**Supplemental Table 4. Study objectives and endpoints**

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Primary Efficacy</strong></td>
<td></td>
</tr>
<tr>
<td>To compare the effect of a 30-week course of mavacamten with placebo on Valsalva LVOT gradient peak as determined by Doppler echocardiography</td>
<td>Change from baseline to Week 30 in Valsalva LVOT peak gradient</td>
</tr>
<tr>
<td><strong>Secondary Efficacy</strong></td>
<td></td>
</tr>
<tr>
<td>To compare the effect of a 30-week course of mavacamten with placebo on LVOT obstruction</td>
<td>Change from baseline to Week 30 in resting LVOT peak gradient</td>
</tr>
<tr>
<td></td>
<td>Proportion of participants achieving a Valsalva LVOT peak gradient &lt; 30 mmHg at Week 30</td>
</tr>
<tr>
<td></td>
<td>Proportion of participants achieving a Valsalva LVOT peak gradient &lt; 50 mmHg at Week 30</td>
</tr>
<tr>
<td>To compare the effect of a 30-week course of mavacamten with placebo on clinical symptoms</td>
<td>Proportion of participants with at least 1 class improvement in NYHA functional classification from baseline to Week 30</td>
</tr>
<tr>
<td>To compare the effect of a 30-week course of mavacamten with placebo on Participant-Reported health status individually</td>
<td>Change from baseline to Week 30 in KCCQ Clinical Summary Score (CSS)</td>
</tr>
<tr>
<td>To compare the effect of a 30-week course of mavacamten on cardiac biomarkers</td>
<td>Change from baseline to Week 30 in NT-proBNP</td>
</tr>
<tr>
<td></td>
<td>Change from baseline to Week 30 in cardiac troponin</td>
</tr>
<tr>
<td>To compare the effect of a 30-week course of mavacamten with placebo on LV mass evaluated by CMR imaging</td>
<td>Change from baseline to Week 30 in LV mass index</td>
</tr>
<tr>
<td><strong>Exploratory Efficacy</strong></td>
<td></td>
</tr>
<tr>
<td>To assess the effect of a 30-week course of mavacamten on cardiac function and structure as evaluated by echocardiography</td>
<td>Proportion of participants achieving NYHA Class I and resting and Valsalva LVOT peak gradient &lt; 30 mmHg at Week 30</td>
</tr>
<tr>
<td></td>
<td>Change from baseline to Week 30 in echocardiographic indices of cardiac structure and systolic and diastolic function</td>
</tr>
<tr>
<td>To assess the effect of a 30-week course of mavacamten on Cardiac function and structure as evaluated by CMR imaging</td>
<td>Change from baseline to Week 30 in myocardial fibrosis</td>
</tr>
<tr>
<td></td>
<td>Change from baseline to Week 30 in cellular hypertrophy, cardiac structure, and function</td>
</tr>
<tr>
<td>To assess the effect of a 30-week course of mavacamten on Participant-Reported health status</td>
<td>Change from baseline to Week 30 in Total Symptom Score and Overall Summary Score from KCCQ</td>
</tr>
<tr>
<td><strong>Safety</strong></td>
<td></td>
</tr>
</tbody>
</table>
To assess the safety of mavacamten during the 30-week double-blinded, placebo-controlled treatment period

- Incidence of LVEF < 50% determined by TTE
- Incidence and severity of TEAEs, and treatment-emergent SAEs
- Incidence of major adverse cardiac events (MACEs; CV death, non-fatal stroke, non-fatal myocardial infarction)
- Incidence of hospitalizations (due to CV and non-CV events)
- Incidence of HF events, including hospitalizations and urgent emergency room/outpatient visits for HF
- Incidence of atrial fibrillation/flutter (new from screening, and recurrent)
- Incidence of ICD therapy and resuscitated cardiac arrest
- Incidence of ventricular tachyarrhythmias including ventricular tachycardia, ventricular fibrillation, and Torsades de Pointe
- Incidence of adverse events of special interest (AESIs; symptomatic overdose, outcomes of pregnancy, LVEF ≤ 30%)

**Long-Term Extension**

To assess the effects of mavacamten on clinical symptoms, cardiac biomarkers, health status, echocardiographic measures, and CMR measures over time

- Change from baseline in NYHA class, echocardiographic and CMR parameters, cardiac biomarkers, and KCCQ results through End of Study (EOS)

To assess the safety of mavacamten over time

- Incidence of safety events, including: LVEF < 50%, TEAEs and treatment-emergent SAEs, MACEs, hospitalizations, HF events, atrial fibrillation/flutter, ICD therapy and resuscitated cardiac arrest, ventricular tachyarrhythmias, or AESIs

**Pharmacokinetics**

To describe the PK characteristics of mavacamten

- Mavacamten plasma concentration over time
- PK parameters using a population PK approach