Targeting the Mechanism of Hypertrophic Cardiomyopathy

Session: Progress in Designing Hypertrophic Cardiomyopathy Trials

Marc J. Semigran MD
Chief Development Officer
Edgewise Therapeutics

Disclosure & Disclaimer

Dr. Semigran is a full-time employee of Edgewise Therapeutics

This presentation contains forward-looking statements that involve substantial risks and uncertainties of Edgewise Therapeutics, Inc. ("Edgewise" or the "Company"). All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, results of operations, business strategy and plans, and objectives of management for future operations, as well as statements regarding industry trends, are forward-looking statements. Such forward-looking statements include, among other things, statements regarding the potential of, and expectations regarding, Edgewise's drug discovery platform, Edgewise's product candidates and programs, including EDG-7500; Edgewise's ability to advance additional programs; the expected milestones and timing of such milestones including for EDG-7500 and the Company's cardiac HCM program; and statements regarding Edgewise's financial position including its liquidity and the sufficiency of its cash resources. In some cases, you can identify forward-looking statements by terminology such as "estimate," "intend," "may," "plan," "potentially" "will" or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: negative impacts of the COVID-19 pandemic on Edgewise's operations, including clinical trials; risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics and operating as an early clinical stage company; Edgewise's ability to develop, initiate or complete preclinical studies and clinical trials for, obtain approvals for and commercialize any of its product candidates or research programs; changes in Edgewise's plans to develop and commercialize EDG-7500 or any other product candidates or research programs; the potential for clinical trials of EDG-7500 or any other product candidates to differ from preclinical, interim, preliminary, topline or expected results; Edgewise's ability to enroll patients in its ongoing and future clinical trials; Edgewise's ability to raise funding it will need to continue to pursue its business and product development plans; regulatory developments in the United States and foreign countries; Edgewise's reliance on third parties, including contract manufacturers and contract research organizations; Edgewise's ability to obtain and maintain intellectual property protection for its product candidates; risks associated with access to capital and credit markets; the loss of key scientific or management personnel; competition in the industry in which Edgewise operates; Edgewise's ability to develop a proprietary drug discovery platform to build a pipeline of product candidates; general economic and market conditions; and other risks. Information regarding the foregoing and additional risks may be found in the section entitled "Risk Factors" in documents that Edgewise files from time to time with the Securities and Exchange Commission. These risks are not exhaustive. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

This presentation contains information that is highly confidential and/or privileged. The information is intended only for the use of individuals or entities to which it is addressed. If you are not the intended recipient, you are hereby notified that any reliance, disclosure, copying, distribution, or taking of any action on the contents of this material is strictly prohibited.

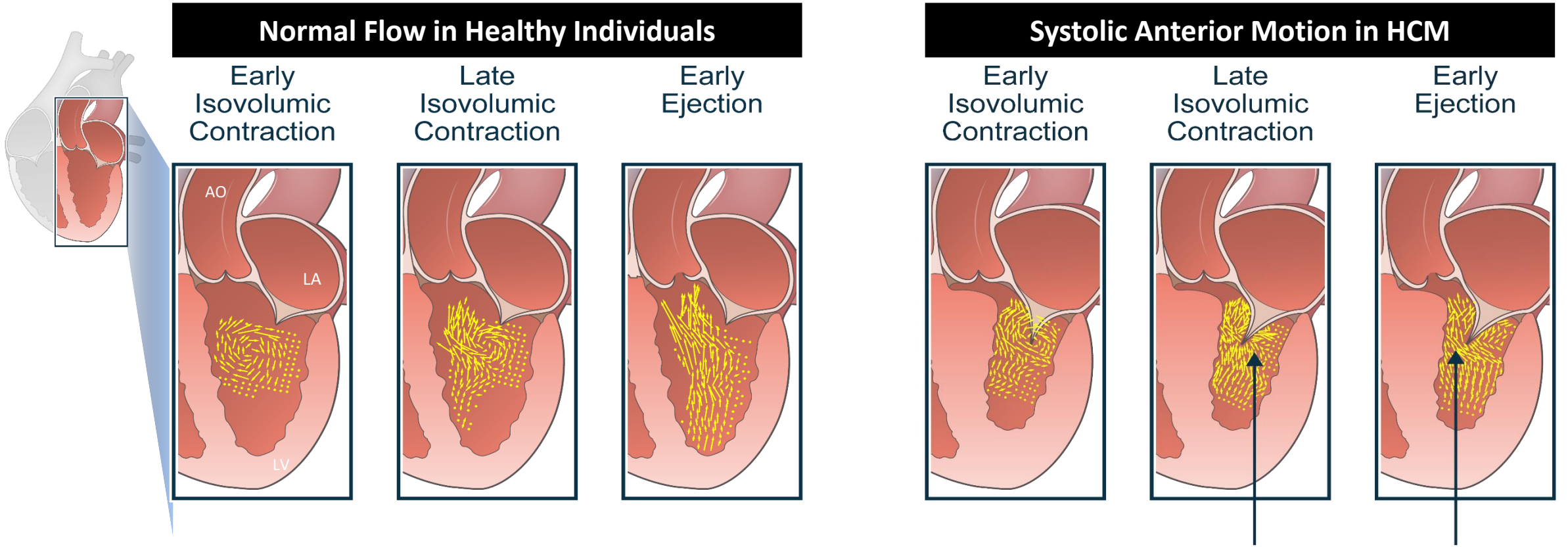
This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

