



Cytokinetics

**ACTIVATE. INHIBIT.
EMPOWER.**

Changing the Course
of Cardiovascular Disease

July 15, 2020

Forward-Looking Statements

This Presentation contains forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995 (the “Act”). Cytokinetics disclaims any intent or obligation to update these forward-looking statements, and claims the protection of the Act's Safe Harbor for forward-looking statements. Examples of such statements include, but are not limited to, statements related Cytokinetics' and its partners' research and development and commercial readiness activities, including the initiation, conduct, design, enrollment, progress, continuation, completion, timing and results of clinical trials, projections regarding growing prevalence, low survival rates and market opportunity in heart failure; Cytokinetics' commercial readiness for *omecamtiv mecarbil*; Cytokinetics' ability to earn and receive milestone payments; the timing and results of clinical trials of AMG 594 and CK-274; the timing of any potential commercial launch of our product candidates, if approved; commercial opportunities for our product candidates; Cytokinetics' cash runway; interactions with the FDA; the properties, potential benefits and commercial potential of CK-274, *omecamtiv mecarbil*, AMG 594, *reldesemtiv* and Cytokinetics' other drug candidates. Such statements are based on management's current expectations; but actual results may differ materially due to various risks and uncertainties, including, but not limited to, potential difficulties or delays in the development, testing, regulatory approvals for trial commencement, progression or product sale or manufacturing, or production of Cytokinetics' drug candidates that could slow or prevent clinical development or product approval, including risks that current and past results of clinical trials or preclinical studies may not be indicative of future clinical trial results, patient enrollment for or conduct of clinical trials may be difficult or delayed, Cytokinetics' drug candidates may have adverse side effects or inadequate therapeutic efficacy, the FDA or foreign regulatory agencies may delay or limit Cytokinetics' or its partners' ability to conduct clinical trials, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Astellas', Amgen's or Ji Xing's decisions with respect to the design, initiation, conduct, timing and continuation of development activities for *reldesemtiv*, *omecamtiv mecarbil* or CK-274, respectively; Cytokinetics' ability to satisfy and conditions to the sale of its royalty interest in *mavacamten* or disbursement of funding from RTW; Cytokinetics may incur unanticipated research, development and other costs or be unable to obtain financing necessary to conduct development of its products; standards of care may change, rendering Cytokinetics' drug candidates obsolete; competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target; and risks and uncertainties relating to the timing and receipt of payments from its partners, including milestones and royalties on future potential product sales under Cytokinetics' collaboration agreements with such partners. These forward-looking statements speak only as of the date they are made, and Cytokinetics undertakes no obligation to subsequently update any such statement, except as required by law. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission (the “SEC”).

Agenda

<ul style="list-style-type: none"> • Introduction <ul style="list-style-type: none"> • <i>A Transformative Time for Cytokinetics</i> • <i>Modulating Contractility for Multiple Unmet Needs</i> 		08:30 – 09:00 AM ET
Activate		
<ul style="list-style-type: none"> • Omecamtiv Mecarbil: <ul style="list-style-type: none"> • <i>The Origin Story</i> • <i>Where We Are Now</i> • <i>Why We Believe</i> • <i>Predictive Value of Key Measures in COSMIC-HF</i> • <i>The Commercial Opportunity</i> 		09:00 – 09:40 AM ET
<ul style="list-style-type: none"> • Panel Discussion: <i>Optimizing Therapy in a New Treatment Landscape</i> 		09:40 – 10:00 AM ET
<ul style="list-style-type: none"> • Questions 		10:00 – 10:05 AM ET
Inhibit		
<ul style="list-style-type: none"> • CK-274: <ul style="list-style-type: none"> • <i>Body of Evidence</i> • <i>Opportunities for Development</i> 		10:05 – 10:25 AM ET
<ul style="list-style-type: none"> • Panel Discussion: <i>Embracing a New Era in the Treatment of HCM</i> 		10:25 – 10:45 AM ET
<ul style="list-style-type: none"> • Questions 		10:45 – 10:50 AM ET
Empower		
<ul style="list-style-type: none"> • Panel Discussion: <i>The Patient Perspective</i> 		10:50 – 11:10 AM ET
<ul style="list-style-type: none"> • Building a Cardiovascular Franchise 		11:10 – 11:20 AM ET
<ul style="list-style-type: none"> • Closing Remarks 		11:20 – 11:30 AM ET

Engaging in Today's Meeting

- **Customize Your View:** Resize the components on your screen, and restore the view with the first button at the bottom center of your screen
- **Features:** Q&A, speaker bios and today's agenda in the lower left box
- **Questions:** Type your questions at any time in the Q&A
- **Technical Issues:** Type in the Q&A box and tech support will respond directly
- **Recording:** A recording of today's event will be available online at www.cytokinetics.com

Company Speakers



Robert Blum
President & CEO



Fady Malik, M.D., Ph.D.
EVP, Research & Development



Stuart Kupfer, M.D.
SVP, Chief Medical Officer



Andrew Wolff, M.D.
SVP, Senior Fellow, Clinical
Research & Development



Steve Heitner, M.D.
Senior Medical Director, Clinical
Research, Cardiovascular



Laura Robertson, M.D.
Medical Director, Clinical
Research, Cardiovascular



Scott Jordan
SVP, New Product Planning &
Commercial Development



Durga Bobba
VP, Global Franchise General
Manager, Cardiovascular



Diane Weiser
SVP, Corporate
Communications & IR

Expert Guests



John McMurray, M.D.

Professor of Medical Cardiology & Honorary Consultant Cardiologist, Institute of Cardiovascular & Medical Sciences, BHF Cardiovascular Research Centre, University of Glasgow



Adrian Hernandez, M.D., M.H.S.

Executive Director, Duke Clinical Research Institute, Vice Dean, Duke University School of Medicine



Larry Allen, M.D., M.H.S.

Professor of Medicine, Kenneth Poirier Chair; Associate Head for Clinical Affairs, Cardiology; Medical Director, Advanced Heart Failure, University of Colorado School of Medicine



Martin Maron, M.D.

Director, Hypertrophic Cardiomyopathy Center; Director, Cardiac CT & MRI, Tufts University School of Medicine



Anjali Tikun Owens, M.D.

Medical Director, Center for Inherited Cardiac Disease, Assistant Professor of Medicine, University of Pennsylvania



Andrew Wang, M.D.

Professor of Medicine, Vice Chief for Clinical Services, Duke University School of Medicine

Patient Guests



Linda Moczowski

Former nurse, patient advocate living with heart failure



Lindsay Davis

Miss Ohio 2011, patient advocate living with hypertrophic cardiomyopathy

INTRODUCTION

A Transformative Time for Cytokinetics

Robert Blum, President & CEO

Sarcomere Directed Therapies

OUR MISSION

To bring forward new medicines to improve the healthspan of people with devastating cardiovascular and neuromuscular diseases of impaired muscle function.

VISION 2025

Leading with Science,
Delivering for Patients

As always, we will support disease advocacy groups elevating the patient voice and live by our values of integrity, fairness and compassion in all that we do.

Our vision is to be the leading muscle biology biopharma company that meaningfully improves the lives of patients with diseases of impaired muscle function through access to our pioneering medicines

Achieve regulatory approvals for at least two drugs arising from our pipeline

Build commercial capabilities to market and sell our medicines reflective of their innovation and value

Generate sustainable and growing revenues from product sales

Double our development pipeline to include ten therapeutic programs

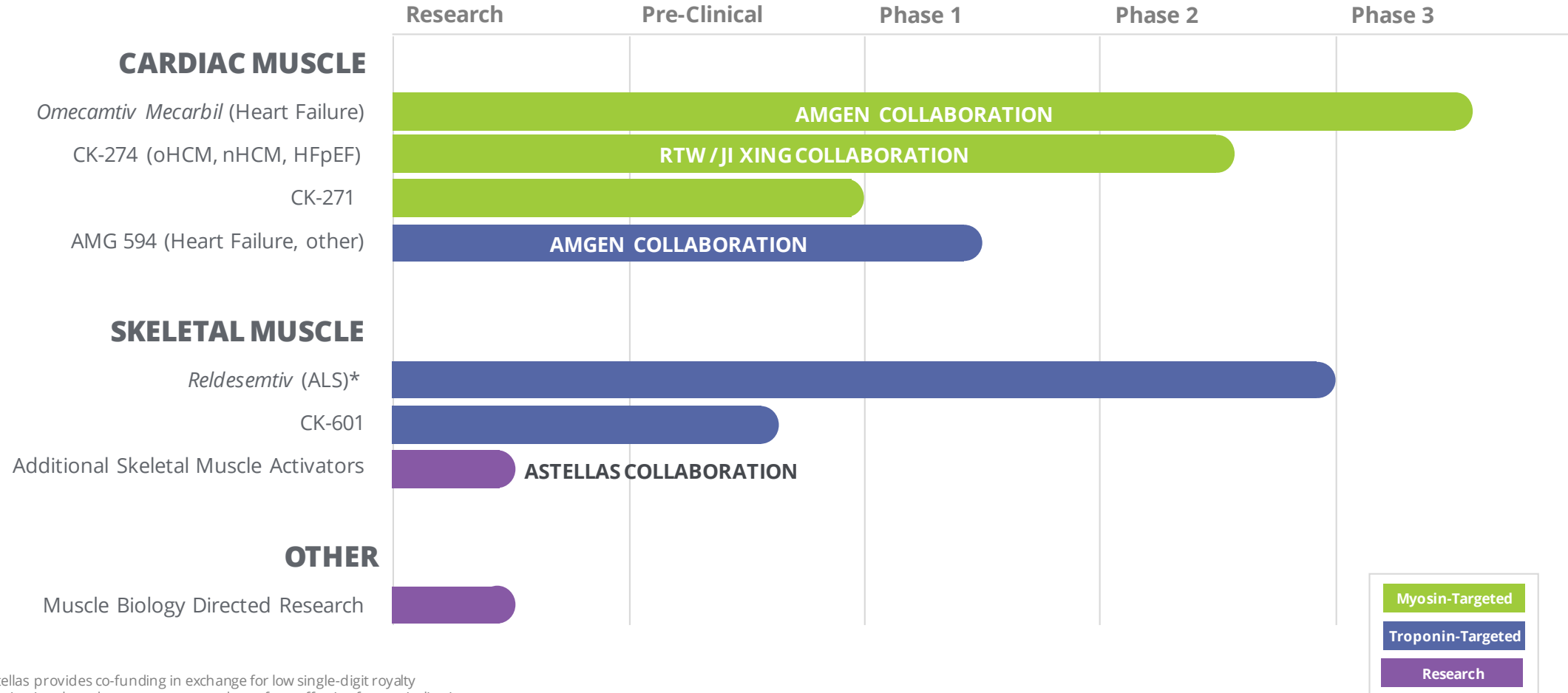
Expand our discovery platform to muscle energetics, growth and metabolism

Be the science-driven company people want to join and partner with

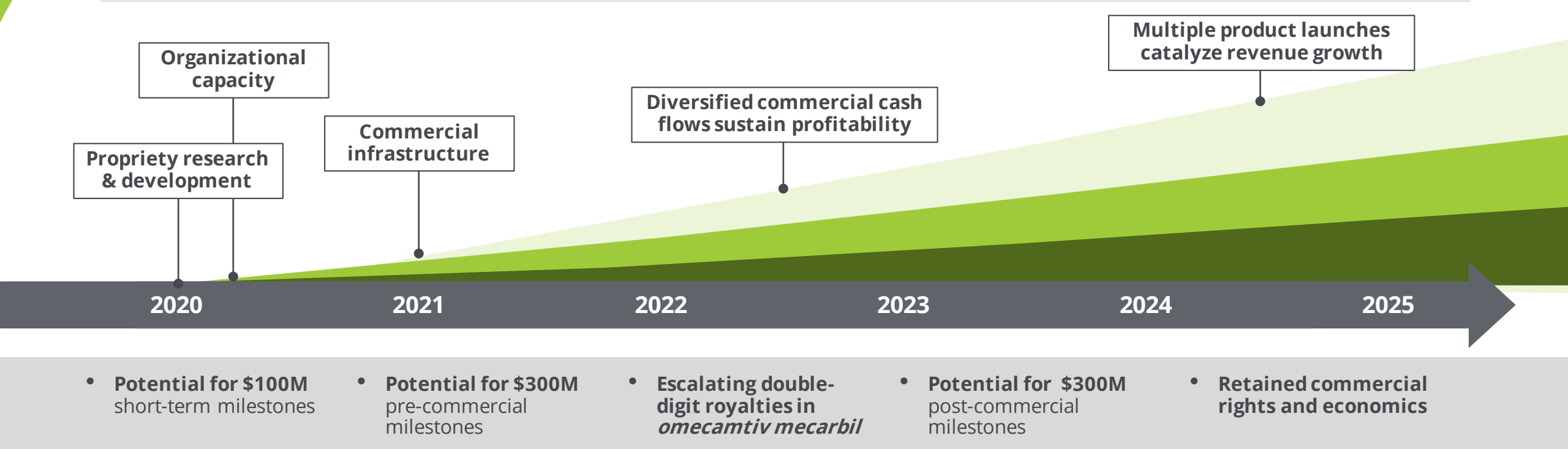
How Do We Get There?



Pipeline of Novel Muscle-Directed Drug Candidates



Corporate Development Strategy



RTW
Investments
CK-274
oHCM, nHCM
COMMITTED CAPITAL FOR
DEVELOPMENT/LICENSING
COLLABORATION IN CHINA

AMGEN
omecamtiv mecarbil
Heart Failure
CO-PROMOTION:
NORTH AMERICA

 **astellas**
reldesemtiv
ALS
CO-FUNDING PHASE 3
CLINICAL DEVELOPMENT

Above illustrative timelines are based on current assumptions and projections. All such timelines are subject to change and may be materially delayed based on a variety of factors, including patient enrollment, clinical trial results, regulatory review, our partners' ability to manufacture products and other factors.

Omecamtiv Mecarbil: Collaborations & Agreements

Amgen & Royalty Pharma



Amgen Collaboration

Purchase Option: 2006

Exercise Option Ex-Japan: 2009

Expanded to Include Japan/Purchase Equity: 2013

Received >\$220M over 13 Years

Amgen responsible for development and commercialization subject to Cytokinetics' participation rights*

Cytokinetics could earn over \$600M in milestone payments

Commercialization:

- Cytokinetics may receive escalating double-digit royalties
- Cytokinetics to co-fund Phase 3 development program
- Co-fund enables co-promote NA
- Cytokinetics reimbursed for certain sales force activities



Royalty Monetization

Royalty Pharma paid \$100M for 4.5% royalty on worldwide sales of *omecamtiv mecarbil*: 2017

Cytokinetics gains right to co-promote *omecamtiv mecarbil*, if approved, in institutional care settings in North America, with reimbursement from Amgen for certain sales force activities

Joint commercial operating team responsible for commercialization program

- Royalty rate may increase up to additional 1% associated with timing of US approval
- Cytokinetics agreed to exercise option to co-invest \$40M in Ph 3 development program in exchange for up to incremental 4% royalty on increasing worldwide sales outside of Japan
- Cytokinetics retains right to receive >\$600M in additional potential milestone payments and escalating double-digit royalties that may exceed 20% on tiered worldwide sales outside Japan; lower royalty rate in Japan

*Servier has a sub-license from Amgen to commercialize *omecamtiv mecarbil* in Europe and certain other countries.

CK-3773274: Collaborations & Agreements

RTW Investments, LP & Ji Xing Pharmaceuticals Limited



RTW & Ji Xing Pharma Licensing Collaboration, Funding Commitments & Royalty Monetization

RTW Investments committed capital, funding and sale proceeds of \$250M to Cytokinetics

Ji Xing Pharma to develop & commercialize CK-274 in China, subject to royalties and up to \$200M in milestone payments

RTW Investments purchases equity and agrees to purchase royalty; provides access to capital for development of CK-274

Ji Xing Pharma

Ji Xing to develop & commercialize CK-274 in Greater China and Taiwan

Cytokinetics receives **\$25M upfront**; eligible to receive **\$200M** in development & commercial milestones & double-digit royalties on sales of CK-274 in licensed territory

RTW: Funding for Development of CK-274

Cytokinetics receives options for additional funding for further development of CK-274 in HCMs:

- Eligible for **\$45M** in each of 2 tranches (upon initiation of global registration programs in oHCM and nHCM) in exchange for 2% royalty on sales in U.S. & certain European countries
- If **full \$90M** received, Cytokinetics pays RTW 4% royalty on sales of CK-274 in U.S. & certain European countries, subject to royalty reductions for potential other indications

RTW: Other Purchases

RTW agrees to purchase Cytokinetics' royalty rights **on future sales of mavacamten** for **\$85M**

RTW purchases **\$50M of Cytokinetics' common stock** at \$25 per share

Commercialization Strategy

Leveraging partnership with Amgen to finance the build of our commercial business

Amgen to reimburse Cytokinetics' commercialization costs in North America

Potential royalties and milestone payments from Amgen expected to support Cytokinetics' commercialization of CK-274, *reldesemtiv* in North America and Europe

AMGEN

omecamtiv mecarbil
Heart Failure

RTW

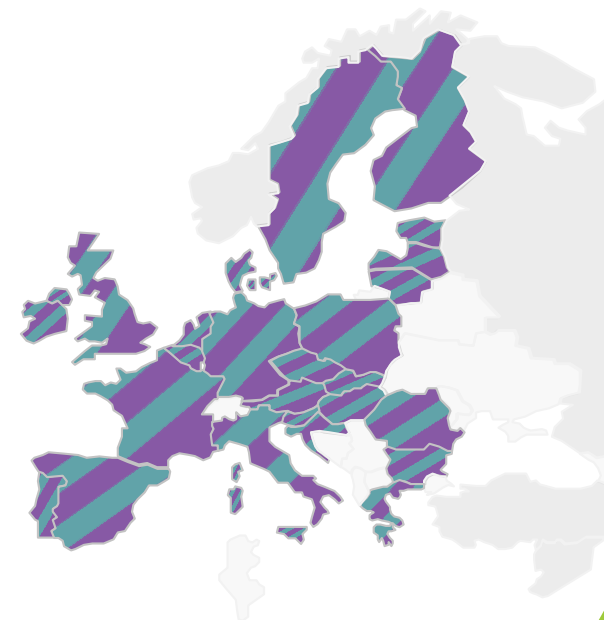
Investments

CK-274
oHCM, nHCM



astellas
reldesemtiv
ALS

Focus to Concentrated Customer Segments
(e.g. Centers of Excellence)



INTRODUCTION

Modulating Contractility for
Multiple Unmet Needs

Fady Malik, M.D., Ph.D., EVP, Research & Development

Targeting Muscle Contractility

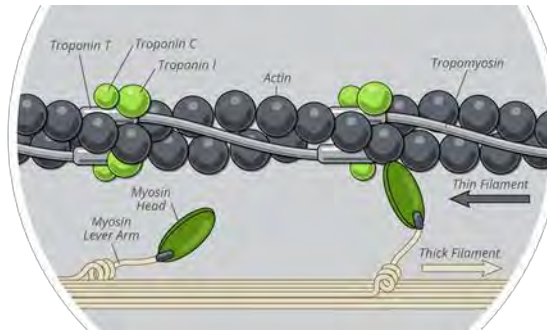
	Cardiac Muscle	Skeletal Muscle	Smooth Muscle
Diversity of Contractile Function	Ventricular ejection Ventricular filling	Mobility Strength	Bronchial tone Pulmonary vascular tone Systemic vascular tone
Diversity of Potential Therapeutic Application	Systolic heart failure Diastolic heart failure	Neuromuscular diseases Conditions of muscle weakness/wasting	Asthma/COPD Pulmonary hypertension Systemic hypertension

Pioneers in the Pharmacology of Muscle Contractility

- Novel molecular targets require novel assays
- Faithful representation of biological function from *in vitro* to *in vivo* setting
- Correlation of molecular findings with functional effects
- Purpose-built measurement technologies

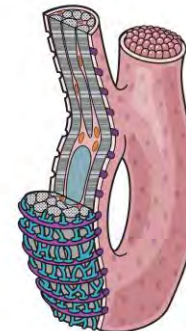
Reconstituted Sarcomere

Flexible Biochemical Assay



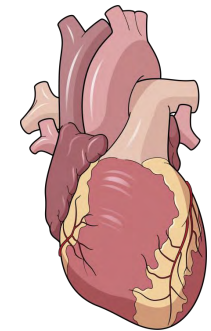
Muscle Fiber

Assay in Native Context



Organ and *In Vivo*

Functional Outcome



Low complexity

High complexity

High Throughput

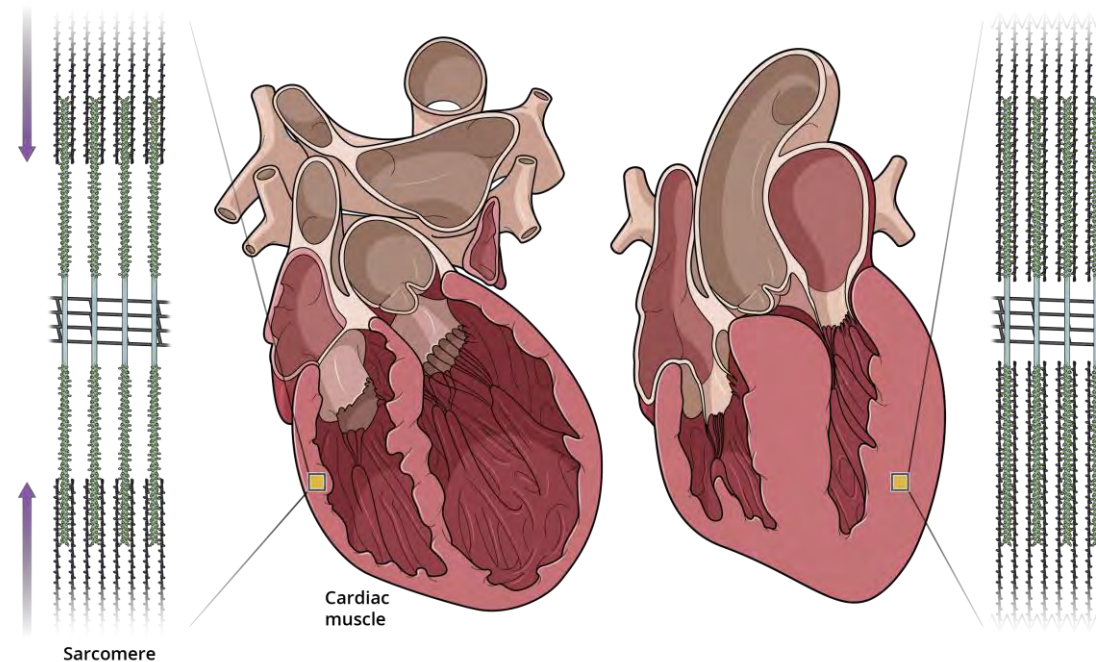
Low Throughput

Coherence

Heart Failure: Multiple Phenotypes with Unmet Need

Decreased Cardiac Contractility

- Heart Failure with Reduced Ejection Fraction (HFrEF)
- Genetic Dilated Cardiomyopathy
- Pulmonary Hypertension with Right Ventricular Heart Failure

