SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Stent, Superficial Femoral Artery
Device Trade Name:	BioMimics 3D Vascular Stent System
Device Procode:	NIP
Applicant's Name and Address:	Veryan Medical Limited Block 11, Galway Technology Park, Parkmore, Galway, Co. Galway, Ireland, H91 VE0H
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P180003
Date of FDA Notice of Approval:	October 04, 2018

II. INDICATIONS FOR USE

The BioMimics 3D Vascular Stent System is indicated to improve luminal diameter in the treatment of symptomatic de novo or restenotic lesions in the native superficial femoral artery and/or proximal popliteal artery, with reference vessel diameters ranging from 4.0 - 6.0 mm and lesion lengths up to 140 mm.

III. CONTRAINDICATIONS

All customary contraindications for angioplasty must be considered when using the BioMimics 3D Vascular Stent System.

There are additional contraindications:

- Patients whose lesions cannot be crossed with a wire and/or balloon catheter and cannot be dilated sufficiently to allow passage of the delivery system.
- Patients who are judged to have a lesion that prevents proper placement or deployment of the stent.
- A lesion that is within an aneurysm or an aneurysm with a proximal or distal segment to the lesion.
- Patients with known intolerance to antiplatelet and/or anticoagulation therapies.
- Patients with a known hypersensitivity to nickel, titanium or tantalum.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the BioMimics 3D Vascular Stent System labeling.

V. DEVICE DESCRIPTION

The BioMimics 3D Vascular Stent System comprises an implantable, self-expanding, nickel-titanium alloy (Nitinol) stent and a delivery system for endovascular placement and release of the stent at the treatment site.

Description of the Stent

The BioMimics 3D Stent (see Figure 1) is laser cut from a straight Nitinol tube and helical curvature is stored in the Nitinol shape memory. Three tantalum radiopaque markers are located at each end of the stent.

Figure 1: BioMimics 3D Stent with Helical Centerline

The BioMimics 3D Stent is provided in a matrix of stent lengths and diameters (see Table 1) to accommodate the morphology of the treatment site within the superficial femoral and proximal popliteal arteries.

Table 1: BioMimics 3D Vascular Stent System: Stent Size Configurations

Stent Diameter	Stent Length				
	60 mm	80 mm	100 mm	125 mm	150 mm
5 mm	✓	✓	✓	✓	✓
6 mm	✓	✓	✓	✓	✓
7 mm	✓	✓	✓	✓	✓

Description of the Delivery System

The BioMimics 3D Vascular Stent System is shown in Figure 2 and consists of the inner shaft (2) and outer shaft (5) secured together via the Tuohy Borst valve (3). The operating length of the stent delivery system (SDS) is 113 cm. All stent sizes are delivered in the same delivery system, which is compatible with 6 French introducer sheaths and recommended for delivery over a 0.035" guidewire.

The inner shaft (2) and Luer hub (1) acts as the guidewire lumen. The outer shaft includes a bifurcated Luer (4) with a Tuohy Borst valve (3). The bifurcated Luer allows for flushing through the system while the valve is opened to facilitate stent deployment. The BioMimics 3D Stent (7) is crimped and loaded into the space between the inner shaft and the outer sheath at the distal end of the SDS. Radiopaque markers are positioned proximal (6) and distal (8) to the stent to facilitate stent placement at the treatment site.

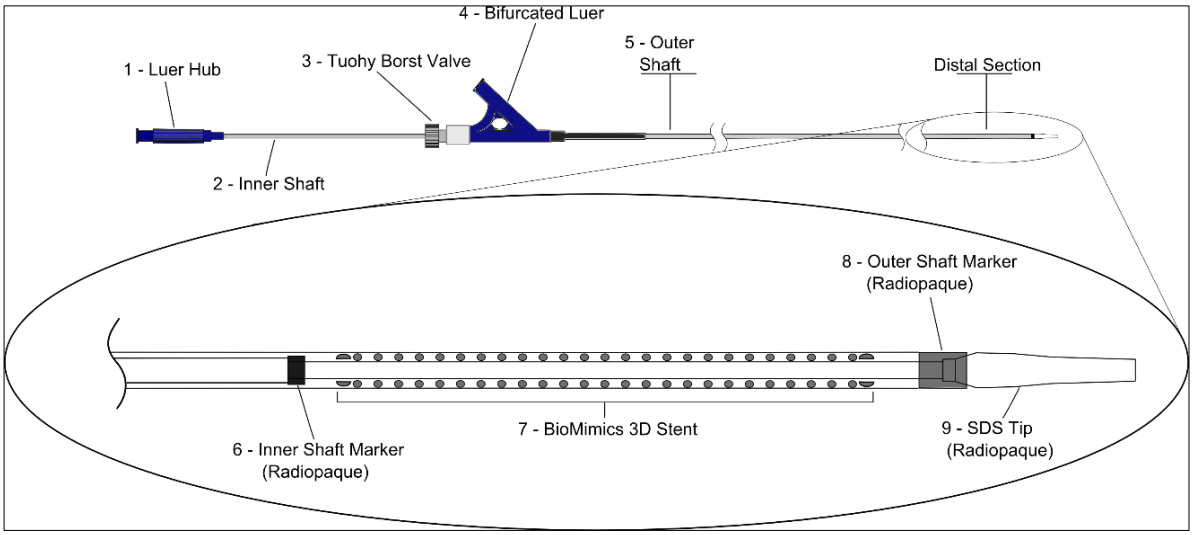


Figure 2: BioMimics 3D Vascular Stent System

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Atherosclerotic disease of the superficial femoral and proximal popliteal arteries can be treated by a range of alternative practices and procedures. Non-invasive approaches include exercise and drug therapy. Minimally-invasive approaches include endovascular intervention using percutaneous transluminal angioplasty using a plain or drug-coated balloon, stents (bare metal, drug-eluting and covered) and various modalities of atherectomy. Invasive approaches include surgical bypass. Each approach has its own advantages and disadvantages. A patient should discuss these alternative approaches with a physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The first commercial sale of the BioMimics 3D Vascular Stent System was in Europe in February 2015, following CE Mark approval. There has been no market withdrawal, correction or removal of the device. A list of countries in which the BioMimics 3D Vascular Stent System has been distributed is provided in Table 2.

Table 2: List of Countries where BioMimics 3D Vascular Stent System has been distributed

Austria	Denmark	Ireland	Norway
Belgium	Spain	Iceland	Portugal
Switzerland	Finland	Italy	Sweden
Germany	France	Netherlands	United Kingdom

VIII. PROBABLE ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

- Stent system events: device embolization; device malfunction; serious injury or surgical intervention; stent strut fracture(s), stent migration, stent misplacement/jumping.
- Vascular events: aneurysm; arterial dissection; arterial perforation; arterial rupture; arterial spasm; arteriovenous fistula; embolism and/or arterial thrombosis; hematoma; hypotension; ischemia; vascular complications which may arise during placement of a bailout stent; pseudoaneurysm; restenosis of the treated segment; stenosis; total occlusion of the peripheral artery; abrupt occlusion of the peripheral artery; vascular complications which may require surgical repair (conversion to open surgery) or endovascular intervention; worsening of peripheral arterial disease leading to additional surgical intervention, endovascular intervention or amputation: vasospasm.
- Bleeding events: access-site complications including bleeding or hemorrhage; gastrointestinal bleed; bleeding complications requiring transfusion.
- Procedural events: Allergic reaction to contrast media / medications; extravasation of contrast media; fracture of the guidewire or any component of the BioMimics 3D Vascular Stent System that may or may not lead to device embolism; radiation exposure.
- Angina
- Bradycardia
- Cardiac arrest
- Cardiac arrhythmia
- Death
- Emergency or non-emergency arterial bypass surgery
- Infection or fever
- Leg pain/claudication
- Myocardial infarction or coronary ischemia

- Nausea/vomiting
- Neurological deficit
- Renal insufficiency or failure
- Respiratory distress or failure
- Serious injury requiring surgical intervention
- Stroke or transient ischemic attack

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

IX. SUMMARY OF NONCLINICAL STUDIES

A. Biocompatibility Studies

The biocompatibility of the BioMimics 3D Vascular Stent System was evaluated per the requirements of FDA Guidance Use of ISO 10993-1, *Biological Evaluation of Medical Devices – Part 1: Evaluation and testing within a risk management framework (2016).* Each test was performed in accordance with the requirements of 21 CFR 58 – *Good Laboratory Practices for Non-Clinical Laboratory Studies.* Tests were conducted separately on sterilized products to support the biocompatibility of (1) the BioMimics 3D delivery system and (2) the BioMimics 3D Stent. The delivery system was categorized as an externally-communicating device with limited contact duration (<24 hours) with vascular tissue and circulating blood. The BioMimics 3D Stent was categorized as a permanent implant device in permanent contact with vascular tissue and circulating blood (>30 days). A summary of all biocompatibility testing performed is provided in Table 3 below.

