sheath?** | 100.0% (219/219) |
| **Duo Stent deployed?** | 100.0% (219/219) |

| | ITT Subjects |
|---|---|
| **Deployed at the intended target site?** | 99.1% (217/219) |
| **Withdrawal of delivery catheter from the introducer sheath?** | 100.0% (219/219) |
| **Duo Stent was post-dilated** | 90.4% (198/219) |
| **Duo Stent implant remained in position from initial deployment through completion of procedure?** | 99.5% (218/219) |

*Data presented as Mean ± SD (N) (Min, Median, Max) or % (#/#)*

**Table 13** provides the size and lengths of all Duo Hybrid Stent and Duo Extend Stent placed. Almost all available stent diameters and lengths were utilized in the study.

**Table 13. VIVID Duo Hybrid Stent and Duo Extend Stent Size and Length**

| Stent Diameter (mm) | Stent Length (mm) | | | | | | |
|---|---|---|---|---|---|---|---|
| | **40** | **60** | **80** | **100** | **120** | **140** | **160** |
| **Duo Hybrid (N=166)** | | | | | | | |
| 12 | N/A[1] | -- | -- | -- | 1 | -- | -- |
| 14 | | 4 | 1 | 15 | 15 | -- | 16 |
| 16 | | 13 | -- | 27 | 28 | -- | 9 |
| 18 | | -- | 22 | -- | 15 | -- | -- |
| **Duo Extend (N=53)** | | | | | | | |
| 12 | -- | -- | 4 | -- | -- | -- | N/A[2] |
| 14 | 4 | -- | 17 | -- | -- | 12 | |
| 16 | -- | -- | 13 | -- | 1 | 2 | |

[1] *Duo Hybrid is not available in 40mm length.*
[2] *Duo Extend is not available in 160mm length.*

## D. Safety and Effectiveness Results

### 1. Safety Results

The primary safety endpoint for the VIVID study is freedom from major adverse events (MAEs) at 30 days post index procedure, as adjudicated by the Clinical Events Committee (CEC) or Core Laboratory. There were only two patients who had a CEC Adjudicated MAE at 30 days, both of whom had new thrombus in the stented segment requiring surgical or endovascular intervention. Both patients were in the chronic post-thrombotic cohort. **Table 14** displays the analysis of all FAS subjects. In each case the lower confidence bound was >95% which met the pre-defined performance goal ($p<0.0001$).

**Table 14. VIVID Primary Safety Endpoint - CEC Adjudicated MAEs at 30 Days**

| Study Group | Freedom from MAE at 30 Days % (#/#) (95% CI) [1] | Performance Goal | p-value[1] | Study Endpoint |
|---|---|---|---|---|
| FAS – All | 98.7% (157/159) (95.5%, 99.8%) | 89% | <0.0001 | MET |

[1] *One sample exact test for one proportion, p-value is one-sided, Exact Two-Sided 95% confidence interval*

**Adverse effects that occurred in the PMA clinical study**

**Table 15** and **Table 16** present an overall summary of adverse events and serious adverse events that have been reported through 390 days by Body System Organ Class. No events were determined to be unanticipated. The types and occurrences of events that were reported are within expected rates.