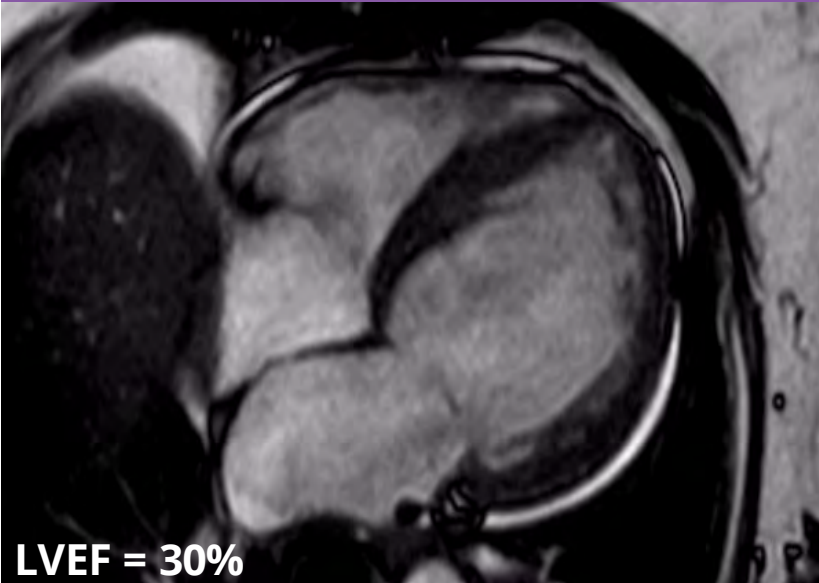


Increased / Preserved Cardiac Contractility

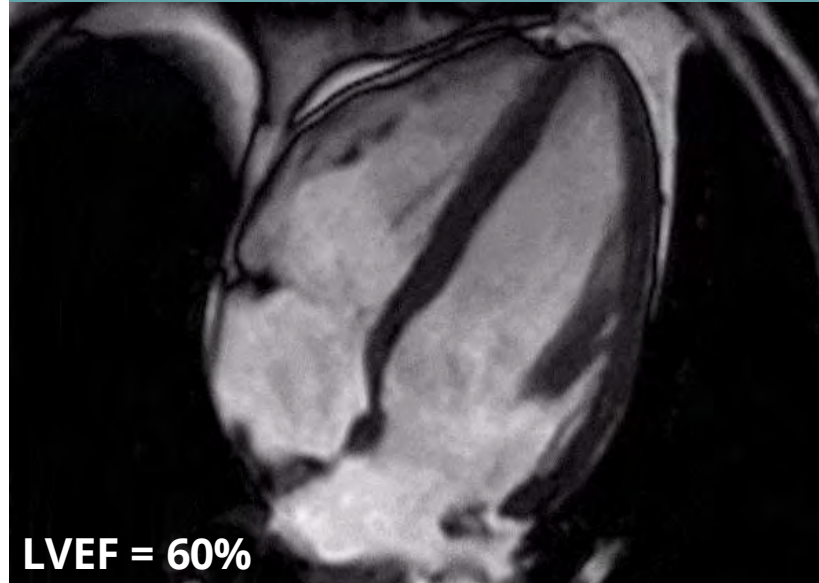
- Non-obstructive Hypertrophic Cardiomyopathy (nHCM)
- Obstructive Hypertrophic Cardiomyopathy (oHCM)
- Heart Failure with Preserved Ejection Fraction (certain HFpEF subsets)

The Spectrum of Cardiac Contractility in Health & Disease

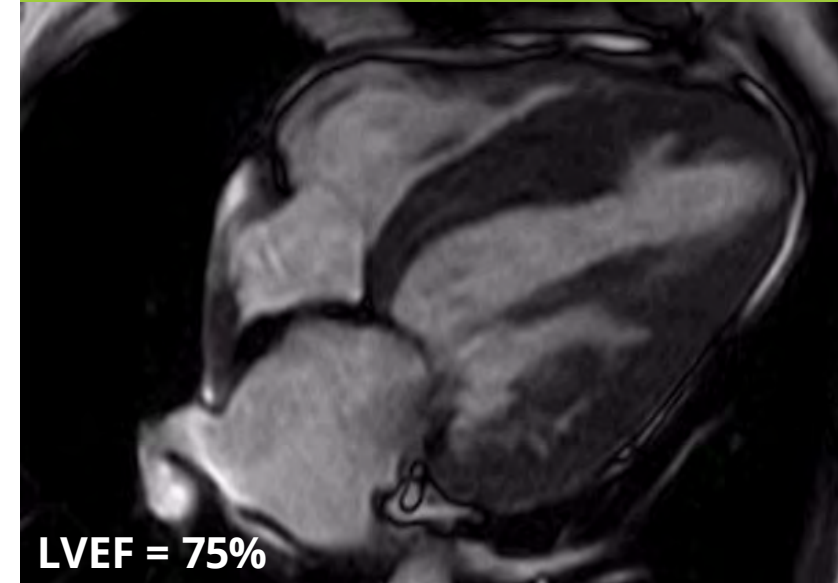
HFrEF (Low Contractility)



Normal Contractility



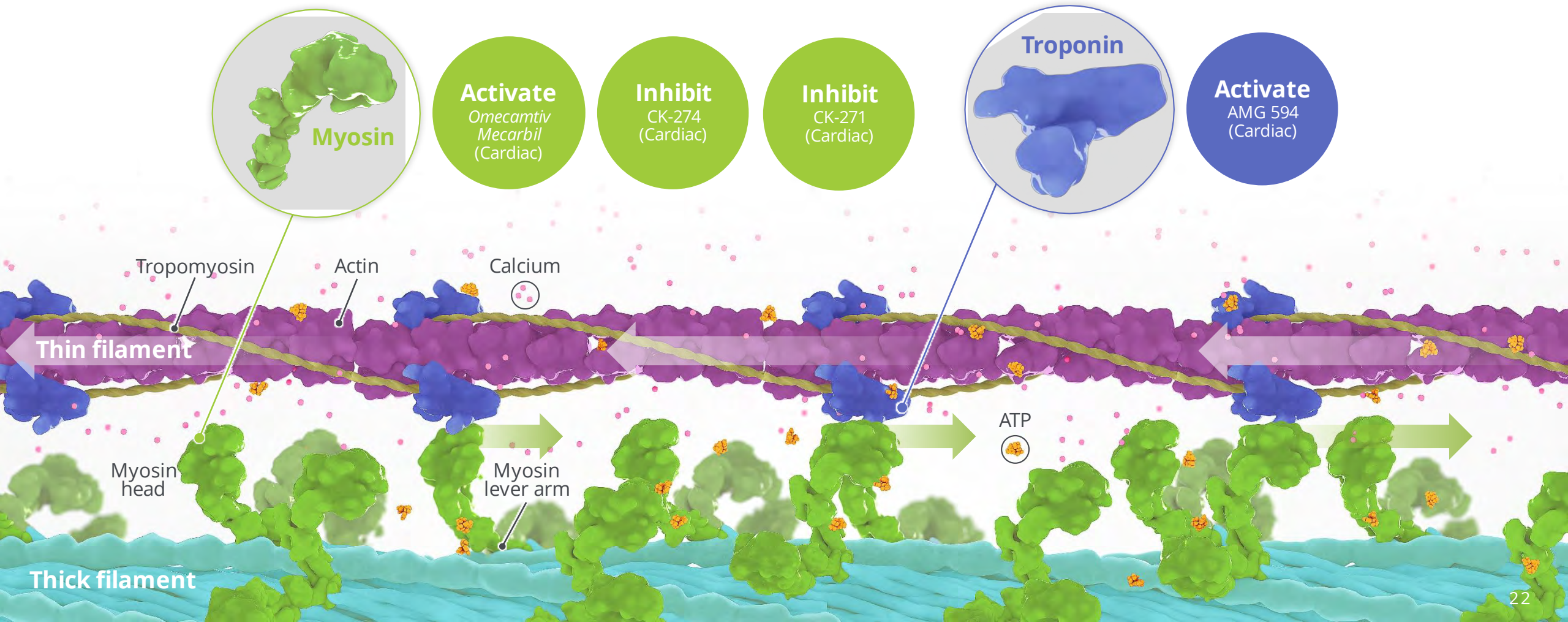
HCM & HFpEF (subset) (Hypercontractility)



LVEF = Left Ventricular Ejection Fraction

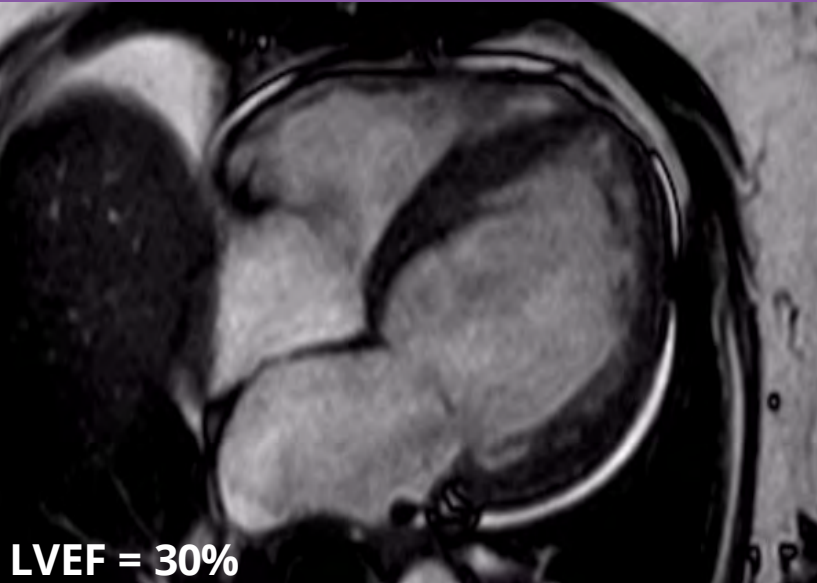
Sarcomere Directed Drug Development

The sarcomere is a molecular machine found in skeletal and cardiac muscle that enables muscle to contract and generate force

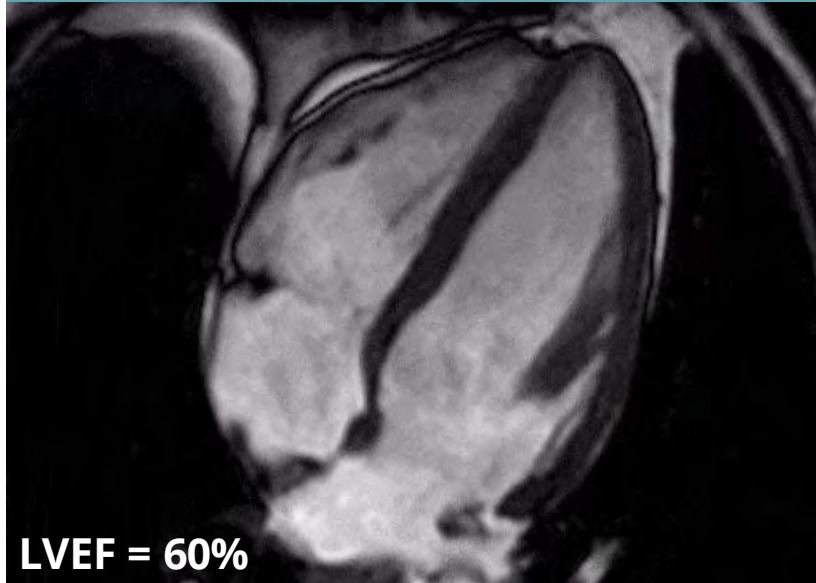


The Spectrum of Cardiac Contractility in Health & Disease

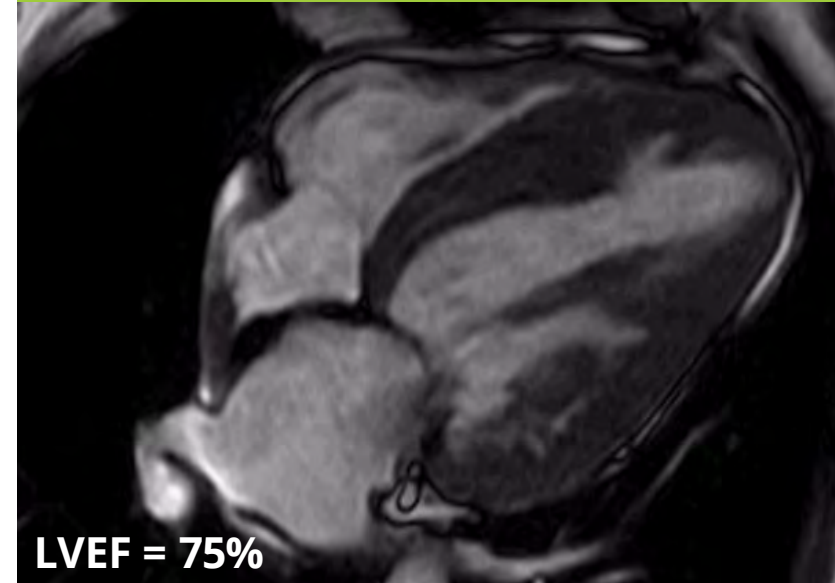
HFrEF (Low Contractility)



Normal Contractility



HCM & HFpEF (subset) (Hypercontractility)



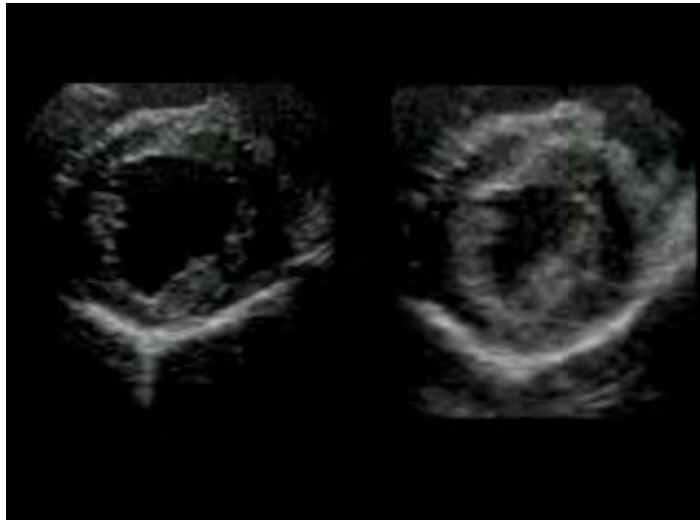
omecamtiv mecarbil

CK-274 & CK-271

LVEF = Left Ventricular Ejection Fraction

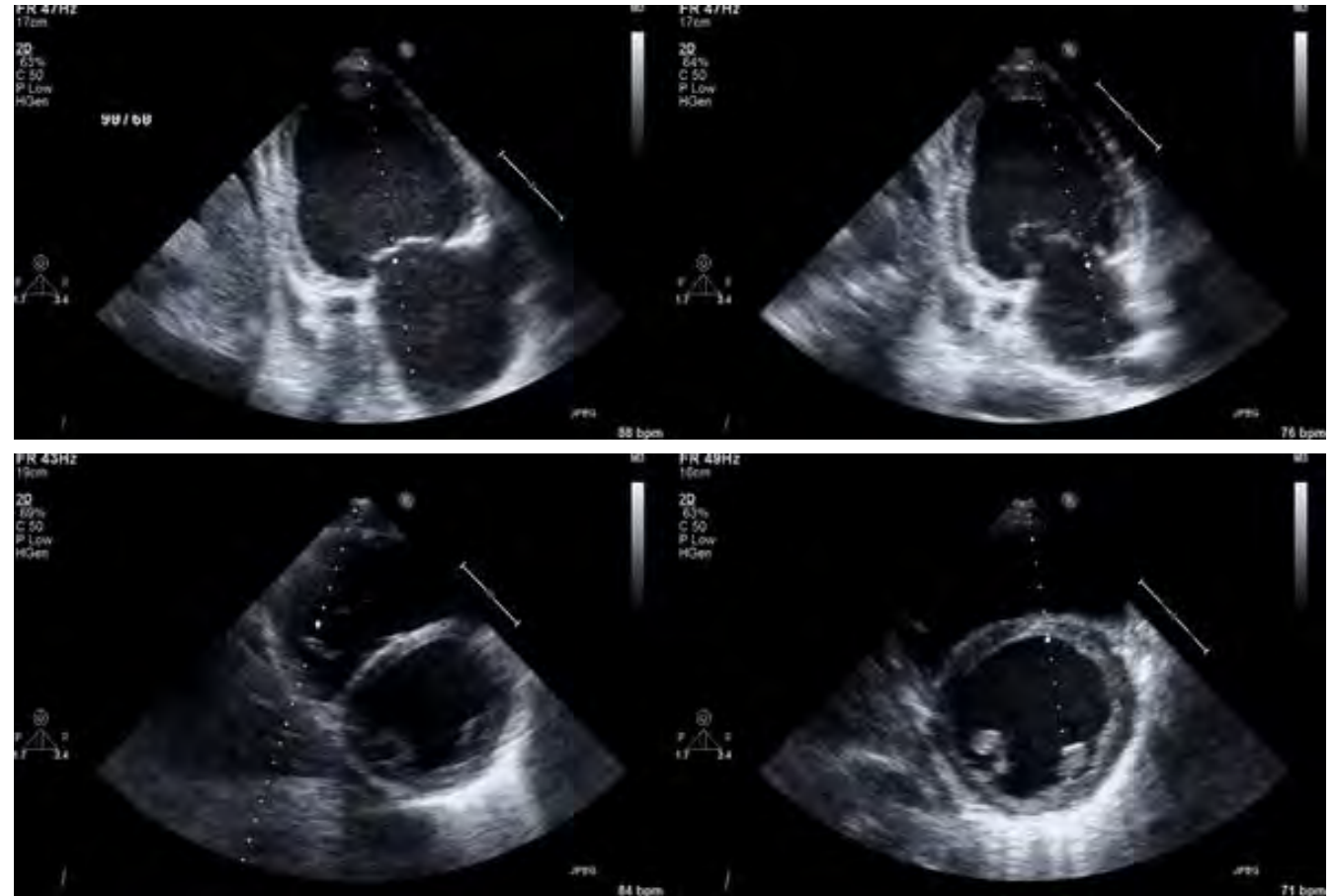
Omecamtiv Mecarbil: Effects on Cardiac Function

Preclinical Model



Prior to Dosing – left image
During Dosing – right image

Human Translation



Images and data from patient enrolled in CY 1121

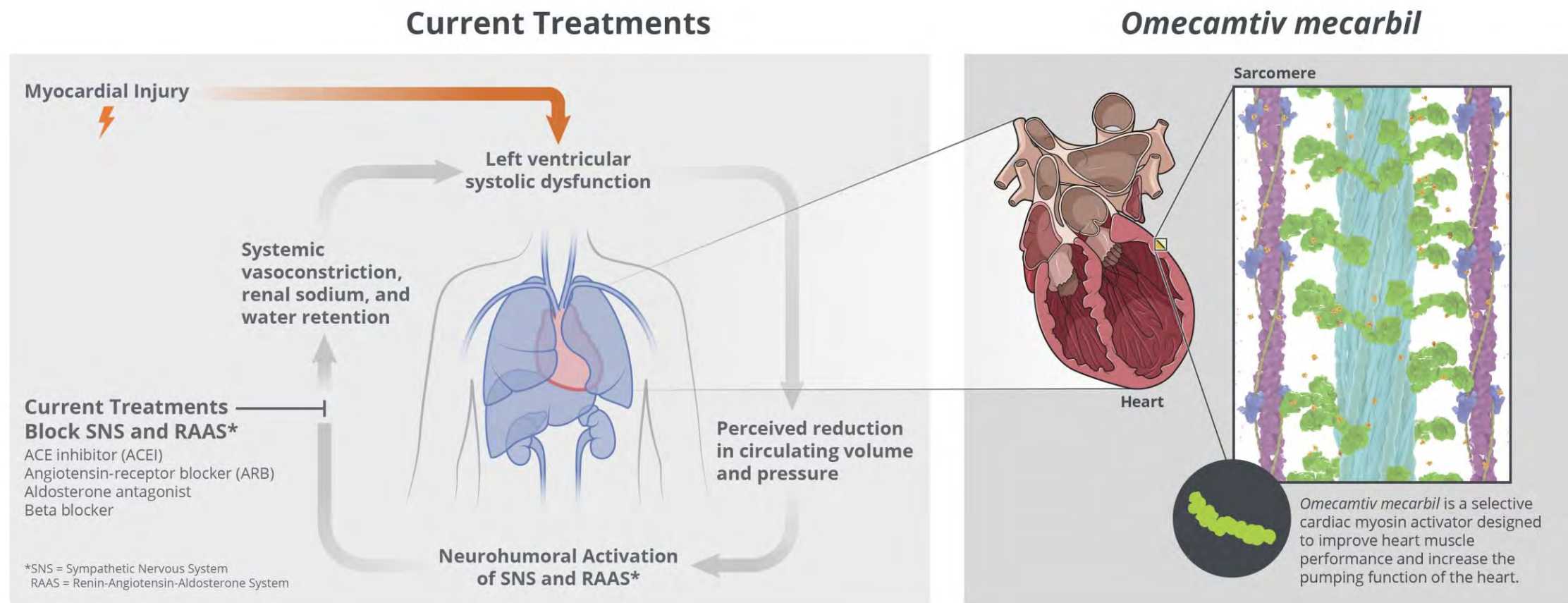
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OMECAMTIV MECARBIL

The Origin Story

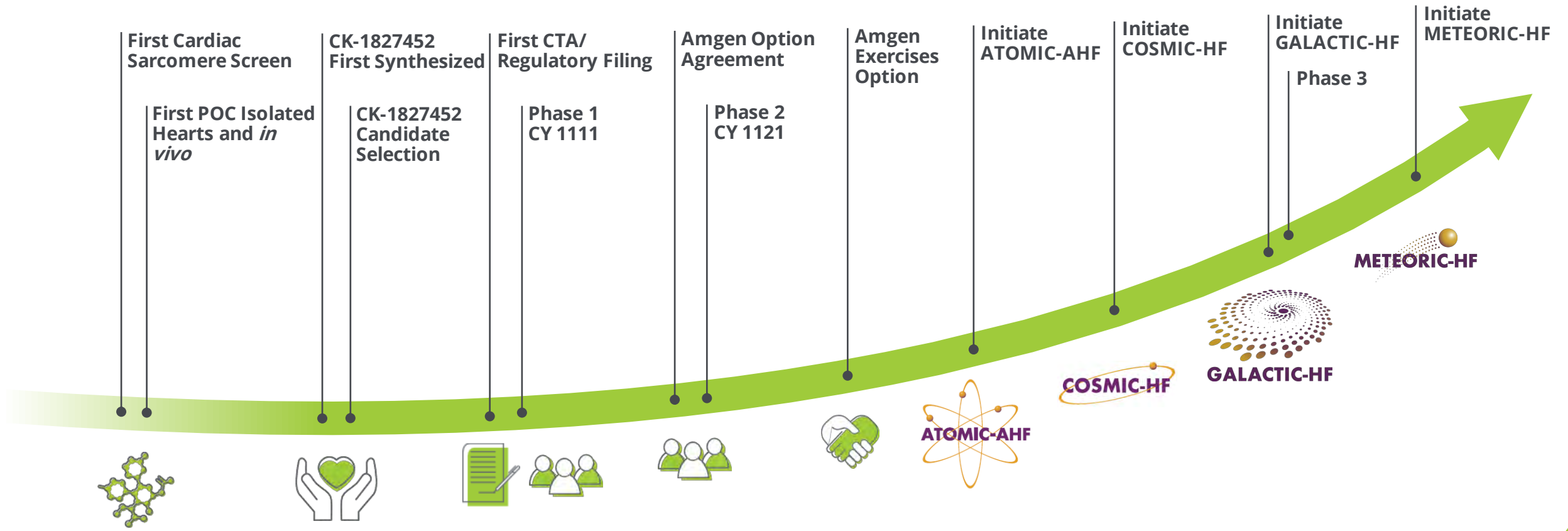
Fady Malik, M.D., Ph.D., EVP, Research & Development

Omecamtiv Mecarbil: Novel Mechanism Approach



Omecamtiv Mecarbil: Pivotal Phase 3 Results Q4 2020

11 Phase 1 studies with over 300 patients, 7 Phase 2 trials with over 1,400 patients



OMECAMTIV MECARBIL

Where We Are Now: GALACTIC-HF

Fady Malik, M.D., Ph.D., EVP, Research & Development

Pivotal Phase 3 Trial Completed Enrollment

GALACTIC-HF continuing following second planned interim analysis



Topline results expected in Q4 2020

Overview

Enrolled 8,256 patients at ~1,000 sites in 35 countries

Primary Endpoint

Composite of time to cardiovascular (CV) death or first HF event*, whichever occurs first

