



Cytokinetics

*Sarcomere Directed Therapies*

EMPOWERING  
**MUSCLE**  
EMPOWERING  
**LIVES**



*John, diagnosed with heart failure*



*Jillian, diagnosed with HCM*



*Chuck, diagnosed with ALS*

# 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' 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, hypertrophic cardiomyopathy (HCM) or amyotrophic lateral sclerosis (ALS); projections regarding the size of the addressable patient population for *omecamtiv mecarbil*, *aficamten* or *reldesemtiv*; Cytokinetics' commercial readiness for *omecamtiv mecarbil*; the likelihood of approval and timing for regulatory approval of *omecamtiv mecarbil* or any of our other drug candidates; the submission of a new drug application (NDA) to the FDA for *omecamtiv mecarbil* in 2021; the timing of commencement of COURAGE-ALS, a phase 3 clinical trial of *reldesemtiv* or the timing of commencement of a phase 3 clinical trial of *aficamten*; 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 *aficamten*, *omecamtiv mecarbil*, *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' ability to conduct clinical trials, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; 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; and competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target. 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”).

*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

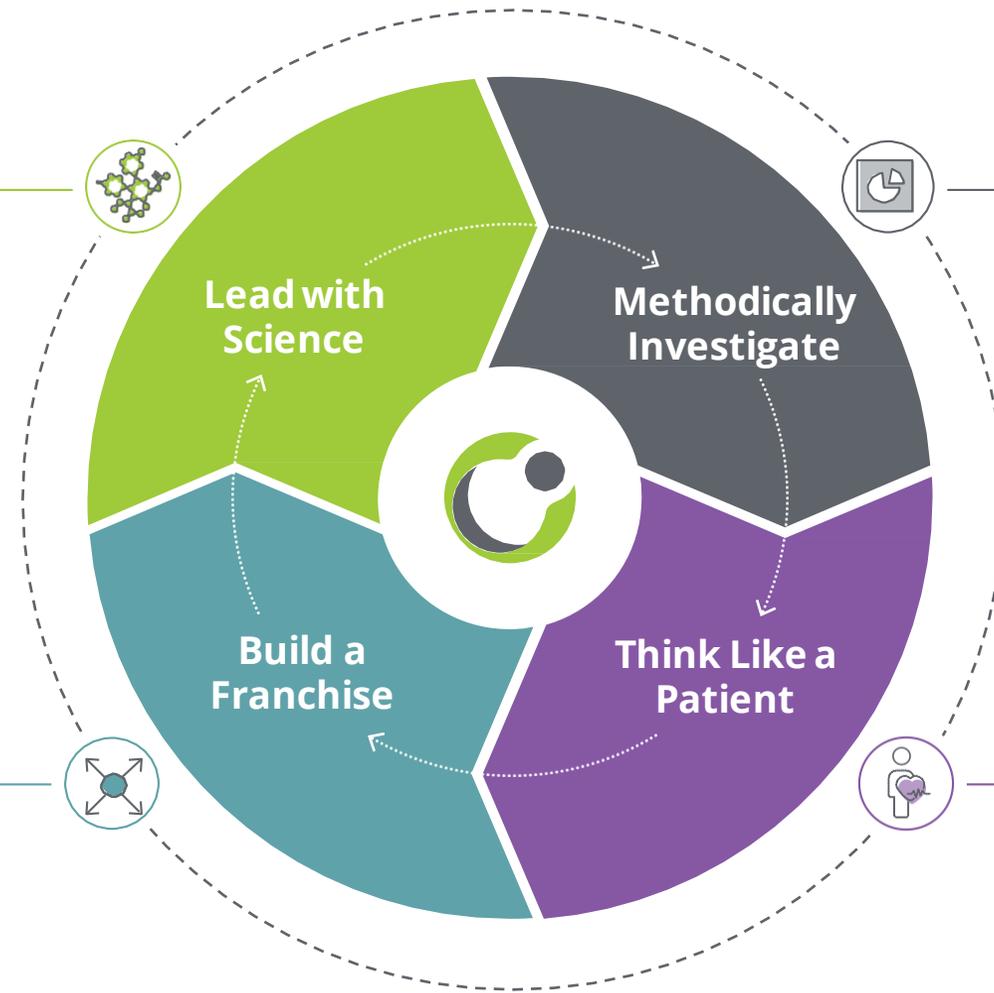
Expand our discovery platform to muscle energetics, growth and metabolism