EDG-7500 is an investigational agent and is not approved in any territory

Advancing EDG-7500, a First-In-Class Sarcomere Modulator for Hypertrophic Cardiomyopathy (HCM)

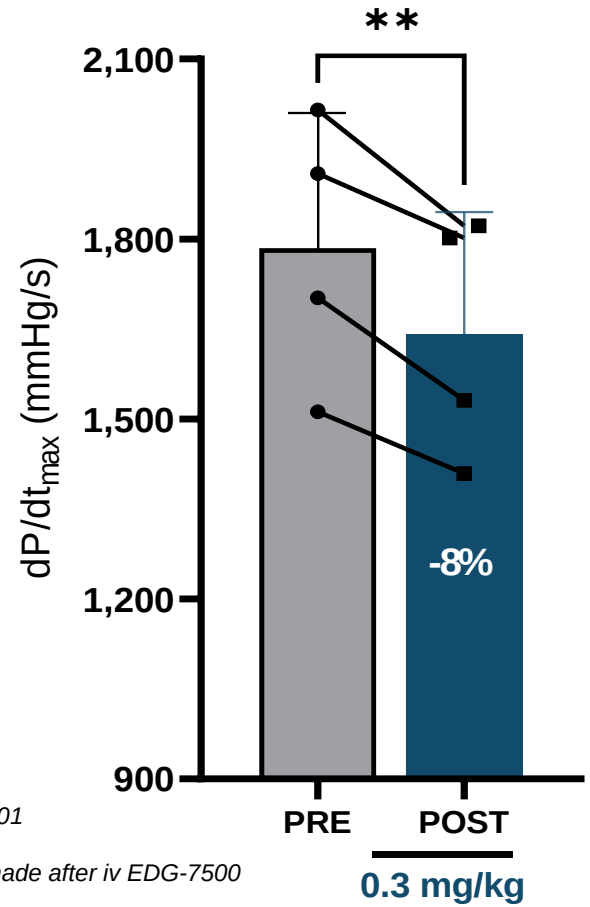
- Edgewise Therapeutics' robust discovery platform is yielding novel compounds targeting important unmet needs of patients suffering from disorders of cardiac and skeletal muscle.
- EDG-7500 is first-in-class oral, selective, cardiac sarcomere modulator for HCM designed to slow myocardial contraction velocity and improve impaired relaxation, hallmarks of patients with either obstructive or nonobstructive pathophysiology.
- Preclinical data of EDG-7500 support beneficial activity in models of both obstructive and non-obstructive HCM with minimal changes in overall LV systolic performance.