Secondary Endpoints

- Time to CV death
- Change in Kansas City Cardiomyopathy Questionnaire Total Symptoms Score (KCCQ TSS) from baseline to Week 24
- Time to first HF hospitalization
- Time to all-cause death

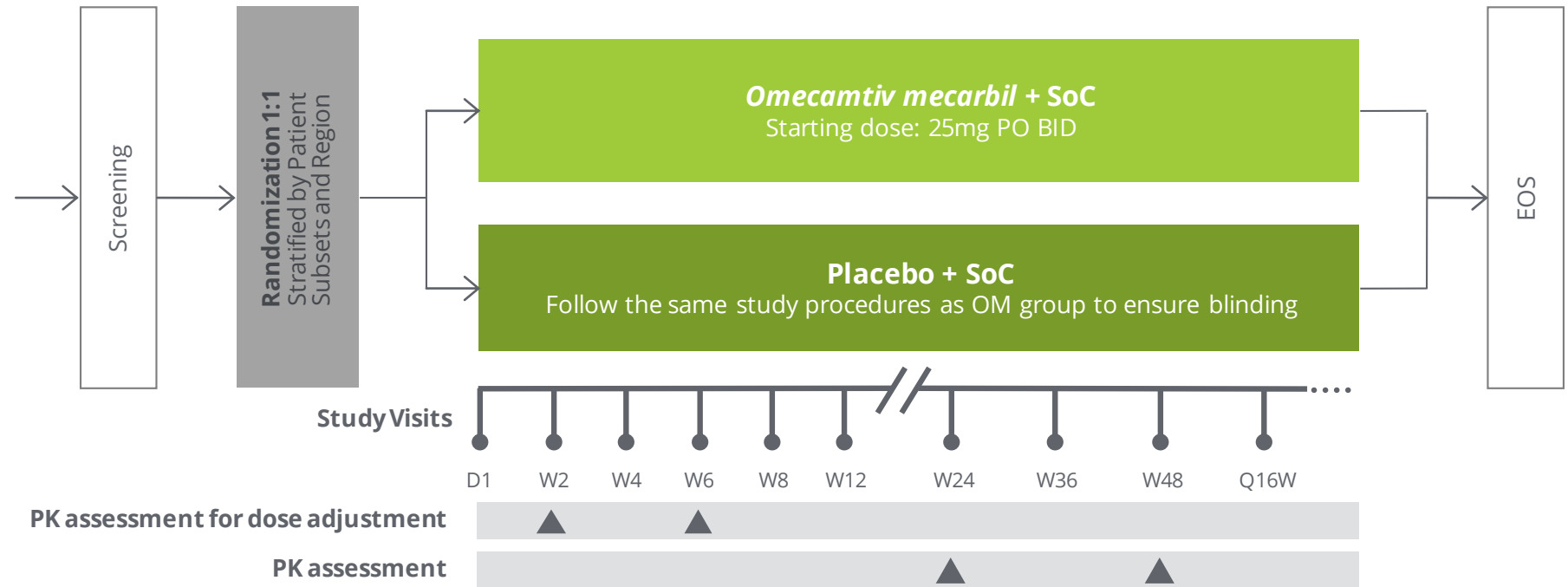
Key Design Points

- Dose optimization based on trough concentration of *omecamtiv mecarbil* at 2 weeks and 6 weeks
- High risk patients enrolled from inpatient and outpatient settings
- Designed to provide 90% statistical power to assess risk of CV death

*An HF event defined as the presentation of the subject for an urgent, unscheduled clinic/office/ED visit, or hospital admission, with a primary diagnosis of HF, where the patient exhibits new or worsening symptoms of HF on presentation, has objective evidence of new or worsening HF, and receives initiation or intensification of treatment specifically for HF (Hicks et al, 2015). Changes to oral diuretic therapy do not qualify as initiation or intensification of treatment.

Clinical Trial Overview

Chronic HFrEF patients currently hospitalized for a primary reason of HF or with history of hospitalization or ER/ED admission for a primary reason of HF within 1 year



Baseline Characteristics: High Risk Population

- 8,256 patients enrolled in 35 countries
- Population at high risk for cardiovascular events despite being well-treated on standard of care
 - Inpatient population: **25%**
 - Time from most recent HF hospitalization/ED visit (months), median (Q1-Q3): **2 (1-5)**
 - NT-proBNP, median (Q1-Q3): **1,998 pg/mL (990-4,078)**
 - LVEF, mean: **27%**
 - ENTRESTO® use: **19%**

	Overall (N=8,256)	Inpatient (N=2,083)	Outpatient (N=6,173)
Time from most recent HF hospitalization/ED visit (months), median (Q1-Q3)	2 (1-5)	-	3 (2-6)
Age (years), mean (SD)	65 (11)	65 (11)	64 (11)
Male, %	79	80	78
White, %	78	82	76
LVEF (%), mean (SD)	27 (6)	27 (6)	27 (6)
NYHA Class II/III/IV, %	53/ 44/ 3	37/ 57/ 6	59/ 39/ 2
NT-proBNP (pg/mL), median (Q1-Q3)	1998 (990-4078)	2509 (1240-5133)	1884 (923-3772)
Ischemic Heart Disease Etiology, %	55	56	54
KCCQ Total Symptom Score, mean (SD)	66 (25)	53 (25)	71 (23)
Atrial Fibrillation or Flutter History, %	42	48	40
Chronic Kidney Disease, %	36	39	35
eGFR (mL/min/1.73m ²), median (Q1-Q3)	59 (44-74)	54 (41-70)	60 (45-75)
SBP (mmHg), mean (SD)	117 (15)	114 (14)	117 (16)
ACEi, ARB or ARNi, %	87	83	88
ARNi (ENTRESTO®) %	19	14	19
Beta Blocker, %	94	93	95
MRA, %	77	81	76
Diuretics other than MRAs, %	90	92	89
Digitalis Glycosides, %	17	17	17
SGLT2 Inhibitors, %	3	3	3

Comparing Patients in Large Heart Failure Trials

Highest risk patients in VICTORIA; lower risk in PARADIGM-HF, DAPA-HF



	GALACTIC-HF (N=8,256)	VICTORIA (N=5,050)	PARADIGM-HF (N=8,339)	DAPA-HF (N=4,744)
Age (y, mean (SD))	65 (11)	67.3 (12.2)	63.8 (11.4)	66 (11)
Race				
White	6,358 (77.0%)	3,239 (64.1%)	5,544 (65.7%)	3,333 (70.2%)
Black or African American	561 (6.7%)	249 (4.9%)	428 (5.1%)	226 (4.7%)
Asian	710 (8.6%)	1,132 (22.4%)	1,509 (17.9%)	1,109 (23.3%)
Other	627 (7.6%)	430 (8.5%)	918 (11.0%)	76 (1.6%)
Geographic Region				
Eastern Europe	2,705 (32.7%)	1,694 (33.5%)	2,826 (33.5%)	1,604 (33.8%)
Western Europe	1,921 (23.3%)	889 (17.6%)	2,051 (24.3%)	550 (11.6%)
Asia Pacific	670 (8.1%)	1,183 (23.4%)	1,487 (17.6%)	1,096 (23.1%)
Latin and South America	1,575 (19.1%)	724 (14.3%)	1,433 (17.0%)	816 (17.2%)
North America	1,386 (16.8%)	560 (11.1%)	602 (7.1%)	678 (14.3%)
Ejection fraction at screening (% mean (SD))	26.6 (6.3)	28.9 (8.3)	29.5 (6.2)	31.1 (6.8)
Concomitant Medications				
ACE-I or ARB	5,803 (70.3%)	3,700 (73.4%)	8,339 (100%)	3,986 (83.6%)
Beta blocker	7,763 (94.0%)	4,691 (93.1%)	7,811 (93.6%)	4,558 (96.0%)
MRA	6,363 (77.1%)	3,545 (70.3%)	4,671 (55.3%)	3,370 (71.0%)
ARNI sacubitril/valsartan	1,595 (19.3%)	731 (14.5%)	-	508 (10.7%)
NT-proBNP at Screening (pg/ml, median (25th, 75th))	1,998 (990-4078)	2,816 (1556-5314)	1,608 (886-3,221)	1,428 (857-2,649)
NYHA Class at Baseline				
Class II	4,376 (53.0%)	2,975 (59.0%)	5,919 (70.1%)	3,203 (67.5%)
Class III	3,633 (44.0%)	2,003 (39.7%)	2,018 (23.9%)	1,498 (31.6%)
Class IV	248 (3.0%)	66 (1.3%)	60 (0.7%)	43 (0.9%)

GALACTIC-HF: Design Paper & Interim Analyses



- **Passed first interim analysis: Q1 2019**
 - Assessed futility only (HR>1.0)
 - Triggered at 1/3 of target 1,590 deaths
- **Passed second interim analysis: Q1 2020**
 - Assessed futility & superiority
 - Triggered at 2/3 of target 1,590 deaths
 - Superiority: p-value for efficacy <0.0005 (one-sided alpha)



JACC
Heart Failure



OMECAMTIV MECARBIL

Where We Are Now: METEORIC-HF

**Steve Heitner, M.D., Senior Medical Director, Clinical
Research, Cardiovascular**

Why METEORIC-HF?

- Despite improvements in overall mortality with medical and device-based therapies, **mortality remains at approximately 50% over 5 years**¹
- Despite new medications having shown significant impact on morbidity and mortality, **still little ability to improve health related quality of life**²
- Despite the prognostic power of LVEF, patients with persistent or severe symptoms and poor functional capacity **tend to experience worse outcomes**³



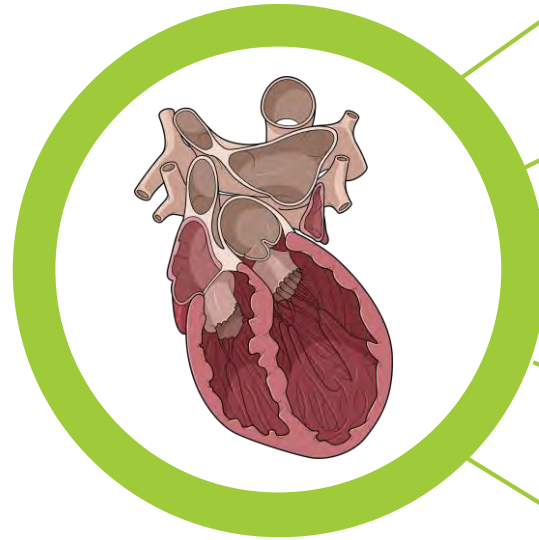
1. Roger - JAMA 292(3): 344-350

2. Mark - 2016 Nat Rev Cardiol 13(5): 286-308

3. SOLVD Investigators -1992 N Engl J Med 327(10): 685-691.

Exercise Capacity Is Powerful Predictor of Outcomes in HF¹

- METEORIC-HF rounds out knowledge of the physiologic impact of *omecamtiv mecarbil* on patients' lives
- **Accelerometry-derived daily physical activity (ADPA):** Highest content activity data, correlates well with HF severity and performance metrics²
- **Cardiopulmonary exercise testing (CPET):** Best physiological and highest fidelity assay of exercise capacity



Outcomes Assessed in Phase 3 Program



Mortality



HF Hospitalization



Symptoms



Exercise Performance



Daily Activity

1. O'Connor – 2012 Circ Heart Fail 5(1): 63-71

2. Snipelisky – 2017 Circ Heart Fail 10(6): e003878.

Second Phase 3 Clinical Trial Underway

Investigating effect of *omecamtiv mecarbil* on exercise tolerance



Trial enrolling patients in 9 countries in North America and Europe

Primary Endpoint

Change in peak VO₂ on CPET from baseline to Week 20

Second Endpoints

- Change in total workload during CPET from baseline to Week 20
- Change in ventilatory efficiency (VE/VCO₂ slope) during CPET from baseline to Week 20
- Change in average daily activity units measured over 2 weeks from baseline to Week 18-20 by accelerometry

Study Plan

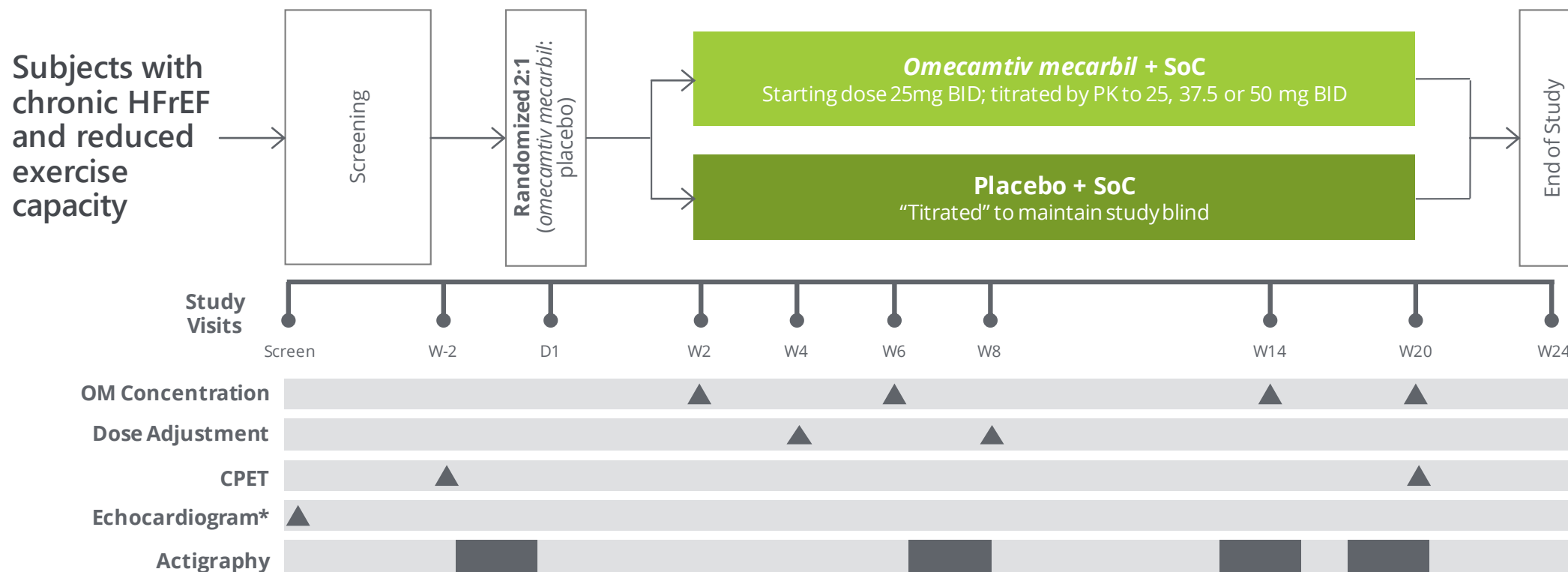
Total Countries Planned	9
Active Countries	4
Total Sites Planned	92
Activated Sites	69
Total Patients Planned	270

Key Design Points

- Designed to enroll approximately 270 patients
- 90% power
- Patients must have LVEF ≤35 percent, be NYHA heart failure class II or III, and have reduced exercise capacity
- Patients randomized 2:1 to *omecamtiv mecarbil*

VO₂ = Oxygen Uptake; CPET = Cardio-Pulmonary Exercise Testing; VE = Ventilatory Efficiency

Clinical Trial Overview



*Screening echocardiogram is not required if an appropriate LVEF assessment has been performed within one year

OMECAMTIV MECARBIL

Why We Believe

**Andrew Wolff, M.D., SVP, Senior Fellow, Clinical
Research & Development**

What Did We Learn from COSMIC-HF?



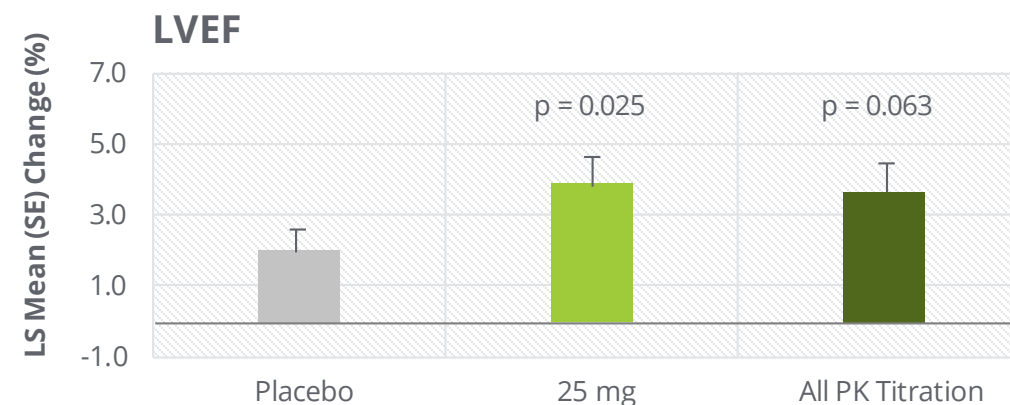
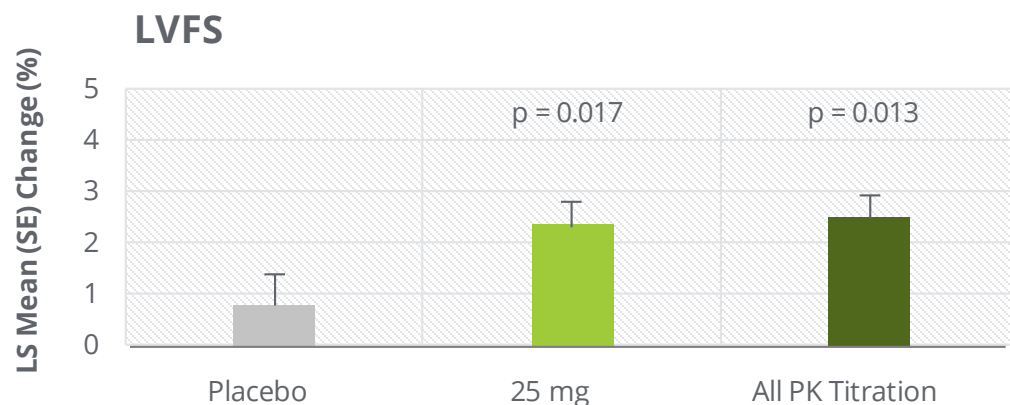
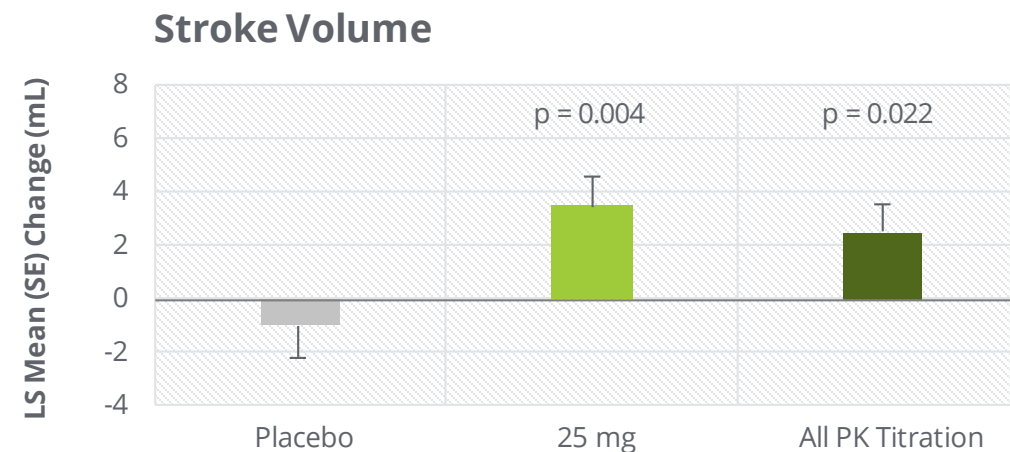
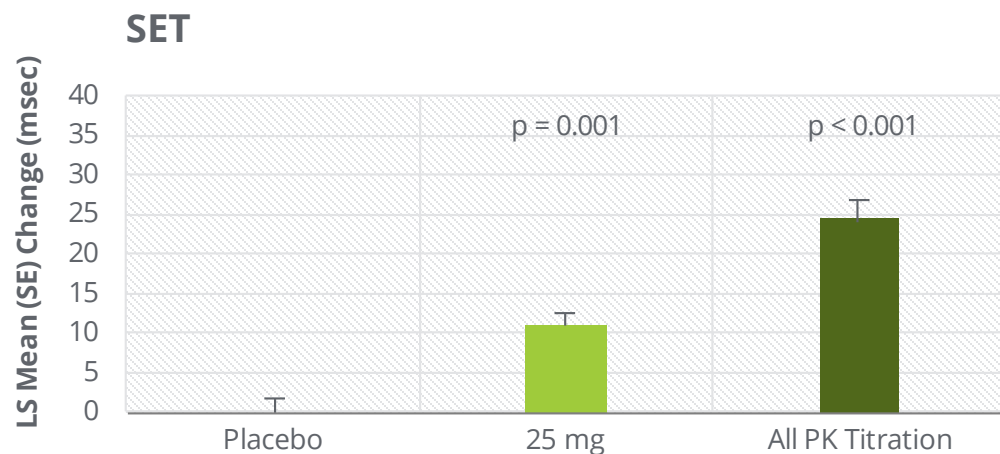
Phase 2 clinical trial of *omecamtiv mecarbil*



- First demonstration of the **effectiveness of PK-guided dose titration to prevent excessive exposures to *omecamtiv mecarbil***
- **Demonstrated improvement** in several different measures that **predict improved prognosis**
 - Decreased left ventricular volumes
 - Decreased NT-proBNP
 - Decreased heart rate
- Demonstrated **favorable tolerability** over 20 weeks of treatment