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

# Executing On Our Vision

- Scientific innovation driven by modulating cardiac myosin
- First-in-class myosin activator
- Next-in-class myosin inhibitor
- Expansion beyond contractility to muscle energetics, metabolism

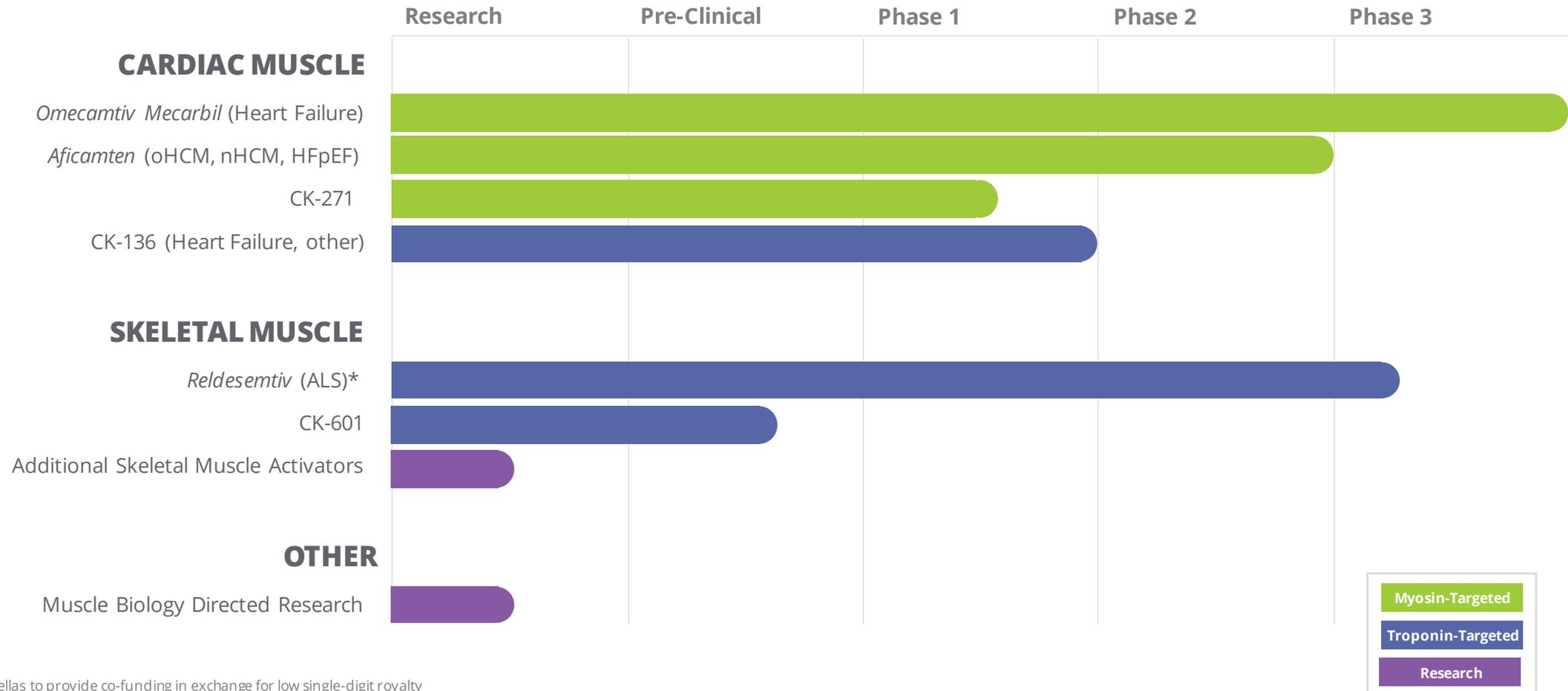
- Customer-centric approach to portfolio management
- Overlap between HFREF and HCM accounts
- Commercial build in HFREF supports future HCM business
- Lifecycle management extends and expands franchise