**Table 15. Adverse Events and Device or Procedure Related Events in Body System Organ Classes in ITT Subjects**

| Body System Organ Class | Adverse Events | | | | | | Device or Procedure Related Events | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Any | | Within 30 Days | | Within 390 Days | | Any | | Within 30 Days | | Within 390 Days | |
| | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts |
| Blood and lymphatic system disorders | 6 | 3.1% (5/162) | 1 | 0.6% (1/162) | 4 | 1.9% (3/162) | | | | | | |
| Cardiac disorders | 17 | 7.4% (12/162) | 2 | 1.2% (2/162) | 14 | 6.8% (11/162) | | | | | | |
| Congenital, familial and genetic disorders | 3 | 1.2% (2/162) | | | 3 | 1.2% (2/162) | | | | | | |
| Ear and labyrinth disorders | 1 | 0.6% (1/162) | | | 1 | 0.6% (1/162) | | | | | | |
| Gastrointestinal disorders | 22 | 11.7% (19/162) | 1 | 0.6% (1/162) | 16 | 9.3% (15/162) | 1 | 0.6% (1/162) | | | 1 | 0.6% (1/162) |
| General disorders and administration site conditions | 44 | 19.1% (31/162) | 14 | 7.4% (12/162) | 36 | 15.4% (25/162) | 10 | 5.6% (9/162) | 6 | 3.1% (5/162) | 8 | 4.3% (7/162) |
| Immune system disorders | 2 | 1.2% (2/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) |
| Infections and infestations | 51 | 24.1% (39/162) | 6 | 3.7% (6/162) | 41 | 19.1% (31/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) |
| Injury, poisoning and procedural complications | 14 | 8.0% (13/162) | 3 | 1.9% (3/162) | 12 | 6.8% (11/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) |
| Investigations | 2 | 1.2% (2/162) | | | 1 | 0.6% (1/162) | | | | | | |
| Metabolism and nutrition disorders | 2 | 1.2% (2/162) | | | 2 | 1.2% (2/162) | | | | | | |
| Musculoskeletal and connective tissue disorders | 47 | 19.8% (32/162) | 11 | 6.2% (10/162) | 37 | 17.9% (29/162) | 6 | 3.1% (5/162) | 5 | 2.5% (4/162) | 6 | 3.1% (5/162) |
| Neoplasms benign, malignant and unspecified (incl cy | 2 | 1.2% (2/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | | | | | | |
| Nervous system disorders | 23 | 9.9% (16/162) | 3 | 1.9% (3/162) | 20 | 9.3% (15/162) | | | | | | |
| Pregnancy, puerperium and perinatal conditions | 1 | 0.6% (1/162) | | | | | | | | | | |

| Body System Organ Class | Adverse Events | | | | | | Device or Procedure Related Events | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Any | | Within 30 Days | | Within 390 Days | | Any | | Within 30 Days | | Within 390 Days | |
| | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts |
| Product issues | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) |
| Psychiatric disorders | 2 | 1.2% (2/162) | | | 2 | 1.2% (2/162) | | | | | | |
| Renal and urinary disorders | 5 | 2.5% (4/162) | | | 3 | 1.2% (2/162) | | | | | | |
| Reproductive system and breast disorders | 5 | 2.5% (4/162) | 1 | 0.6% (1/162) | 5 | 2.5% (4/162) | | | | | | |
| Respiratory, thoracic and mediastinal disorders | 17 | 8.0% (13/162) | 2 | 1.2% (2/162) | 15 | 8.0% (13/162) | 1 | 0.6% (1/162) | | | 1 | 0.6% (1/162) |
| Skin and subcutaneous tissue disorders | 14 | 6.2% (10/162) | 5 | 1.9% (3/162) | 11 | 4.3% (7/162) | 2 | 0.6% (1/162) | 2 | 0.6% (1/162) | 2 | 0.6% (1/162) |
| Surgical and medical procedures | 4 | 1.9% (3/162) | 1 | 0.6% (1/162) | 3 | 1.2% (2/162) | | | | | | |
| Vascular disorders | 33 | 16.7% (27/162) | 3 | 1.9% (3/162) | 27 | 14.2% (23/162) | 10 | 6.2% (10/162) | 2 | 1.2% (2/162) | 10 | 6.2% (10/162) |
| Not Coded | 7 | 3.7% (6/162) | | | 1 | 0.6% (1/162) | | | | | | |
| **Total** | **325** | **63.0% (102/162)** | **56** | **23.5% (38/162)** | **257** | **55.6% (90/162)** | **34** | **18.5% (30/162)** | **19** | **9.9% (16/162)** | **32** | **17.3% (28/162)** |