Dose-Dependent Increases in Cardiac Performance

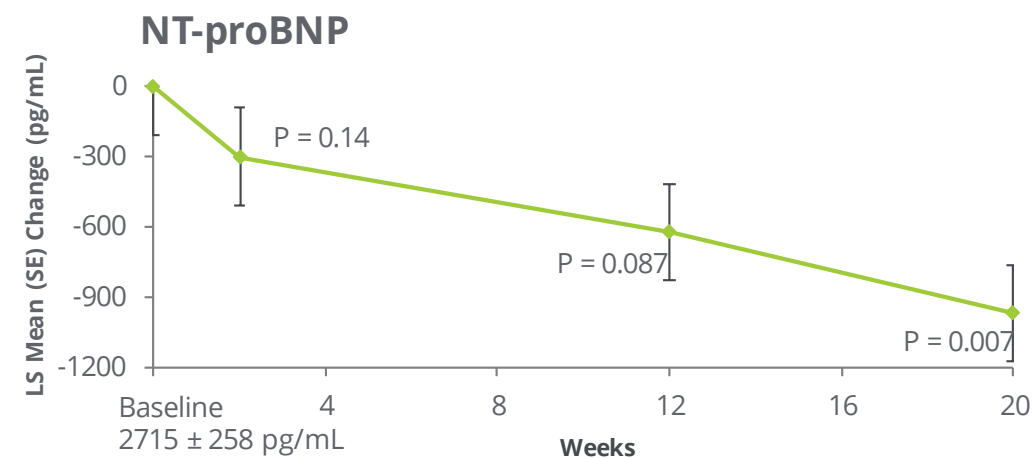
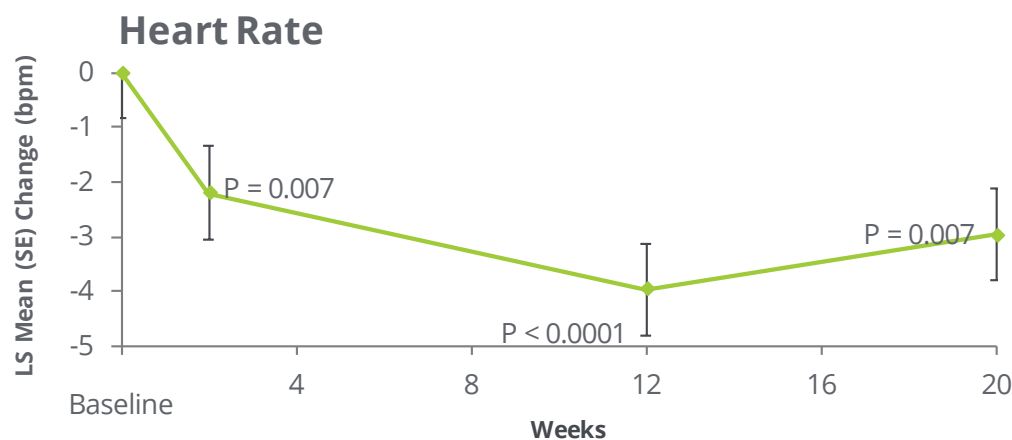
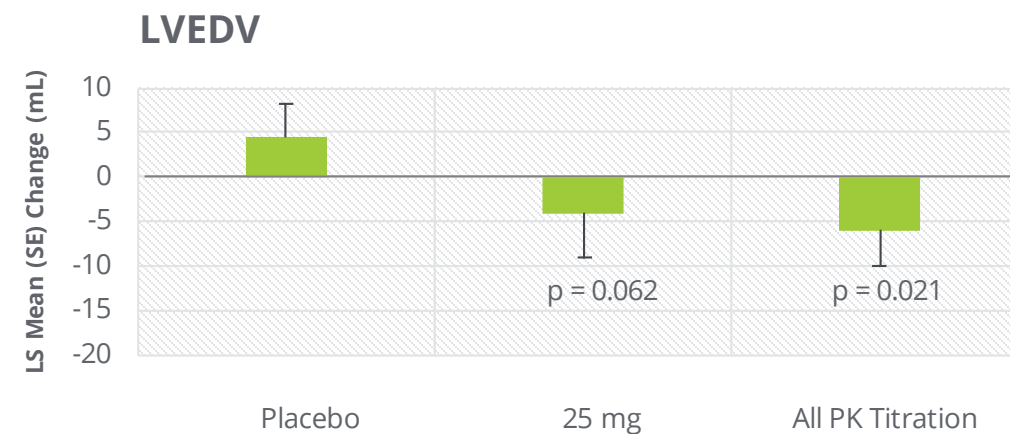
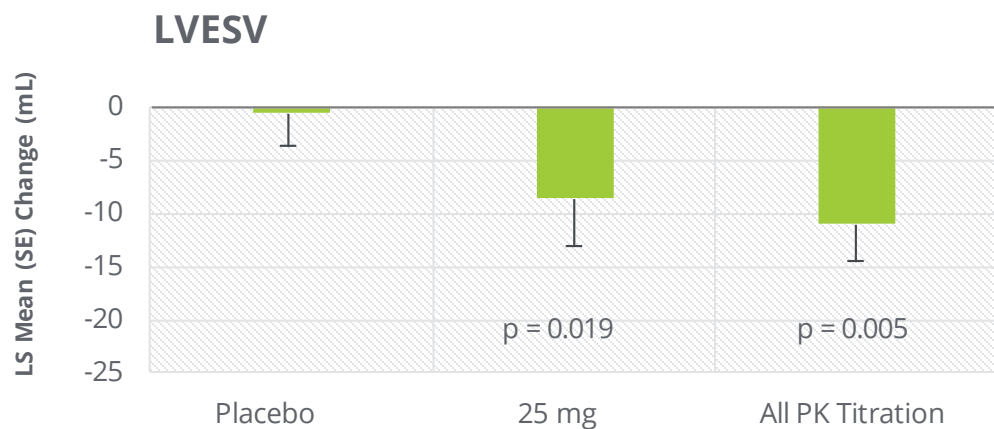
Pharmacodynamic results after 20 weeks of double-blind treatment



LVEF, left ventricular ejection fraction; LVFS, left ventricular fractional shortening;
SE, standard error; SET, systolic ejection time ; all p values are nominal without multiplicity adjustment.

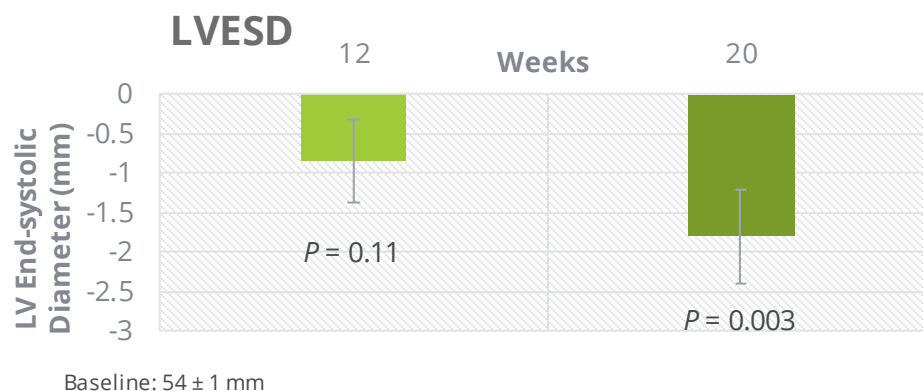
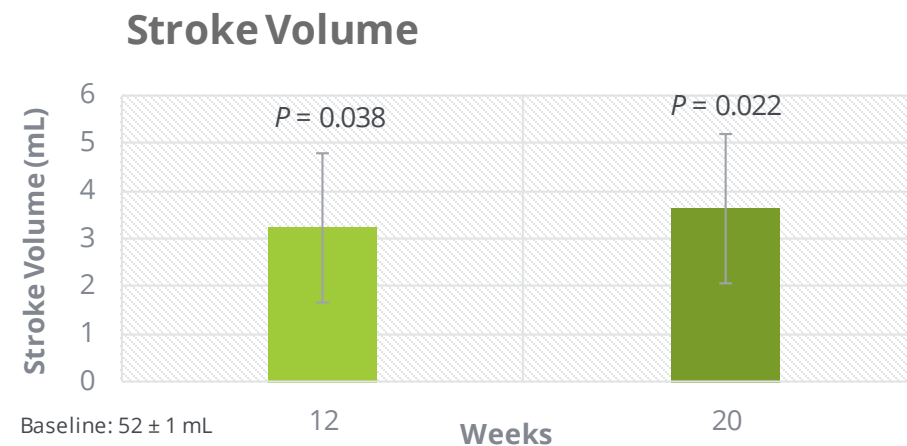
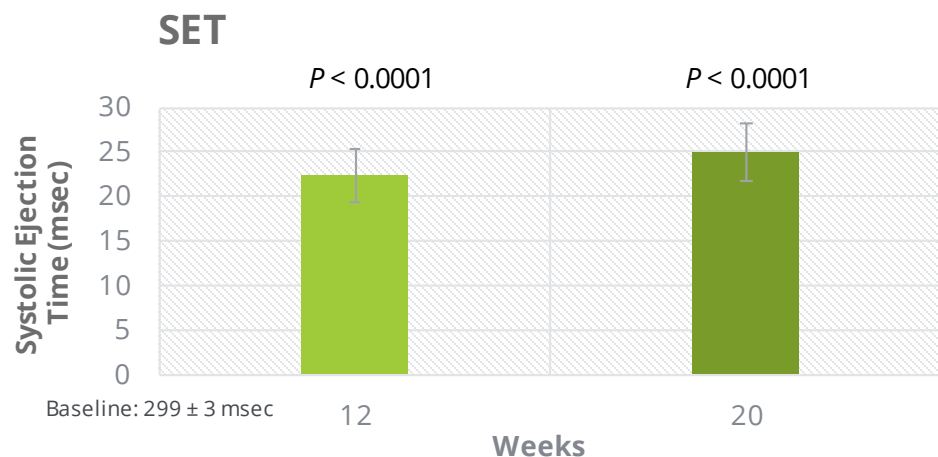
Improved Physiology & Decreased Cardiac Risk

Reductions in heart volumes, heart rate, & wall stress



LVESV left ventricular end systolic volume; LVEDV left ventricular end diastolic volume
All p values are nominal without multiplicity adjustment

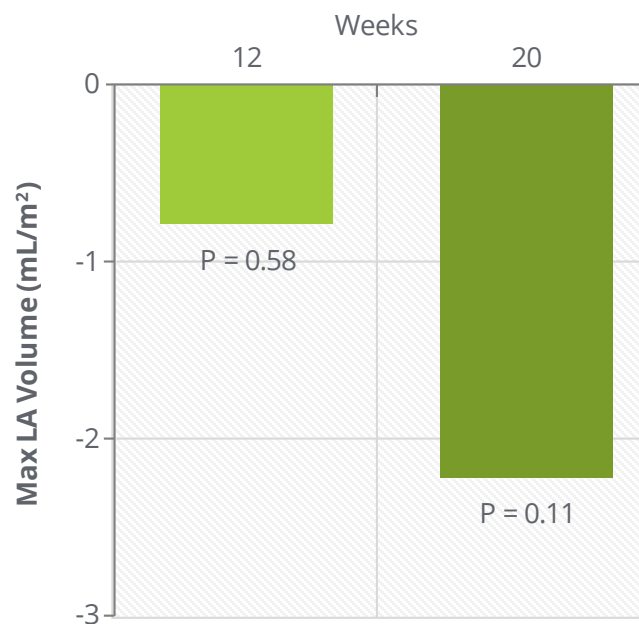
Sustained Increase in LV Systolic Function



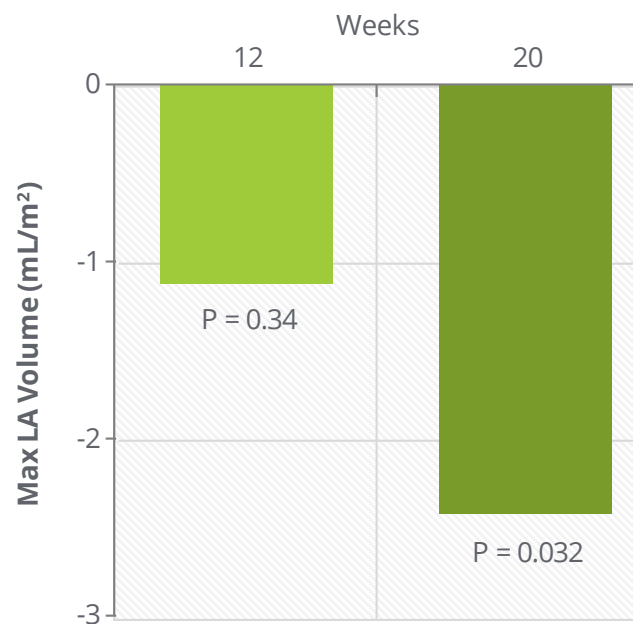
SET, systolic ejection time ; LVESD, left ventricular end systolic diameter;
LVEDD, left ventricular end diastolic diameter

Improved Left Atrial Systolic Function

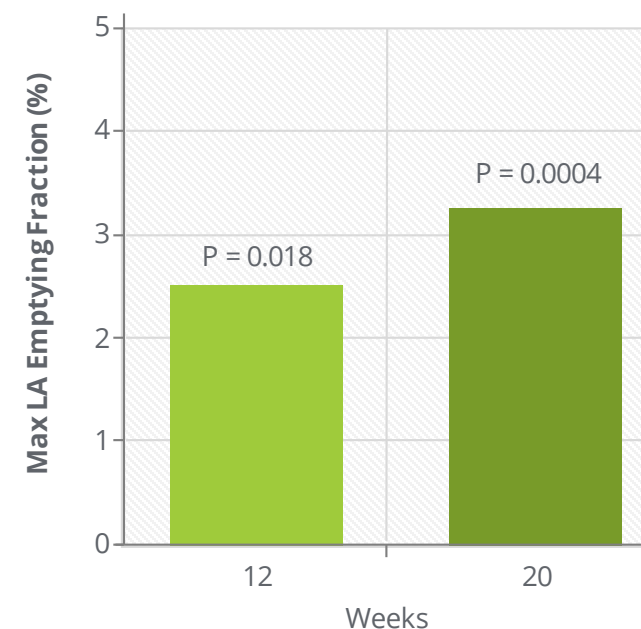
Placebo-corrected LS Mean Change from Baseline in Max LA volume for the OM PK Titration Group



Placebo-corrected LS Mean Change from Baseline in Min LA volume for the OM PK Titration Group

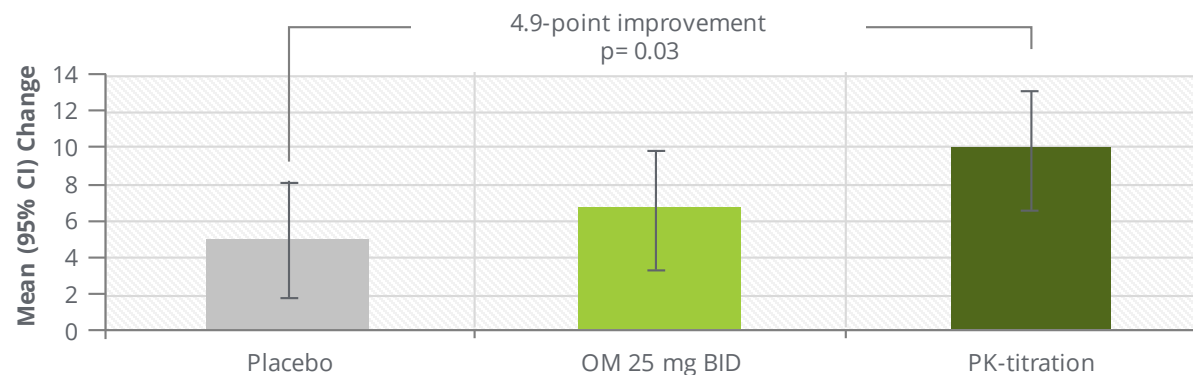


Placebo-corrected LS Mean Change from Baseline in LA Emptying Fraction of the OM PK Titration Group

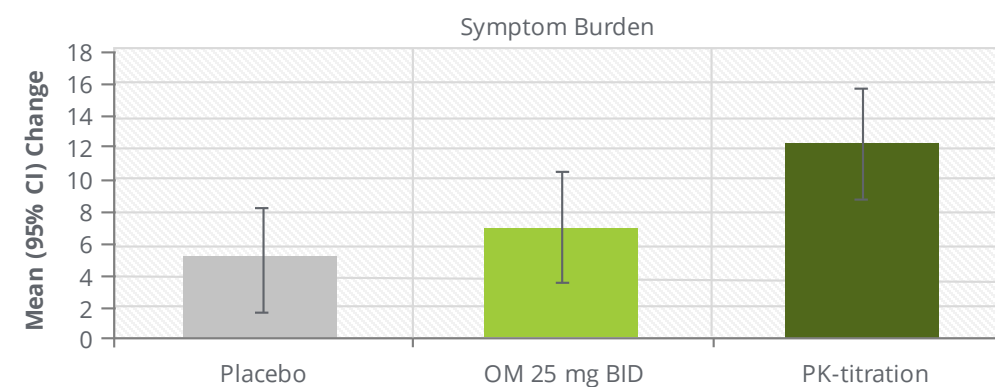
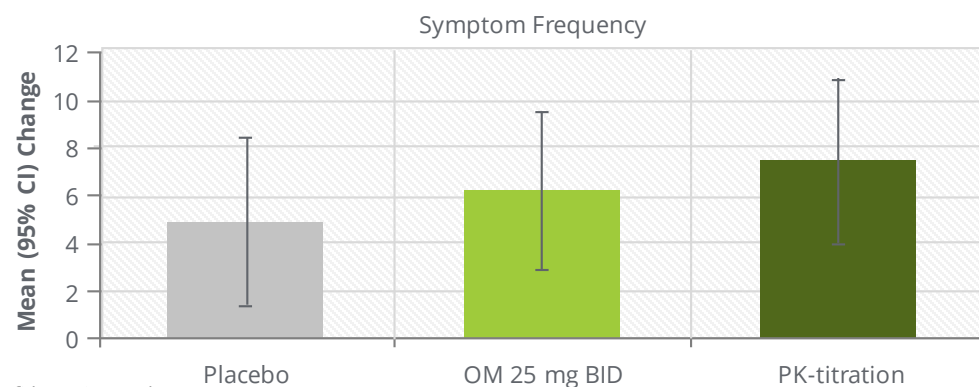


Improvements in Symptoms

Change from Baseline in KCCQ Total Symptoms Score at Week 20



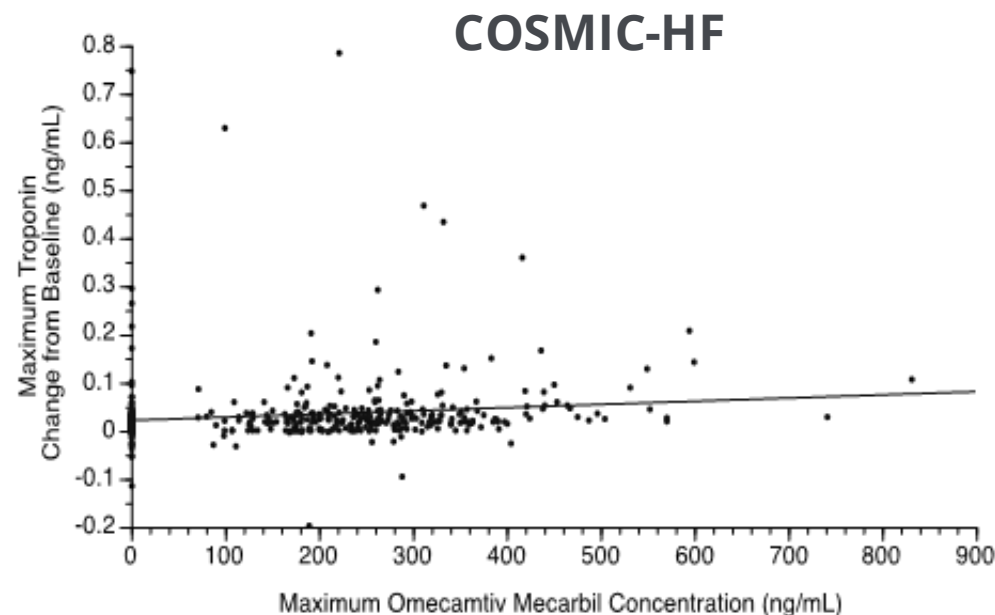
Change from Baseline in KCCQ Subdomain Scores at Week 20



CI: confidence interval

Troponins: Small Increases, Unrelated to Exposures to *Omecamtiv Mecarbil*

- Baseline troponin I levels were above the diagnostic limit for myocardial infarction (0.04 ng/mL) for ~25% in COSMIC-HF
- Events of increased troponin I (n=278 across all treatment groups) were independently adjudicated and **none were determined to be myocardial ischemia or infarction.**¹



Troponin I Levels in COSMIC-HF (ng/mL)				
	Placebo	25 mg BID	All PK Titration	All OM
Median at Baseline (Q1, Q3)	0.025 (0.016, 0.041)	0.022 (0.016, 0.039)	0.022 (0.016, 0.042)	0.022 0.016, 0.040
Median Change from Baseline to Week 20 (Q1, Q3)	0.000 (-0.007, 0.004)	0.001 (0.000, 0.012)	0.006 (0.000, 0.024)	0.004 (0.000, 0.019)

1. Teerlink, et al. The Lancet 2016; 2895-2903

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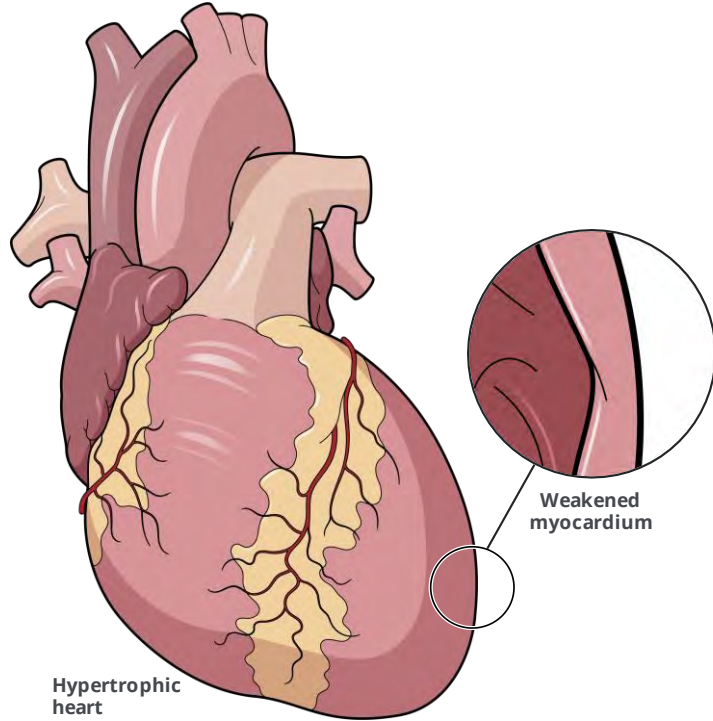
Predictive Value of Key Measures
in COSMIC-HF

Stuart Kupfer, M.D., SVP, Chief Medical Officer

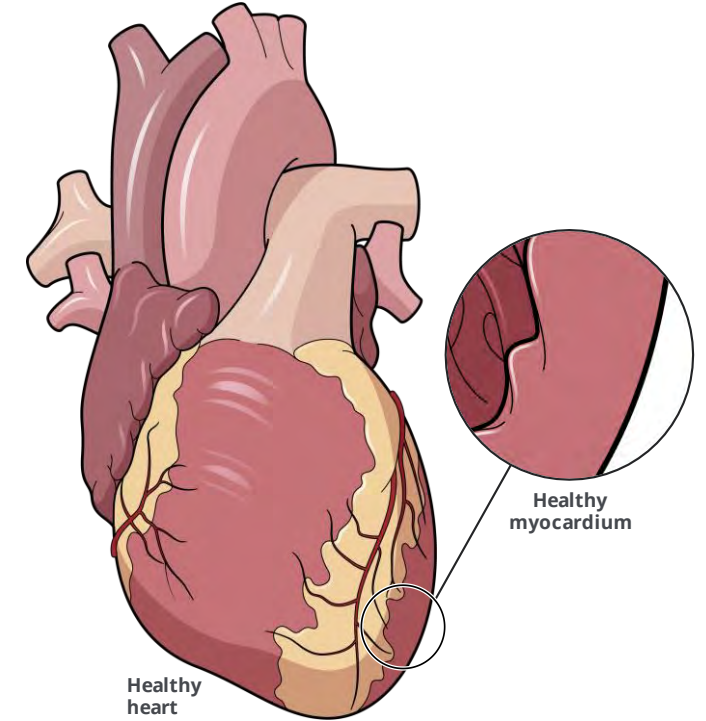
NT-proBNP: Predictive Biomarker in Heart Failure