- Positive Phase 3 results from GALACTIC-HF; NDA submission expected in 2H 2021
- Positive Phase 2 results from REDWOOD-HCM; Phase 3 clinical trial expected by year-end
- Clinical trial results from METEORIC-HF expected in early 2022

- Regular input, collaboration and guidance
- Elevate patient voice
- Improve function, performance and healthspan

# Pipeline of Novel Muscle-Directed Drug Candidates



\* Astellas to provide co-funding in exchange for low single-digit royalty  
 All drug candidates above are investigational products and are not approved as safe or effective for any indication.

*Sarcomere Directed Drug Development*

# CARDIAC MUSCLE

*Omecamtiv Mecarbil*

CK-136

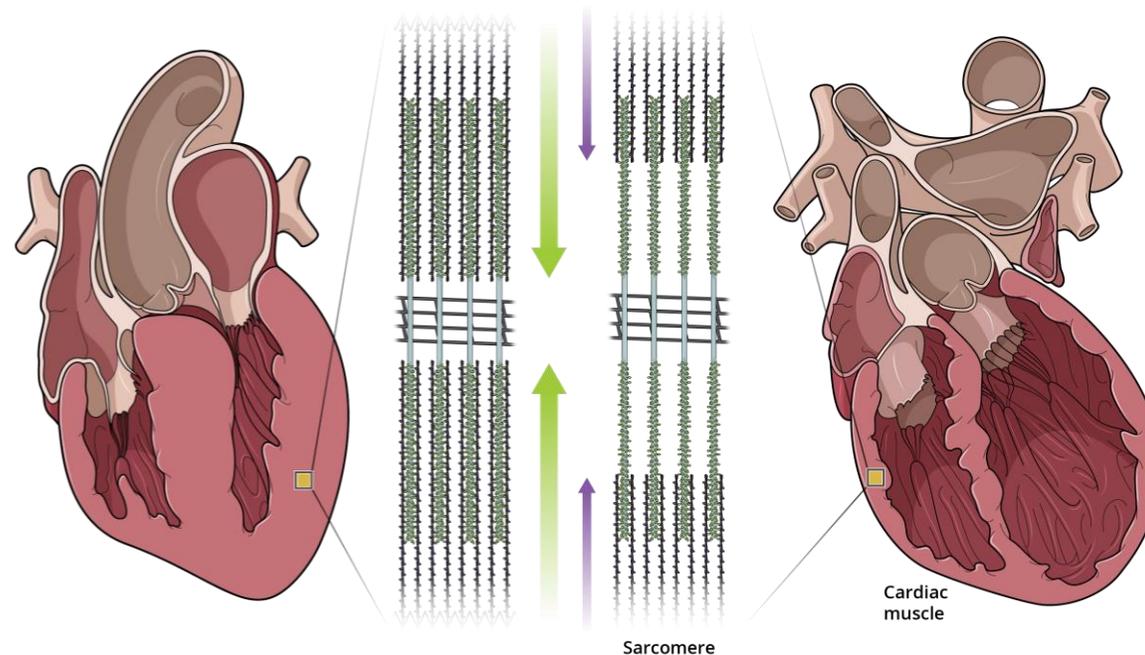
*Aficamten, CK-271*

# ***Omeamtiv*** ***Mecarbil***

# Contractile Dysfunction Underlies Heart Failure

## Increased / Preserved Cardiac Contractility

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



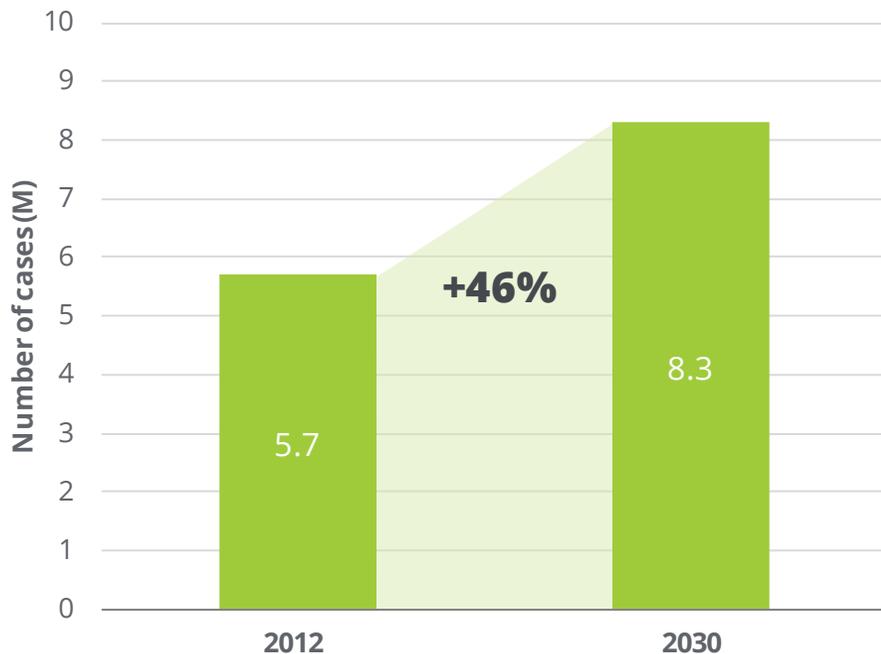
## Decreased Cardiac Contractility

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

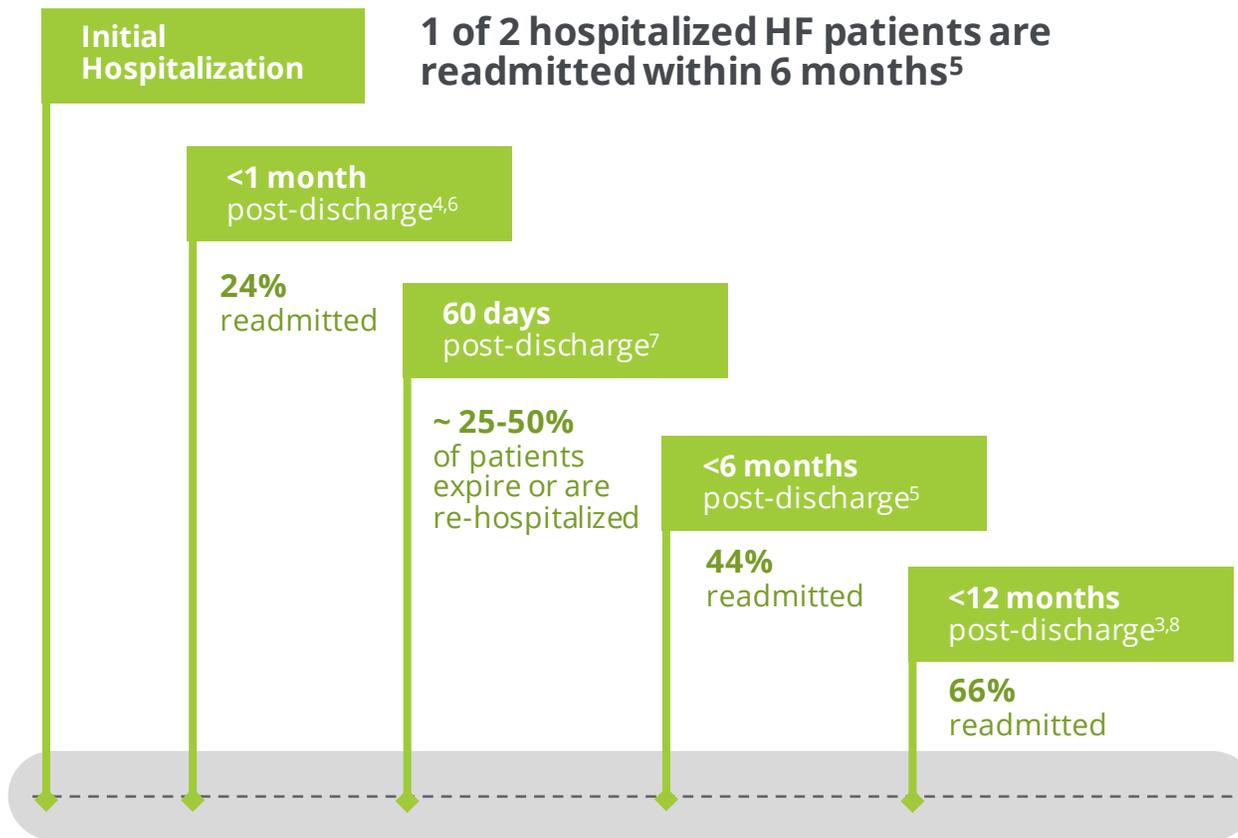
# Heart Failure: Growing Prevalence and High Readmission Rates

