GROWTH: A Multicenter Pivotal Study of Neonatal, Infant, and Young Child Vascular Stenoses Studying the Renata Minima Stent

Clinical Protocol

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Study Sponsor: Renata Medical

Protocol Synopsis

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Title	Multicenter Pivotal Study of Neonate, Infant, and Young Child Vascular Stenoses Studying the Renata Minima Stent
Phase	Pivotal Study
Sponsor	Renata Medical
Investigational Device	Minima Stent
Study Objectives	To assess device performance and clinical safety and effectiveness of the Minima Stent in neonates, infants and young children requiring intervention for coarctation of the aorta or pulmonary artery stenosis who are indicated for treatment.
Study Design	Single arm, prospective, non-randomized, multi-center, open-label, Pivotal study.
Study Population	The study population will be comprised of patients with a clinically relevant pulmonary artery or aortic vascular stenosis who are indicated for treatment. For each treatment location (pulmonary artery or aortic vascular), a minimum of 10 patients will be treated.
Inclusion Criteria	Inclusion criteria include: • The subject's legally authorized representative has been informed of the nature of the clinical investigation, agrees to its provisions, and has provided written informed consent • Requiring treatment* of: o native, acquired, or recurrent aortic coarctation, or o native, acquired, or recurrent pulmonary artery stenosis *As defined by the patient's medical team • Patency of at least one femoral vein, femoral artery, jugular vein or both carotid arteries able to accommodate the delivery system • Adjacent vessel to stenosis measuring > or equal to 4 mm
Exclusion Criteria	Exclusion criteria include: • Active bloodstream infection requiring antibiotic therapy within 3 days prior to stent implantation

	• History of or active endocarditis (active treatment with antibiotics) within 180 days prior to stent implantation • Aortic or pulmonary artery aneurysm in the location targeted for treatment • Body weight < 1.5 kg • Anatomic location of lesion judged by the investigator to not lend to the safe placement of a stent • Target vessels larger or smaller than the Minima System balloon size ranges • Known genetic syndrome known to be associated with vasculopathies such as but not limited to Williams syndrome, Loeys-Dietz syndrome, etc • Clinical scenario requiring that more than one vessel needs stent implantation at the time of the trial procedure. • Currently participating in an investigational drug study or another device study • Major or progressive non-cardiac disease resulting in a life expectancy of less than six months • Known hypersensitivity to aspirin or heparin and cannot be treated with other antiplatelet and/or antithrombotic medications • Known hypersensitivity to cobalt-chromium or contrast media that cannot be adequately pre-medicated
Number of Subjects	Maximum of 42 US subjects
Number of Study Sites	8 US sites, with the possibility of additional Japanese and/or European Union sites pending the appropriate regulatory approvals.
Location of Study Sites	Children's Hospital Los Angeles Cedars Sinai Medical Center Seattle Children's Hospital Cincinnati Children's Hospital Boston Children's Hospital Nationwide Children's Hospital Le Bonheur Children's Hospital
Visit Schedule	Screening/baseline, discharge, 1 month, 3 months, 6 months, 12 months, and annually thereafter through 5 years

	Enrollment is expected to take up to 6 months and will be ongoing throughout the study.
Primary Efficacy Endpoint	The primary efficacy endpoint will be assessed as the rate of clinical success, with the performance goal defined as a clinical success rate of greater than 77%. Clinical success is defined as: • Stenosis relief, defined by stent outer diameter ≥ 75% of the surrounding vessel immediately after deployment. • Freedom from open surgical intervention required to treat Minima Stent disfunction through 6 months. • Maintenance of stented vessel diameter ≥ 50% of post-implant diameter at 6 months; as measured using CT angiography and/or angiography.
Primary Safety Endpoint	The primary safety endpoint will be assessed as the percentage of cases with freedom from procedure- or device-related SAEs resulting in an event listed below, with the performance goal defined as greater than 78% of cases: o Death o Cardiac arrest and/or emergency ECMO cannulation o Stroke o Limb loss o Vessel dissection of target lesion o Device thrombosis/occlusion o Cardiac perforation requiring percutaneous or open surgical intervention o Persistent cardiac arrhythmia requiring a pacemaker
Secondary Efficacy Endpoints	• Peak-to-peak pressure gradient (ventricle to arterial or arterial to arterial) < 20 mmHg after stent placement, when applicable. • Successful stent re-dilation (when indicated) at re-catheterization, defined as an increase in the intra stent angiographic luminal diameter within 2mm of the adjacent native vessel diameter immediately after re-dilation.
Secondary Safety Endpoints	• Freedom from stent embolization or migration through 6 months. • Freedom from stent fracture that led to reintervention through 6 months • Freedom from non-elective Minima Stent explant at 90-days post re-dilation • Freedom from procedure- or device-related SAE during re-dilation that results in the following: o Death o Cardiac arrest and/or emergency ECMO cannulation o Stroke o Limb loss o Vessel dissection of target lesion

	○ Device thrombosis/occlusion ○ Cardiac perforation requiring percutaneous or open surgical intervention ○ Persistent cardiac arrhythmia requiring a pacemaker
Sample Size Considerations	The study intends to enroll a maximum of 42 subjects within the United States. For each treatment location (pulmonary artery or aortic vascular), a minimum of 10 patients will be treated. Additionally, no site will be permitted to enroll more than one third of the total subjects implanted in the study. The chosen sample size is appropriate, as it allows for the analysis of each co-primary endpoint, with the appropriate power level. See section 10 for details.
Statistical Analysis Methods	Descriptive statistics will be the primary analysis method. The proportion of subjects with device success will be calculated along with the associated 95% confidence interval. Other categorical endpoints will be described with percentages. Continuous variables will be presented as mean with the standard deviation or median. Time-to-event endpoints will be described with Kaplan Meier graphs as appropriate. Other statistical analysis methods and graphing methods can be used in addition to those listed above, as appropriate.