⬆ Increases with worsening HF

⬇ Decreases with treatment benefits

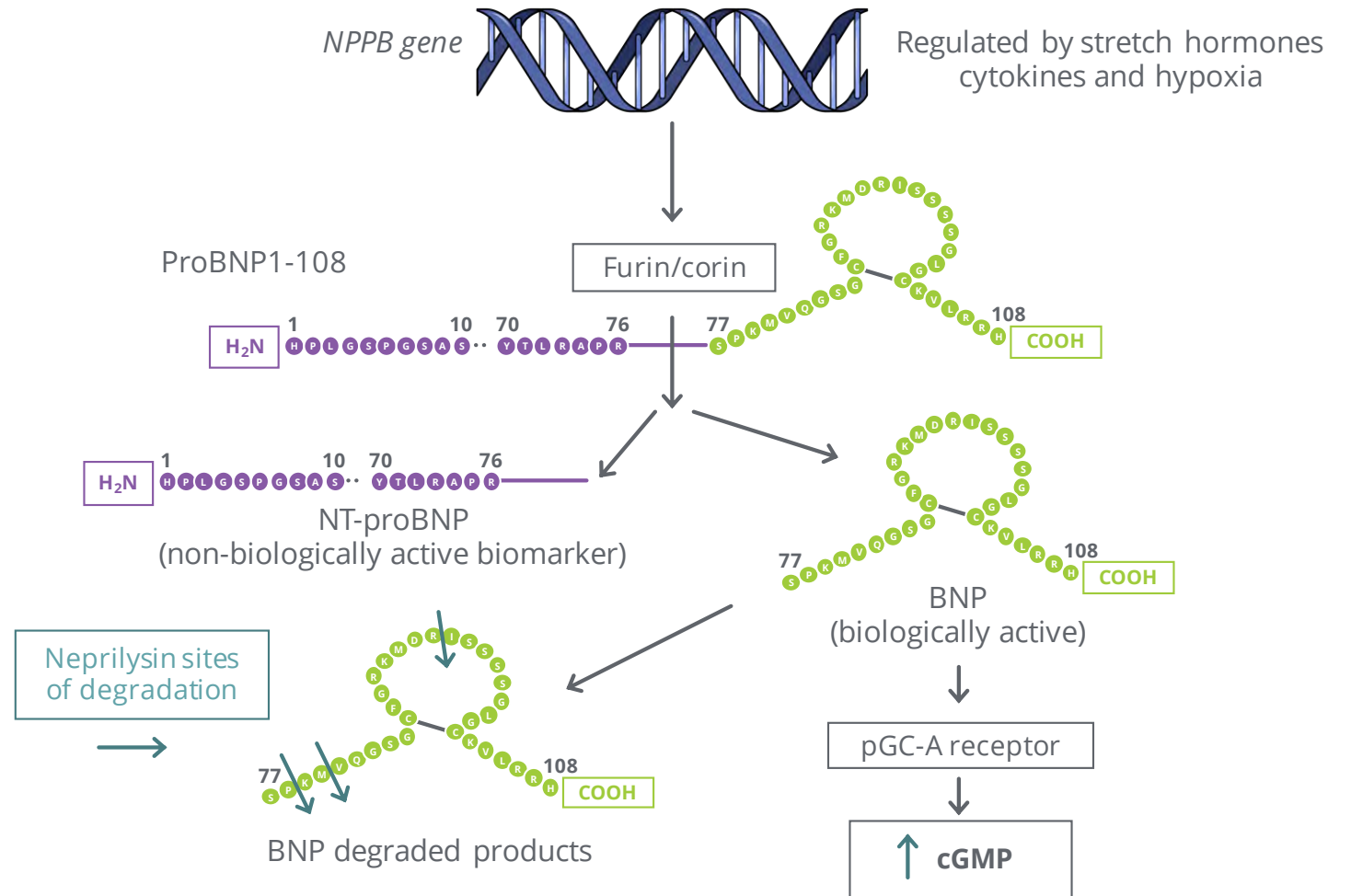


- Biomarker of increased cardiac wall stress
- Correlates with adverse cardiac remodeling
- Prognosticates worsening HF and CV death



NT-proBNP: Predictive Biomarker of Heart Failure

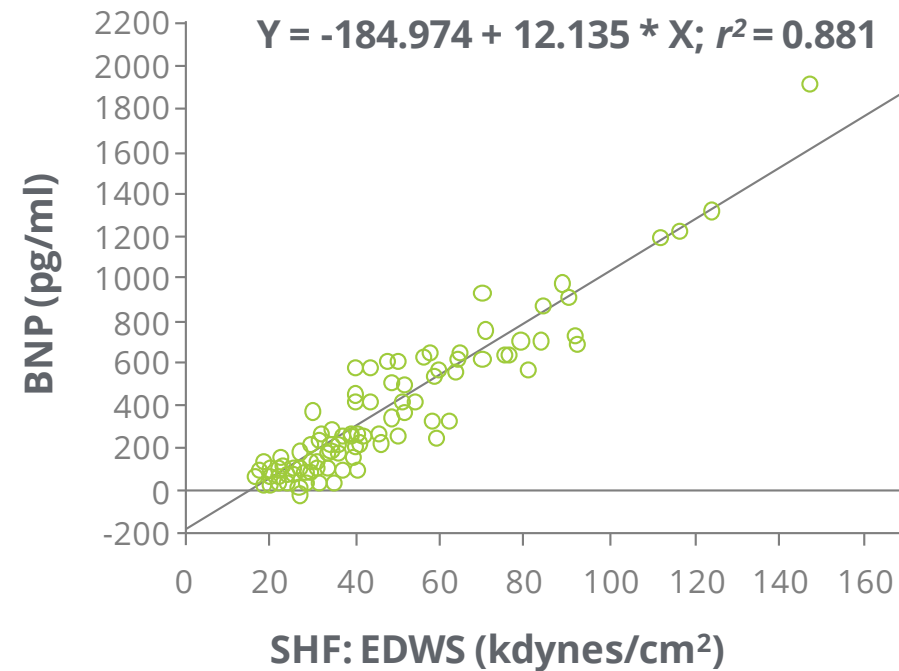
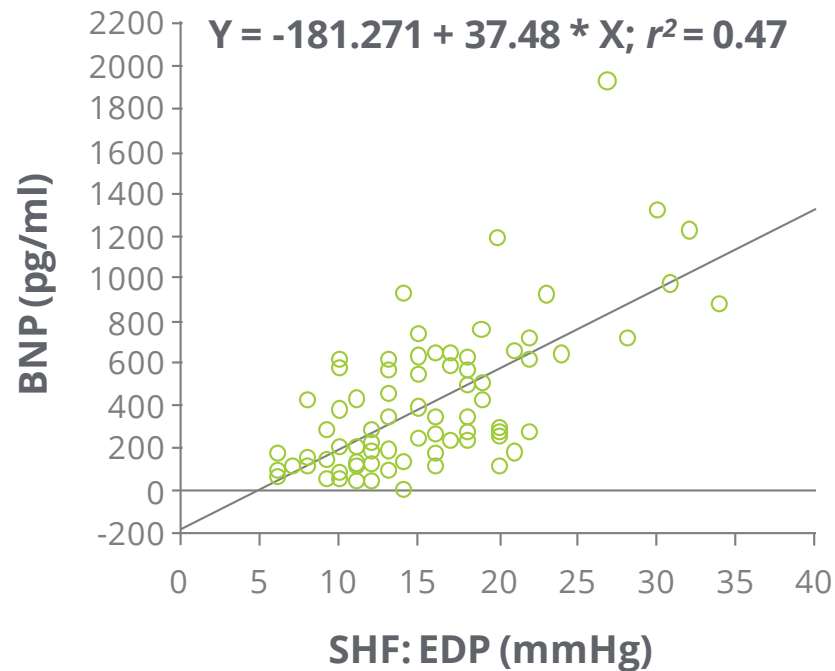
- **NT-proBNP** is an inactive peptide produced during proBNP processing
- **ProBNP** is secreted by myocytes in the LV in response to pressure overload or volume expansion
- **BNP** is biologically active
 - Vasodilation
 - Diuresis
 - Reverse remodeling



McKie PM et al. *JACC* – 2016 – 68:2437-9

BNP Correlates with LV Dysfunction in HF

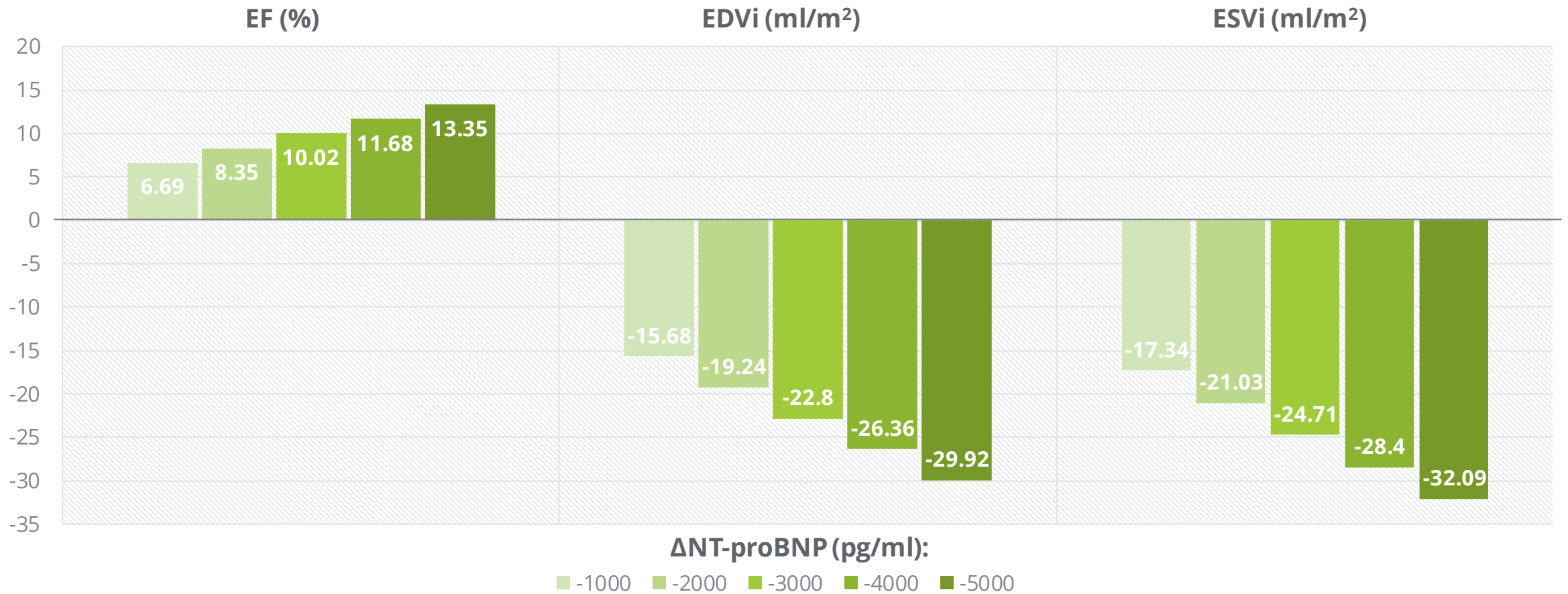
Elevated BNP associated with increased LV end-diastolic pressure and wall stress



Iwanaga Y et al. JACC – 2006 – 47:742-8

Decreased NT-proBNP Correlates with Reverse Remodeling

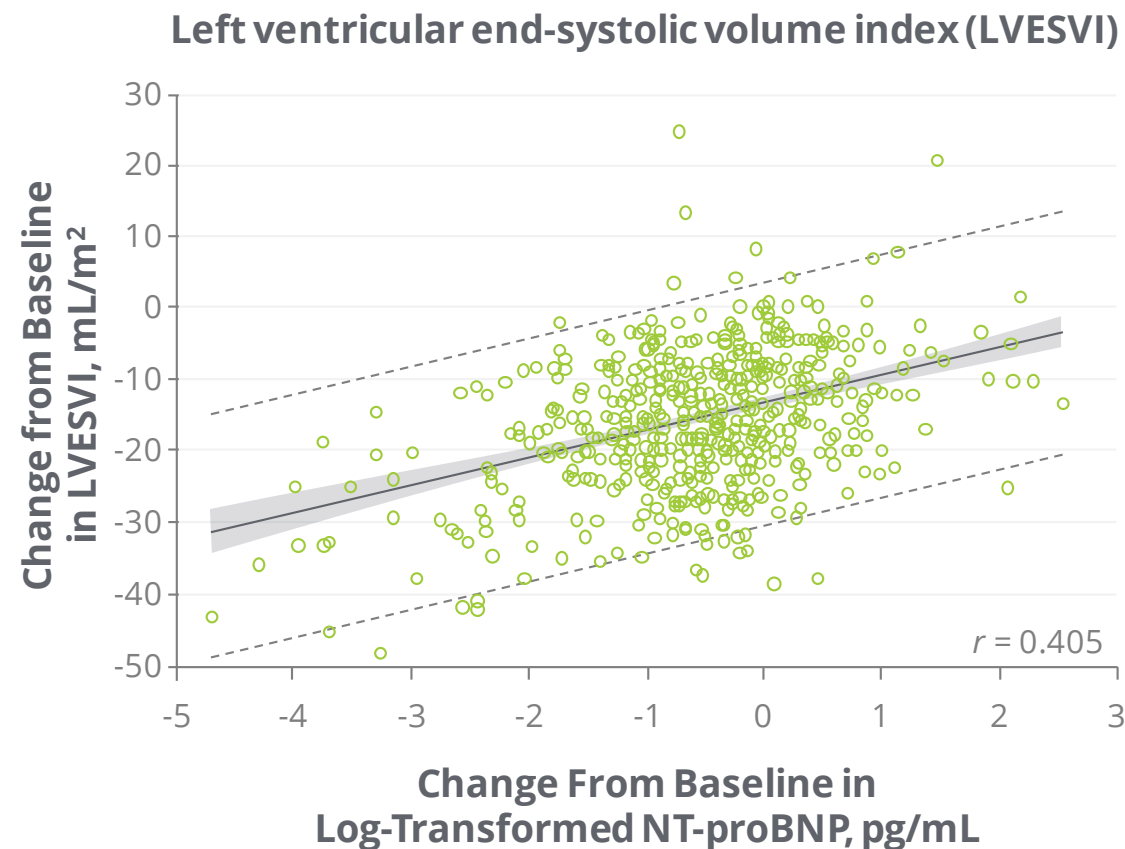
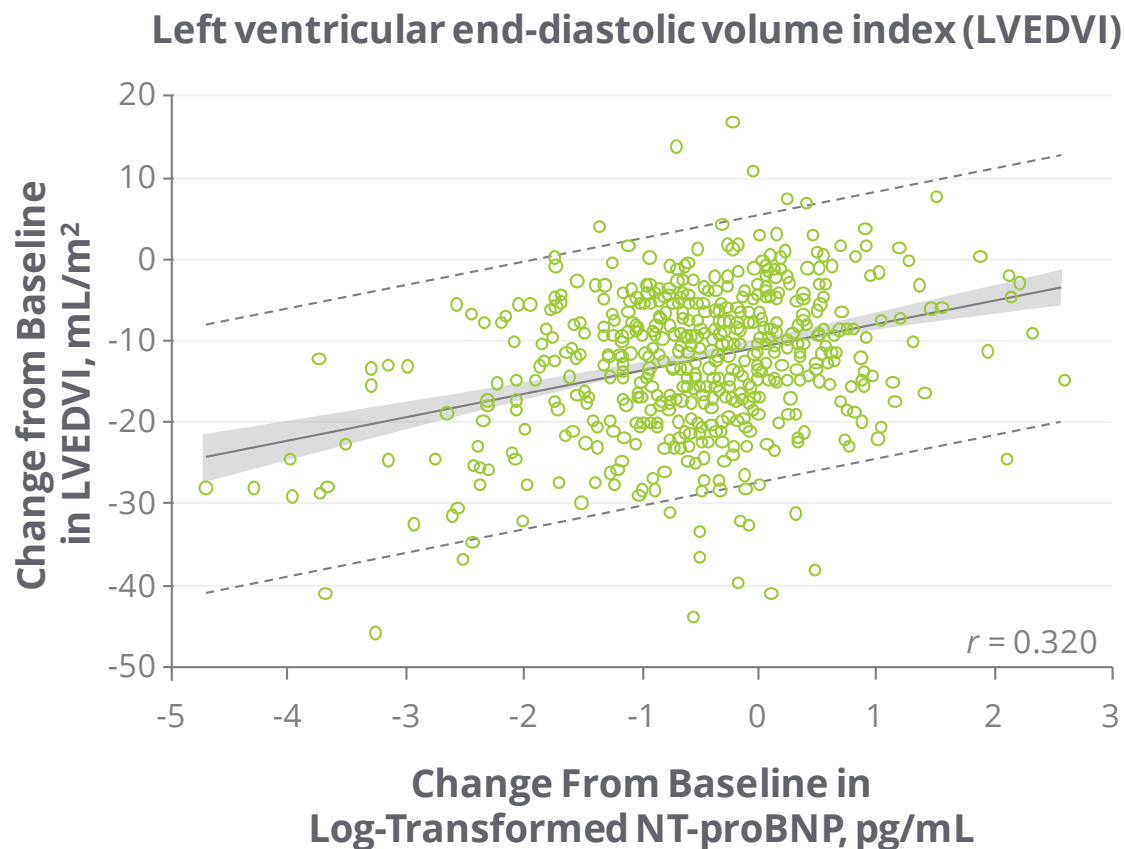
GUIDE-IT: NT-proBNP-guided HF therapy



Daubert MA et al. *JACC Heart Failure* – 2018 – 7:158-68

Decreased NT-proBNP Correlates with Reverse Remodeling

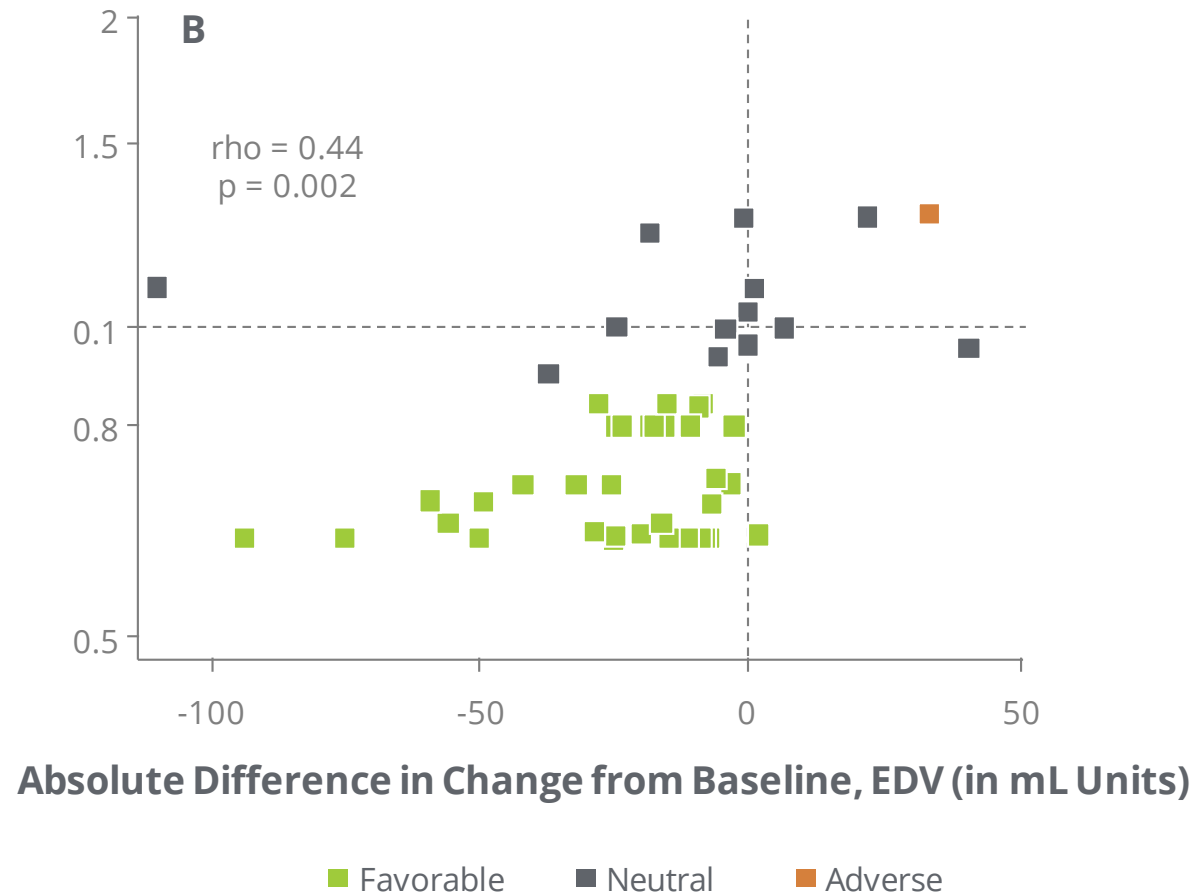
Sacubitril-Valsartan



Januzzi JL et al. *JAMA* – 2019 – 322:1085-95

LV Remodeling Correlates with HF Mortality

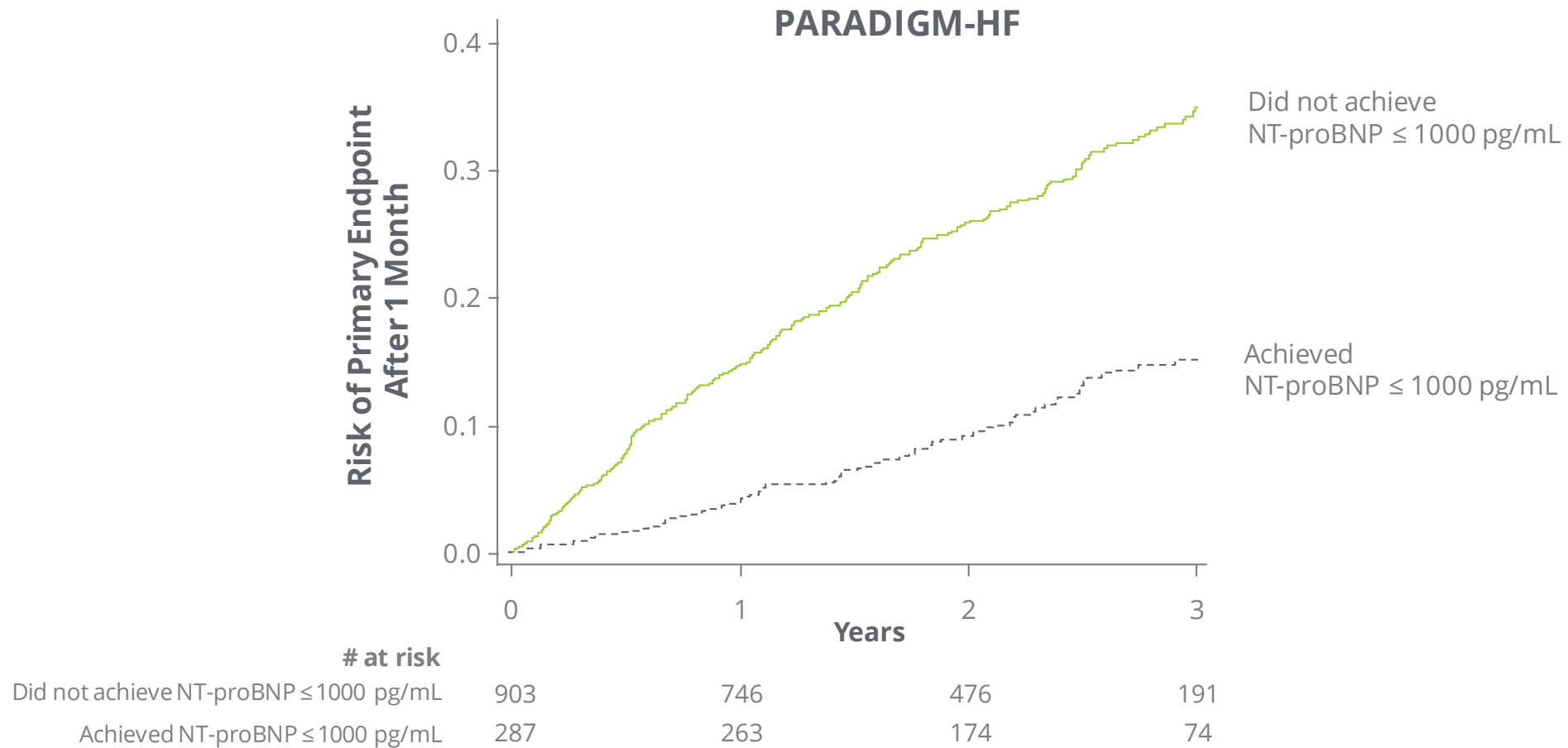
Drugs/devices that reverse LV remodeling are associated with reduced mortality