**Table 16. Serious Adverse Events and Serious Device or Procedure Related Events in Body System Organ Classes in ITT Subjects**

| Body System Organ Class | Serious Adverse Events | | | | | | Serious Device or Procedure Related Events | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Any | | Within 30 Days | | Within 390 Days | | Any | | Within 30 Days | | Within 390 Days | |
| | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts |
| Blood and lymphatic system disorders | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | | | | | | |
| Cardiac disorders | 6 | 3.1% (5/162) | | | 4 | 2.5% (4/162) | | | | | | |
| Congenital, familial and genetic disorders | 1 | 0.6% (1/162) | | | 1 | 0.6% (1/162) | | | | | | |

| Body System Organ Class | Serious Adverse Events | | | | | | Serious Device or Procedure Related Events | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Any | | Within 30 Days | | Within 390 Days | | Any | | Within 30 Days | | Within 390 Days | |
| | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts |
| Gastrointestinal disorders | 5 | 3.1% (5/162) | 1 | 0.6% (1/162) | 4 | 2.5% (4/162) | | | | | | |
| General disorders and administration site conditions | 7 | 4.3% (7/162) | 2 | 1.2% (2/162) | 4 | 2.5% (4/162) | 5 | 3.1% (5/162) | 1 | 0.6% (1/162) | 3 | 1.9% (3/162) |
| Infections and infestations | 9 | 4.9% (8/162) | 1 | 0.6% (1/162) | 7 | 3.7% (6/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) |
| Injury, poisoning and procedural complications | 4 | 2.5% (4/162) | | | 2 | 1.2% (2/162) | | | | | | |
| Metabolism and nutrition disorders | 1 | 0.6% (1/162) | | | 1 | 0.6% (1/162) | | | | | | |
| Musculoskeletal and connective tissue disorders | 2 | 0.6% (1/162) | | | 2 | 0.6% (1/162) | | | | | | |
| Nervous system disorders | 5 | 1.9% (3/162) | 2 | 1.2% (2/162) | 5 | 1.9% (3/162) | | | | | | |
| Pregnancy, puerperium and perinatal conditions | 1 | 0.6% (1/162) | | | | | | | | | | |
| Product issues | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) | 1 | 0.6% (1/162) |
| Psychiatric disorders | 1 | 0.6% (1/162) | | | 1 | 0.6% (1/162) | | | | | | |
| Renal and urinary disorders | 1 | 0.6% (1/162) | | | | | | | | | | |
| Reproductive system and breast disorders | 4 | 1.9% (3/162) | 1 | 0.6% (1/162) | 4 | 1.9% (3/162) | | | | | | |
| Respiratory, thoracic and mediastinal disorders | 3 | 1.9% (3/162) | 1 | 0.6% (1/162) | 3 | 1.9% (3/162) | 1 | 0.6% (1/162) | | | 1 | 0.6% (1/162) |
| Skin and subcutaneous tissue disorders | 1 | 0.6% (1/162) | | | 1 | 0.6% (1/162) | | | | | | |
| Surgical and medical procedures | 3 | 1.2% (2/162) | 1 | 0.6% (1/162) | 3 | 1.2% (2/162) | | | | | | |

| Body System Organ Class | Serious Adverse Events | | | | | | Serious Device or Procedure Related Events | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Any | | Within 30 Days | | Within 390 Days | | Any | | Within 30 Days | | Within 390 Days | |
| | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts | # of events | #(%) of pts |
| Vascular disorders | 11 | 5.6% (9/162) | 2 | 1.2% (2/162) | 8 | 4.3% (7/162) | 5 | 3.1% (5/162) | 1 | 0.6% (1/162) | 5 | 3.1% (5/162) |
| **Total** | **67** | **28.4% (46/162)** | **13** | **7.4% (12/162)** | **52** | **22.2% (36/162)** | **13** | **8.0% (13/162)** | **4** | **2.5% (4/162)** | **11** | **6.8% (11/162)** |

Note, the two subject deaths were not related to the study device or procedure. One subject died from motor vehicle accident trauma at 225 days post-procedure. The other subject died from sepsis at 125 days post-procedure. Overall, MAEs remained low through 12 months. In total, eight (8) subjects experienced an MAE within 390 days of the procedure. These subjects were in both the ITT and PP cohorts. Seven (7) of the MAEs were categorized as "Presence of new thrombus within the stented segment requiring surgical or endovascular intervention" and one was a "clinically significant pulmonary embolism confirmed by CT angiography".

