COSMIC-HF: Secondary Objectives

- To characterize its pharmacokinetics (PK) after 12 weeks of treatment
- To select an oral modified release (MR) formulation and dose of OM for chronic twice daily (BID) dosing in subjects with HF and left ventricular systolic dysfunction (LVSD).

OM increases stroke volume, decreases filling pressures, and improves left ventricular volumes.

OM prolongs duration of systole.

OM increases entry rate of myosin into force-producing state; hence increasing the number of "force generators" (myosin heads) interacting with actin.4

While several interventions have been shown to reduce the rate of HF hospitalizations and improve HF outcomes (e.g., angiotensin converting enzyme [ACE] inhibitors, beta-blockers, aldosterone antagonists, coronary revascularization, and biventricular pacing),1 mortality and morbidity still remain high.

HF is a condition most commonly marked by cardiac systolic dysfunction.

We will evaluate changes in heart rate (HR) and QTc intervals.

OM increases stroke volume; decreases filling pressures, and improves left ventricular volumes.

OM increases entry rate of myosin into force-producing state; hence increasing the number of "force generators" (myosin heads) interacting with actin.4

COSMIC-HF: Primary Objectives

- To ask an oral modified release (MR) formulation and dose of OM for chronic twice daily (BID) dosing in subjects with HF and left ventricular systolic dysfunction (LVSD).

COSMIC-HF: Secondary Objectives

- To evaluate the safety and tolerability of oral OM.

COSMIC-HF: Trial: Study Design

- Multicenter, randomized, double-blind, parallel, placebo-controlled, dose escalation study.

- Study population: up to approximately 420 subjects with HF and LVSD.

- Study duration: 30 days; screening (30 days), escalation phase (7 days each), and expansion phase (24 weeks).

COSMIC-HF: Trial: Dose Escalation Phase (Cohorts 1–3)

<table>
<thead>
<tr>
<th>Cohort</th>
<th>OM Formulation</th>
<th>Dose Level</th>
<th>PK Sampling (Day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OM Formulation A</td>
<td>25 mg BID</td>
<td>D1 D5 D8 D10 D14</td>
</tr>
<tr>
<td>2</td>
<td>OM Formulation B</td>
<td>50 mg BID</td>
<td>D1 D5 D8 D10 D14</td>
</tr>
<tr>
<td>3</td>
<td>OM Formulation C</td>
<td>100 mg BID</td>
<td>D1 D5 D8 D10 D14</td>
</tr>
</tbody>
</table>

COSMIC-HF is a Global Study

- United States
- Canada
- United Kingdom
- France
- Italy
- Germany
- Belgium
- Poland
- Czech Republic
- Hungary
- Lithuania
- Poland
- United States

References