Kramer DG et al. JACC - 2010 - 56:392-406

Reductions in NT-proBNP Correlate with Improved HF Outcomes

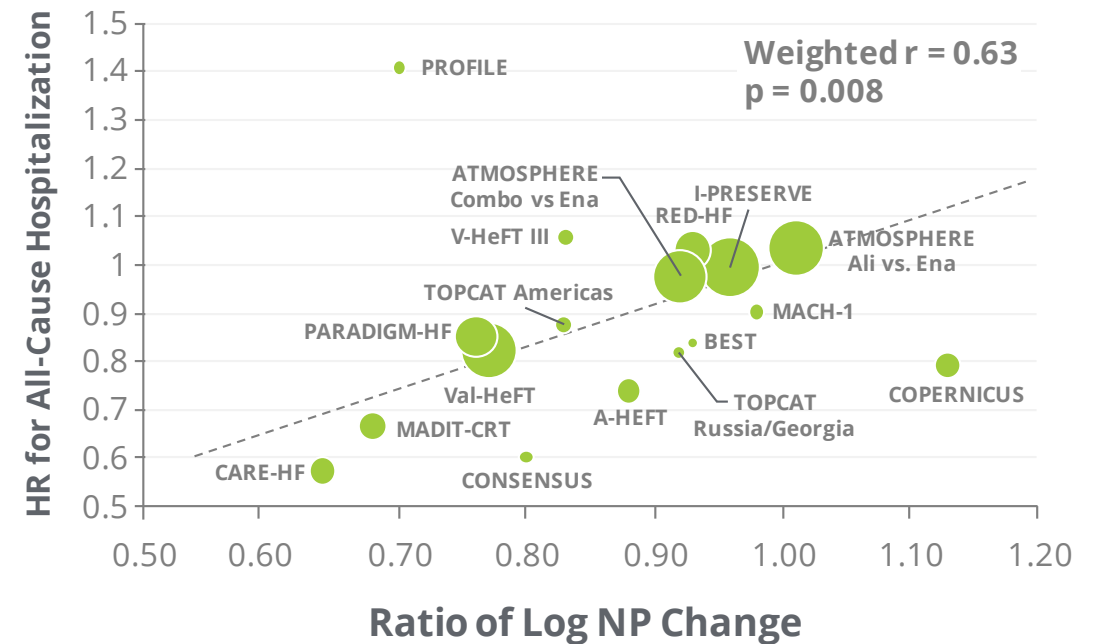
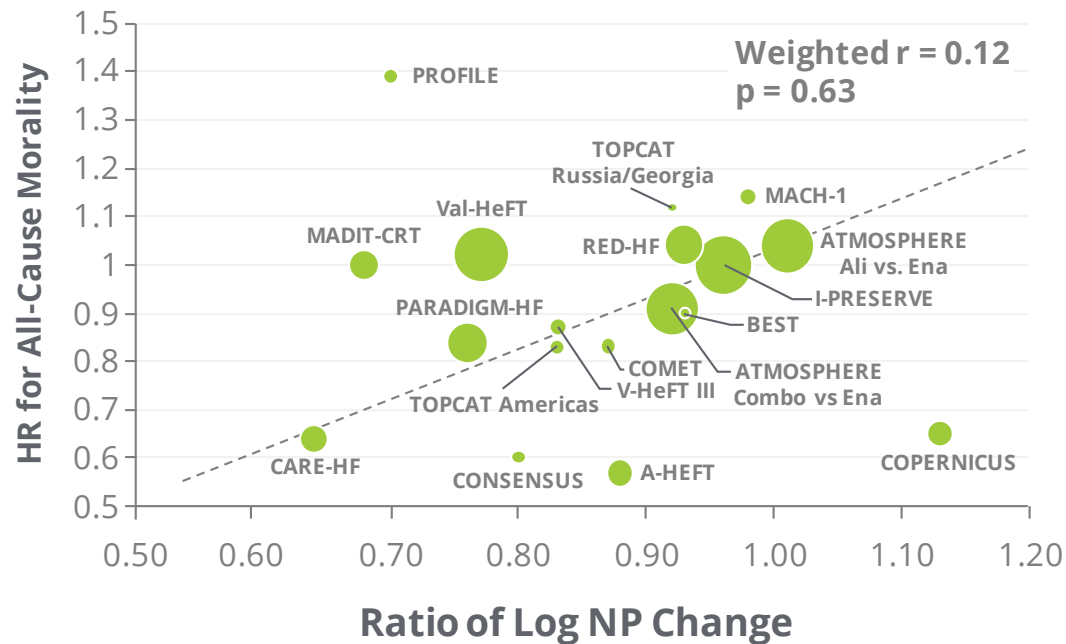
PARADIGM-HF



Zile MR et al. JACC – 2016 – 68:2425-36

Reductions in NT-proBNP Correlate with Improved HF Outcomes

Meta-analysis of 16 heart failure trials



Vaduganathan M et al. *JACC Heart Failure* – 2018 – 6:564-9

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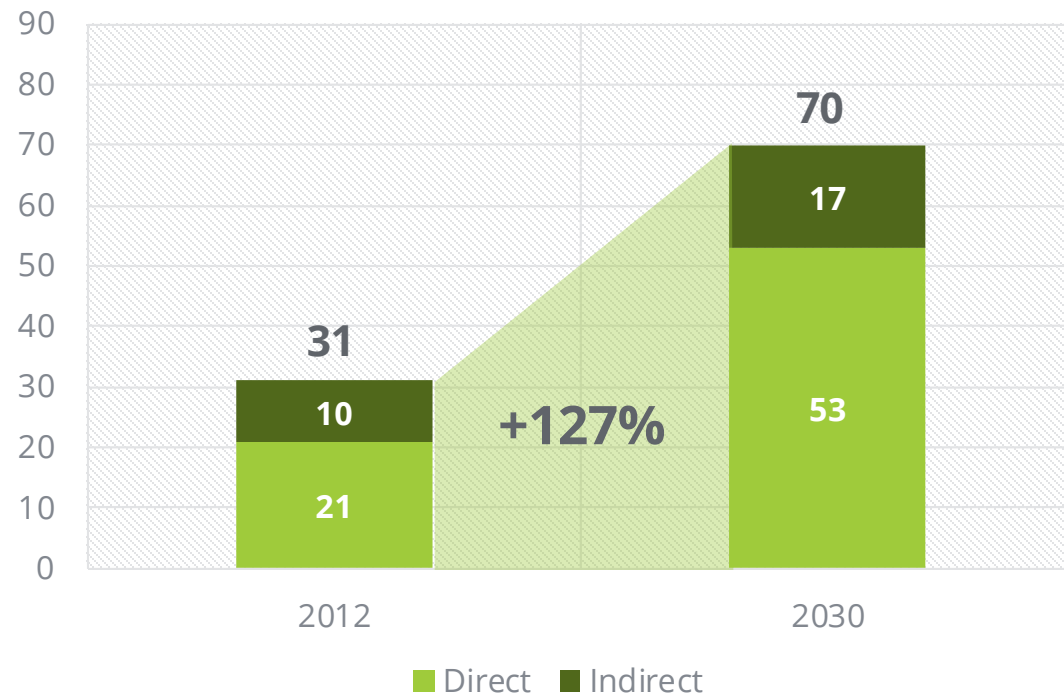
The Commercial Opportunity

**Scott Jordan, SVP, New Product Planning &
Commercial Development**

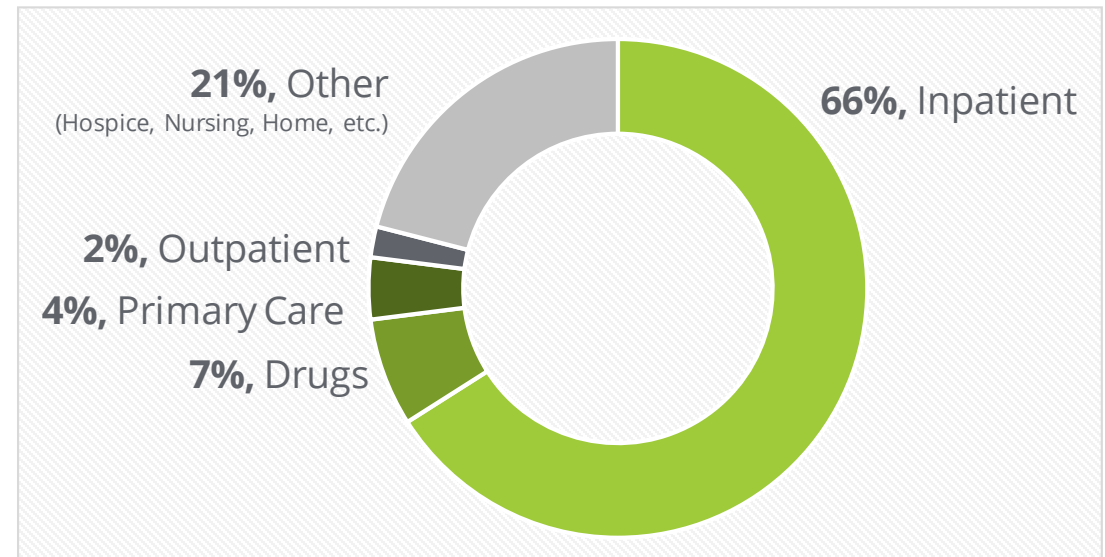
Cost Of HF: Over \$30B and Increasing

Two-thirds of HF spending is for inpatient care

Total Cost Of HF In The U.S. (\$ Billions)¹



Allocation of HF Costs in U.S.²



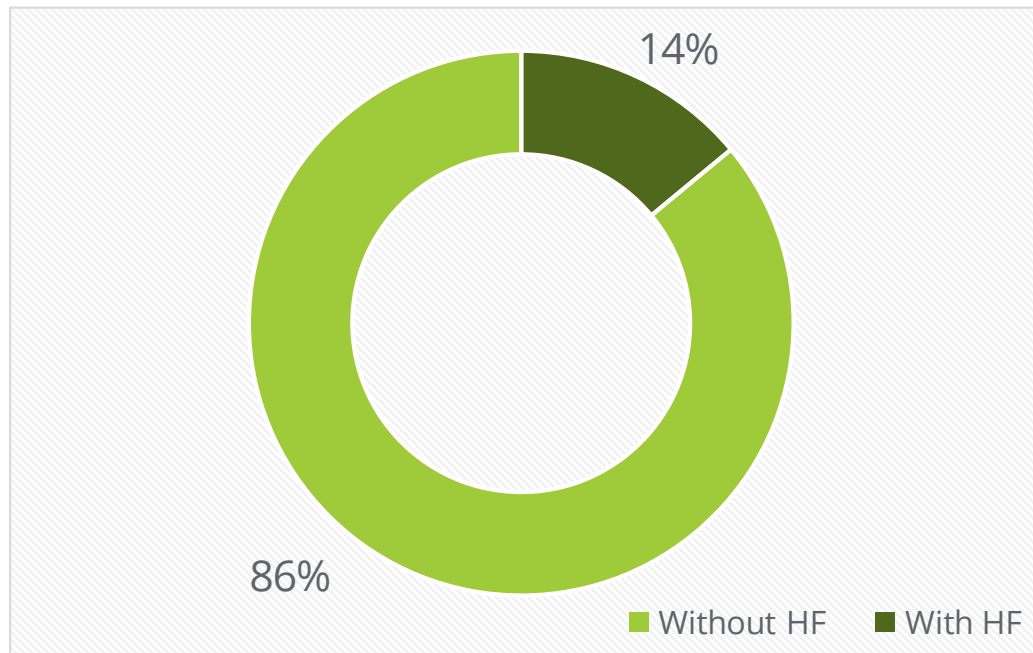
1. Heidenreich PA, et al. Forecasting the impact of heart failure in the United States; A policy statement from the AHA, Circ Heart Fail 2013.

2. Voigt, J. et al., A reevaluation of the costs of heart failure and its implications for allocation of health resources in the United States. (2014) Clin Cardiol. 2014 May;37(5): 312-2.

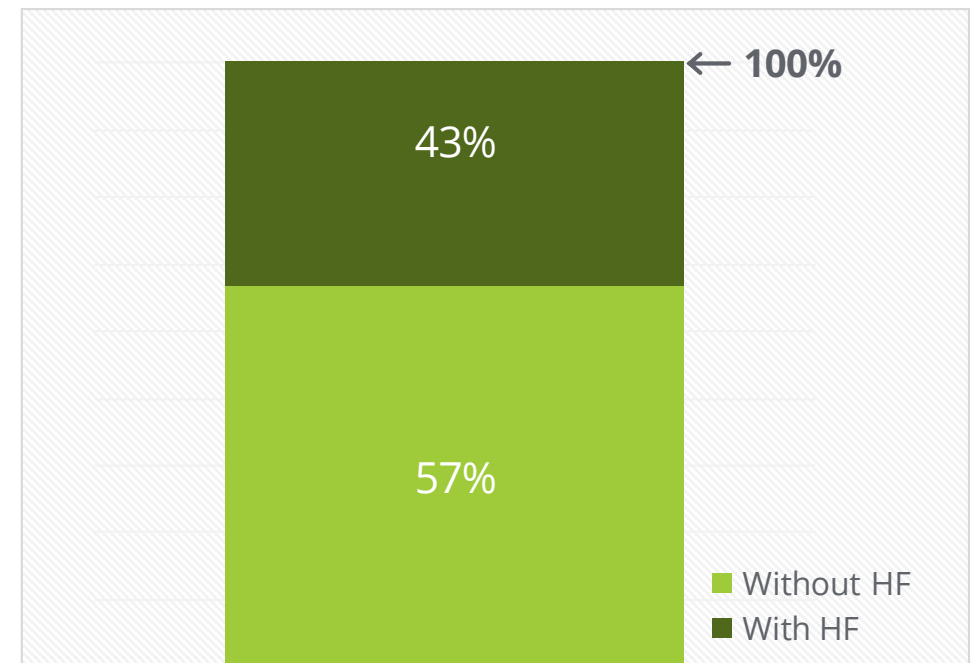
Disproportionate Medical Spending for Heart Failure

HF prevalence and proportion of spending in Medicare population

Prevalence of HF In Medicare Population

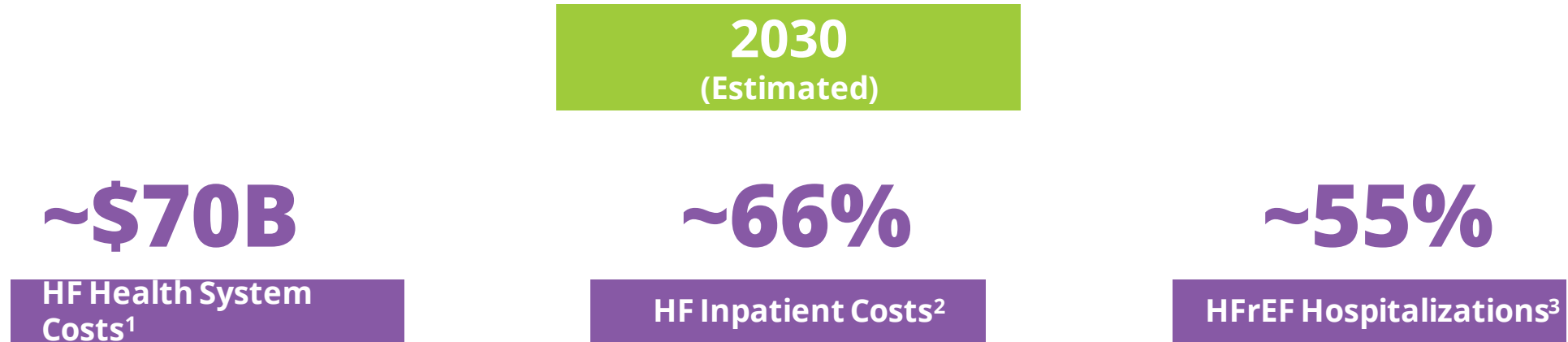


Medicare Spending



"The High Cost of Heart Failure for Medicare Population: An Actuarial Cost Analysis," Milliman, February 2015; Centers for Medicare and Medicaid Services. Medicare health support overview.

Reducing Health System Costs



In 2030, a 20% reduction in HFrEF hospitalizations could result in a savings of ~\$5B to the US Health Care System in just initial hospitalizations alone

1. Heidenreich PA, et al. Forecasting the impact of heart failure in the United States; A policy statement from the AHA, Circ Heart Fail 2013.

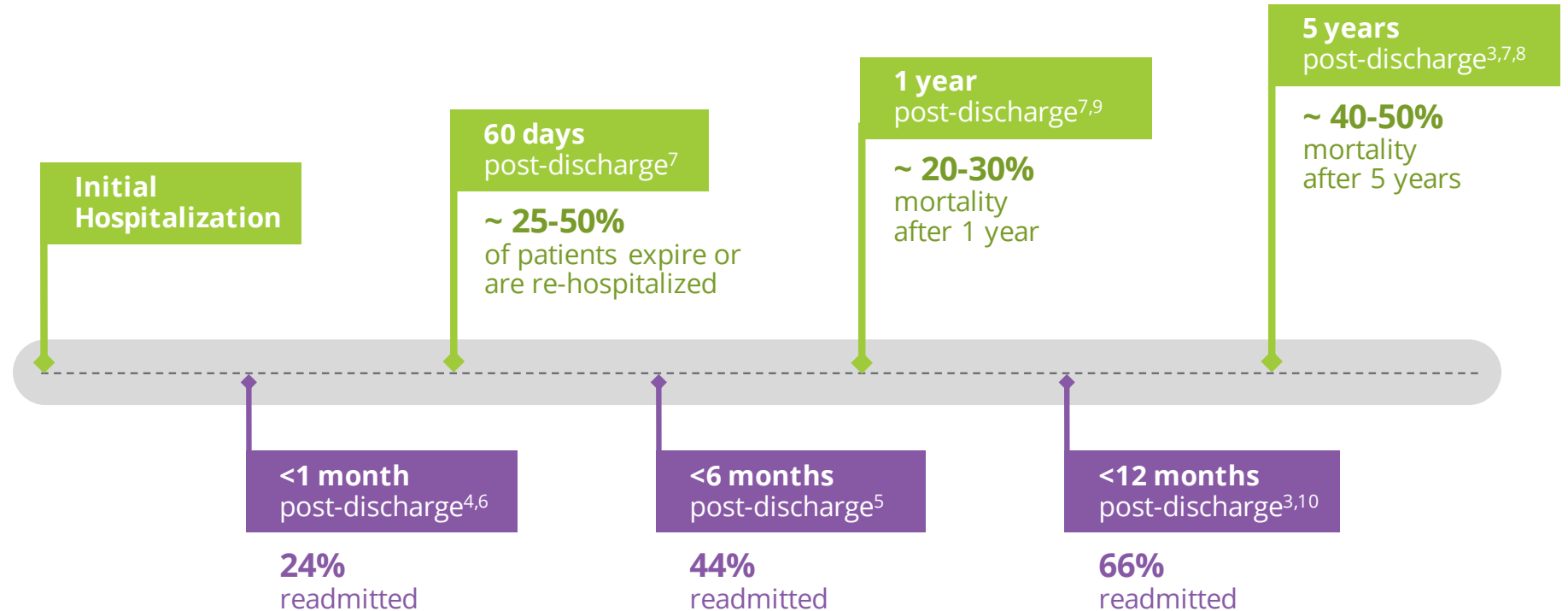
2. Voigt, J. et al., A reevaluation of the costs of heart failure and its implications for allocation of health resources in the United States. (2014) Clin Cardiol. 2014 May;37(5): 312-2.

3. CVrg

High Mortality and Hospital Readmission Rates

Acute heart failure is the most frequent cause of hospitalization in people > 65^{1,2}

1 of 2
hospitalized
HF patients are
readmitted
within 6 months⁵



1. Adams et al. *Am Heart J* 2006; 149:209-16

2. Chen et al. *JAMA* 2011;306:1669-78

3. Dickstein et al. *Eur Heart J* 2008;29:2388-442

4. Korda, et al. *BMC Health Serv Res.* 2017;21;17(1):220.

5. Krumholz et al. *Arch Intern Med* 1997;15799 – 105

6. Krumholz et al. *Circ Cardiovasc Qual Outcomes* 2009;2(5):407-13

7. Loehr et al. *Am J Cardiol* 2008;101:1016-22

8. Roger et al. *Circulation* 2012;125:32-220

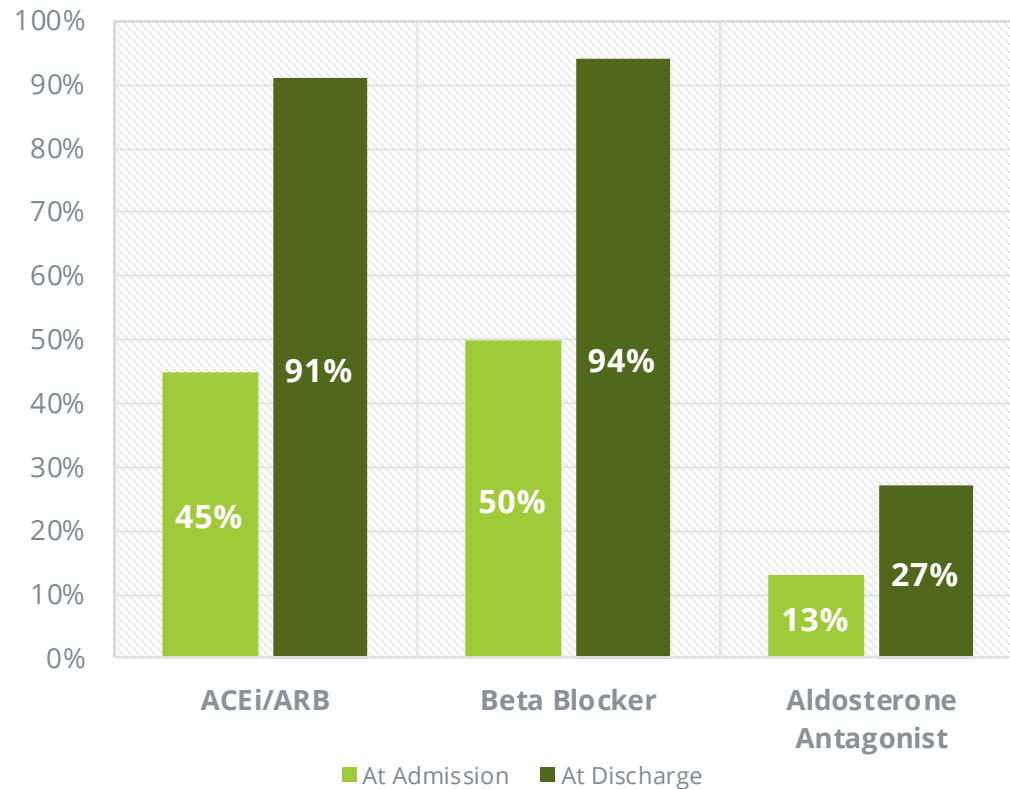
9. Shahar, et al. *J Card Fail* 2004; 10(5):374-9

10. Whellan et al. *Circulation* 2010 Jan;3(1):33-40

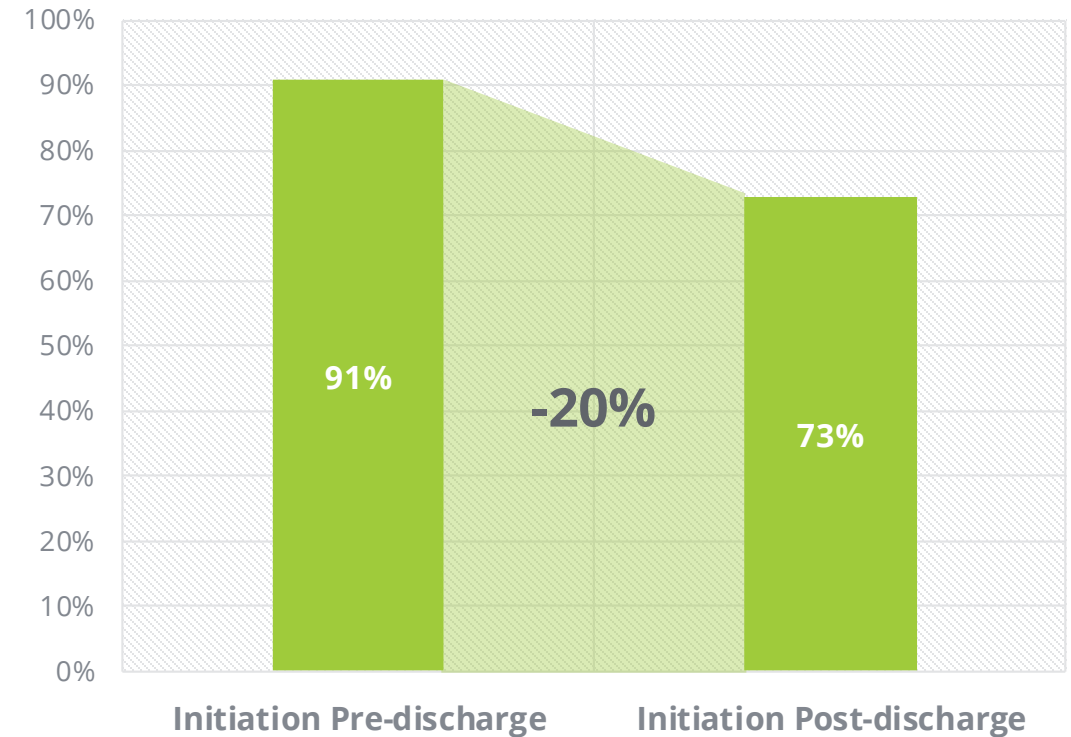
Hospitalization: An Opportunity To Optimize HF Medications

Initiation of therapy pre-discharge improves compliance

Patients With Prescription (%)¹



Beta Blocker Use At 60 Days Post Hospital Discharge (%); Data From IMPACT-HF²



1. Allen LA, et. al, Circulation 2015. Hospitals Participating in Get With The Guidelines Quality Improvement Initiative.

