EDG-15400, A NOVEL SARCOMERE MODULATOR, PREVENTS THE DEVELOPMENT OF DIASTOLIC DYSFUNCTION IN THE ZSF1 RAT MODEL OF HEART FAILURE WITH PRESERVED EJECTION FRACTION

Marcus Henze[1], Yangsong Wu[1], Amy Perry[1], Kayla Wald[1], Sarah Larkin[1], Craig Emter[1], Alan J Russell[1]

[1]Edgewise Therapeutics, Boulder, CO, USA

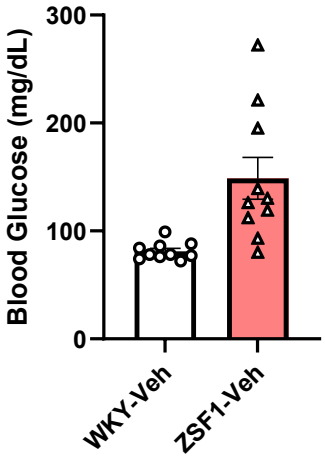
Craig A. Emter, PhD | Senior Director, Cardiovascular Pharmacology & Discovery
Edgewise Therapeutics

DISCLOSURE SLIDE

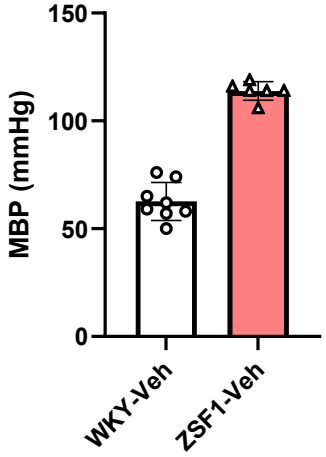
Craig A. Emter, PhD, is an employee of Edgewise Therapeutics,

EDG-15400 is an investigational agent that is not approved for use by any regulatory authority in any territory and its safety and efficacy have not been established.

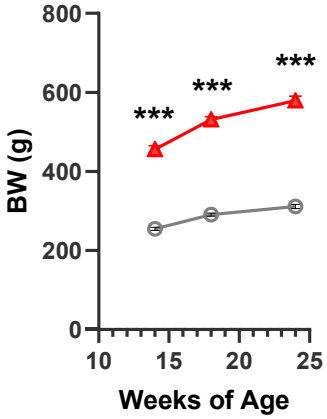
ZSF1 RATS DEVELOP SYMPTOMS CONSISTENT WITH COMORBIDITIES OF HFpEF WITH DIASTOLIC IMPAIRMENT