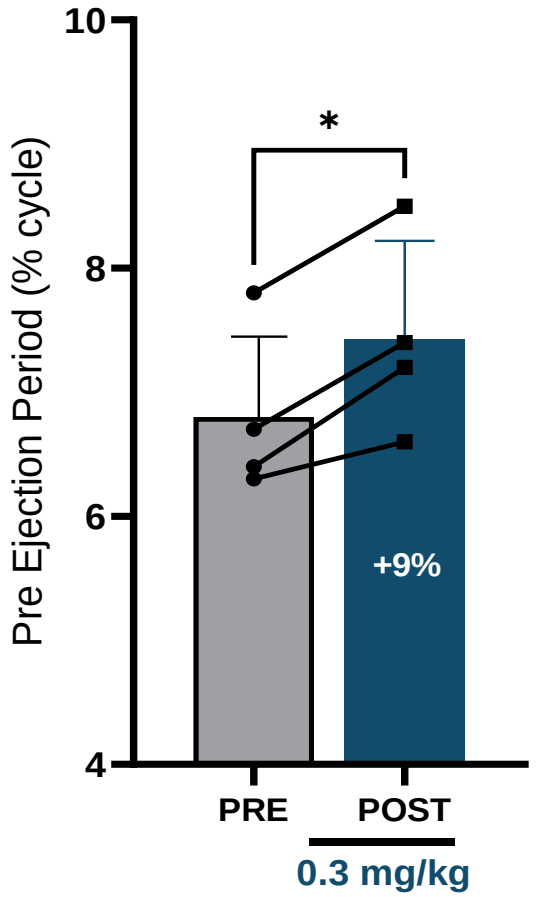
LVOT Obstruction Results from Abnormalities in Early Systolic Blood Flow & Mitral Structure

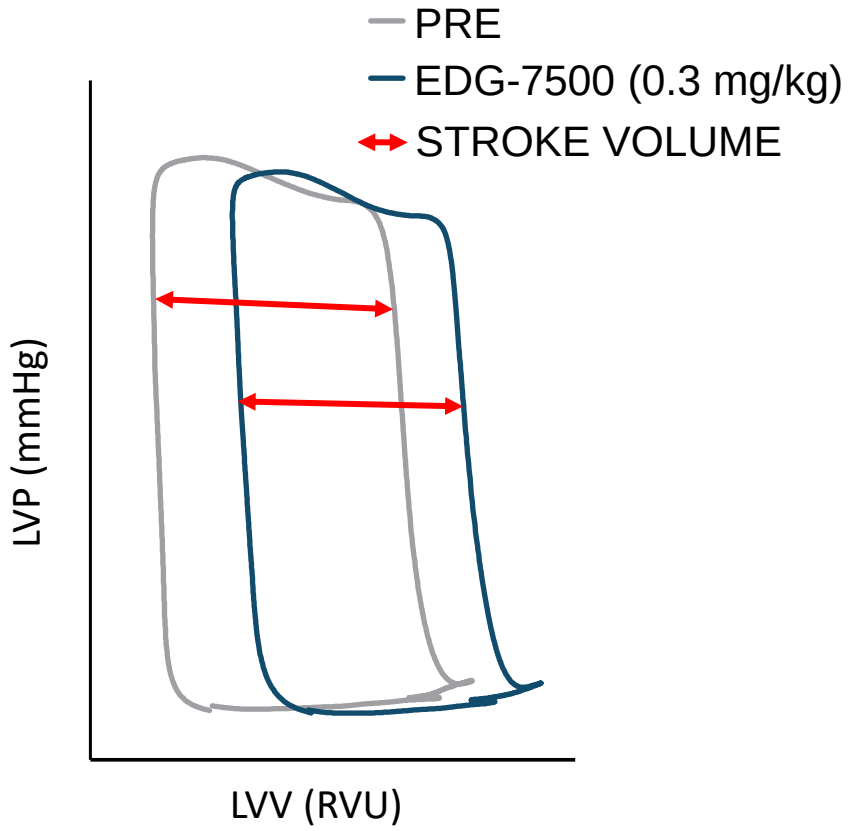


Adapted from Ro R, et al. J Am Coll Cardiol. 2014;64:1984-1995

Systolic Function: EDG-7500 Reduces +dP/dt$_{max}$ during Isovolumic Contraction and Prolongs Pre Ejection Period in Healthy Canines; Stroke Volume is Preserved



