For IMB-1018972 this consisted of:
- 24 subjects received single doses (IR) of 50 to 400 mg
- 18 subjects received 50 mg/mg (MR) BID for 5 days
- 12 subjects received single doses of 50 to 200 mg (MR) BID for 14 days
- 12 subjects received multiple doses of 200 mg (MR) BID for 5 days

**METHODS**

- First-in-human, phase 1, randomized, double-blind, placebo-controlled study.
- Part 1 evaluated IMB-1018972 in single ascending doses of 50, 150 (fed/fast), and 400 mg of an immediate-release (IR) formulation, N=6/2 active/placebo and a single dose of 35 mg trimetazidine MR as comparator; N=8 (Figure 1).
- Part 2 evaluated IMB-1018972 in multiple doses of 50 and 150 mg given twice daily (BID) for 14 days, N=6/3 active/placebo.
- Part 3 evaluated IMB-1018972 with 4 or 8 hour modified release (MR) profiles:
  - Single doses of 50 or 200 mg, given fed or fasted, N=12 active
  - Multiple doses of 200 mg 8-hour MR formulation given BID for 5 days, N=12 active
- Serial blood and urine samples were collected and analyzed for IMB-1018972, IMB-1028814, and trimetazidine with validated assays for PK analyses.
- Safety assessments included adverse event (AE) reporting, physical exam, clinical laboratories, 12-lead ECG and telemetry collection.

**RESULTS**

- 88 healthy adult subjects participated in the study comprised of: 66 receiving IMB-1018972; 14 receiving placebo; 8 receiving trimetazidine.

**IMB-1018972 (IMB-101) is a novel, investigational cardiac mitrope under development for the treatment of cardiovascular disease**

IMB-101 acts as a partial fatty acid oxidation (pFOX) inhibitor to increase pyruvate dehydrogenase (PDH) activity and enhance carbohydrate oxidation.

**IMB-101 is a pro-drug of three active metabolites**

- Niacin
- IMB-101
- Trimetazidine

**IMB-101 is well tolerated and exhibits predictable PK characteristics in a phase 1 healthy volunteer study**

**IMB-101 is currently being investigated in 3 phase 2, proof-of-concept studies in patients with hypertrophic cardiomyopathy, stable angina and type 2 diabetes**

**DISCLOSURE INFORMATION**

Author Disclosure. PC, LB, NB, GM, LT, and JP are employees/shareholders of Imbria. JdvW and Tvl are employees of PRA Health Sciences.

**CONCLUSIONS**

The study design was made in accordance with the principles of formulation design space (McDermott & Schioles, Ther Deliv 2015).