2. Effectiveness Results

The primary effectiveness endpoint was primary patency of the stented segment at 12 months defined as freedom from:

- Duplex Ultrasound (DUS) core laboratory adjudicated stenosis or occlusion >50% within the stented segment. If DUS showed >50% stenosis or occlusion, confirmation by diagnostic intravascular ultrasound (IVUS) is required.
- CEC adjudicated clinically driven target lesion reintervention (CD-TLR) defined as endovascular or surgical procedure for new, recurrent, or worsening symptoms and core lab adjudicated >50% stenosis or occlusion within the stented segment confirmed by diagnostic IVUS.

In the FAS group, 132/162 patients were evaluable for the 12M primary effectiveness endpoint. The primary endpoint was met by 90.2% of subjects with a lower confidence bound of 83.1% thus meeting the target performance goal (p=0.0002). In the PP group, 115/162 patients were evaluable for 12M primary for the 12M primary effectiveness endpoint. The primary endpoint was met by 89.8% of subjects with a lower confidence bound of 82.7% thus meeting the target performance goal (p=0.0003).

**Table 17. Primary Effectiveness Endpoint – Primary Patency at 12 Months in FAS and PP Subjects**

| Analysis Group | % (#/#) (95% CI)[1] | Target Performance Goal | p-value[1] | Study Endpoint |
|---|---|---|---|---|
| FAS | 90.2% (119/132) (83.1%, 97.2%) | 77.3% | 0.0002 | MET |
| PP | 89.8% (115/128) (82.7%, 97.0%) | | 0.0003 | MET |

[1] *One sample Z-test for a proportion, p-value is one-sided, Two-Sided 95% confidence interval. The variation in the proportion is estimated under the null (see statistical plan).*

**Table 18** summarizes additional analyses conducted in FAS subjects by baseline disease state. Primary patency by disease state in the FAS cohort was 86.7% in the acute thrombotic cohort, 95.2% in the non-thrombotic cohort, and 79.4% in the chronic post-thrombotic cohort.

**Table 18. Primary Effectiveness Endpoint at 12 Months in FAS Subjects Overall and by Disease State**

| | FAS Subjects | Acute Thrombotic | Non-Thrombotic | Chronic Post Thrombotic |
|---|---|---|---|---|
| Primary Patency at 12M | 90.2% (119/132) | 86.7% (13/15) | 95.2% (79/83) | 79.4% (27/34) |
| ◆ CD-TLR | 7 | 0 | 3 | 4 |
| ◆ Not patent finding in the absence of CD-TLR | 6 | 2 | 1 | 3 |

*Data shown as % (n/N)*

3. Secondary Endpoints

Secondary endpoints are summarized in **Table 19 - Table 20**. As seen in **Table 19**, there was a sustained decrease in Venous Clinical Severity Score (VCSS) – Pain Score from baseline to 12 months.

**Table 19. VCSS Pain Score and Changes in VCSS from Baseline in ITT Patients**

| Parameter | Baseline | 6 months | 12 months |
|---|---|---|---|
| At Follow-up | 2.0 ± 0.8 (160)<br>(0.0, 2.0, 3.0) | 0.5 ± 0.8 (149)<br>(0.0, 0.0, 3.0) | 0.5 ± 0.8 (138)<br>(0.0, 0.0, 3.0) |
| Change from Baseline | -- | -1.4 ± 1.1 (148)<br>(-3.0, -2.0, 3.0) | -1.4 ± 1.1 (137)<br>(-3.0, -2.0, 2.0) |

*Data shown as mean ± SD (N) (min, median, max)*

Primary assisted patency was defined as freedom from DUS core laboratory adjudicated occlusion or stenosis > 50% within the stented segment following a clinically driven target lesion reintervention (CD-TLR) due to a > 50% but < 100% stenosis at 12 months while secondary patency was defined as freedom from DUS core laboratory adjudicated occlusion or stenosis > 50% within the stented segment following a clinically driven target lesion reintervention at 12 months due to greater than 50% stenosis or occlusion within the stented segment. For both endpoints, if site reported or core laboratory adjudicated DUS showed > 50% stenosis or occlusion, confirmation by diagnostic IVUS was required. As with the primary patency endpoint, DUS, IVUS and venogram imaging were used to evaluate the endpoint. As shown in **Table 20**, primary assisted patency and secondary patency at 12M were 94.7% (124/131) and 95.4% (125/131), respectively.