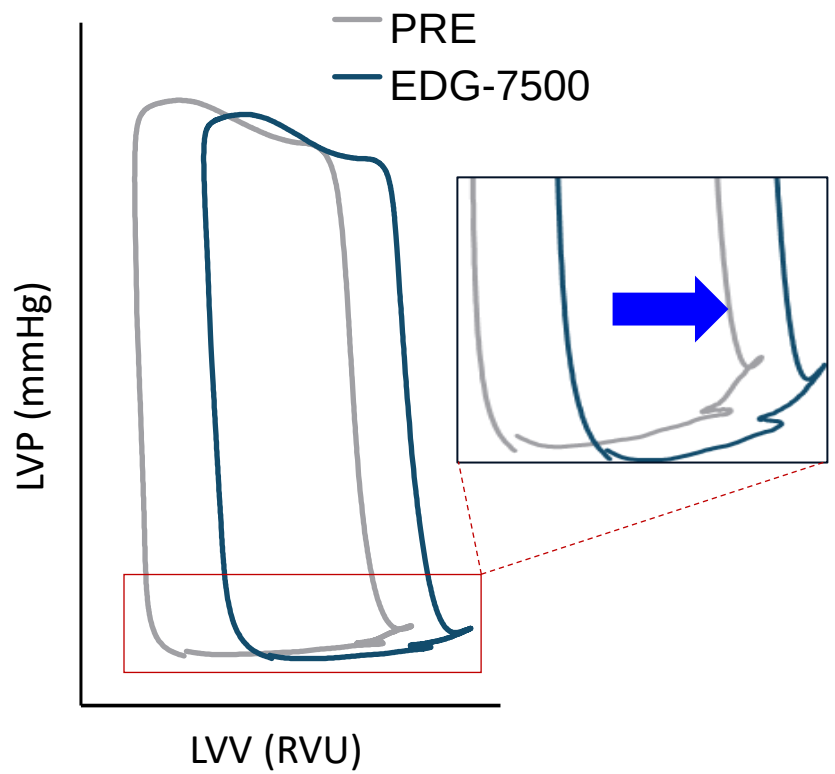


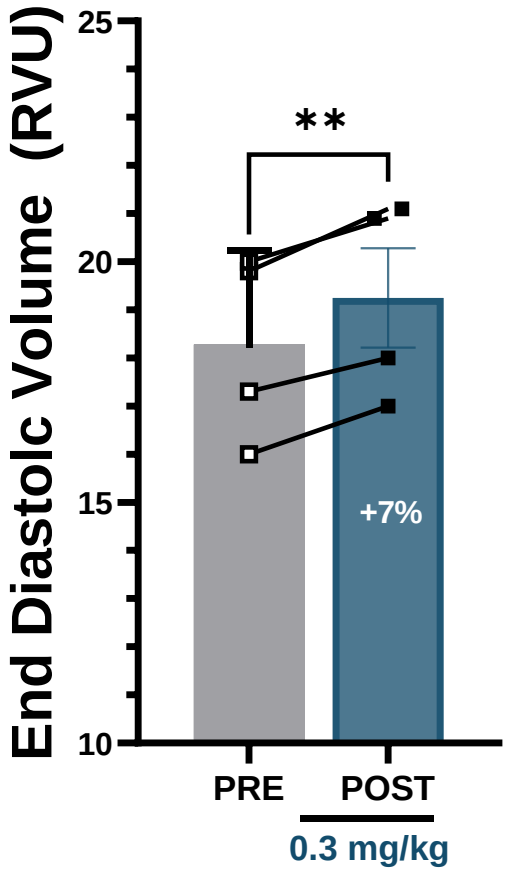


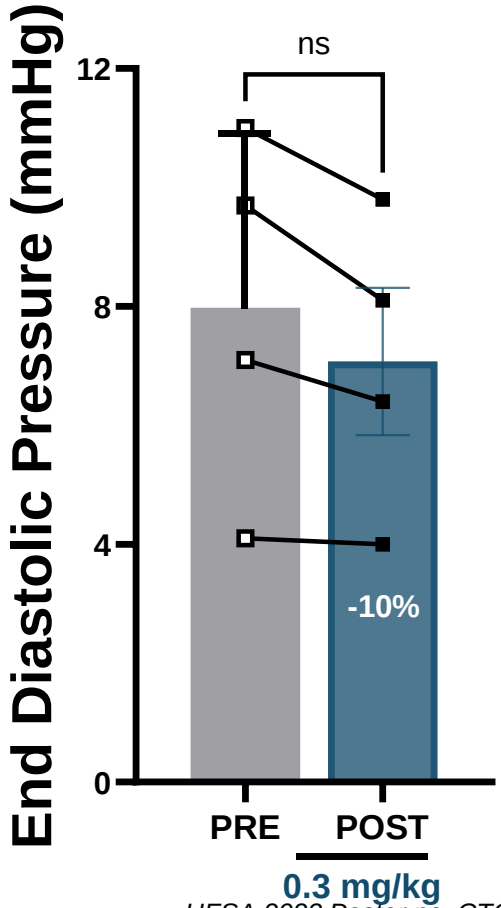
*p< 0.05; ** p < 0.01*
N=4 animals
Measurements made after iv EDG-7500 administration