Table 3: Summary of biocompatibility testing performed on the BioMimics 3D Vascular Stent

Test Performed	Test Description	Stent	Delivery System	Results
Cytotoxicity	ISO MEM Elution Assay	✓	✓	Non-toxic
Sensitization	ISO Guinea Pig Maximization	✓	✓	Non-sensitizing
Irritation	ISO Intracutaneous Reactivity	✓	✓	Non-irritating
Pyrogenicity	USP Material-Mediated Pyrogenicity	✓	✓	Non-pyrogenic
Acute Systemic Toxicity	ISO Systemic Toxicity Study	✓	✓	Non-toxic
Hemocompatibility	ASTM Hemolysis Study (Direct and Indirect Contact)	✓	✓	Non-hemolytic
	Complement Activation Assay (SC5b-9)	✓	✓	Not a complement activator

Stent implantation and stent and delivery system thrombogenicity were evaluated as part of other *in-vivo* studies conducted to evaluate the safety and performance of the device as outlined in Section IX.E. Chemical characterization and toxicological risk assessment were used to assess the endpoints of subchronic/chronic toxicity, genotoxicity, and carcinogenicity of the stent. The data demonstrated that the medical device materials and processing agents used in the manufacture of the BioMimics 3D Vascular Stent System have an acceptable biological safety profile.

B. *In-Vitro* Bench Testing

In-vitro bench testing was performed to assess the functional characteristics of the BioMimics 3D Vascular Stent System. Testing was performed in accordance with FDA Guidance: *Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, April 2010* and updated guidelines *Select Updates for Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stent and Associated Delivery systems, August 2015*. The relevant bench testing outlined in the Guidance documents was performed in support of the BioMimics 3D Vascular Stent System and is summarized in Table 4 below.

Table 4: Non-Clinical Engineering Tests of Stents and Delivery Systems

Test	Test Purpose	Acceptance Criteria	Results
IMPLANT			
Stent Material Composition	To verify that the composition of the Nitinol and tantalum stent materials conform to medical grade materials Standards.	The chemical composition of the Nitinol material must conform to ASTM F2063 for medical grade Nitinol. The chemical composition of the Tantalum material must conform to ISO 13782.	Pass
Shape Memory and Superelasticity	To determine the temperature (Austenite finish temperature (*Af*)) at which the stent achieves full radial expansion.	All stents must have an Af temperature of 20 ± 5°C.	Pass
Fretting Corrosion	To determine the potential for fretting corrosion after simulated use durability testing, with stents deployed in an overlapping configuration.	The stent must have a minimum breakdown potential above 300 mV.	Pass
Pitting and Crevice Corrosion Potential	To determine the potential for pitting and crevice corrosion of the stent.	The stent must have a minimum breakdown potential above 300 mV.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Galvanic Corrosion	To determine the potential for galvanic corrosion of the stent.	The galvanic corrosion rate shall be < 0.001 mpy.	Pass
Deployed Outer Diameter/ Labeled Diameter	To determine the outer diameter of the stent after deployment.	The stent diameter must meet relevant design specifications.	Pass
Uniformity of Expansion	To determine the stent diameter uniformity after deployment.	The stent diameter must meet relevant design specifications.	Pass
Mounted (Undeployed) Length	To determine the length of the stent in the delivery system.	The stent mounted length must be ± 2 mm from the specified length.	Pass
Stent Wall Thickness / Strut and Bridge Thickness	To determine the stent strut thickness.	0.220 mm ± 0.028 mm	Pass
Percent Surface Area	To determine the surface coverage of the stent in the vessel	The stents are characterized for information only	The percent surface area was determined
Stent Form Profile	To determine if the stent has the correct unconstrained three-dimensional shape after deployment.	The curvature must be such that the stent passes through the associated curvature check tool.	Pass
Foreshortening	To determine how much the stent shortens by comparing the stent length when constrained inside the catheter to that when deployed in the vessel.	The stent deployed across the specified vessel range shall not foreshorten more than 10%.	Pass
Stent Integrity	To ensure that the stent has no clinically relevant flaws after deployment.	Stents must adhere to visual inspection requirements after deployment.	Pass
Radial Resistive Force RRF	To determine RRF generated by the stent at the clinically relevant diameter.	The force exerted by the stent on the vessel, under the conditions of radial compression shall be ≥0.29 N/mm.	Pass
Chronic Outward Force COF	To determine radial COF generated by the stent at the clinically relevant diameter.	The force exerted by the stent on the vessel under the conditions of radial expansion shall be between 0.06 N/mm and 0.44 N/mm.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Stress/Strain Analysis and Fatigue Analysis	The purpose of the stress/strain analysis is to evaluate the strains the stent experiences during manufacture and during *in-vivo* use when subjected to clinically relevant loading conditions.	Finite element analysis of the strain levels of the BioMimics 3D Stent during manufacture, deployment and physiological loading conditions must indicate that the stent does not experience unsafe strains. The stent must demonstrate acceptable fatigue safety performance using a Constant Life fatigue analysis.	Pass
Accelerated Durability Testing - Pulsatile	To determine the fatigue resistance of the stent deployed in an overlapping configuration after 380 million pulsatile radial load cycles equivalent to 10 years of implanted life.	The stent must maintain structural integrity over a 10-year equivalent in-vitro loading, simulating arterial conditions within the indicated use range. Type 2-5 fractures are not acceptable.	Pass. No stent fractures (Type 1 – 5) observed.
Accelerated Durability Testing – Combined Loading (walking and stair climbing)	To determine the fatigue resistance of the stent deployed in an overlapping configuration and subjected to a simulated walking and stair climbing load equivalent to 10 years of implanted life.	The stent must maintain structural integrity over a 10-year equivalent in-vitro loading, simulating arterial conditions within the indicated use range. Type 2 - 5 fractures are not acceptable.	Pass. No stent fractures (Type 1 – 5) observed.
MRI Safety and Compatibility	To assess the safety and compatibility of the stent in the MRI environment	The stent shall be MR conditional to 1.5 and 3 Tesla.	The results show that the stent may be labelled as MR Conditional in accordance ASTM F2053
Radiopacity	To determine the visibility of the stent and delivery system under X-ray	The delivery system and stent must be visible under fluoroscopy	Pass

Test	Test Purpose	Acceptance Criteria	Results
Stent Crush Resistance	To determine the ability of a deployed stent to recover its original diameter after being subjected to a crush load.	The stent must have a minimum Crush Resistance Force, FCrush, of 0.031 N/mm. The stent must have a minimum Collapse Resistance Force, FCollapse, of 0.062 N/mm. The stent outer diameter must be within specification after stent crush and collapse testing.	Pass
Stent Local Compression Resistance	To determine the ability of the stent to recover its original diameter after being subjected to a focal crush load.	The stent must meet the deployed outer diameter specification, after application and removal of a local compressive load which results in a diameter reduction of at least 50 %.	Pass
Stent Kink Resistance	To characterize the smallest radius of curvature the stent can withstand without kinking.	The stent must not kink at a centerline radius of curvature ≥ 17 mm.	Pass
DELIVERY SYSTEM			
Delivery System Dimensional Verification	To determine the dimensional characteristics of the delivery system	The delivery system must meet relevant design specifications.	Pass
Crossing Profile	To purpose of this test is to confirm that the delivery system will fit in the indicated introducer sheath/guide catheter.	The delivery system crossing profile must meet relevant design specifications.	Pass
Delivery Deployment and Retraction	To assess the ability of the delivery system to deliver and deploy the stent at the intended location and to assess the subsequent removal of the delivery system.	The stent must be easily deployed from the delivery system after introducing and tracking the SDS over a 0.035'' guidewire through a clinically relevant anatomical model without kinking. The delivery system must be easily retracted after stent deployment.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Compatibility with accessory devices	To assess the compatibility of the stent and delivery system with accessory devices.	The stent and delivery system must be compatible with required ancillary devices.	Pass
Surface Contamination (After Deployment)	To determine if particulate contamination is present on the device after deployment.	No catheter materials should be visible on the deployed stent surface when inspected under 2.5X magnification.	Pass
Accuracy of Deployment	To assess the accuracy of deploying the stent at the target location.	The stent shall be deployed ± 5.0 mm from the intended deployment location.	Pass
Stent/System Force to Deploy	To assess the force required to deploy the stent	The maximum force shall not exceed 19.6 N.	Pass
Catheter Bond Strength	To evaluate the strength of delivery system bonds	The delivery system bonds must maintain integrity above the specified load levels during stent deployment and delivery system retraction.	Pass
Tubing Tensile Strength	To determine the tensile strength of the delivery system outer braid	The tensile strength of the delivery system outer braid must exceed the maximum load specified during stent deployment.	Pass
Delivery System Torque Strength	To assess the ability of the delivery system to withstand torsional load.	When the distal tip is not free to rotate, catheter functionality and integrity should be maintained after multiple rotations of the proximal support shaft luer.	Pass
Catheter Flexibility and Kink Resistance	To assess the catheter flexibility and kink resistance by tracking it to the intended location over a guide wire	The catheter must be able to accommodate the pre-determined clinically relevant angle during access and delivery without kinking.	Pass
Package Integrity	To assess the integrity of the device packaging	The packaging and labeling must withstand the hazards of environment and distribution and maintain sterility of the device.	Pass

C. Sterilization

The BioMimics 3D Vascular Stent Delivery System is sterilized with ethylene oxide gas to a sterility assurance level (SAL) of 10^{-6}. Validation and revalidation are completed in compliance with ISO 11135:2014 *Sterilization of health care products -- Ethylene oxide -- Requirements for development, validation and routine control of a sterilization process for medical devices*.

D. Packaging and Shelf Life

Packaging qualification and device verification testing was performed on the BioMimics 3D Vascular Stent System. The device is protected in a plastic hoop on a backing card and sealed in a Tyvek pouch. A shelf life of 18 months has been established for the BioMimics 3D Vascular Stent System based on product and packaging shelf life testing.