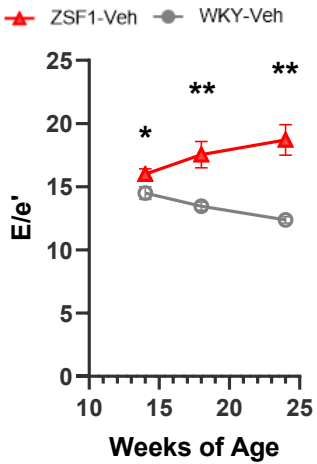
Hyperglycemia

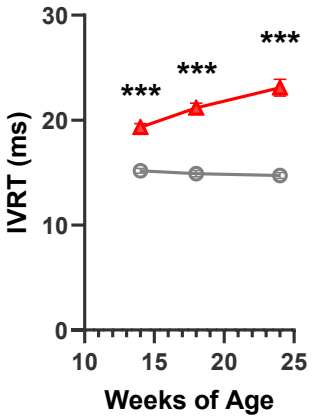


Hypertension



Obesity

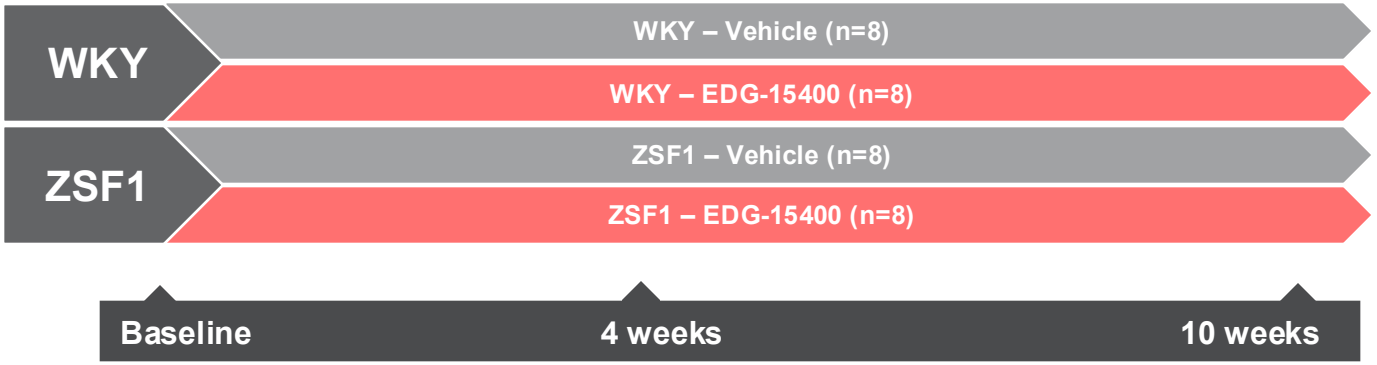




Impaired diastolic function

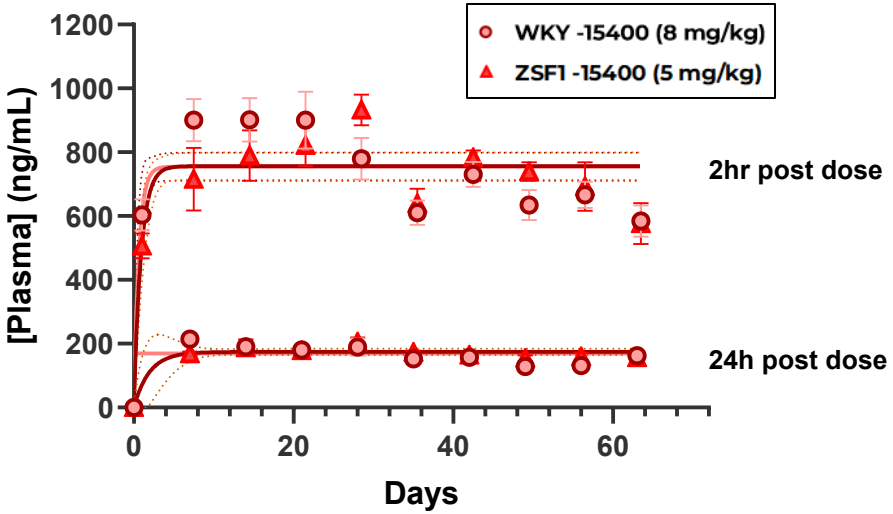
ZSF1 rats display "HFpEF" phenotype compared to age-matched Wistar-Kyoto (WKY) controls

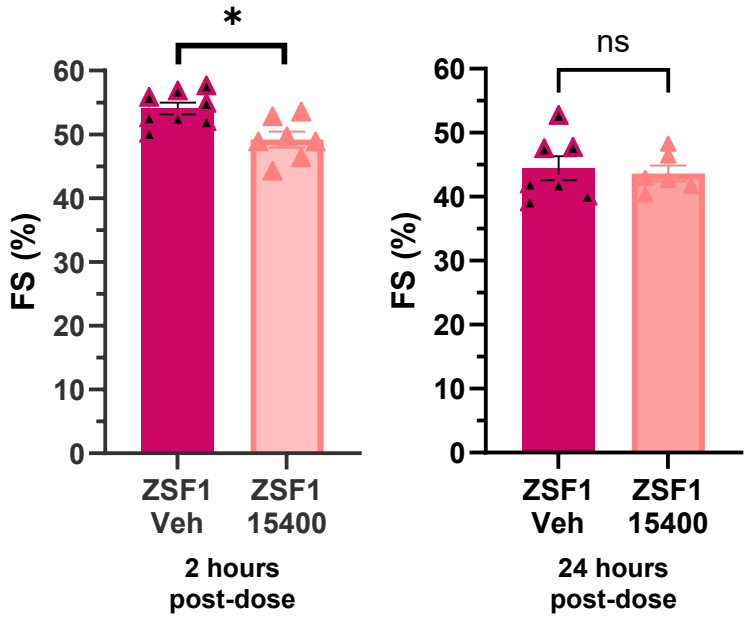
STUDY DESIGN : A PRECLINICAL MODEL OF HFpEF



Study Aim: To determine if 10-weeks of daily oral administration of EDG-15400 can prevent the development of impaired diastolic dysfunction in the ZSF1 rat, a preclinical model of HFpEF

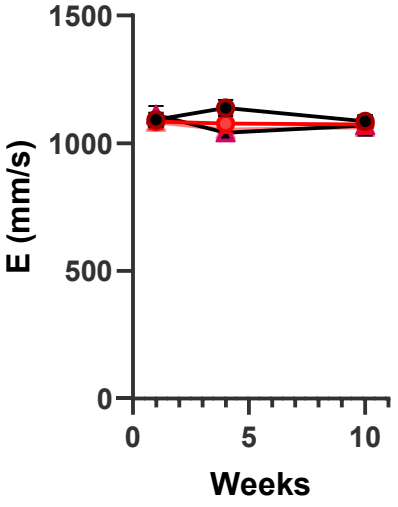
EDG-15400: LIMITED AND TRANSIENT SYSTOLIC EXCURSIONS