HFSA 2023 Poster no. CTC-010

Diastolic Function: EDG-7500 Increases Left Ventricular Compliance in Healthy Canines







** p < 0.01
N=4
Measurements made after iv EDG-7500 administration

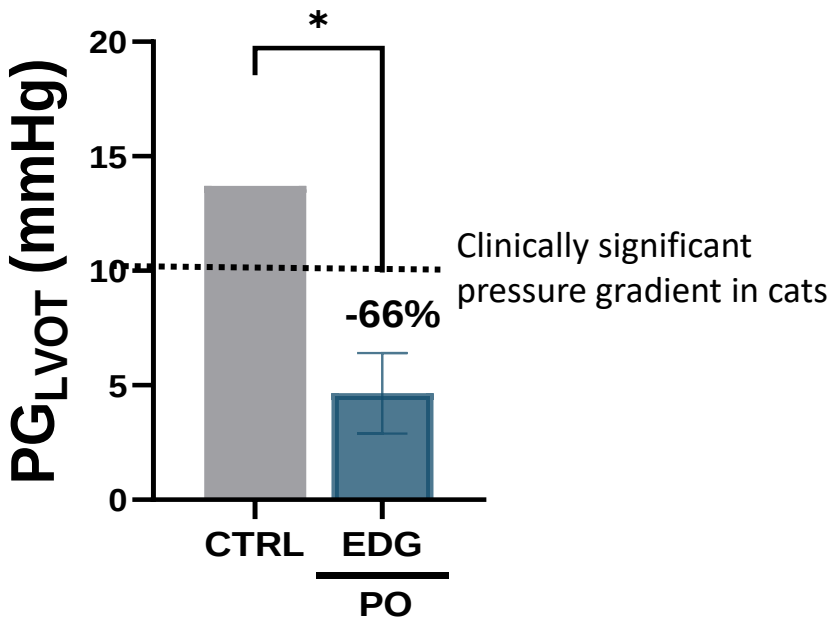
HFSA 2023 Poster no. CTC-010

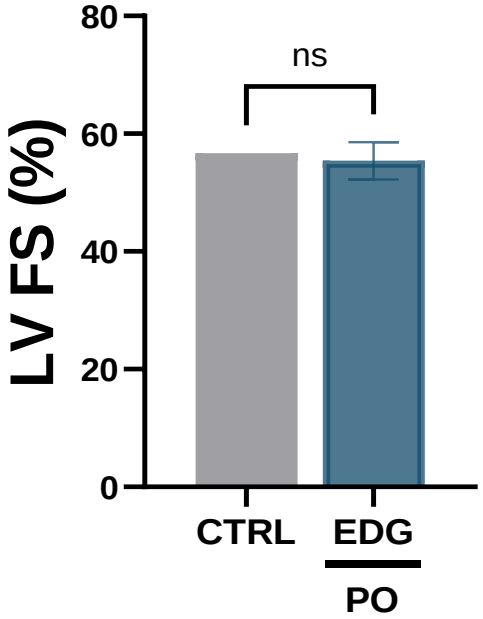
EDG-7500 Relieves LVOT Gradient Without Changing Fractional Shortening in Cats with Genetic oHCM

A31P MyBP-C Mutation Cat Model of oHCM (n=6).

Measurements made after single fixed dose oral EDG-7500 administration.

Plasma EDG-7500 levels: 68-560 ng/mL.