E. Preclinical *In-Vivo* Studies

The BioMimics 3D Stent was subjected to preclinical *in-vivo* evaluation to demonstrate safety and performance. The porcine carotid artery was selected as a suitable model and the study was performed in accordance with *21 CFR 58 – Good Laboratory Practices for Non-Clinical Laboratory Studies*. The study showed that use of the BioMimics 3D Stent produces similar acute and chronic biological response to that following deployment of a Nitinol control stent. The results support the safety and performance of the BioMimics 3D Stent.

Table 5: Results of *in vivo*, preclinical testing of the BioMimics 3D Stent

Study Type	Study Design	Findings
90-day Swine Study	Porcine carotid model utilized 6 Swine (11 BioMimics 3D Stents (Test) and 1 Everflex stent (Control) Ilio-femoral artery approach Explants at 90 ± 5 days	The performance of the BioMimics 3D Stent met the pre-specified acceptance criteria. The majority of Test tissues were similar to Control tissues at 90 & 180 days and included mild wall injury, inflammation, fibrin, and hemorrhage, with mild neointima formation and extensive endothelialization of the luminal surface, without intraluminal thrombus formation. These findings suggest that when deployed as intended, the BioMimics 3D Stent results in a similar biological response to the Control stent. There was no evidence of stent fracture under fluoroscopy at follow-up intervals through 90 & 180 days.
180-day Swine Study	Porcine carotid model utilized 6 Swine (11 BioMimics 3D Stents (Test) and 1 Everflex stent (Control) Ilio-femoral artery approach Explants at 180 ± 5 days	

X. SUMMARY OF PRIMARY CLINICAL STUDY

A prospective, multi-center, single arm clinical study ("MIMICS-2 Study") was conducted to establish a reasonable assurance of safety and effectiveness of stenting with the BioMimics 3D Vascular Stent System for peripheral artery disease of the femoropopliteal arteries in the US, Germany and Japan under IDE #G140182. Data from this clinical study were the basis for the PMA approval decision. Results from an additional clinical study ("MIMICS Study") performed in Germany were used to evaluate the subject device. A summary of the MIMICS-2 clinical study is presented below, followed by the Mimics Study in Section XI.

A. Study Design

Patients were treated between June 29, 2015 and October 18, 2016. The database for this PMA reflected data collected through November 8, 2017 and included 271 patients at 43 investigational sites (31 in US; 6 in Germany; and 6 in Japan).

The study was a prospective, multi-center, single-arm clinical study. Safety and effectiveness outcomes in the MIMICS-2 Study were compared to established performance goals defined by VIVA Physicians, Inc. for the clinical evaluation of safety and effectiveness of Nitinol stents used in the treatment of symptomatic disease of the femoropopliteal artery. The primary safety endpoint was a composite of major adverse events (MAE) comprising death, any major amputation performed on the index limb or clinically-driven target lesion revascularization (CDTLR) through 30 days. The primary effectiveness endpoint was primary stent patency rate at 12 months as defined as no significant reduction in luminal diameter (i.e. < 50% diameter stenosis) since the index procedure, or where angiography reveals >50% stenosis, or intervening CDTLR.

Statistically powering the primary effectiveness endpoint at the 85% level required 230 subjects, evaluable at 12 months. For a sample size of 230 subjects, the power for the primary safety endpoint was >99%, keeping the overall study power at approximately 85%. To declare trial success, both primary endpoint hypotheses were required to be satisfied, thus no adjustment to alpha was necessary to account for multiple endpoints. Allowing for 15% attrition, 271 subjects were enrolled in the MIMICS-2 Study to obtain 230 evaluable subjects.

Independent core laboratories conducted reviews of duplex ultrasound, X-ray and angiographic images from index procedure and follow-up visits. In addition, all adverse events potentially contributing to determination of primary outcome measurement, were reviewed by an independent and experienced Clinical Events Committee (CEC). Events were evaluated as to a relationship with the BioMimics 3D stent placement procedure and/or the BioMimics 3D stent and whether any revascularization events during follow-up were clinically-driven. A range of secondary outcome measures were defined in the MIMICS-2 Study Protocol including longer-term assessment of safety and stent patency, together with clinical and functional outcomes.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment was limited to those subjects that met the following inclusion criteria:

Subject inclusion criteria

1. Subject is male or female, with age >18 and ≤85 years at date of enrollment.
2. Subject or authorized representative provides written informed consent before any study-specific investigations or procedures.
3. Subject is willing to undergo all follow-up assessments according to the specified schedule over 36 months.
4. Subject is a suitable candidate for angiography and endovascular intervention and, if required, is eligible for standard surgical repair.
5. Subject has symptomatic peripheral arterial disease (PAD) of the lower extremities requiring intervention to relieve de novo obstruction or occlusion of the native femoropopliteal artery.
6. Subject has PAD classified as Rutherford clinical category 2, 3 or 4.
7. Subject has documented PAD by either (i) a resting ankle-brachial index (ABI) of ≤0.90 (or ≤0.75 after exercise of the target limb). Resting toe brachial index (TBI) is performed only if unable to reliably assess ABI. TBI must be <0.70; or (ii) Normal ABI with angiographic or ultrasound evidence of ≥60% diameter stenosis.

Angiographic inclusion criteria

8. Subject has single or multiple stenotic or occlusive lesions within the native femoropopliteal artery ("target lesions") that can be crossed with a guidewire and fully dilated. (Note: multiple target lesions must be treated as a single lesion.)
9. Single or multiple target lesions must be covered by a single stent or two overlapping stents. In the case of tandem lesions, the gap between lesions must be ≤ 3 cm.
10. Target lesion(s) eligible for treatment under the Protocol are at least 1 cm distal to the origin of the deep femoral artery and at least 3 cm above the bottom of the femur.
11. Target lesion(s) reference vessel diameter is between 4.0 mm and 6.0 mm by operator's visual estimate.
12. Single or multiple target lesions measure ≥40 mm to ≤140 mm in overall length, with ≥60% diameter stenosis by operator's visual estimate.
13. Subject has a patent popliteal artery (no stenosis ≥50%) distal to the treated segment.
14. Subject has at least one patent infrapopliteal vessel (<50% stenosis) with run-off to the ankle.

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

Subject Exclusion Criteria

1. Subject is unable or is unwilling to comply with the procedural requirements of the study Protocol or will have difficulty in complying with the requirements for attending follow-up visits.
2. Subject has a comorbidity that in the investigator's opinion would limit life expectancy to less than 36 months.

3. Subject has an iliac stent in target limb that has required re-intervention within 12 months prior to index.
4. Subject has any planned major surgical procedure (including any amputation of the target limb) within 30 days after the index procedure for this Study.
5. Subject has a target vessel that has been treated with any type of surgical or endovascular procedure prior to enrollment.
6. Subject has a target vessel that has been treated with bypass surgery.
7. Subject has PAD classified as Rutherford clinical category 0, 1, 5 or 6.
8. Subject has known or suspected active systemic infection at the time of enrollment.
9. Subject has a known coagulopathy or has bleeding diatheses, thrombocytopenia with platelet count less than 100,000/microliter or INR (international normalized ratio) >1.8.
10. Subject has a stroke diagnosis within 3 months prior to enrollment.
11. Subject has a history of unstable angina or myocardial infarction within 60 days prior to enrollment.
12. Subject has a contraindication to antiplatelet, anticoagulant, or thrombolytic therapies.
13. Subject has known allergy to contrast agents or medications used to perform endovascular intervention that cannot be adequately pre- medicated.
14. Subject has known allergy to titanium, nickel or tantalum.
15. Subject has received thrombolysis within 72 hours prior to the index procedure.
16. Subject has acute or chronic renal disease (e.g., as measured by a serum creatinine of >2.5 mg/dL or >220 µmol/L), or on peritoneal or hemodialysis.
17. Subject requiring coronary intervention within 7 days prior to enrollment.
18. Subject is pregnant or breast-feeding.
19. Subject is participating in another research study involving an investigational product (pharmaceutical, biologic, or medical device).
20. Subject has other medical, social or psychological problems that, in the opinion of the investigator, preclude them from receiving this treatment, and the procedures and evaluations pre- and post-treatment.

Angiographic exclusion criteria

21. Subject has significant disease or obstruction (≥50%) of the inflow tract that has not been successfully treated at the time of the index procedure (success measured as ≤30% residual stenosis, without complication).
22. Subject has a lesion in the contralateral limb requiring intervention during index procedure or within next 30 days.
23. Subject has no patent (≥50% stenosis) outflow vessel providing run-off to the ankle.
24. There is a lack of full expansion in the predilatation balloon.
25. Target lesion(s) requires percutaneous interventional treatment, beyond standard balloon angioplasty alone, prior to placement of the study stent.
26. Evidence of aneurysm or acute thrombus in target vessel.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30-days (± 7), 12 months (365 days ± 30) and 24 months (730 days ± 60) postoperatively. A 36-month (1095 days ± 60) surveillance visit shall be completed at the clinic or remotely by telephone. At follow-up visits to the site, subjects are assessed for vascular patency (Duplex ultrasound); clinical status (medical history / physical exam; adverse event assessment; ankle-brachial index; Rutherford clinical category); exercise capability and capacity (walking impairment questionnaire; 6-minute walk test (in a sub-group of investigational sites)), and X-ray of the treated area.

A summary of the schedule of MIMICS-2 Study follow-up assessments is provided in Table 6. Adverse events and complications were recorded through the Month 12 visit. Thereafter, only Major Adverse Events (MAE), Serious Adverse Events (SAE), revascularizations in the target leg and unanticipated adverse device effects (UADE) were recorded.

