METEORIC-HF

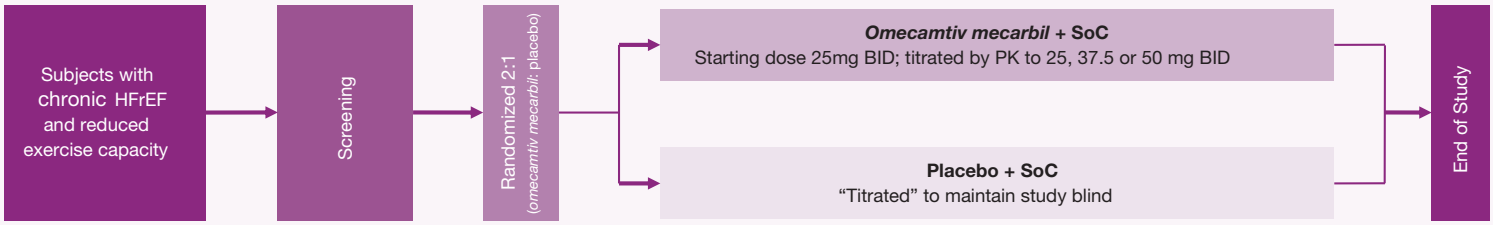
Multicenter **E**xercise **T**olerance **E**valuation of ***O****mecamtiv Mecarbil* **R**elated to **I**ncreased **C**ontractility in **H**eart **F**ailure

Study to Assess the Effect of *Omecamtiv Mecarbil* on Exercise Capacity in Subjects With Heart Failure

Cytokinetics Clinical Study: CY 1031 NCT Clinical Study: 03759392

A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Assess the Effect of *Omecamtiv Mecarbil* on Exercise Capacity in Subjects With Heart Failure With Reduced Ejection Fraction and Decreased Exercise Tolerance

PHASE 3 STUDY DESIGN:



STUDY PURPOSE:

To evaluate the effect of treatment with *omecamtiv mecarbil* compared with placebo on exercise capacity as determined by cardiopulmonary exercise testing (CPET) following 20 weeks of treatment with *omecamtiv mecarbil* or placebo

PRIMARY ENDPOINT:

Change in peak oxygen uptake (VO_2) on CPET from baseline to Week 20

SECONDARY ENDPOINTS:

- Change in exercise capacity, as measured by the change in total workload during CPET from baseline to Week 20
- Change in ventilatory efficiency, as measured by the change in Ventilation (VE)/Carbon dioxide output (VCO_2) slope during CPET from baseline to Week 20
- Change in the average daily activity units measured over a 2-week period from baseline (Week -2 to Day 1) to Week 18-20

KEY INCLUSION CRITERIA:

- Male or female, ≥ 18 to ≤ 85 years of age
- History of chronic HF, defined as requiring continuous treatment with medications for HF for a minimum of 3 months before screening
- New York Heart Association (NYHA) class II or III at screening
- Left ventricular ejection fraction ≤ 35%
- On maximally tolerated HF SoC therapies consistent with regional clinical practice guidelines, if not contraindicated and according to investigator judgment of the subject's clinical status. Beta blocker dose must be stable for 30 days prior to randomization
- N-terminal (NT)-proBNP level ≥ 200 pg/mL
- Peak VO_2 ≤ 75% of the predicted normal value with respiratory exchange ratio (RER) ≥ 1.05 on a screening CPET, confirmed by a CPET core laboratory

KEY EXCLUSION CRITERIA:

- Paroxysmal atrial fibrillation or flutter documented within the previous 6 months, direct-current (DC) cardioversion or ablation procedure for atrial fibrillation within 6 months, or plan to attempt to restore sinus rhythm within 6 months of randomization. Subjects with persistent atrial fibrillation and no sinus rhythm documented in the prior 6 months are permitted.
- Ongoing or planned enrollment in cardiac rehabilitation.
- Major medical event or procedure within 3 months prior to randomization, including: hospitalization, surgery, renal replacement therapy or cardiac procedure. This includes episodes of decompensated HF that require IV HF treatment.
- Chronotropic incompetence (including inadequate pacemaker rate response) during CPET at screening, defined as a maximum heart rate <60% of the maximum predicted heart rate
- Other exclusion criteria may apply

ADDITIONAL INFORMATION:

Study ID: CY 1031 www.clinicaltrials.gov (Identifier: 03759392)

SoC = Standard of Care

METEORIC-HF Cytokinetics

Omecamtiv mecarbil is an investigational cardiac myosin activator. Efficacy and safety have not been established.