PATHFINDER I: POST-MARKET REGISTRY OF AURYON* ATHERECTOMY DEVICE IN SUBJECTS AFFECTED WITH INFRAINGUINAL PERIPHERAL ARTERY DISEASE (PATHFINDER-REGISTRY, EX-PAD-05)

PROTOCOL NUMBER: EX-PAD-05

IRB NUMBER: 20200044

SPONSOR: ANGIODYNAMICS

VERSION NUMBER: 1.2

DATE: 13 OCT 2020

1 STATEMENT OF COMPLIANCE

The study will be conducted in compliance with the US FDA Title 21 CFR Part 50 – Protection of Human Patients and Part 56 – Institutional Review Boards; the International Council for Harmonisation for Pharmaceuticals for Human Use (ICH) GCP guidelines E6R2 (November 09, 2016) as they apply to observational studies; the Belmont Report; US Title 45 CFR Part 164 Subpart E – Privacy of Individually Identifiable Health Information and the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule (2002); and any applicable national guidelines.

The protocol, informed consent form(s), and all participant's materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before a participating site may enroll participants. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

The Principal Investigator will assure that no deviation from or changes to the protocol will take place without prior agreement from the registry study sponsor and documented approval from the Institutional Review Board (IRB).

2 PROTOCOL SUMMARY

TITLE:	PATHFINDER I: Post-Market Registry of Auryon Atherectomy Device in Subjects Affected with Infrainguinal Peripheral Artery Disease (PATHFINDER-Registry, EX-PAD-05)
DEVICE DESCRIPTION:	The AURYON System consists of two sub-units: 1) a single use catheter ("AURYON catheter"); and 2) a laser system. The AURYON catheter is a single use catheter that is made of an array of optic fibers and surrounded by a circumferential blunt blade at its distal tip. The AURYON catheter is connected to the laser system via its connector and transmits energy at pre-set fluence levels of 50 and 60 mJ/mm2 to the occluded or narrowed artery. The AURYON System must work over a commercially available 300cm 0.014" guide wire (GW) that crosses the lesion intraluminally. - For the small size catheters (i.e., 0.9mm and 1.5mm), there is a designated lumen tube for a guidewire at the center of the inner blunt blade. Please note that 0.9mm and 1.5mm catheters do not have an aspiration feature and have not been tested in ISR lesions. These devices should not be used in ISR cases. The larger AURYON catheters (i.e., 2.0mm and 2.35mm) have an eccentric guidewire lumen, and include additional features consisting of an aspiration feature (both catheters) and an "off-center" feature (2.35mm only). The aspiration feature is intended for debris and thrombus collection and removal from the vessel during the atherectomy procedure. The "off-center" feature is included in the 2.35 mm catheter only and is designed to facilitate debulking of lesions in blood vessels beyond the catheter's diameter.
INDICATION FOR USE:	The AURYON system is indicated for use in the treatment, including atherectomy, of infra-inguinal stenoses and occlusions, including in-stent restenosis (ISR).
REGULATORY STATUS:	The device is cleared for sale in the US (K181642).
STUDY DESCRIPTION:	The PATHFINDER I Registry is a prospective, non-randomized, single arm, multicenter observational study. It is a pilot registry study towards a subsequent large pivotal phase registry. This pilot registry is aimed to evaluate the performance (peri-procedural) and clinical outcomes (intermediate and long-term) of the AURYON Atherectomy System, within the initial launch phase of the product in the market. After signing an informed consent form, eligible PAD subjects treated with the AURYON Atherectomy

	System in a post-market (commercial device use) setting will be enrolled and will be followed for 24 months post index procedure. Enrolled subjects will undergo endovascular PAD treatment that includes atherectomy using the AURYON system, according to institutional standard of care. Data collection will include prospective data collection and medical record review of procedures performed according to standard of care, at the study protocol specific follow up time-points.
OBJECTIVES:	To evaluate the safety and efficacy of AURYON Atherectomy System in the treatment of de novo, re-stenotic and ISR lesions in infra-inguinal arteries of Peripheral Artery Diseases (PAD) subjects, in a real-world setting. This is a pilot registry study towards a subsequent large pivotal registry (PATHFINDER II).
ENDPOINTS:	Primary Endpoints: 1. Primary Efficacy: Acute Procedural Success Percentage of subjects with successful revascularization of target vessel defined as ≤30% residual stenosis at the index lesion post atherectomy using the AURYON system and final adjunctive treatment (if required), as evaluated by angiographic corelab. 2. Primary Safety: Percentage of subjects with freedom from peri-procedural major adverse events (PPMAE), defined as (a) flow-limiting dissection, (b) clinically significant distal embolization, (c) bailout stenting, (d) major/unplanned amputation, (e) target vessel perforation requiring endovascular or surgical repair or (f) death, till discharge. Secondary endpoint(s): 1. Rate of device related complications requiring intervention, defined as peri procedural MAEs, reported by the operating physician as caused directly due to the use of the AURYON device. 2. Rates of post-discharge MAEs over time; defined as: (a) Unplanned target limb amputation, (b) cardiovascular death, (c) clinically driven target lesion revascularization[1], (d) target vessel revascularization (TVR). 3. Patency rate, defined as (1) <50% stenosis at the treated lesion, with peak systolic velocity ratio (PSVR) of <2.5, as