Table 6: MIMICS-2 Study Follow-up Schedule

Assessment	Baseline[1]	Day 0 Index Procedure	Day 30	Month 12	Month 24	Month 36[8]
Informed Consent[2]	X					
Medical History / Physical Exam[3]	X		X	X	X	
Laboratory Assessments: Creatinine, platelets	X					
Coagulation Studies[4]	X					
Urine pregnancy test if female[5]	X					
Ankle Brachial Index	X		X	X	X	
Rutherford Clinical Category	X		X	X	X	
Walking Impairment Questionnaire[10]	X		X	X	X	
Six-Minute Walk Test	X		X	X	X	
Index Angiogram / Stent Deployment		X				
Medications: Aspirin / Clopidogrel[6]		X	X	X	X	X
Duplex Ultrasound		X[7]		X	X	X[7]
X-Rays of Treatment Area[9]				X	X	X
Adverse Event Assessment	X	X	X	X	X	X

[1] Standard of care evaluations were done up to 30 days before the procedure
[2] Consent was obtained within 14 days prior to enrollment
[3] Medical history is required at baseline only
[4] PT/INR (prothrombin time or international normalized ratio) obtained only if subject on chronic warfarin therapy
[5] Negative pregnancy test was required within 14 days of enrollment for women of childbearing potential
[6] Dual anti-platelet therapy was required through 30 days and then continued per physician / institutional standards of care. Aspirin therapy was continued indefinitely
[7] Post-procedure DUS was obtained post-procedure through Day 30 (+7 days). DUS at 36 months only if clinical signs or symptoms are present suggestive of worsening claudication

[8] 36-Month surveillance visit may be completed via clinic or telephone visit.
[9] X-ray imaging was permitted at a facility remote to the investigational site.
[10] WIQ obtained 30 days prior to index procedure through the peri-procedural period (e.g., within 24 hours of index procedure.)

3. Clinical Endpoints

The primary safety endpoint was measured as a composite of independently-adjudicated major adverse events (MAE) comprising death, any major amputation performed on the index limb, or CDTLR through 30 days. The primary safety objective is achieved if the one-sided lower 97.5% Agresti-Coull confidence limit for the proportion of subjects treated with BioMimics 3D who are free from MAE through 30 days, is greater than the VIVA Physicians' performance goal of 88%.

The primary effectiveness endpoint was primary stent patency rate at 12 months. Patency was defined as no significant reduction in luminal diameter (i.e. < 50% diameter stenosis) since the index procedure or intervening CDTLR. Luminal diameter was determined by the independent core laboratory. Loss of primary stent patency is deemed when Doppler ultrasound (DUS) peak systolic velocity ratio (PSVR) >2.0, or where angiography reveals >50% diameter stenosis, or where the subject undergoes CDTLR. When both DUS and angiography imaging modalities were available, angiography took precedence. Success in the primary effectiveness objective was established if the one-sided lower 97.5% Agresti-Coull confidence limit for the proportion of subjects treated with BioMimics 3D that continue to have treated segment patency through 12 months was greater than 66%.

With regard to success/failure criteria, both primary endpoint hypotheses were required to be satisfied, thus no adjustment to alpha was necessary to account for multiple endpoints.

Secondary Endpoints

The clinical study evaluated the following secondary endpoints:

- Contribution of individual MAE rates to the primary safety endpoint;
- MAE rate at Month 12 and contribution of individual event rates to the overall MAE;
- Rates of all adverse events and serious adverse events not included in primary safety endpoint determination;
- Core lab reported technical success (≤50% residual diameter stenosis at index procedure);
- Comparison of Rutherford Clinical Category at Baseline, Day 30, Months 12 and 24;
- Comparison of 6-minute walk test at Baseline, Day 30, Months 12 and 24 (selected sites);
- Comparison of ankle-brachial index at Baseline, after stenting and Months 12 and 24;
- Comparison of the walking impairment questionnaire at Baseline, after stenting and Months 12 and 24; and
- Core lab determined stent fracture rate at 12, 24 and 36 Months.

B. Accountability of PMA Cohort

At the time of database lock, of 271 patients enrolled in the PMA study, 94.5% (256/271) of the intention-to-treat (ITT) cohort completed their 12 month post-operative visit and their data are available for analysis. Table 7 describes compliance for the clinical trial subjects through 12 months with regard to determination of primary study endpoints.

Table 7: MIMICS-2 Study Follow-up Compliance Through 12 months (ITT Cohort)

	N=271	
Available for Primary Safety Endpoint determination:	99.3% (269/271)	
• Day 30 visit completed	268	
• Day 30 visit missed but subject attended 12-month visit	1	
• Lost to follow-up without Day 30 visit		2
Available for Primary Effectiveness Endpoint determination:	91.5% (248/271)	
• Scheduled, diagnostic DUS at Month 12 visit	242	
• Subjects without DUS at Month 12 but with intervening TLR	4	
• Subjects without DUS at Month 12 but with patent DUS at Month 24 and no intervening TLR	2	
• Withdrew consent		4
• Lost to follow-up		6
• Died		3
• Missed Month 12 visit, no DUS and without TLR		5
• Month 12 Visit/DUS was prior to start of visit window		2
• Month 12 Visit DUS was non-diagnostic		3

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a pivotal study performed in the US. Baseline demographics, medical history and risk factors were generally similar across the populations enrolled in the US (N=162), Japan (N=31), and Germany (N=78) without evidence of any significant difference in risk factors for Nitinol stenting between the cohorts.

Data for the consolidated MIMICS-2 Study population are summarized in Table 8 (subject demographics and relevant medical history) and Table 9 (clinical status).

Table 8: MIMICS-2 Study Baseline Demographics and Medical History

Parameter (n)	ITT Subjects; N=271
Age (n/N) Median [IQR (interquartile range)]	(271/271) 69.0 [62.0,76.0]

Parameter (n)	ITT Subjects; N=271
Mean ± SD; Range (Min, Max)	68.4 ± 9.5; (45.0, 94.0)
Gender: Male	66.4% (180/271)
Race:	
White	79.3% (215/271)
Asian	11.4% (31/271)
Black or African American	5.9% (16/271)
Native Hawaiian or Pacific Islander	0.0% (0/271)
American Indian or Alaska Native	0.0% (0/271)
Other	0.4% (1/271)
Refuse to disclose	3.0% (8/271)
Ethnicity:	
Not Hispanic or Latino	93.4% (253/271)
Hispanic or Latino	3.7% (10/271)
Unknown	0.0% (0/271)
Refuse to disclose	3.0% (8/271)
Relevant Medical History:	
Hypertension	90.0% (244/271)
Hypercholesterolemia / dyslipidemia	81.9% (222/271)
Unstable angina	3.3% (9/271)
Previous myocardial infarction	18.5% (50/271)
Previous percutaneous coronary intervention	33.6% (91/271)
Previous coronary artery bypass graft	20.7% (56/271)
Congestive heart failure	6.6% (18/271)
Cerebrovascular accident or stroke	7.7% (21/271)
Renal insufficiency	0.7% (2/271)
Diabetes	45.4% (123/271)
Previous revascularization (endovascular or surgery) in leg(s)	36.2% (98/271)
Smoking:	
Current	40.2% (109/271)
Former	40.6% (110/271)

Table 9: MIMICS-2 Study - Clinical Status ITT Subjects

Parameter (n)	N=271
ABI (Target Limb):	
(n/N)	(257/271)
Median [IQR]	0.67 [0.57, 0.81]
Mean ± SD; Range (min. max)	0.70 ± 0.20; (0.00, 1.73)
> 0.9	11.3% (29/257)
> 0.4 ≤ 0.9	85.6% (220/257)
≤ 0.4	3.1% (8/257)
Rutherford Clinical Category:	
(n/N)	(271/271)
Median [IQR]	3.0 [2.0,3.0]
Mean ± SD; Range (min. max)	2.8 ± 0.5; (2.0, 5.0)

Parameter (n)	N=271
0	0.0% (0/271)
1	0.0% (0/271)
2	26.9% (73/271)
3	67.5% (183/271)
4	5.2% (14/271)
5	0.4% (1/271)
6	0.0% (0/271)

Table 10 summarizes the baseline lesion characteristics determined by the core laboratory, together with quantitative vascular angiographic data for the target lesion in all enrolled subjects at the index procedure. There was 100% enrollment compliance with *de novo* target lesion eligibility. Lesions were moderately to severely calcified in 45.9% of subjects according to the Peripheral Arterial Calcium Scoring System (PACSS) and 30.0% had total occlusions. Mean lesion length was 81.2 mm and the mean BioMimics 3D stented length was 112.3 mm. Technical success (defined as ≤ 50% diameter stenosis in final stent angiogram) was reported by the core laboratory as 100%.

Table 10: Core Laboratory Reported Baseline Lesion & Index / Quantitative Vascular Angiography

Lesion Characteristic[1]	Category	ITT Subjects; N=271
Lesion type[2]	*De novo*	100% (271/271)
Lesion location within superficial femoral and proximal popliteal arteries	Proximal Mid Distal	11.5% (31/270) 48.1% (130/270) 40.4% (109/270)
Reference vessel diameter (mm)	Mean ± SD	5.2 ± 0.9 (269/271)
Pre-procedure diameter stenosis %	Mean ± SD	77.8 ± 18.3 (269/271)
Lesion length (mm)	Mean ± SD Median [IQR[3]] Range	81.2 ± 38.4 (269/271) 73.8 [54.4, 108.6] 9.3, 217.2
Calcification % (moderate + severe)		45.9 (124/270)
Total occlusion %		30.0 (81/270)
Tibial vessel runoff % (<50% stenosis in 1 or more vessel)		98.8 (237/240)
Post-stent diameter stenosis %	Mean ± SD	12.6 ± 7.5 (269/271)
Deployed stent length (mm)	Mean ± SD Median [IQR] Range	112.3 ± 36.3 (269/271) 104.0 [82.8, 146.8] 54.3, 238.7
Technical success % (final stent ≤ 50% diameter stenosis)		100.0% (269/269)

[1] Core laboratory reported data, unless indicated
[2] Investigator reported

[3] *IQR: Interquartile Range*

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the cohort of 269 ITT subjects who were available for the 30-day evaluation. The key safety outcomes for this study are presented below in Table 11. Serious adverse events are reported in Table 12.