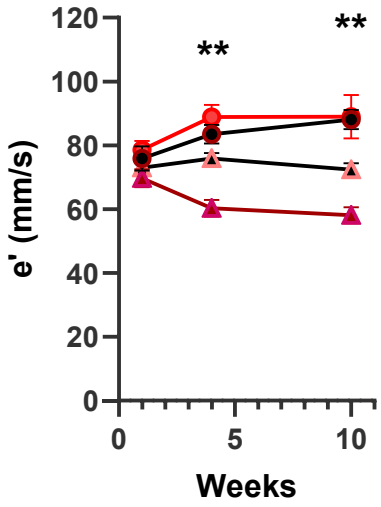


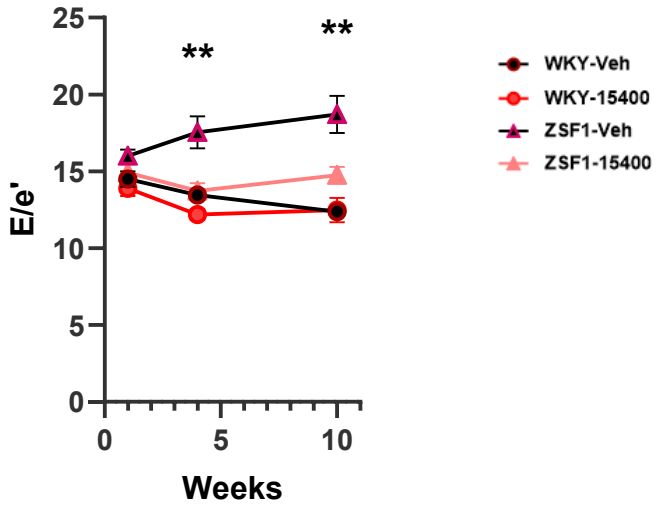


Plasma exposures in WKY and ZSF1 rats following daily oral administration of EDG-15400 over 10 weeks were similar.

DIASTOLIC FUNCTION: IMPROVED WITH EDG-15400 IN ZSF1 RATS





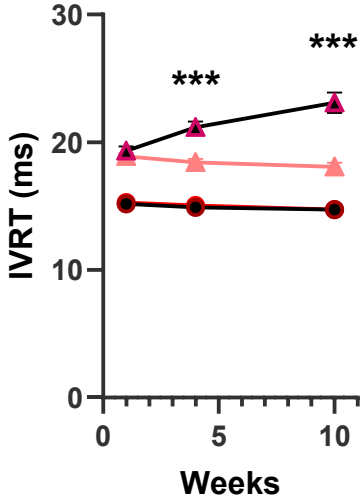


No Change in early filling velocity (E)

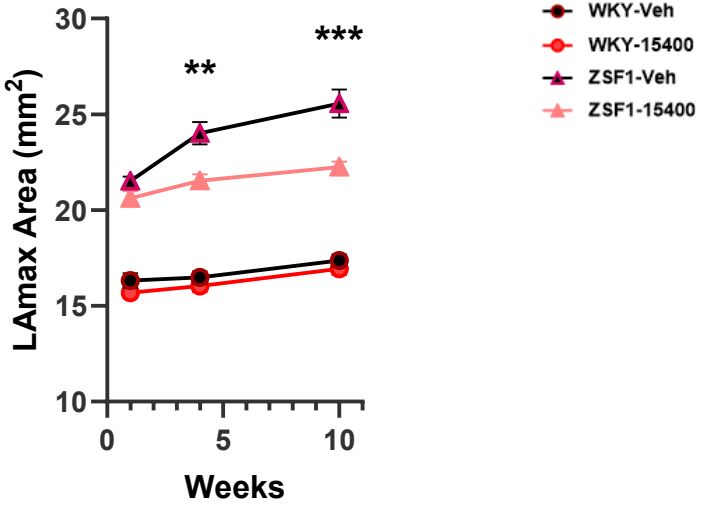
Preserved mitral annular velocity (e')

Prevents pathological increase in LV filling pressure (E/e')

EDG-15400 IMPROVES RELAXATION AND ATTENUATES PATHOLOGICAL INCREASES IN LEFT ATRIAL SIZE IN ZSF1 RATS



Prevents pathological increase in isovolumic relaxation time (IVRT).



Prevents pathological left atrial enlargement

EDG-15400, A NOVEL SARCOMERE MODULATOR, PREVENTS THE DEVELOPMENT OF DIASTOLIC DYSFUNCTION IN THE ZSF1 RAT MODEL OF HEART FAILURE WITH PRESERVED EJECTION FRACTION

1

Ten weeks of daily EDG-15400 treatment **prevents the continuing development of diastolic dysfunction and atrial enlargement in ZSF1 rats.**

2

This is evident by signatures of **improved early diastolic filling kinetics and decreased LV filling pressure,** supporting further exploration of EDG-15400 for the treatment of HFpEF.

THANK YOU

Scientific Sessions

#ScientificSessions26