**Table 20. Primary Assisted Patency and Secondary Patency at 12 Months in ITT Subjects**

| Parameter | Patency at 12M |
|---|---|
| Primary Assisted Patency at 12M | 94.7% (124/131)<br>(89.4, 97.4) |
| ◆ CD-TLR for 100% occlusion | 1 |
| ◆ Not patent finding in the absence of CD-TLR for 100% occlusion | 6 |
| Secondary Patency at 12M | 95.4% (125/131)<br>(90.4%, 97.9%) |

*Data shown as % (n/N) (Wilson's 95% CI)*

4. Observational Endpoints

Device, lesion, and procedural success were evaluated using the following definitions:

- Device success is defined as successful deployment at the intended target site and successful withdrawal of the delivery catheter from the introducer sheath. The following must be met to be considered a Device Success:
    - Successful deployment of the Duo Stent(s) at the intended target site,

AND

- Successful withdrawal of the delivery catheter(s) from the introducer sheath, AND
- The Duo Stent remaining at the intended deployment location through completion of the index procedure as determined by the Principal Investigator (PI)

- Lesion success is defined as target lesion patency of ≤50% residual diameter or area stenosis of the stented segment at the completion of the procedure (core laboratory adjudicated).
- Procedural success is defined as lesion success without the occurrence of major adverse events from the time of treatment to discharge (CEC and/or core laboratory adjudicated).

As summarized in **Table 21**, all subjects met the criteria for lesion and procedural success and 159/162 (98.1%) met the criteria for device success. Of the three subjects that did not meet the criteria for device success, two subjects did not have successful deployment at the target site and one subject did not have the stent remaining at the intended target location through the index procedure. No adverse events were associated with these failures.

**Table 21. Device, Lesion, and Procedural Success in ITT Subjects**

| | ITT Subjects |
|---|---|
| Device Success per stent introduced | 98.6% (216/219)<br>(97.1%, 100.2%)[1] |
| Device Success per subject | 98.1% (159/162)<br>(94.7%, 99.4%)[2] |
| Lesion Success per subject | 100.0% (162/162)<br>(97.7%, 100.0%)[2] |
| Procedural Success per subject | 100.0% (162/162)<br>(97.7%, 100.0%)[2] |

*Data shown as % (n/N) (Wilson's 95% CI). No hypothesis tests were pre-specified, and no multiplicity adjustment were applied.*
*[1] Generalized estimating equations.*
*[2] Wilson's 95% confidence interval.*

Stent fracture and migration were evaluated via X-ray through 36 months and stent embolization via X-ray or venogram through 36 months. There were no instances of stent fracture, migration, or embolization through 12 months.

Several quality-of-life measures were also included as observational endpoints. The clinical CEAP score, all EQ-5D-3L categories, Vilalta score, VEINES-QOL and VEINES-Sym scores all improved from baseline to 12 months as summarized in **Table 22**.