The primary safety endpoint was defined as the composite of MAE comprising death, any major amputation performed on the index limb, or CDTLR through Day 30. All site-reported adverse events were reviewed by the independent CEC and those events reported or potentially qualifying as MAE, or interventions performed on the target limb, were adjudicated.

The observed rate of freedom from MAE through Day 30 was 99.6% (268/269) based on the ITT population. Two subjects were lost to follow-up without any event reported, and without an ascertainment of status past the Day 23 lower window for the Day 30 visit, these subjects were ineligible for the primary safety endpoint analysis according to the Protocol and Statistical Analysis Plan. One subject had a CEC-adjudicated MAE, a CDTLR, three days after the index procedure, following abrupt closure of the treated segment. No additional adverse events were reported or adjudicated as MAE through Day 30. The data supporting the determination of the primary safety endpoint are presented in Table 11.

Table 11: Summary of Major Adverse Events in MIMICS-2 Study through 30 Days and 12 Months

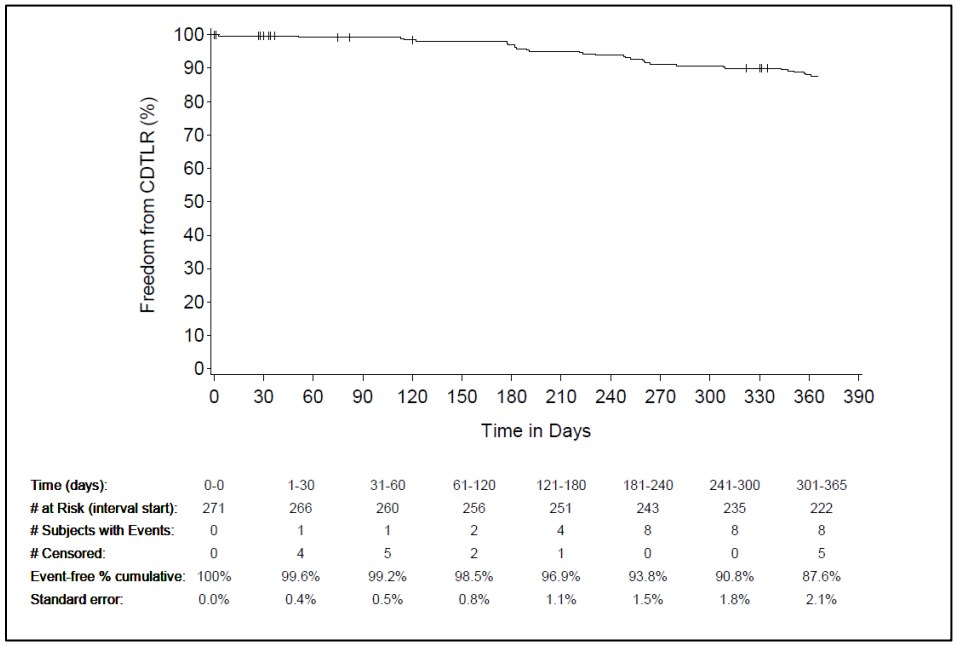
Event	Rate of Freedom from Event in ITT Cohort (n/N)	
	30 Days	12 Months[1]
Major Adverse Event	99.6% (268/269)	86.4% (223/258)
• Death	100% (269/269)	98.8% (253/256)
• Major Amputation	100% (269/269)	100% (254/254)
• Clinically-driven Target Lesion Revascularization	99.6% (268/269)	87.5% (224/256)

[1] Subjects appear in the denominator if (i) they have sufficient follow-up (at least 12 months less 30 days), or (ii) they have had the event of interest (each event is considered separately).

The lower 97.5% one-sided Agresti-Coull confidence limit for the proportion of subjects treated with the BioMimics 3D Vascular Stent System that were free from MAE at Day 30 was 97.7%, which exceeds the performance goal of 88%. The primary safety endpoint of the MIMICS-2 Study was therefore met.

The CEC-adjudicated rate of MAE occuring on or before Day 365 was 13.6% (35/258), as summarized in Table 11. There were three deaths (one non-cardiovascular: metastatic disease; two cardiovascular: both heart failure) within 365 days (1.2%; 3/256). Additionally, 32 subjects had CDTLR within 365 days (12.5%; 32/256). No major amputations were reported.

For those MAE that were adjudicated by CEC as CDTLR, the Kaplan-Meier survival analysis in Figure 3 estimates that the 12-month freedom from CDTLR after treatment with BioMimics 3D is 87.6%.



Time (days):	0-0	1-30	31-60	61-120	121-180	181-240	241-300	301-365
# at Risk (interval start):	271	266	260	256	251	243	235	222
# Subjects with Events:	0	1	1	2	4	8	8	8
# Censored:	0	4	5	2	1	0	0	5
Event-free % cumulative:	100%	99.6%	99.2%	98.5%	96.9%	93.8%	90.8%	87.6%
Standard error:	0.0%	0.4%	0.5%	0.8%	1.1%	1.5%	1.8%	2.1%

Figure 3: Kaplan-Meier Survival Estimate for CEC-Adjudicated CDTLR through 12 Months

Adverse effects that occurred in the PMA clinical study

Table 12 provides a summary of all serious adverse events reported through 12 months. A serious adverse event (SAE) was defined as an adverse event that:

- Led to death,
- Led to a serious deterioration in the health of the subject, that either resulted in:
  - a life-threatening illness or injury, or
  - a permanent impairment of a body structure or a body function, or
  - in-patient hospitalization or prolongation of existing hospitalization
  - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to body structure or a body function, or
- Led to fetal distress, fetal death or a congenital abnormality or birth defect.

No adverse event occurring in the MIMICS-2 Study qualified for an unanticipated adverse device effect (UADE) report.

Table 12: Investigational Site Reported Serious Adverse Events through 12 Months

AE Category	Event Description[1]	% (n/N)
All Serious Adverse Events	All Serious Adverse Events	42.1% (114/271)
Vascular disorders	Restenosis of treated segment	12.2% (33/271)
	Arterial stenosis (non-target)	9.2% (25/271)
	Restenosis	2.2% (6/271)
	Restenosis of treated vessel	1.5% (4/271)
	Thrombosis	1.5% (4/271)
	Dissection	0.7% (2/271)
	Hypotension	0.7% (2/271)
	Limb ischemia	0.7% (2/271)
	Pseudoaneurysm	0.7% (2/271)
	Abrupt occlusion	0.4% (1/271)
	Amputation (unplanned, spontaneous)	0.4% (1/271)
	Aneurysm	0.4% (1/271)
	Dissection (≥ Grade C) in target vessel requiring intervention	0.4% (1/271)
	Embolization, distal	0.4% (1/271)
	Hypertension	0.4% (1/271)
	Total occlusion of the peripheral artery	0.4% (1/271)
Cardiac disorders	Angina	2.2% (6/271)
	Congestive heart failure (CHF)	2.2% (6/271)
	Atrial fibrillation	1.8% (5/271)
	Myocardial infarction	1.1% (3/271)
	Myocardial ischemia	1.1% (3/271)
	Cardiac arrhythmia	0.4% (1/271)
	Ventricular tachycardia	0.4% (1/271)
Blood & lymphatic system disorders	Anemia	0.4% (1/271)
Gastrointestinal disorders	Gastro-intestinal bleeding	0.7% (2/271)
Infections & infestations	Sepsis	1.1% (3/271)
	Infected peripheral wound	0.4% (1/271)
	Urinary tract infection (UTI)	0.4% (1/271)
Injury, poisoning & procedural complications	Arterial occlusion/thrombus at puncture site	0.7% (2/271)
	Vascular access complications	0.7% (2/271)
	Groin hematoma ≥ 5 cm, with or without surgical repair	0.4% (1/271)
	Seizure	0.4% (1/271)

AE Category	Event Description[1]	% (n/N)
Nervous system disorders	Stroke or other neurological complications	0.4% (1/271)
Renal & urinary disorders	Renal failure/renal insufficiency	0.7% (2/271)
Respiratory, thoracic & mediastinal disorders	Respiratory distress	0.7% (2/271)
	Pneumonia	0.4% (1/271)
Other event[2]	Other	16.2% (44/271)

[1] Site reported term
[2] "Other event" category comprises 69 SAE in 44 subjects across 17 different categories.

The use of the BioMimics 3D Vascular Stent System in the MIMICS-2 Study was associated with a rate of procedure and device-related SAE (see Table 13) comparable to similar devices during the index procedure, through discharge, 30-day and 12-month visits.