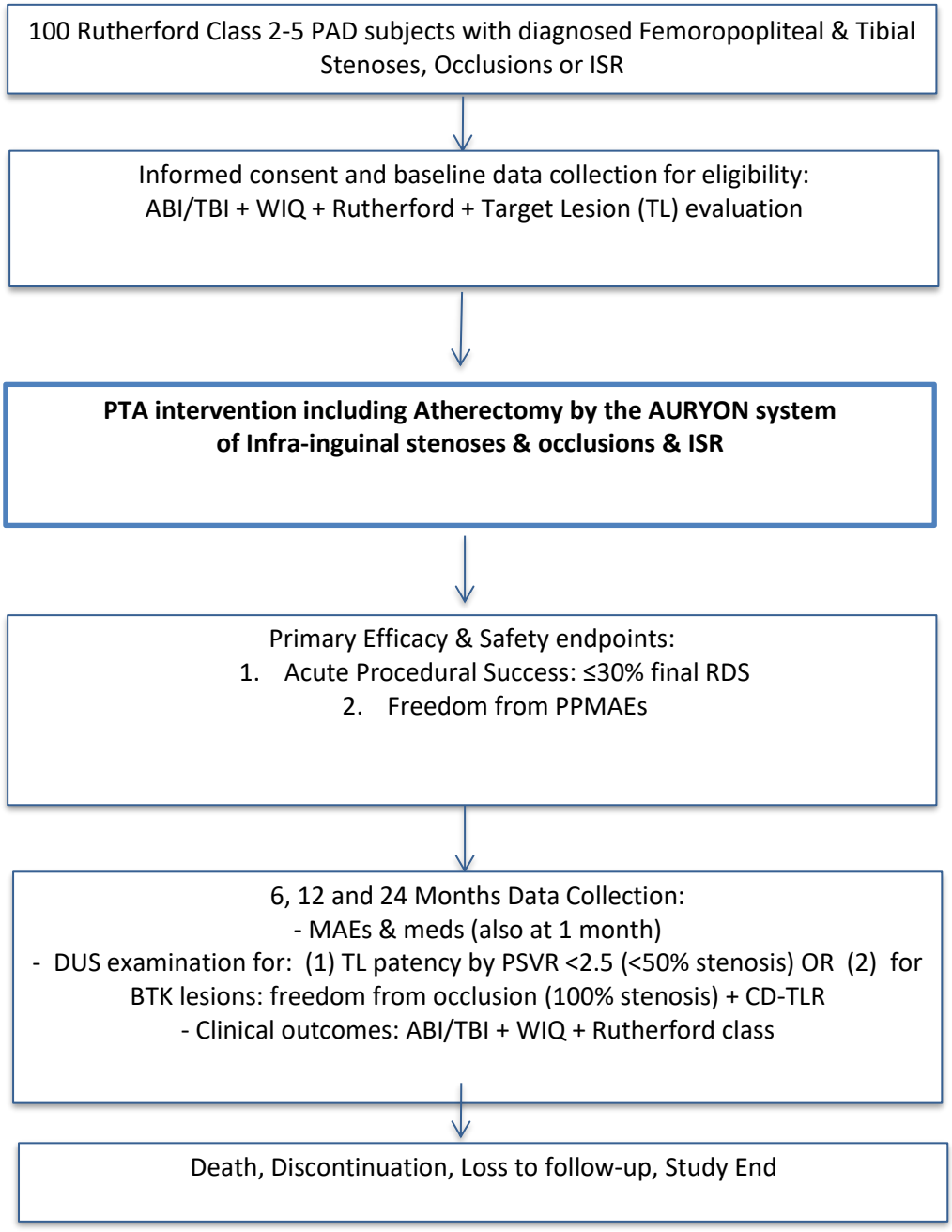
[1] Clinically-Driven Target Lesion Revascularization (CD-TLR), defined as a reintervention performed for ≥50% diameter stenosis (confirmed by angiography) within 5 mm of the target lesion after documentation of recurrent clinical symptoms of PAD following the index procedure.

	assessed quantitatively by Duplex ultrasonography (DUS); OR, (2) for BTK lesions: freedom from occlusion (100% stenosis by DUS) combined with freedom from CD-TLR, at 6, 12, and 24 months. 4. Clinical outcomes, defined as change in ankle brachial index (ABI or TBI if needed), walking impairment questionnaire (WIQ), and Rutherford category at 6, 12, and 24, months, compared to baseline Exploratory endpoint(s): 1. Intravascular ultrasound assessment pre- and post-Auryon and correlation with angiographic findings (e.g. lesion length, MLA -minimal lumen area gain, calcium severity and removal, etc.). This endpoint will be analyzed only for cases that used IVUS as a routine practice in the index procedure.
STUDY POPULATION:	Patients with infra-inguinal PAD undergoing atherectomy with the AURYON Atherectomy System. <u>Inclusion Criteria</u> A potential subject will be included in the study if he/she meets all the following inclusion criteria: 1. Subject is ≥ 18 years old. 2. Subject is a candidate for atherectomy for infra-inguinal peripheral artery disease. 3. Documented symptomatic atherosclerotic peripheral artery disease with claudication or critical limb ischemia (CLI) (Rutherford Classification 2-5). 4. Subject is capable and willing to comply with the scheduled follow up 5. Subject is able and willing to sign a written Informed Consent Form (ICF). <u>Exclusion Criteria</u> A potential subject will be excluded from the study if he/she meets any of the following exclusion criteria: 1. Target lesion is in an arterial bypass. 2. Planned use of another atherectomy device in the same procedure 3. Co-morbid condition(s) with less than 1yr anticipated survival that could limit the subject's ability to participate in the trial or to comply with follow-up requirements or impact the scientific integrity of the study.