**Table 22. Quality of Life Measures at Baseline and Follow-up in ITT Subjects**

| Clinical Measure | Time Point | | |
|---|---|---|---|
| | Baseline | 6M | 12M |
| **Clinical CEAP Score** | | | |
| C0 | 1.2% (2/162) | 30.9% (46/149) | 31.2% (43/138) |
| C1 | 0.6% (1/162) | 8.7% (13/149) | 8.0% (11/138) |
| C2 | 0.6% (1/162) | 8.1% (12/149) | 5.8% (8/138) |
| C2r | 0.0% (0/162) | 0.0% (0/149) | 2.2% (3/138) |
| C3 | 66.0% (107/162) | 32.2% (48/149) | 31.2% (43/138) |
| C4 | 5.6% (9/162) | 2.7% (4/149) | 2.9% (4/138) |
| C4a | 13.0% (21/162) | 6.0% (9/149) | 7.2% (10/138) |
| C4b | 1.9% (3/162) | 2.0% (3/149) | 2.2% (3/138) |
| C5 | 4.9% (8/162) | 6.0% (9/149) | 8.7% (12/138) |
| C6 | 5.6% (9/162) | 2.7% (4/149) | 0.7% (1/138) |
| C6r | 0.6% (1/162) | 0.7% (1/149) | 0.0% (0/138) |
| **EQ-5D-3L Questionnaire** | **Baseline** | **6M** | **12M** |
| **EQ-5D-3L Mobility Score** | | | |
| 1 – No problems | 47.8% (76/159) | 66.4% (93/140) | 64.9% (85/131) |
| 2 – Some problems | 51.6% (82/159) | 33.6% (47/140) | 35.1% (46/131) |
| 3 – Extreme problems | 0.6% (1/159) | 0.0% (0/140) | 0.0% (0/131) |
| **EQ-5D-3L Self-Care Score** | | | |
| 1 – No problems | 83.0% (132/159) | 91.4% (128/140) | 93.1% (122/131) |
| 2 – Some problems | 15.7% (25/159) | 8.6% (12/140) | 6.9% (9/131) |
| 3 – Extreme problems | 1.3% (2/159) | 0.0% (0/140) | 0.0% (0/131) |
| **EQ-5D-3L Usual Activity Score** | | | |
| 1 – No problems | 49.1% (78/159) | 67.1% (94/140) | 75.4% (98/130) |
| 2 – Some problems | 45.9% (73/159) | 30.7% (43/140) | 23.8% (31/130) |
| 3 – Extreme problems | 5.0% (8/159) | 2.1% (3/140) | 0.8% (1/130) |
| **EQ-5D-3L Pain/Discomfort Score** | | | |
| 1 – No problems | 25.2% (40/159) | 52.1% (73/140) | 50.4% (66/131) |
| 2 – Some problems | 59.7% (95/159) | 45.7% (64/140) | 47.3% (62/131) |
| 3 – Extreme problems | 15.1% (24/159) | 2.1% (3/140) | 2.3% (3/131) |
| **EQ-5D-3L Anxiety/Depression Score** | | | |
| 1 – No problems | 54.1% (86/159) | 70.7% (99/140) | 76.3% (100/131) |
| 2 – Some problems | 39.0% (62/159) | 25.0% (35/140) | 21.4% (28/131) |
| 3 – Extreme problems | 6.9% (11/159) | 4.3% (6/140) | 2.3% (3/131) |
| **EQ-VAS Score** (0 = worst imaginable health state and 100 = best imaginable health state) | | | |
| At follow-up | 67.7 ± 23.6 (158) | 77.7 ± 18.1 (140) | 79.7 ± 16.7 (130) |

| Clinical Measure | Time Point | | |
|---|---|---|---|
| | **Baseline** | **6M** | **12M** |
| Change from Baseline | -- | 8.6 ± 23.2 (137) | 10.6 ± 22.1 (127) |
| **Villalta Score** | **Baseline** | **6M** | **12M** |
| At follow-up | 10.4 ± 4.8 (159) | 3.4 ± 4.1 (149) | 3.3 ± 3.9 (138) |
| Change from Baseline | -- | -6.7 ± 5.5 (146) | -6.9 ± 5.7 (135) |
| **VEINES-QOL/Sym Score** | **Baseline** | **6M** | **12M** |
| **VEINES - Sym** | | | |
| At follow-up | 52.6 ± 24.9 (157) | 75.9 ± 22.7 (139) | 76.9 ± 21.9 (132) |
| Change from Baseline | -- | 22.6 ± 23.8 (135) | 23.4 ± 25.8 (128) |
| **VEINES - QOL** | | | |
| At follow-up | 51.4 ± 23.8 (157) | 75.0 ± 22.7 (139) | 75.9 ± 23.6 (132) |
| Change from Baseline | -- | 23.6 ± 24.7 (135) | 24.3 ± 25.8 (128) |

*Data presented as Mean ± SD (N) or % (n/N)*

5. Subgroup Analyses

**Table 23** displays the results of the primary analysis by the pre-determined subgroups of FAS subjects: Gender, geography (US vs OUS), age (≤ 61 vs > 61), race, and ethnicity. In general, there were no differences in the primary effectiveness endpoint between any of the pre-defined sub-groups, with the exception of US vs OUS. The OUS sample size was only 8.5% of the total FAS subject population, so the differences may be due to the small numbers of OUS subjects.