Table 13: Rate and Incidence of Site-Reported, Serious Adverse Events to 12 months (ITT Subjects)

Event Category	Number of Events; % Subjects with Event (n/N)		
	In-hospital	30 Days	12 Months
Any SAE	15; 4.8% (13/271)	33; 9.6% (26/271)	217; 42.1% (114/271)
Potential MAVE*	3; 1.1% (3/271)	4; 1.5% (4/271)	54; 15.9% (43/271)
Device- or Procedure-related[1]	10; 3.3% (9/271)	12; 4.1% (11/271)	47; 15.5% (42/271)
Device- related	0; 0.0% (0/271)	1; 0.4% (1/271)	35; 11.8% (32/271)
Procedure-related[1]	10; 3.3% (9/271)	12; 4.1% (11/271)	21; 7.0% (19/271)

[1] As determined by the investigator to be probably or definitely related to the procedure.
* Potential MAVE event, defined as any: Abrupt occlusion; Access site complication requiring surgery or transfusion; Arterial perforation or rupture; Dissection (Grade C or greater) in target vessel requiring intervention; Embolization, distal; Limb ischemia; Necrosis, target limb; Pseudoaneurysm, access site; Pseudoaneurysm, target limb; Restenosis, target lesion; Restenosis, target vessel; or Thrombosis

The rate of serious adverse events reported up to 12 months that were categorized as device-related by the investigational site was 11.8% (30/271). These included: restenosis of treated segment (10.7%; 29/271); restenosis of treated vessel (0.4%; 1/271); abrupt occlusion (0.4%; 1/271); total occlusion of the peripheral artery (0.4%; 1/271).

The rate of serious adverse events reported up to 12 months that were categorized as procedure-related by the investigational site was 7.0% (19/271). These included: abrupt occlusion (0.4%; 1/271); arterial occlusion/thrombus at puncture site (0.7%; 2/271); dissection (0.7%; 2/271); dissection (Grade C or >) in target vessel requiring intervention (0.4%; 1/271); groin hematoma ≥ 5cm with or without surgical repair (0.4%); pseudoaneurysm (0.4%; 1/271); renal failure/renal insufficiency (0.4%; 1/271); restenosis of treated segment (3.0%; 8/271); vascular access complications (0.7%: 2/271); hypoglycemia (0.4%; 1/271).

2. Effectiveness Results

There were 248 ITT subjects evaluable for the primary effectiveness endpoint, primary stent patency at 12 months. Primary patency was defined as no significant reduction in luminal diameter (< 50% diameter stenosis) since the index procedure. Loss of patency was determined by an independent core laboratory when the peak systolic velocity ratio (PSVR) exceeds 2.0, or where angiography revealed > 50% diameter stenosis, or where the subject had a CDTLR. CDTLR is adjudicated by the Clinical Events Committee as revascularization of the target lesion with objective evidence of recurrent symptoms associated with an angiographic determination of ≥50% stenosis and new distal ischemic signs (worsening ABI or worsening Rutherford Category associated with the index limb); or angiographically-determined ≥70% diameter stenosis in the absence of objective evidence of recurrent symptoms. Where both imaging modalities were available, angiography took precedence.

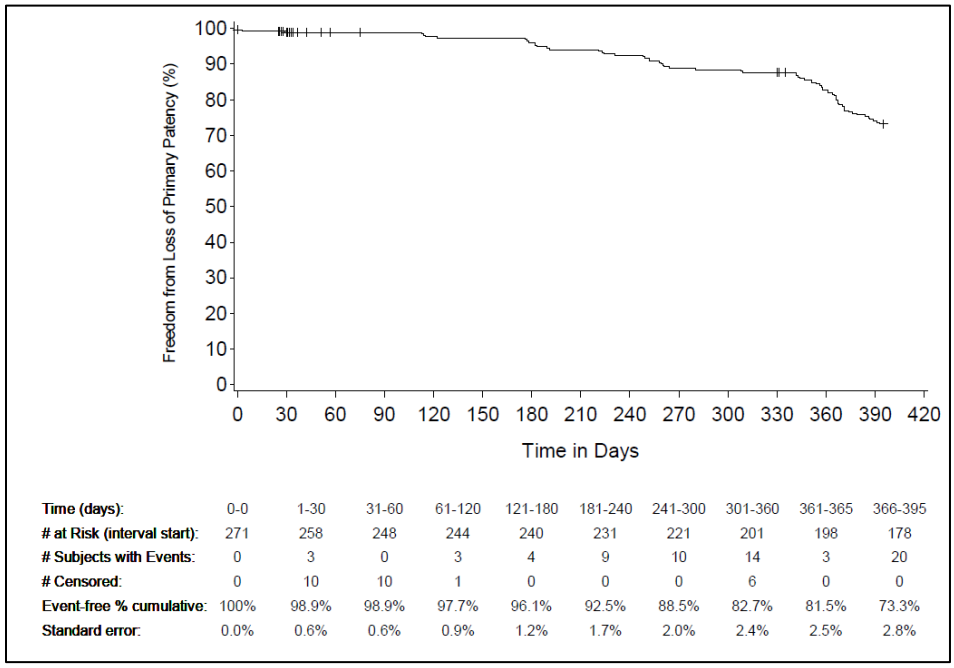
Based on core laboratory determination, the observed primary stent patency rate in the ITT population at Day 395 was 73.0% (181/248). The primary effectiveness endpoint results are summarized in Table 14.

Table 14: MIMICS-2 Study Primary Effectiveness Endpoint Result (ITT Subjects)

Endpoint	Rate (n/N) [95% CI]
Primary stent patency rate at 12 Months *(end of window, Day 395)*	73.0% (181/248) [67.1%, 78.1%]

The lower 97.5% one-sided Agresti-Coull confidence interval for the proportion of subjects treated with BioMimics 3D who continued to have treated segment patency through 12 months was 67.1%, which exceeded the performance goal of 66%. The primary effectiveness endpoint of the MIMICS-2 Study was therefore met.

A further analysis of MIMICS-2 primary patency data was conducted using a Kaplan Meier survival estimate of the probability of a subject being free from loss of primary stent patency through 12 months. In this ITT analysis, subjects were censored at the date of their DUS follow-up, or at the time of Study exit due to either death, consent withdrawal or lost to follow-up. Subjects confirmed by the core laboratory to have primary stent patency at their 12-month 12 DUS, were censored at the end of the 12-month-12 follow-up window – (Day 395). The output of this Kaplan-Meier analysis for primary patency presented in Figure 4 indicates the probability of freedom from loss of primary patency at 12 months (Day 395) after treatment with BioMimics 3D is 73.3%. For Day 360, a commonly used Kaplan-Meier metric for comparative review of peripheral endovascular interventional studies, the KM freedom from loss of primary patency value is 82.7%.



Time (days):	0-0	1-30	31-60	61-120	121-180	181-240	241-300	301-360	361-365	366-395
# at Risk (interval start):	271	258	248	244	240	231	221	201	198	178
# Subjects with Events:	0	3	0	3	4	9	10	14	3	20
# Censored:	0	10	10	1	0	0	0	6	0	0
Event-free % cumulative:	100%	98.9%	98.9%	97.7%	96.1%	92.5%	88.5%	82.7%	81.5%	73.3%
Standard error:	0.0%	0.6%	0.6%	0.9%	1.2%	1.7%	2.0%	2.4%	2.5%	2.8%

Figure 4. Kaplan-Meier Survival Estimate for Primary Stent Patency (ITT Subjects)

3. Secondary Endpoints

Analyses were conducted for protocol-defined secondary study endpoints. These were to provide descriptive statistics without hypothesis testing. As MIMICS-2 is an ongoing Study with follow-up in progress, the secondary endpoint data presented in Table 15 are limited to the 12-Month visit window.

Table 15: Summary of Secondary Endpoint Outcomes through 12 Months (ITT Subjects)

Outcome measure (n)	Baseline/ Index Procedure	30 Days	12 Months
Technical Success[1]	100% (269/269)		
Rutherford Clinical Category (RCC) Mean ± SD Median [IQR] Range (Min, Max)	 2.8 ± 0.5 (271) 3.0 [2.0, 3.0] 2.0, 5.0	 0.8 ± 1.0 (268) 0.0 [0.0; 1.0] 0.0, 4.0	 0.9 ± 1.1 (254) 1.0 [0.0; 1.0] 0.0, 4.0
Proportion of matched subjects with improvement of 1 or more RCC		86.9% (233/268)	85.0% (216/254)
Proportion of matched subjects with worsening of 1 or more RCC		0% (0/268)	2.0% (5/254)
Ankle-Brachial Index (ABI) Target Limb Mean ± SD Median [IQR] Min, Max	 0.70 ± 0.20 (257) 0.67 [0.57, 0.81] 0.00, 1.73	 0.98 ± 0.16 (263) 0.97 [0.90, 1.05] 0.52, 2.27	 0.92 ± 0.19 (247) 0.93 [0.83, 1.00] 0.33, 1.86
Walking Impairment Questionnaire (WIQ) Overall Score: Mean ± SD Median [IQR] Min, Max	 0.28 ± 0.24 (266) 0.22 [0.07, 0.45] 0.00, 1.00	 0.58 ± 0.32 (264) 0.63 [0.30, 0.86] 0.00, 1.00	 0.58 ± 0.31 (253) 0.66 [0.33, 0.86] 0.00, 1.00
Stent Fracture[2]			0% (0/229)

[1] Technical success reported by the core lab as the percentage of treated lesions in which a final result of ≤50% residual diameter stenosis (in-stent) was achieved at index procedure.
[2] Stent fracture reported by core laboratory on review of X-ray images of treated area

Technical Success

Technical success was reported by the core laboratory as the percentage of treated lesions in which a final result of ≤50% residual diameter stenosis (in-stent) was achieved at the BioMimics 3D index procedure. Technical success was achieved in 100% (269/269) of the reviewed baseline angiograms.

