

# **SUPPLEMENTAL MATERIAL**

**Table S1. UNIVERSE Inclusion/Exclusion criteria.**

<p><b>Inclusion Criteria:</b></p> <ol style="list-style-type: none"><li>1. Boys or girls 2 to 8 years of age with single ventricle physiology and who have completed the initial Fontan procedure within 4 months prior to enrollment</li><li>2. Considered to be clinically stable by the investigator and able to tolerate oral or enteral administration of a suspension formulation and oral/enteral feedings</li><li>3. Satisfactory initial post-Fontan transthoracic echocardiographic screening as defined in the Post-Fontan Echocardiographic Examination Research Protocol</li><li>4. Parent/legally acceptable representative must sign an informed consent form (ICF) and child assent will also be provided, if applicable, according to local requirements</li></ol>
<p><b>Exclusion Criteria:</b></p> <ol style="list-style-type: none"><li>1. Evidence of thrombosis, including those that are asymptomatic confirmed by post-Fontan procedure transthoracic echocardiogram, or other imaging techniques, during the screening period of the study</li><li>2. History of gastrointestinal disease or surgery associated with clinically relevant impaired absorption</li><li>3. History of or signs/symptoms suggestive of protein-losing enteropathy</li><li>4. Active bleeding or high risk for bleeding contraindicating antiplatelet or anticoagulant therapy, including a history of intracranial bleeding</li><li>5. Criterion modified per Amendment INT-2<ol style="list-style-type: none"><li>5.1 Indication for anticoagulant or antiplatelet therapy other than current study, however:<ul style="list-style-type: none"><li>– A subject who has received vitamin K antagonist (VKA) after the Fontan procedure may be eligible provided that the subject has discontinued VKA before the screening visit. Baseline laboratory samples must be obtained at least 7 days after the last dose of VKA.</li><li>– A subject who is receiving ASA at the time of the screening visit may be eligible and may continue receiving ASA provided the last dose is taken at least 24 hours prior to the first dose of study drug.</li><li>– A subject who is receiving heparin or LMWH after the Fontan procedure may be eligible and may continue receiving either of these anticoagulants during the screening period provided the study drug (rivaroxaban or ASA) is started 0 to 2 hours prior to the next scheduled administration of either of these anticoagulants and omit their administration thereafter.</li></ul></li></ol></li><li>6. Chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs)</li><li>7. Platelet count <math>&lt;50 \times 10^9/L</math> at screening</li><li>8. Criterion modified per Amendment INT-2<ol style="list-style-type: none"><li>8.1 Estimated glomerular filtration rate (eGFR) <math>&lt;30 \text{ mL/min/1.73m}^2</math></li></ol></li><li>9. Known clinically significant liver disease (eg, cirrhosis, acute hepatitis, chronic active hepatitis, or alanine aminotransferase (ALT) <math>&gt;3x</math> upper limit of normal (ULN) with concurrent total bilirubin <math>&gt;1.5x</math> ULN with direct bilirubin <math>&gt;20\%</math> of the total at screening)</li><li>10. Criterion modified per Amendment INT-2<ol style="list-style-type: none"><li>10.1 Known contraindication to ASA, or has or is recovering from chicken pox or flu-like symptoms (subjects participating in Part B only)</li></ol></li><li>11. Criterion modified per Amendment INT-2<ol style="list-style-type: none"><li>11.1 Known allergies, hypersensitivity, or intolerance to rivaroxaban, ASA or its excipients</li></ol></li><li>12. Inability to cooperate with study procedures</li><li>13. Combined P-glycoprotein (P-gp) and strong cytochrome P450 3A4 (CYP3A4) inhibitors (such as but not limited to ketoconazole, telithromycin, or protease inhibitors) use within 4 days before enrollment, or planned use during the study. Itraconazole use within 7 days before enrollment or planned use during the study.</li><li>14. Combined P-gp and strong CYP3A4 inducers (such as but not limited to rifampin/rifampicin, rifabutin, rifapentine, phenytoin, phenobarbital, carbamazepine, or St. John's Wort) use within 2 weeks before enrollment, or planned use during the study.</li><li>15. Planned use of drugs that are moderate CYP3A4 inhibitors (such as erythromycin) during the Initial PK, PD, and Safety Assessment Period of Part A only</li><li>16. Participation in a clinical study with an investigational drug or medical device in the previous 30 days prior to enrollment</li><li>17. Any condition for which, in the opinion of the investigator, participation would not be in the best interest of the subject (eg, compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments</li><li>18. Family member of an employee of the investigator or study site with direct involvement in the proposed study or other studies under the direction of that investigator or study site</li></ol>

**Table S2. Study Committees: List of Collaborators.**

<b>Executive committee</b>	
Brian McCrindle	Hospital for Sick Children, Toronto, ON
Jennifer Li	Duke University Medical Center, Durham, NC
Alan Michelson	Boston Children's Hospital, Harvard Medical School, Boston, MA
Henri Justino	Texas Children's Hospital, Houston, TX
<b>Central independent adjudication committee</b>	
Ken Mahaffey	Stanford University School of Medicine, Stanford, CA
Christopher Almond	Stanford University School of Medicine, Stanford, CA
Doff McElhinney	Stanford University School of Medicine, Stanford, CA
Sarah Lee	Stanford University School of Medicine, Stanford, CA
<b>Independent data monitoring committee</b>	
Alain Leizorovicz	University of Lyon, Lyon, France
Lisa Bomgaars	Baylor College of Medicine, Houston, TX
Lawrence Lesko	University of Florida, Department of Pharmaceutics, Gainesville, FL