**Table 23. Subgroup Analyses of Primary Patency at 12M in FAS Subjects**

| | FAS | Acute Thrombotic | Non-Thrombotic | Chronic Post Thrombotic |
|---|---|---|---|---|
| **Gender** | | | | |
| Male | 87.8% (43/49) | 83.3% (5/6) | 100.0% (26/26) | 70.6% (12/17) |
| Female | 91.6% (76/83) | 88.9% (8/9) | 93.0% (53/57) | 88.2% (15/17) |
| **Geography** | | | | |
| Inside United States (US) | 93.3% (112/120) | 92.9% (13/14) | 95.1% (77/81) | 88.0% (22/25) |
| Outside United States (OUS) | 58.3% (7/12) | 0.0% (0/1) | 100.0% (2/2) | 55.6% (5/9) |
| **Age** | | | | |
| ≤ Median Age=61 | 88.6% (62/70) | 88.9% (8/9) | 97.6% (40/41) | 70.0% (14/20) |
| > Median Age=61 | 91.9% (57/62) | 83.3% (5/6) | 92.9% (39/42) | 92.9% (13/14) |
| **Race** | | | | |
| White | 89.2% (99/111) | 90.9% (10/11) | 94.1% (64/68) | 78.1% (25/32) |
| Black | 90.9% (10/11) | 75.0% (3/4) | 100.0% (7/7) | 0 |
| Other/Decline/Unknown | 100.0% (10/10) | 0 | 100.0% (8/8) | 100.0% (2/2) |

| | FAS | Acute Thrombotic | Non-Thrombotic | Chronic Post Thrombotic |
|---|---|---|---|---|
| **Ethnicity** | | | | |
| Not Hispanic or Latino | 89.3% (100/112) | 83.3% (10/12) | 94.4% (68/72) | 78.6% (22/28) |
| Hispanic or Latino | 93.3% (14/15) | 100.0% (2/2) | 100.0% (7/7) | 83.3% (5/6) |
| Unknown | 100.0% (5/5) | 100.0% (1/1) | 100.0% (4/4) | 0 |

6. COVID-19 Analyses

Given that COVID-19 has been associated with a hypercoagulable state, which has the potential to increase MAE occurrence and decrease patency, the study included a test of both the primary safety and effectiveness hypotheses in both the SARS-CoV-2 negative subset and all subjects (regardless of SARS-CoV-2 status). The performance goals for both primary safety and primary effectiveness were met for both cohorts. COVID-19 status did not affect primary outcomes in this study.

7. Pediatric Extrapolation

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

### E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 32 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.

## XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

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

## XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

### A. Effectiveness Conclusions

The non-clinical testing conducted on Duo Venous Stent System demonstrated that the performance characteristics of the device met the product specifications. The test results obtained from sterilization testing demonstrated that the product can be adequately sterilized and is acceptable for clinical use. A shelf life of two years has been established for the Duo Venous Stent System (Pin/Pull) based on product and package shelf-life testing. A shelf life of one year has been established for the Duo Venous Stent System

(Triaxial Handle) based on product and package shelf-life testing.

Vesper Medical performed a prospective, multi-center, single-arm study (VIVID) to investigate the safety and effectiveness of the Duo Venous Stent System in treating symptomatic iliofemoral venous outflow obstructions. One-hundred-sixty-two (162) subjects were enrolled and underwent treatment with the Duo Venous Stent System with subsequent follow-ups at 30 days, 6 months, 12 months, 24 months, and 36 months.