Rutherford Clinical Category (RCC)

At baseline, 94.5% (256/271) of subjects had moderate (RCC 2) or severe (RCC3) intermittent claudication. Only 5.2% (14/271) of subjects had rest pain (RCC 4). One subject was a protocol eligibility criteria deviation, due to minor tissue loss at baseline (RCC 5 = 0.4%; 1/271). No subject was either asymptomatic (RCC 0) or complained of mild claudication (RCC 1).

At 30 days, for the 268 subjects assessed, there was a mean improvement in RCC of 2.0 ± 1.1 categories, and no subject was worse compared to baseline. At 12 months, for the 254 subjects with matched assessments, there was a maintained improvement over baseline of 1.9 ± 1.1 categories. An improvement of ≥1 category was reported in 86.9% of subjects at 30 days and in 85% at 12 months. Five subjects (2%, 5/254) had deteriorated compared to baseline at 30 days, and 4 of those due to worsening of both the treated (index) leg and the non-treated leg.

6-Minute Walk Test

In accordance with the protocol, the 6-minute walk test was conducted among a subgroup of investigational sites. Baseline walking test data were available from 22 subjects from 8 sites, 8.1% (22/271). Using a matched-baseline analysis, the mean walking distance increased 49.1% for the cohort of 21 subjects at 30 days and 29.9% for the cohort of 15 subjects at 12 months, indicating a continued clinical benefit arising from treatment with BioMimics 3D.

Ankle-brachial Index (ABI)

The ABI was measured at baseline, 30 days, and 12 months. At baseline the median ABI for 257 subjects was 0.67 with a mean 0.7. At 30 days, in the 253 subjects assessed, the subjects improved with a median of 0.29 and mean of 0.27. At 12 months, the improvement was maintained in the 236 subjects assessed with a median 0.24 and mean 0.22.

Walking Impairment Questionnaire (WIQ)

Subjects treated with BioMimics 3D also demonstrated sustained improvement in all categories within the WIQ Questionnaire over the 12-month follow-up interval, maintaining the improvement seen at 30 days. Using a matched baseline comparison, there was a 0.30 ± 0.30 improvement in the overall WIQ score at 30 days (259/264 subjects) and 0.29 ± 0.30 (248/253) at 12 months. Data from the component elements of the WIQ (Walking Distance; Walking Speed and Stair Climbing) are presented in Table 16.

Table 16: MIMICS-2 Study - Walking Improvement Questionnaire, Changes from Baseline (ITT Subjects)

Mean Change from Baseline ± SD (N)	30 Days	12 Months
Overall Score	0.30 ± 0.30 (259)	0.29 ± 0.30 (248)
Walking Distance Score	0.37 ± 0.37 (264)	0.37 ± 0.38 (253)
Walking Speed Score	0.29 ± 0.30 (263)	0.26 ± 0.31 (251)
Stair Climbing Score	0.25 ± 0.35 (260)	0.24 ± 0.35 (249)

Stent Integrity

The core laboratory conducted a review of X-ray imaging of the treated area for 229/271 subjects for which imaging collected at the 12-month visit was available. No fracture was reported in any study stent.

Poolability of Results

Poolability of study subjects was investigated by comparing primary outcomes across investigational sites and regions. A chi-square test was conducted without detecting significant difference among sites regarding the primary patency endpoint at 12 months (p=0.52). Poolability of study subjects is not an issue for the safety endpoint at 30 days as there was only one MAE. In conclusion, there does not appear to be

heterogeneity across sites, and the pooling of data over sites appears to be appropriate.

4. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes: gender, cilostazol use, country, 5 mm stent or not, and overlapping stents.

Gender Analysis

The observed 30-day MAE free rate was 99.4% (178/179) for males and 100.0% (90/90) for females, with only one MAE reported for any subject during this assessment window. The observed 12-month primary patency rate was 76.8% (129/168) for males and 65.0% (52/80) for females.

Cilostazol

The observed 30-day MAE free rate was 100.0% (18/18) for subjects taking cilostazol and 99.6% (250/251) for those not taking cilostazol. The observed 12-month primary patency rate was 86.7% (13/15) for subjects taking cilostazol and 72.1% (168/233) for those not taking cilostazol.

Country of investigational site location

The observed 30-day MAE free rate was 100% (31/31) for Japan, 99.4% (159/160) for US and 100% (78/78) for Germany. The observed 12-month primary patency rate was 67.7% (21/31) for Japan, 71.1% (101/142) for US, and 78.7% (59/75) for Germany.

5 mm Stent

The number of subjects evaluable at 12-months that were treated with 5 mm diameter BioMimics 3D stents was small (n=33), relative to those treated with 6 mm or 7 mm stents (n=215). The observed 12-month primary patency rate was 72.7% (24/33) for subjects treated with 5 mm stents and 73.0% (157/215) for those treated with 6 mm or 7 mm stents.

Overlapping Stents

A relatively small number of subjects in the MIMICS-2 Study (12.5%; 34/271) required placement of a second BioMimics 3D stent. The observed 30-day MAE free rate was 99.6% (235/236) for subjects treated with single and 100.0% (33/33) for those treated with overlapped stents. The use of overlapped stents was primarily to treat longer lesions ≥ 120 mm (65%; 22/34), prior to the mid-study introduction of the 150 mm BioMimics 3D stent. The core laboratory reported mean stented segment lengths of 105.1 mm for single stents and 162.2 mm for overlapping stents. Across all stented segment lengths, the observed primary patency in subjects evaluable at 12 months, was higher for single stent (75.9%; 164/216) than in overlap stented segments (53.1%; 17/32). It is of interest that among 55 subjects with long stented segments ≥ 150 mm, where poorer outcomes are typically expected, the observed 12-

month primary patency was 63.6% (21/33) when a single stent was used and 59.1% (13/22) when overlapped stents were used.

5. 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 189 investigators of which none were full-time or part-time employees of the sponsor and 3 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 3
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

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

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

The Mimics Study was a prospective, multicenter, randomized (2:1 BioMimics 3D Stent vs. a straight Nitinol control stent) evaluation of safety and effectiveness in patients with symptomatic peripheral arterial disease undergoing femoropopliteal intervention, conducted in Germany. The study investigated the safety and performance of the BioMimics 3D Stent in improving luminal diameter in the treatment of symptomatic de-novo or restenotic lesions up to 100 mm in length in native superficial femoral and/or proximal popliteal arteries with reference vessel diameters ranging from 3.5 – 7.0 mm. Stent sizes of 5.0 – 7.0 mm (diameter) and 60 – 125 mm (length) were available for this study.

A. Mimics Study Design

A lead-in cohort of 10 subjects was enrolled at one investigational site as a Phase I cohort to gain preliminary acute interventional safety experience with the BioMimics 3D Vascular Stent System. After review of the clinical safety experience of the system in this preliminary cohort, the study was transitioned into Phase II, progressively increasing to a total of 8 investigational sites in Germany, in which a further 76 subjects were enrolled with 2:1 randomization to either BioMimics 3D or the Control stent, such that 50 subjects received treatment with BioMimics 3D Stents. The Mimics study was

not powered to detect a difference between the two cohorts with respect to either safety or performance.

The comparator arm was enrolled specifically to provide a point of anatomical, mechanical and hemodynamic reference for analysis of supplementary outcome measures, including X-ray imaging of the treated area with the limb flexed at the knee, or extended. In total, in Phase I and II studies, 61 BioMimics 3D Stents were placed in 60 subjects.

B. Subject demographics and medical history

A summary of subject demographics and medical history is presented in Table 17.

Table 17: Mimics Study Subject Demographics and Medical History

(n/N)	**BioMimics 3D Phase I (N = 10)**	**BioMimics 3D Phase II (N = 50)**	**BioMimics 3D All subjects (N = 60)**
Age: Mean ± SD; Range (min, max)	65 ± 10 (48, 85)	68 ± 10 (49, 94)	67 ± 10 (48, 94)
Male %	80 (8/10)	66 (33/50)	68 (41/60)
Race: White/Caucasian %	100 (10/10)	100 (50/50)	100 (60/60)
Diabetes %	50 (5/10)	26 (13/50)	30 (18/60)
Type I %	0 (0/10)	0 (0/10)	0 (0/60)
Type II %	50 (5/10)	26 (13/50)	30 (18/60)
Insulin-dependent %	20 (2/10)	10 (5/50)	16.6 (7/60)
Dyslipidemia %	100 (10/10)	76 (38/50)	80 (48/60)
Hypertension %	90 (9/10)	88 (44/50)	88 (53/60)
Smoking (Current + Former) %	90 (9/10)	74 (37/50)	77 (46/60)
Current %	40 (4/10)	42 (21/50)	42 (25/60)
Former %	50 (5/10)	32 (16/50)	35 (21/60)
Carotid artery disease %	20 (2/10)	10 (5/50)	12 (7/60)
Renal disease %	10 (1/10)	4 (2/50)	5 (3/60)
Iliac disease %	40 (4/10)	18 (9/50)	22 (13/60)
Peripheral disease %	50 (5/10)	30 (15/50)	33 (20/60)
Rutherford Clinical Category %			
1	0 (0/10)	6 (3/50)	5 (3/60)
2	20 (2/10)	14 (7/50)	15 (9/60)
3	70 (7/10)	74 (37/50)	73 (44/60)
4	0 (0/10)	6 (3/50)	5 (3/60)
5	10 (1/10)	0 (0/50)	2 (1/60)
ABI Mean ± SD	0.65 ± 0.10	0.59 ± 0.22	0.61 ± 0.21
Range (min,max)	(0.50, 0.76)	(0.25, 1.43)	(0.25, 1.43)

Lesion characteristics

Mean, core-laboratory reported, lesion length and stented segment length for the 60 subjects treated with BioMimics 3D Stents within the randomized Phase II study were 69.5 mm ± 28.5 mm and 103.4 mm ± 30.3 mm, respectively. Further data on lesion characteristics and procedural outcome are presented in Table 18.