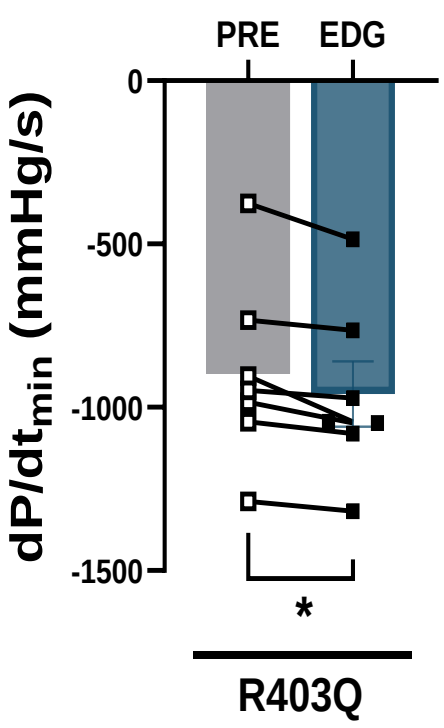


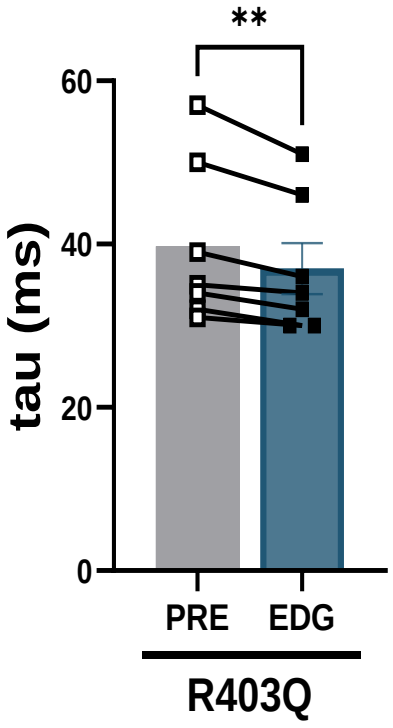
** p < 0.01*

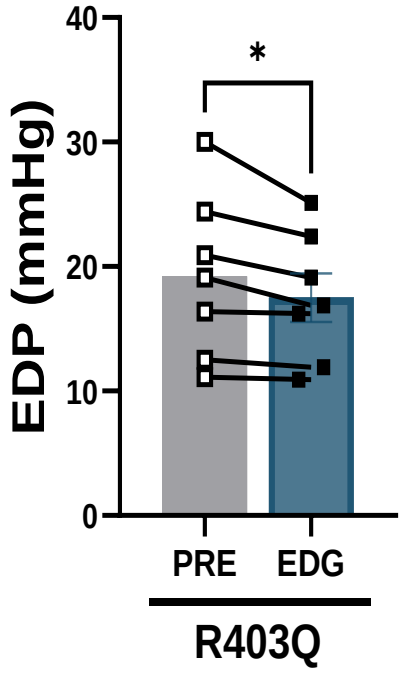
Kaplan J, et al. J Am Coll Cardiol. 2023;81(8 Supplement):349

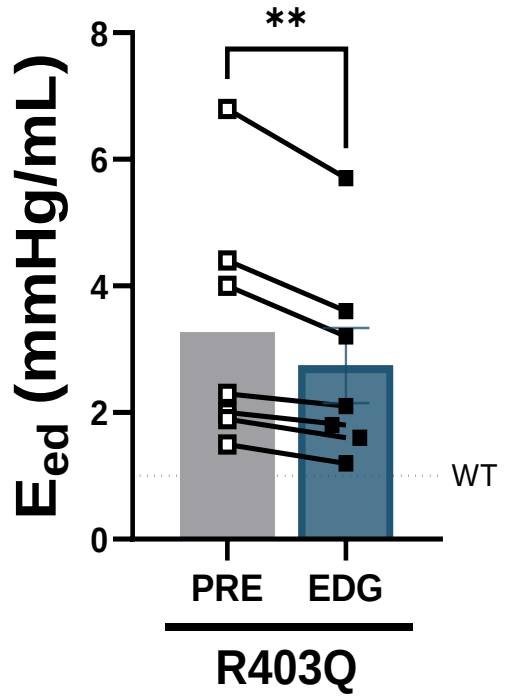
Abnormal LV Relaxation, Filling Pressure, & Diastolic Compliance Acutely Improve with EDG-7500

MYH7 R403Q Minipig Genetic Model of nHCM (n=6)









** P < 0.05, ** P < 0.01*
0.5 mg/kg EDG-7500 IV bolus

delRio C et al.Circulation. 2023;148:A15612

Summary

- Knowledge of muscle biology and the pathophysiologic mechanisms of HCM has informed design of a small molecule that directly targets both early-systolic and diastolic myocardial function with modest effects on overall systolic performance as measured by ejection-phase indices.
- EDG-7500 has been shown to eliminate LVOT obstruction in a cat model of oHCM over a wide range of exposures without altering %FS.
- EDG-7500 efficacy has been observed in preclinical animal models of HCM.
- Single ascending dose human studies of the safety & tolerability of EDG-7500 have begun (NCT06011317).
- EDG-7500's novel mechanism of action supports investigating fixed-dose regimens for treatment of patients with HCM.