The primary effectiveness endpoint was primary patency of the stented segment at 12 months defined as freedom from adjudicated occlusion or stenosis >50% within the stented segment evaluated by DUS and clinically driven target lesion reintervention (CD-TLR). The primary effectiveness endpoint met the performance goal of 77.3% (p=0.0002). Primary patency at 12 months in the FAS cohort was 90.2% with a 95% lower confidence bound of 83.1%. Primary patency by disease state in the FAS cohort was 86.7% in the acute thrombotic cohort, 95.2% in the non-thrombotic cohort, and 79.4% in the chronic post-thrombotic cohort. Additionally, there were improvements in several pain and QoL endpoints at 12 months evaluated by VCSS, Villalta, CEAP, EQ-5D-3L, VEINES SYM and VEINES QOL. Technical and procedural success per subject were also acceptably high rates.

## B. Safety Conclusions

The biocompatibility and animal testing demonstrate that the Duo Venous Stent System support a reasonable assurance of safety for the intended clinical use.

The VIVID study primary safety endpoint was to demonstrate freedom from major adverse events (MAEs) at 30 days post index procedure, as adjudicated by the Clinical Events Committee (CEC) or Core Laboratory.

The primary safety endpoint met the performance goal of 89% (p<0.0001). Freedom from MAEs in the FAS cohort at 30 days was 98.7% with a lower 95% confidence interval of 95.5%. The rates of MAEs remain low through 360 days of follow-up, and the ITT cohort performed similarly. Freedom from CD-TLR and CD-TVR at 360 days was 96.2% (95% CI: 91.7, 98.3) and 95.6% (95% CI: 90.9, 97.9). There were no unanticipated adverse device events.

## C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The probable benefit of using the Duo Venous Stent System to treat symptomatic iliofemoral venous obstructions include restoring blood flow which may improve patient quality of life by reducing the symptoms of venous disease.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The types and occurrences of reported adverse events are within expected rates for the studied patient population and therapeutic area.

1. Patient Perspective

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

In conclusion, given the available information above, the data support that the probable benefits outweigh the probably risks for treating symptomatic iliofemoral outflow obstructions with the Duo Venous Stent System.

### D. Overall Conclusions

The clinical and non-clinical data in this application support the reasonable assurance of safety and effectiveness of Duo Venous Stent System when used in accordance with the indications for use. The Duo Venous Stent System met the safety and effectiveness performance goals in the prospective, multi-center, single-arm, non-blinded VIVID clinical study The non-clinical and clinical data demonstrate that the DUO Venous Stent System is safe and effective in the treatment of iliofemoral venous outflow obstructions when used in accordance with the device labeling and Instructions for Use (IFU).

## XIII. CDRH DECISION

CDRH issued an approval order on [date of approval order]. The final clinical conditions of approval cited in the approval order are described below.

Post-Approval Study – VIVD Continued Follow-Up Study. This study should be conducted per protocol VIVID, PROTOCOL # V-CA 0001 Version E (dated April 23, 2021). This study is a prospective, multi-center follow-up of the VIVID pivotal study (G190030) that enrolled 162 subjects at 30 clinical sites in the United States and European Union. It will evaluate the long-term safety and effectiveness of the Duo Venous Stent System.

All 152 remaining subjects active at the end of the 12-month evaluation will continue to be followed annually through 36 months. The primary endpoint to be assessed is freedom from clinically driven target lesion revascularization (CD-TLR) at 36 months, as defined by the protocol. The secondary endpoints to be assessed include the following:

- Primary patency
- Primary assisted patency
- Secondary patency
- Stent fracture, migration, and embolization
- Changes in CEAP, Villalta, VCSS pain score, and VEINES QOL
- Venous Ulcer Assessment
- Clinically driven target vessel revascularization (CD-TVR)

- Adverse events

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

## XIV. 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.

## XV. REFERENCES

Razavi MK, Jaff MR, Miller LE. Safety and Effectiveness of Stent Placement for Iliofemoral Venous Outflow Obstruction: Systematic Review and Meta-Analysis. Circ Cardiovasc Interv. 2015 Oct 1; 8(10).