Table 18: Mimics Study Target Lesion Characteristics

Target Lesion Characteristics (n/N)	BioMimics 3D Phase I (N = 10)	BioMimics 3D Phase II (N = 50)	BioMimics 3D (N = 60)
Lesion Length (mm) Mean ± SD	88.0 ± 14.9	65.8 ± 29.3	69.5 ± 28.5
Range (min,max)	(62.0, 113.7)	(13.7, 153.8)	(13.7, 153.8)
Pre-proc. Reference Vessel Diameter (mm) Mean ± SD	4.9 ± 0.8	4.7 ± 1.1	4.7 ± 1.11
Range (min,max)	(3.4, 5.65)	(2.3, 7.8)	(2.3, 7.8)
Pre-procedure Stenosis (%) Mean ± SD	80.3 ± 11.5	84.3 ± 16.6	83.6 ± 15.9
Range (min,max)	(63.4, 100)	(51.0, 100)	(51.0, 100)
Calcification %			
None	0 (0/10)	36 (18/50)	30 (18/60)
Mild	60 (6/10)	12 (6/50)	20 (12/60)
Moderate	30 (3/10)	10 (5/50)	13.3 (8/60)
Severe	10 (1/10)	42 (21/50)	36.7 (22/60)
Stent length (mm) Mean ± SD	127.2 ± 18.5	98.7 ± 30.1	103.4 ± 30.3
Range (min,max)	(78.4, 149.3)	(11.9, 162.3)	(11.9, 162.3)
Stent diameter (mm) Mean ± SD	5.8 ± 0.5	5.6 ± 0.9	5.7 ± 0.8
Range (min,max)	(5.1, 6.8)	(3.0, 7.3)	(3.0, 7.3)
Post-procedural stenosis % Mean ± SD	19.1 ± 8.2	22.0 ± 7.7	21.5 ± 7.8
Range (min,max)	(10.3, 30.9)	(8.2, 42.4)	(8.2, 42.4)
Total occlusion %	10 (1/10)	44 (22/50)	38 (23/60)
Occlusion Length (mm) Mean ± SD	50.1 ± 0.0 (1/10)	43.5 ± 21.9 (22/50)	43.8 ± 21.5 (23/60)
Range (min,max)	(50.1, 50.1)	(6.9, 91.3)	(6.9, 91.3)
Run-off vessels %			
0	11.1 (1/10)	0.0 (0/50)	2.1 (1/60)
1	22.2 (2/10)	31.6 (12/50)	29.8 (14/60)
2	66.7 (6/10)	31.6 (12/50)	38.3 (18/60)
3	0.0 (0/10)	36.8 (14/50)	29.8 (14/60)

C. Study Endpoints and Results

The *primary safety endpoint* was defined as a composite of major adverse events (MAE) comprising death, amputation, or target lesion revascularization (TLR) through 30 days. The performance goal (PG) specified that 88% of subjects should be free from MAE through 30 days. All 60 subjects remained free from MAE at 30-days.

The *primary performance endpoint* specified a PG of 67% freedom from clinically driven target lesion revascularization (CDTLR) at 6-months post index

procedure. All Phase I (10 subjects) and Phase II (50 subjects) treated with the BioMimics 3D Stent were free from CDTLR at 6 months.

MIMICS Phase II Study subjects were followed up to 24 months. Analysis of data from the extended follow up period showed that the proportion of patients treated with BioMimics 3D who maintained stent patency (PSVR ≤ 2.0) at 12 and 24 months was 75% and 72% respectively. A Kaplan-Meier survival analysis estimated freedom from loss of primary stent patency for subjects treated with BioMimics 3D at 80% Year 1 and 72% Year 2, compared with 71% and 55% for the Control stent. Kaplan- Meier analysis of independently adjudicated clinical events showed that freedom from CDTLR was 91% for BioMimics 3D vs. 92% for the Control stent at 12 months and 91% versus 76% at 24 months. Core laboratory review of X-ray imaging of the stented area, through 2 years of follow-up, revealed no fractures at any timepoint in any BioMimics 3D Stent.

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

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

Non-clinical and pre-clinical testing conducted on the stent and delivery system demonstrated that the performance characteristics meet the product specifications. The multi-center MIMICS-2 clinical study evaluated the safety and effectiveness of the BioMimics 3D Vascular Stent System. The primary effectiveness endpoint was defined as the 12-month primary stent patency as determined by core-laboratory adjudicated DUS, angiography, and/or freedom from CDTLR. The observed primary effectiveness endpoint of primary patency rate met the performance goal of 66% with a rate of 73.0% [97.5% Agresti-Coull confidence interval: 67.1%, 78.1%]. The effectiveness data are further supported by the first Mimics Study, a randomized, controlled trial with a Nitinol straight stent comparator. The Mimics Study also included core laboratory determination of primary patency. The 12-month patency outcomes are numerically comparable (73.0% for MIMICS-2 and 75.0% for Mimics) albeit within the limitation of differences in the study populations. Regarding secondary endpoints, patients showed improvements in Rutherford category, ABI, 6-minute walk, and WIQ.

B. Safety Conclusions

The risks of the device are based on non-clinical laboratory and animal studies, as well as data collected in the clinical studies described above. The safety of the BioMimics 3D Vascular Stent System was demonstrated in the MIMICS-2 Study through

achievement of the 30-day primary safety endpoint, freedom from MAE, a result also achieved in the Mimics Study. The MAE rate comprised of death, any major amputation performed on the index limb, or CDTLR through Day 30. The lower 97.5% one-sided Agresti-Coull confidence limit for the proportion of subjects treated with the BioMimics 3D Vascular Stent System that were free from MAE at Day 30 was 97.7%, which exceeds the performance goal of greater than 88%. No evidence of stent fracture was noted in the MIMICS- 2 Study through 12 months or in the Mimics study through 24 months, both based on independent core laboratory review.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in clinical studies conducted to support PMA approval as described above. The results of the MIMICS-2 Study provides a basis for concluding with reasonable assurance that the benefits of using the BioMimics 3D Vascular Stent System in patients undergoing interventional treatment for symptomatic femoropopliteal disease, and in accordance with the labeling and Instructions for Use, outweigh the risk of illness or injury.

The primary potential benefit is the improvement or restoration of blood flow in the superficial femoral artery and/or proximal popliteal arteries. In this study, patients demonstrated sustained clinical improvement in functional status and Rutherford category when compared to pre-procedure assessments.

The frequency and types of the adverse events reported throughout the pivotal clinical study are in alignment with what might be expected in the studied patient population and therapeutic area using comparable treatments. No unanticipated device- or procedure-related adverse events were reported in the study.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for the BioMimics 3D Vascular Stent when used for the treatment of symptomatic de novo or restenotic lesions in superficial femoral artery and/or proximal popliteal arteries with reference vessel diameters between 4.0 and 6.0 mm and lesion lengths up to 140 mm.

1. Patient Perspectives

   Patient perspectives considered during the review included Quality of Life assessments, specifically the WIQ. Scores for treated patients improved based on preprocedure assessments. Improvements were also noted in the 6-minute walk test, ABI, and Rutherford category. It is expected that patients would place value on this treatment and are willing to accept the risks of this treatment to achieve the benefit.

D. Overall Conclusions

The clinical and non-clinical data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The clinical study met the pre-specified safety and effectiveness endpoints, and the patients demonstrated quality of life improvements. Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk

of illness or injury when used as indicated in accordance with the labeling and the Instructions for Use.

XIV. CDRH DECISION

CDRH issued an approval order on October 04, 2018. The final conditions of approval cited in the approval order are described below.

Post-Approval Study – MIMICS-2 Continued Follow-Up Study. This study should be conducted per protocol MIMICS-2, CID-100, Issue 09 (dated July 20, 2017). This study is a prospective, multi-center follow-up of the MIMICS-2 pivotal study (G140182) that treated 271 subjects from 43 investigational sites. It will evaluate the long term safety and effectiveness of the BioMimics 3D Vascular Stent System. All 249 remaining subjects (22 subjects have discontinued the study), 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 (CDTLR) at 36 months, as defined by the protocol. The secondary endpoints to be assessed include the following:

a. Overall rate and incidence of type of serious adverse events from Day 0 through completion of Study follow-up at Month 36;

b. Primary stent patency rate: determined at Month 24 per protocol definition of primary stent patency;

c. Clinical outcome: comparison of Rutherford Clinical Category measured at Baseline and Month 24. Worsening of Rutherford Clinical Category is defined as an increase by one or more categories compared to Baseline or unexpected major amputation of the target limb;

d. Comparison of Six-Minute Walk Test measured at Baseline and Month 24 (sub-group of investigational sites);

e. Comparison of the ankle brachial index (ABI) measurement at Baseline and Month 24;

f. Comparison of the Walking Impairment Questionnaire at Baseline and Month 24;

g. Stent integrity measured as freedom from stent fracture, defined as clear interruption of a stent strut observed in a minimum of two projections, determined by core lab examination of X-rays taken with the leg in extension at 24 and 36 Months.

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

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.