Direct **O**ral Anticoagulant **T**herapy with the **H**eart**M**ate **3** LVAD: A Pilot Study

DOT-HM3 Study

Statistical Analysis Plan

Investigator initiated study

The study site:

Institute for Clinical and Experimental Medicine, Prague, Czech Republic

05/15/2021

DOT HM3 Study – Statistical analysis plan

Stable HM3 patients who have not suffered a Major hemocompatibility-related adverse after index hospitalization discharge and are at least 3 months post-implant will be screened for participation in the study. Upon meeting the study criteria and patient informed consent, the individuals will be randomized to either continued therapy with a Vitamin K antagonist and aspirin or conversion to apixaban 5 mg twice a day in a 1:2 manner; the apixaban group will be stratified further by 1:1 randomization to continued use of 100 mg aspirin once daily or cessation. Thus, 45 patients are planned to be enrolled and randomized in 3 subgroups of 15 patients in each arm. The sample size of 45 patients was calculated to be sufficient to elucidate any safety signal. After 180 days follow-up is reached, the Vitamin K antagonist and aspirin arm will be transitioned to apixaban and randomized in a 1:1 manner to groups with or without aspirin.

Survival free of a hemocompatibility-related adverse events event (Stroke ischemic/hemorrhagic, Pump thrombosis, Severe bleeding, Peripheral arterial thromboembolic events) at the endpoint of 90 days will be evaluated as primary endpoint as proportion of success calculated between the apixaban and the warfarin arms. The prevalence (percent of patients with events) and incidence (event rates in events per pt-year) of adverse events and rehospitalizations will be determined. The secondary endpoints include an evaluation of the following adverse events per INTERMACS definitions (version 5.0) throughout the study period:

- Stroke (ischemic/hemorrhagic)
- Pump thrombosis
- Major bleeding
- GI Bleeding
- Peripheral arterial thromboembolic events
- Transient ischemic attack
- Hemolysis
- Venous thromboembolism
- Myocardial infarction
- Right heart failure
- Cardiac arrhythmias
- Liver and kidney dysfunction
- Death due to any cause

Time to event analyses will be done by Kaplan-Meier analysis. The overall outcomes being evaluated for clinical safety as assessed by the study's oversight committee.