2. Gattis WA, et. al, J Am Coll Cardiol 2004.

Co-Promotion Focused on Institutional Care Segments



Top HF Accounts

In North America

Concentrated Customer Segment



~70%

HFrEF Patients



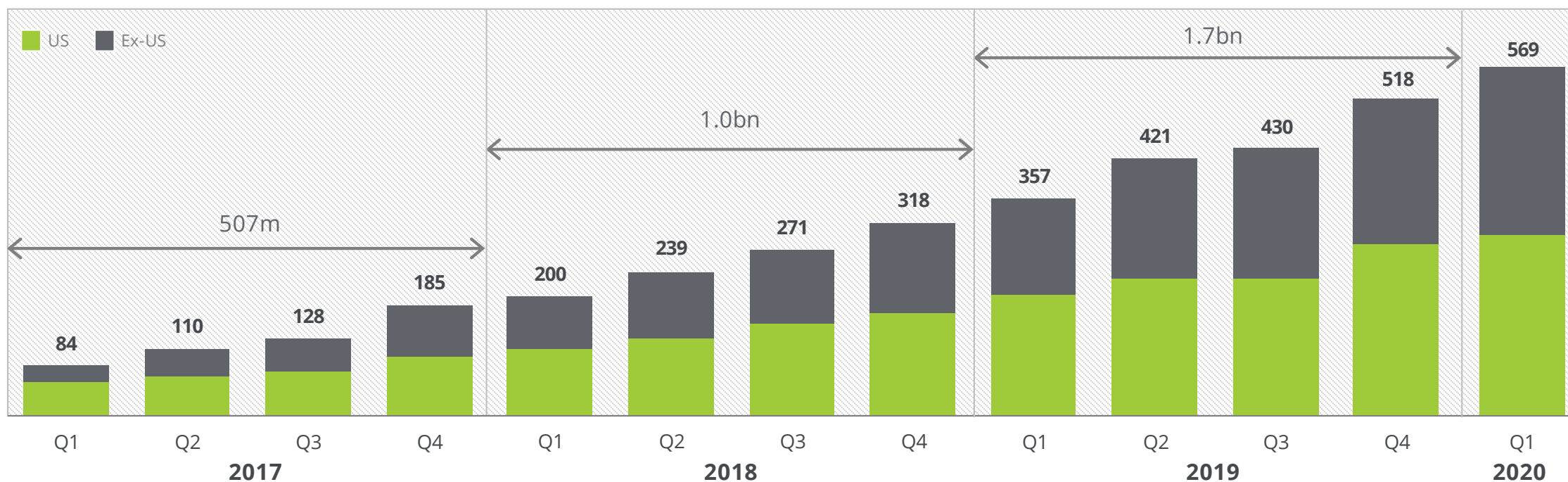
~75%

HF Prescription Sales

Commercial Opportunity for New Heart Failure Therapy

\$1.7B sold in 2019: Q1 2020 sales increased 62% year over year

Entresto® Global Product Sales (M)



*As with all products in Phase 3, the product profile achieved by *omecamtiv mecarbil* in GALACTIC-HF is required to provide a better understanding of the expected revenue.
Source: Novartis public quarterly results presentations

Commercial Readiness for *Omecamtiv Mecarbil*

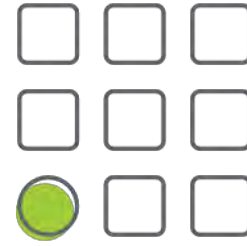
Multiple workstreams in progress to prepare for successful commercial launch



Educate heart failure market



Assess impact for value proposition



Determine areas of differentiation for HCPs



Cultivate advocacy for heart failure patients



Health Economic Impact Varies Across Care Delivery Systems

Payers measure value differently



Integrated
Delivery
Networks
(IDNs)

Pharmacy
Benefit
Managers
(PBMs)






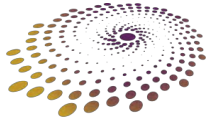



Hospitals

Translating Results from GALACTIC-HF to Value

- Budget Impact (Per member per month)
 - Cost Effectiveness
 - Quality Adjusted Life Years (QALY)
 - Total Cost of Care to System
 - Health System Rating (STAR)
 - Minimize CMS Readmission Penalty
-
- **Hypothesis: *Omecamtiv mecarbil* will provide economic benefit to payers across all parameters that are important to payers**

Opportunity: Potential to Meet Needs of All Groups

		 Physicians	 Patients	 Payers
Decrease Mortality	 GALACTIC-HF	✓	✓	✓
Decrease Hospitalization	 GALACTIC-HF	✓	✓	✓
Improve QOL	 GALACTIC-HF	✓	✓	✓
Increase Activity	 METEORIC-HF	✓	✓	✓

PANEL DISCUSSION

Optimizing Therapy in a New
Treatment Landscape

***Moderator: Andrew Wolff, M.D. SVP, Senior Fellow,
Clinical Research & Development***

Optimizing Therapy in a New Treatment Landscape

Panel Discussion



John McMurray, M.D.
Professor of Medical Cardiology & Honorary Consultant Cardiologist, Institute of Cardiovascular & Medical Sciences, BHF Cardiovascular Research Centre, University of Glasgow



Adrian Hernandez, M.D., M.H.S.
Executive Director, Duke Clinical Research Institute, Vice Dean, Duke University School of Medicine



Larry Allen, M.D., M.H.S.
Professor of Medicine, Kenneth Poirier Chair; Associate Head for Clinical Affairs, Cardiology; Medical Director, Advanced Heart Failure, University of Colorado School of Medicine



Fady Malik, M.D., Ph.D.
EVP, Research & Development, Cytokinetics



Andrew Wolff, M.D.
SVP, Senior Fellow, Clinical Research & Development, Cytokinetics

MODERATED BY

ACTIVATE
INHIBIT
EMPOWER

CK-274

Body of Evidence

Stuart Kupfer, M.D., SVP, Chief Medical Officer

Laura Robertson, M.D., Medical Director, Clinical Research, Cardiovascular

CK-274: Next-In-Class Cardiac Myosin Inhibitor

Potential treatments for patients with HCM

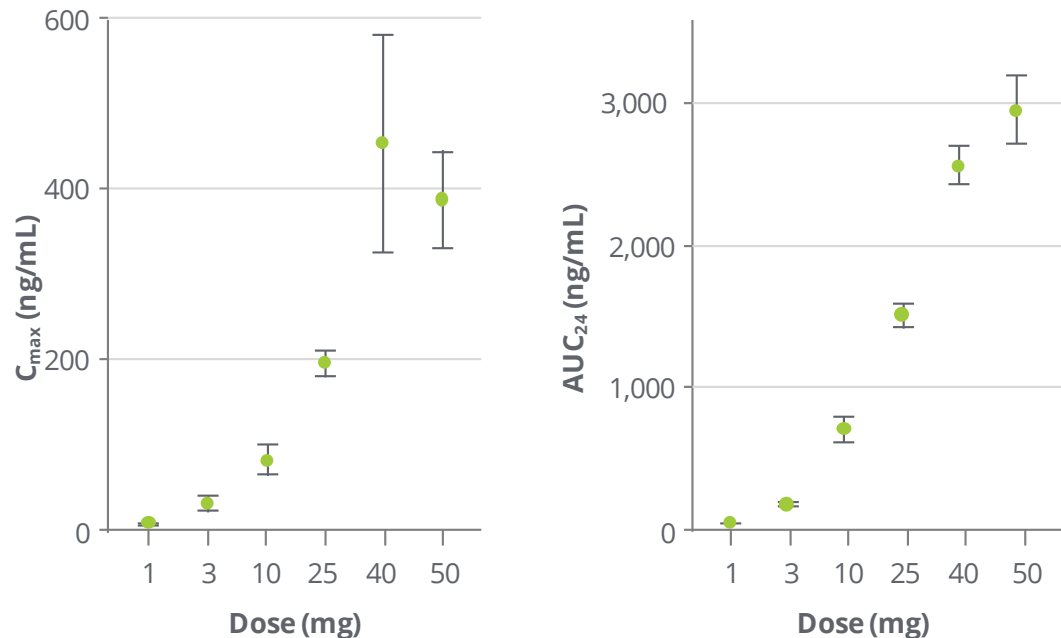


- Discovered by company scientists independent of collaborations
- Selective allosteric inhibitor of cardiac myosin
- No inhibition of smooth muscle myosin observed
- Potential *in vivo* pharmacodynamic advantages related to distinctive binding site
- Optimized to minimize potential drug-drug interactions
- High oral bioavailability observed across pre-clinical species
- Clear pharmacokinetic/pharmacodynamic (PK/PD) relationship observed
- Shallow exposure-response relationship
- Projected once daily dosing to reach steady state in patients expeditiously
- **Goal: Enable flexible and convenient dose optimization in humans as may contribute to its efficacy and safety profile**

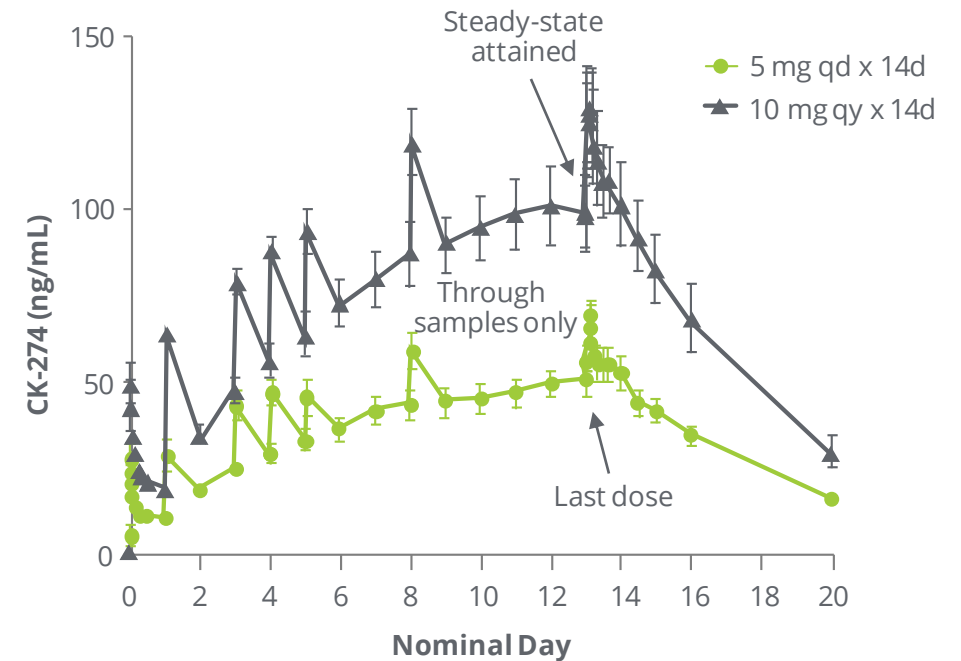
Phase 1 PK Results Support Progression to Phase 2

Phase 1: CK-274 was well tolerated in healthy participants, no SAEs*

SAD PK: Absorption and Elimination Generally Dose Proportional



MAD PK: Steady-State Achieved After 14 Days of Dosing



*No SAEs and no clinically meaningful changes in vital signs, ECGs, or laboratory tests
Data points represent mean \pm standard error of the mean
 C_{max} = maximum drug plasma concentration; AUC = area under the plasma concentration curve; SAD = single ascending dose; d = day; qd = once daily

Phase 1 PK and PK/PD Support Phase 2 Design

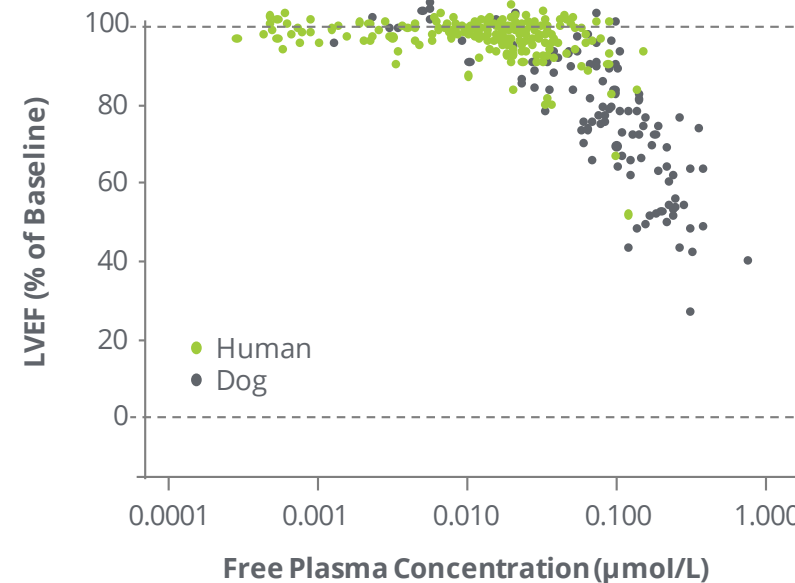
Half-Life of CK-274 at Steady-State was ~81 hours (3.4 days) On Average

PK Parameter, Geometric Mean (%CV)*	Dose (n)	5 mg (6)	7.5 mg (6)	10 mg (6)
	C _{max} (ng/mL)	69 (23.2%)	148 (39.5%)	141 (19.7%)
	t _{max} (h)	2.75 (1.5–4)	1.0 (0.5–5)	2.5 (0.5–3)
	AUC ₂₄ (ng•h/mL)	1,321 (23.0%)	2,518 (25.8%)	2,631 (22.8%)
	t _{1/2} (h)	86.3 (11.9)	76.9 (14.5)	79.7 (14.1)
	AR	4.71	4.5	4.79

*Except data for t_{max} shown as median (minimum-maximum), and t_{1/2} shown as the arithmetic mean (standard deviation).
AR (accumulation ratio) calculated as (AUC₂₄ on Day 14 or 17)/(AUC₂₄ on Day 1).
%CV = percent coefficient of variation; C_{max} = maximum plasma concentration; AUC₂₄ = area under the plasma concentration curve;
MAD = multiple ascending dose; t_{1/2} = apparent plasma terminal elimination half-life; t_{max} = time to maximum observed plasma concentration.

Shallow Exposure-Response Relationship Observed Preclinically Appears to Have Translated to Humans, May Enable Flexible Dose Optimization in Humans

PK/PD Relationship of CK-274 for Ejection Fraction (LVEF)

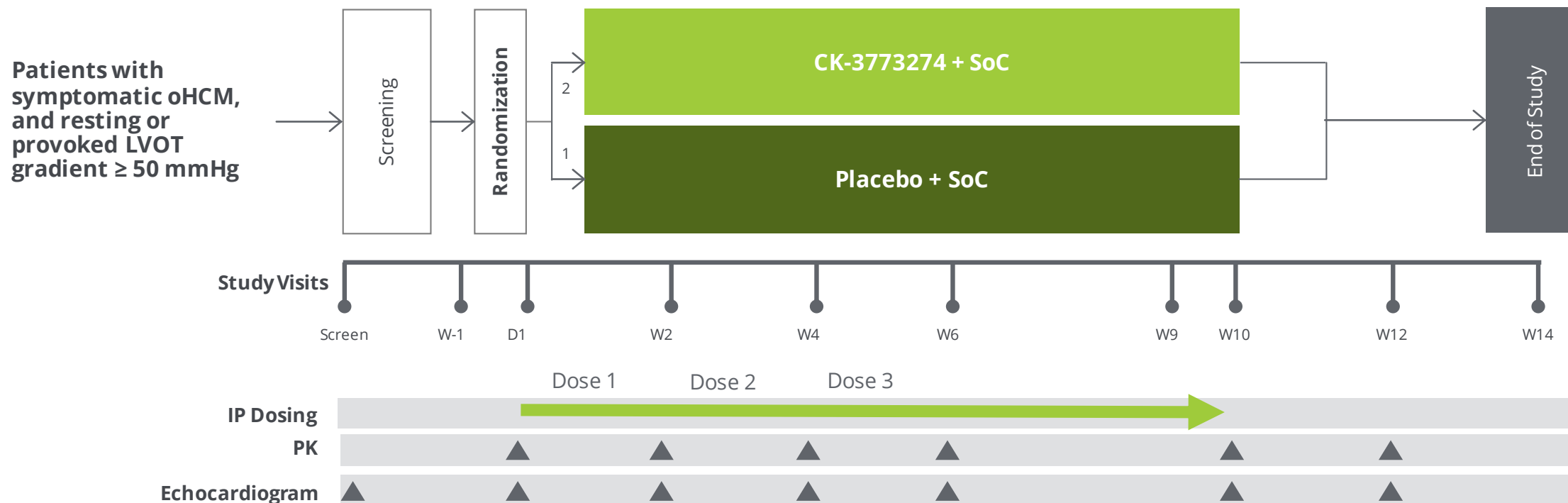


Graphs show LVEF as a function of exposure; data points represent observed values in dogs and humans.

Decrease in LVEF as function of exposure is similar in humans and dogs.

Phase 2 Clinical Trial Design

Two sequential dose-finding cohorts (optional 3rd cohort)



Clinical Sites in REDWOOD-HCM

US



EU & UK



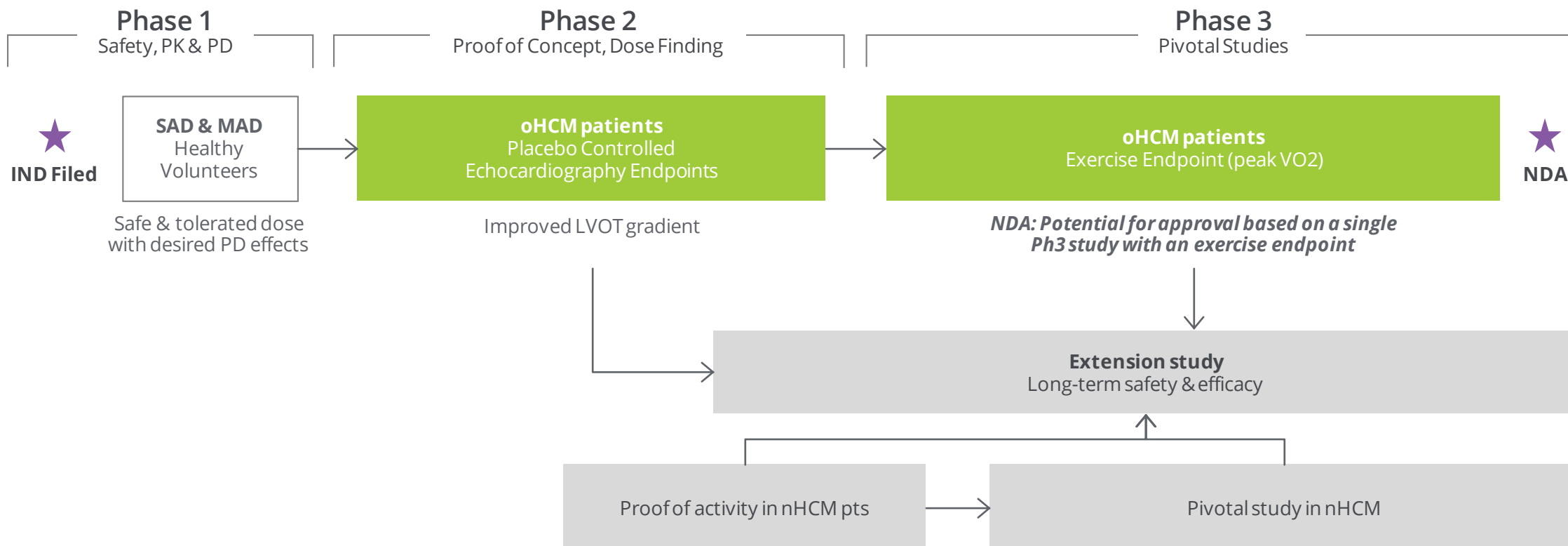
CK-274

Opportunities for Development

Stuart Kupfer, M.D., SVP, Chief Medical Officer

**Laura Robertson, M.D., Medical Director, Clinical
Research, Cardiovascular**

CK-274: Clinical Development Plan for HCM



Obstructive HCM: Potential Phase 3 Trial Endpoints

- **CPET – Cardiopulmonary exercise testing**
 - Peak VO_2 (oxygen uptake)
 - V_E/VCO_2 (ventilatory efficiency)
 - OUES (oxygen uptake efficiency slope)
- **NYHA class**
- **Echocardiographic parameters** – LVOT gradient, Measures of cardiac contractility (LVEF, LVFS, GLS)
- **Biomarkers** – NT-proBNP, Troponins
- **PROs – Patient-Reported Outcomes**
 - PROMIS scores – Dyspnea, Fatigue, Physical Function
 - HCM-specific instruments currently being validated



