Heart failure (HF) is a major cause of mortality in the United States and is characterized by impairment of ventricular filling or ejection of blood.

In preclinical studies and clinical trials, treatment with an investigational ActRIIA ligand trap (ActRIIA-Fc) demonstrated benefits in cardiopulmonary function; however, a dose-limiting increase in red blood cells (RBCs) was also observed.

KER-012 is an investigational, modified ligand trap designed to reduce SMAD3/3 signaling without affecting RBCs.

KER-012, a research form of KER-012 Preventative (RKER-012 Preventative), has significantly reduced heart weight (A), left ventricular posterior wall thickness (B), and interventricular septal end diastole (C) compared to TAC vehicle mice. No significant differences were observed in TGF-β, TIMP, and Collα1 relative to TAC vehicle mice. No significant changes were observed in TGF-β.

These results demonstrate that RKER-012 Treatment mice had significantly reduced left ventricular posterior wall thickness (B) and interventricular septal end diastole (C) compared to TAC-vehicle mice. Heart weight in KER-012 Treatment mice trended towards a decrease compared to TAC-vehicle mice (A).

These results provide preclinical evidence that KER-012 has the potential to benefit heart failure patients as a preventative or treatment option.

**CONCLUSIONS**

- **TAC** mouse model (TAC-vehicle) showed increased HW, LVPtG, IVsd, LV fibrosis, E/E’ ratio, tissue remodelling markers and decreased E/A ratio compared to control animals (Sham).
- KER-012 Preventive mice had significantly reduced HW, LVPtG, IVsd, and LV fibrosis compared to TAC-vehicle mice.
- KER-012 Treatment mice had significantly reduced LVPtG, IVsd, and E/E’ ratio compared to TAC-vehicle mice, while LV fibrosis and HW trended towards a decrease.
- These results demonstrate that KER-012, in a preclinical model of left ventricular pressure overload, lessened the severity of cardiac fibrosis and remodeling, leading to an improvement in left ventricular function.

These results provide preclinical evidence that KER-012 has the potential to benefit heart failure patients as a preventative or treatment option.

**REFERENCES**


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