	4. Participating in another study on an interventional non-cleared device, that could impact the study results
DESCRIPTION OF SITES/FACILITIES ENROLLING PARTICIPANTS:	This study will be conducted at sites where eligible PAD patients are routinely treated with atherectomy by AURYON Atherectomy System. Total enrollment of approximately 100 subjects at approximately 10 sites in the US. To reduce bias by sites, each site may enroll up to 15 eligible subjects whom have successfully completed their index atherectomy treatment with the AURYON system and with analyzable imaging for the primary efficacy analysis.
DESCRIPTION OF STUDY PROCEDURE:	Atherectomy by the AURYON system, of infra-inguinal stenoses, occlusions or in-stent restenosis (ISR).
STUDY DURATION:	The study duration is expected to be two and a half (2.5) years: 6 months to enroll and two (2) years to follow up all subjects.
PARTICIPANT DURATION:	Two (2) years
PRIMARY ANALYSIS PLAN:	As this is a pilot registry study, no formal hypotheses are defined; rather statistical analyses will be descriptive in nature and will serve to provide estimates of the primary and secondary study endpoints. Also, no formal sample size calculation was performed. The number of enrolled subjects will allow for sufficient safety monitoring and evaluation of the safety and efficacy endpoints and will provide point estimates for the large-scale registry. Analysis sets: <u>Intent-to-treat (ITT) population:</u> The intent-to-treat (ITT) population will consist of all subjects who signed the informed consent form and underwent procedure with an attempt of using the AURYON system. <u>Modified Intent-to-treat (mITT) population:</u> The modified Intent-to-treat (mITT) population will consist of all ITT subjects who underwent atherectomy using the AURYON system for at least one lesion. <u>Per-protocol (PP) population</u>

	The per-protocol (PP) population will consist of all mITT subjects for whom the AURYON catheter fully crossed at least one target lesion. If a subject does not undergo complete procedure, either due to early or intraoperative non-eligibility of inclusion/exclusion criteria or due to missing evidence of significant arterial disease (≥50%) by fluoroscopy angiogram in the index procedure, the subject will be considered as a screen failure. Screen failures will not be included into ITT population and will not be followed or part of the analysis. If a subject undergoes an atherectomy attempt but the AURYON system could not be successfully used in any target lesion, the subject will be included into ITT population but excluded from mITT and PP populations. That subject will not be followed-up after discharge. If a subject undergoes atherectomy using the AURYON system but the AURYON catheter cannot fully cross the target lesion, the subject will be included into ITT and mITT populations but excluded from PP population. That subject will be followed-up after discharge at 30-day, 6-month, 12-month and 24-month visits. Analyses of all primary & secondary endpoints will be conducted in both the mITT and PP populations. The ITT population will serve as the primary set for safety assessments.
RATIONALE FOR NUMBER OF PATIENTS:	With a total of 100 patients successfully treated by AURYON system in this study cohort, this study will serve as an unpowered pilot registry, towards a larger powered registry study that is planned to include approximately 1000 patients.

3 STUDY SCHEMA



4 SCHEDULE OF ACTIVITIES

Table 1. Schedule of Events for Screening and Enrollment, AURYON atherectomy Procedure and Post-Procedure Follow-up

Study assessment	Pre-Procedure	Procedure	Post-procedure	Hospital discharge	30 Days (±1 weeks)	6, 12, 24 Months (±1 Month)
Medical history & demographics	X					
Physical Examination	X					X
Informed Consent	X					
Angiographic evaluation of target lesion	X	X	X			
PAD Intervention including AURYON Atherectomy		X				
Quantitative DUS						X
ABI[0]	X					X
Rutherford Classification	X					X
WIQ	X					X
Record of relevant medications[1]	X	X		X	X[3]	X[4]
Record of PPMAEs[2] and other procedural complication		X	X	X		
Record of MAEs[2]					X[3]	X[4]

[0] Toe-brachial index (TBI) will be taken for subjects with non-compressible vessels

[1] Relevant medications: anticoagulant and anti-platelets.

[2] Adverse events should only be captured after signing of the Informed Consent Form.

[3] The visits may be done via phone call for record of any reportable adverse events and relevant medications.

[4] In case that subject is not showing up to one or more of these follow-up visits, the site should contact the subjects by telephone to collect as much data as possible of any reportable adverse events and relevant medications.