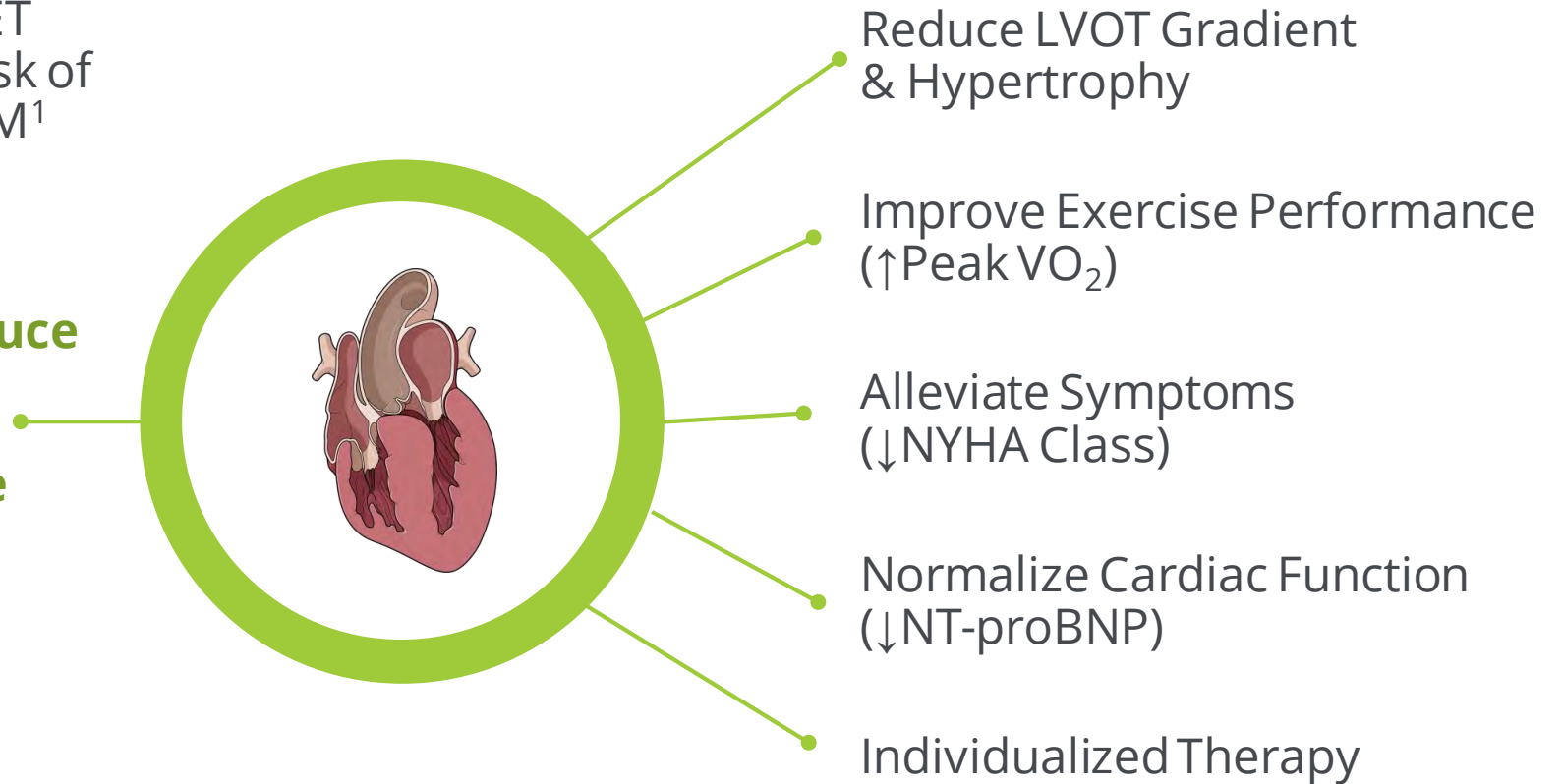
CK-274: Addressing significant disease burden in HCM

Exercise capacity is a powerful predictor of outcomes in HCM¹

Decreased peak VO_2 by CPET correlates with increased risk of death and transplant in HCM¹

CK-274 Designed to powerfully and safely reduce hypercontractility and robustly improve HCM patient health in multiple dimensions

Targeting long-term levels of benefit consistent with surgical myectomy in obstructive HCM²



¹Coates – 2015 Circ Heart Fail 8:1022-31. ²Rastegar – 2017 Ann Cardiothorac Surg 6:353-63.

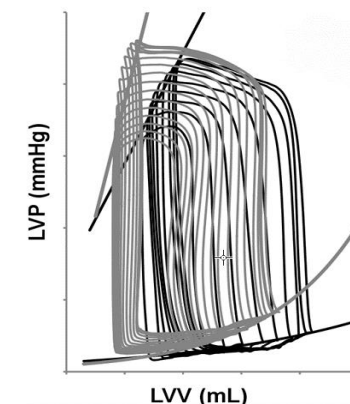
Non-Obstructive HCM – Human Model of HFpEF Subgroup

nHCM patients with similarities to subgroups of HFpEF patients with hypercontractility

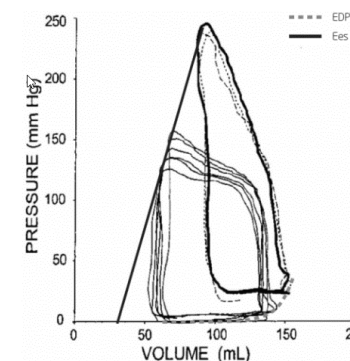
Symptoms and pathophysiology are similar in both conditions

Symptoms	Pathophysiology
Dyspnea	Increased Contractility
Exercise Capacity Diminished	Left Ventricular Hypertrophy
Peripheral Edema	Diastolic Dysfunction
Fatigue	Increased LV Filling Pressure

nHCM

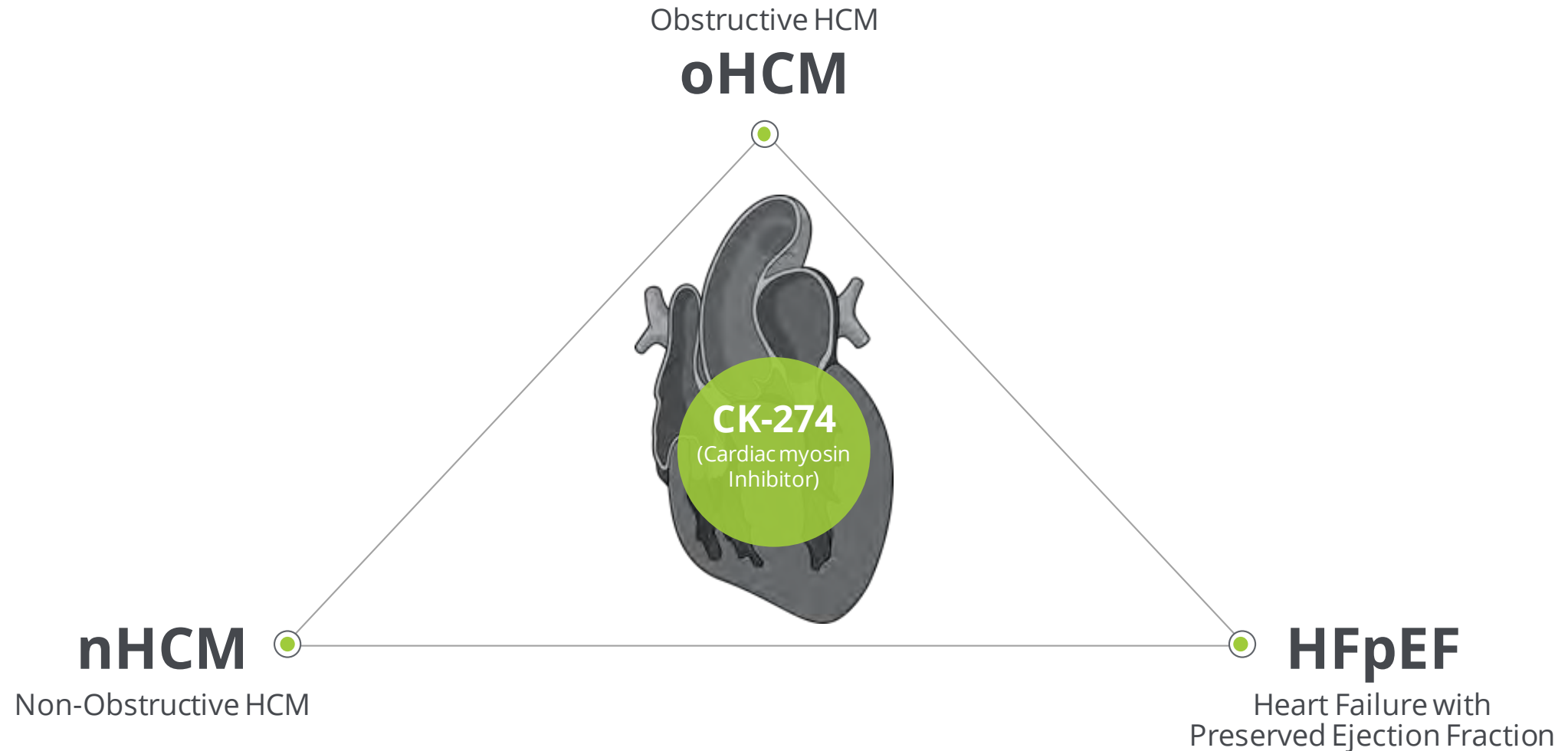


HFpEF Subgroup



Novel Approach Addresses Multiple Unmet Patient Needs

No FDA approved therapies



PANEL DISCUSSION

Embracing a New Era in the
Treatment of HCM

***Moderator: Steve Heitner, M.D., Senior Medical
Director, Clinical Research, Cardiovascular***

Embracing a New Era in the Treatment of HCM

Panel Discussion



Martin Maron, M.D.
Director, HCM Center; Director,
Cardiac CT & MRI, Tufts
University School of Medicine



Andrew Wang, M.D.
Professor of Medicine, Vice Chief
for Clinical Services, Duke
University School of Medicine



Anjali Owens, M.D.
Medical Director, Center for Inherited
Cardiac Disease, Assistant Professor
of Medicine, University of
Pennsylvania



Fady Malik, M.D., Ph.D.
EVP, Research & Development,
Cytokinetics



Steve Heitner, M.D.
Senior Medical Director, Clinical
Research, Cardiovascular,
Cytokinetics

MODERATED BY

ACTIVATE
INHIBIT
EMPOWER

PANEL DISCUSSION

Perspectives in Heart Failure & HCM

**Diane Weiser, SVP, Corporate Communications &
Investor Relations**

Perspectives in Heart Failure & HCM

Panel Discussion



Linda Moczowski

Former nurse, patient advocate
living with heart failure



Lindsay Davis

Miss Ohio 2011, patient advocate
living with HCM

MODERATED BY



Diane Weiser

SVP, Corporate
Communications & IR,
Cytokinetics

EMPOWER

Building a Cardiovascular Franchise

**Durga Bobba, VP, Global Franchise General Manager,
Cardiovascular**

Tremendous Need Exists to Improve CV Care

Novel CV drugs are desperately needed to improve patient healthspan

Heart Disease the **Leading Cause of Death** in the US



#1 Heart disease (185)



#2 Cancer (152)



#3 Respiratory (49)



#4 Stroke (38)

2018 US Deaths per 100,000 Standard Population

CV Disease the **Leading Category in Healthcare Spend**



#1 Cardiovascular (\$327B)



#2 Musculoskeletal (\$300B)



#3 Respiratory (\$231B)



#4 Endocrine (\$227B)

2019 US Expenditure by Disease Category

Lack of Innovation Exists Across CV Conditions



#1 Rare diseases
(211 drugs approved)



#2 Neurologic disease
(139 drugs approved)



#3 Cancer
(133 drugs approved)



#10 Cardiovascular
(43 drugs approved)
... and **just 4 drugs for HF**

of Approved Drugs since 2010

Source: NCHS Data Brief, No. 355 January 2020, Peterson-KFF, Health System Tracker, PharmaProjects.

CV Franchise: Built on Science, Medicine & Patient Healthspan

Foundation for Success:
Continue to build and improve upon novel medicines allowing CV patients to do more, longer

Target Underlying Pathophysiology To Best Address CV Patient Needs

Build Deepest Scientific Expertise

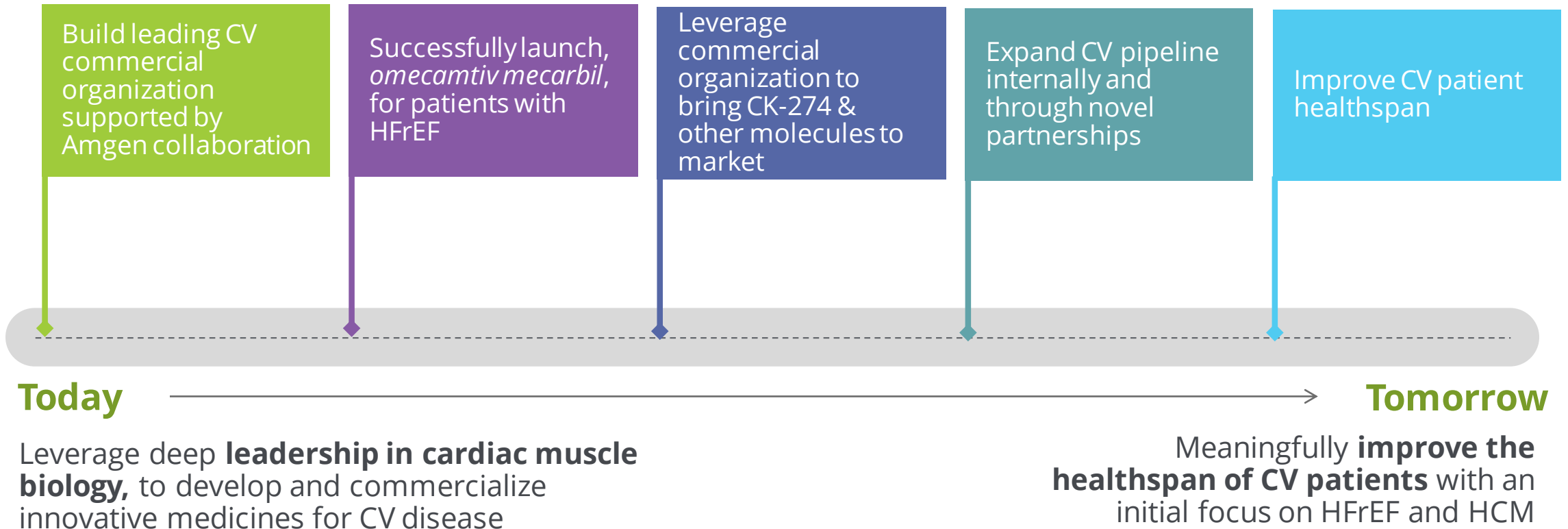
Identify Novel Assets to Address CV Patient Needs and Set New Standard of Care

Ensure Clinical Development Captures Benefits CV Patients Truly Care About

Build Commercial Organization with CV Patient at Center

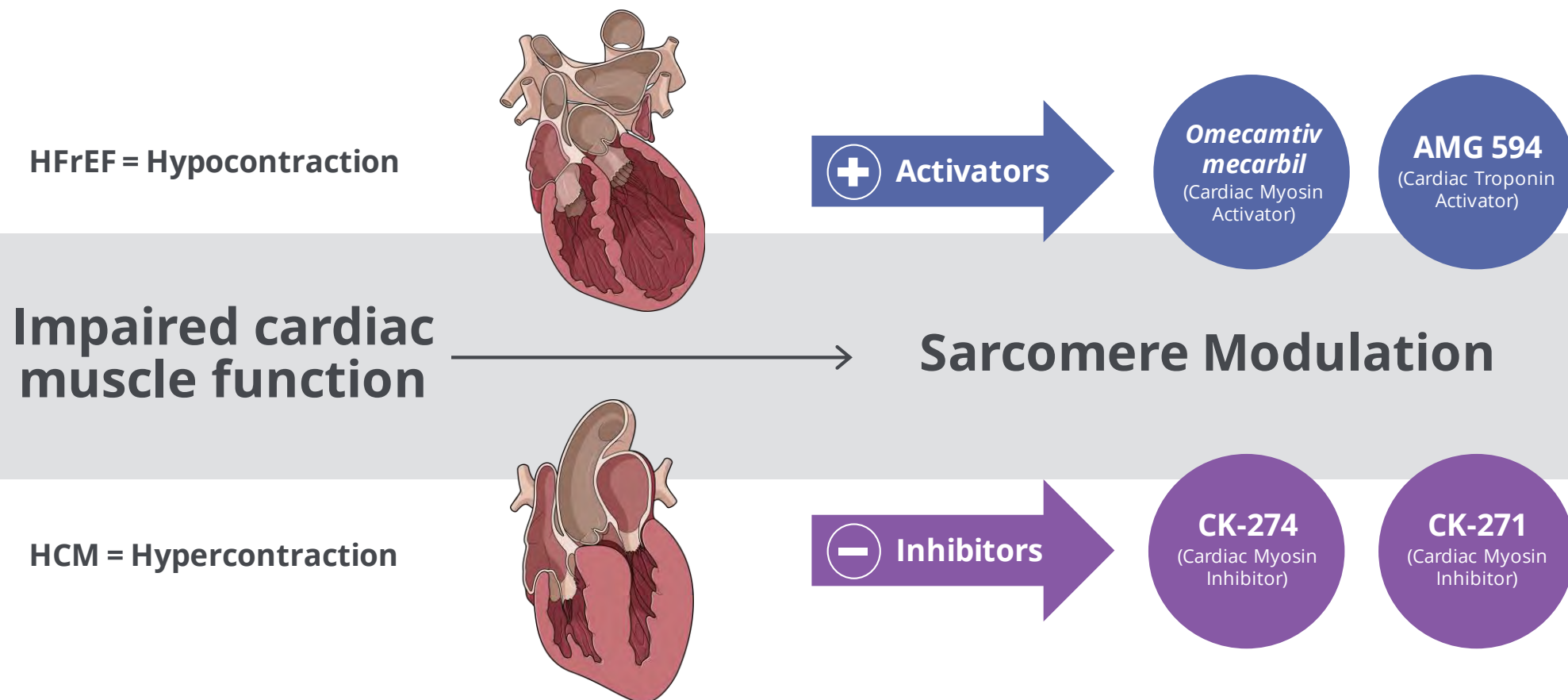


CV Franchise: Built to Improve Patient Healthspan

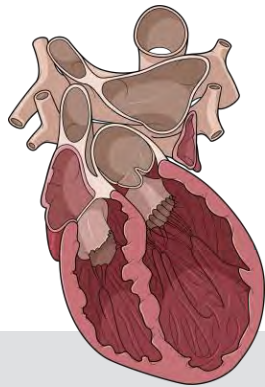


Novel & Built for Purpose Molecules Focused on Cardiac Muscle Biology

Four modulators in pipeline; more in development in contractility & muscle energetics



Novel & Built for Purpose Molecules: Functional & QOL Benefits



~3M HFrEF patients in US

**Omecamtiv
mecarbil**
(Cardiac Myosin
Activator)

AMG 594
(Cardiac Troponin
Activator)

*Multiple, novel assets
designed to benefit patients*

**Impaired cardiac
muscle function**



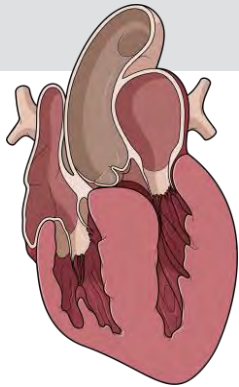
**Sarcomere
Modulation**



**Improved
Healthspan**



**Do More
For Longer**



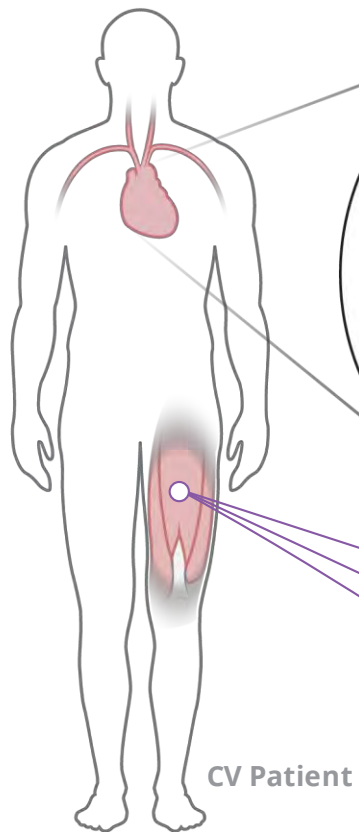
CK-274
(Cardiac Myosin
Inhibitor)

CK-271
(Cardiac Myosin
Inhibitor)

*Multiple novel assets
designed to benefit patients*

~600K HCM patients in US

Convergence of Verticals Addresses CV Conditions & Co-Morbidities



- HFrEF ✓
- HCM ✓
- HFpEF
- Other Cardiomyopathies
- Right Ventricle (RV) Dysfunction

Enhanced Cardiac
Muscle Performance
**Applicable Across
Additional
CV Conditions**

- Frailty
- Reduced Work Capacity
- Muscle Weakness

Enhanced Skeletal
Muscle Performance
Can Address **CV
Patient Co-Morbidities**

Building Synergistic Commercial Capabilities

Building Today...

Building commercial organization focused on hospitalized CV patients and HCPs to optimize opportunity for *omecamtiv mecarbil*

- Leverage funding from Amgen collaboration
- Cultivate advocacy with CV patients and HCPs

To Lead Tomorrow

Establish Cytokinetics as a CV leader by leveraging commercial capabilities for future product launches

- Significant overlap between HFrEF & HCM accounts
- Simultaneously gain experience in HFrEF & HCM



IQVIA HPD – Q3'18 – Q2'19

CLOSING REMARKS

Robert Blum, President & CEO

VISION 2025

Leading with Science,
Delivering for Patients

As always, we will support disease advocacy groups elevating the patient voice and live by our values of integrity, fairness and compassion in all that we do.

Our vision is to be the leading muscle biology biopharma company that meaningfully improves the lives of patients with diseases of impaired muscle function through access to our pioneering medicines

Achieve regulatory approvals for at least two drugs arising from our pipeline

Build commercial capabilities to market and sell our medicines reflective of their innovation and value





Generate sustainable and growing revenues from product sales

Double our development pipeline to include ten therapeutic programs

Expand our discovery platform to muscle energetics, growth and metabolism

Be the science-driven company people want to join and partner with

We're Up To The Challenge

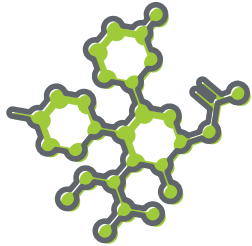
Pipeline*	1 Pivotal trial readout in Q4 2020	2 Pivotal trials in 2021	3 Potential FDA approvals by 2025	5 Clinical stage programs	10 Development programs by 2025
Programs*	Heart Failure <i>Omecamtiv mecarbil</i> <ul style="list-style-type: none">Phase 3 CV outcomes trial results Q4 2020Phase 3 exercise capacity trial results 2H 2021	 AMG-594 <ul style="list-style-type: none">Phase 1	HCM CK-274 <ul style="list-style-type: none">Phase 2 trial initial results 2H 2020	ALS <i>Reldesemtiv</i> <ul style="list-style-type: none">Prepare for potential phase 3 trial starting in Q4 2020	Ongoing R&D Additional research in muscle biology, energetics & metabolism 
Foundations	175 Full time employees 	\$237M At Q1 2020	>\$1B Eligible milestone payments in partnerships 	~20% Eligible for double-digit escalating royalties** on worldwide sales on <i>omecamtiv mecarbil</i>	

*Timelines and milestones reflect Cytokinetics' current expectations and beliefs.

**Outside Japan; lower royalty rate in Japan

Integrated Corporate Development Strategy

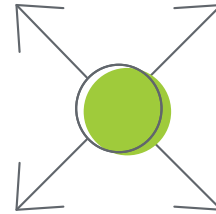
Leveraging expertise in muscle biology to build sustainable cardiovascular business



R&D



**Business
Development**



**Commercial
Development**



**Industry Leading
CV Franchise**

Empowering Muscle, Empowering Lives

**a relentless dedication
to PATIENTS**

Video Playing

Watch the full video on our YouTube Channel here:
[Behind HF: One Hundred Percent, The John Crofut Story](#)



THANK YOU

Sarcomere Directed Therapies



John, diagnosed with heart failure



Jillian, diagnosed with HCM



Chuck, diagnosed with ALS