## 6 million people have heart failure in the United States

Prevalence Expected to Increase by 46% from 2012 – 2030



Mozzafarian, et al. *Circulation* 2016; 133: e38-360



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

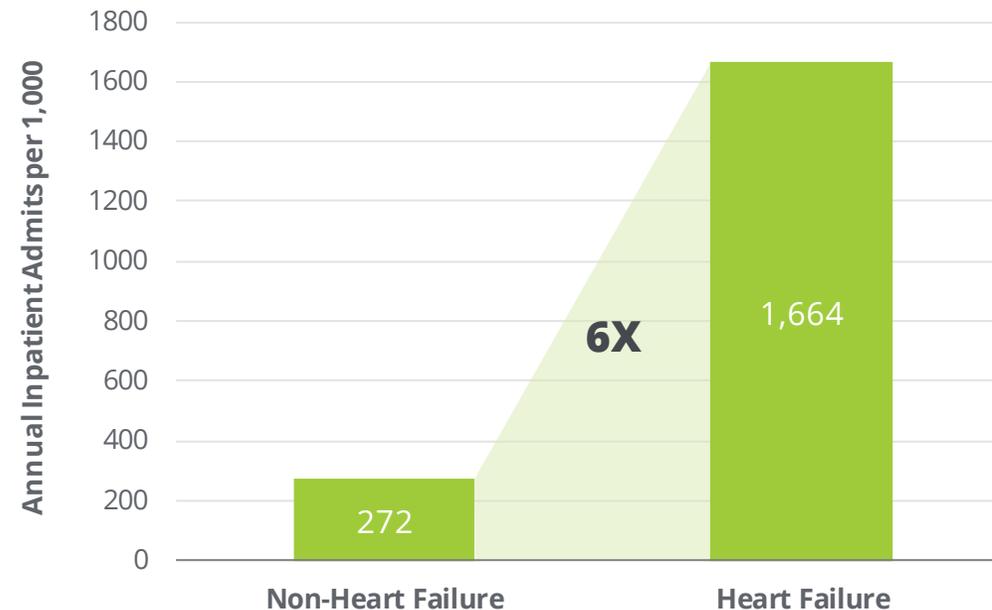
6. Krumholz et al. *Circ Cardiovasc Qual Outcomes* 2009;2(5):407-13  
 7. Loehr et al. *Am J Cardiol* 2008;101:1016-22  
 8. Whellan et al. *Circulation* 2010 Jan;3(1):33-40

# High Economic Burden of Heart Failure

Heart failure costs ~\$123 billion annually, representing 33% of total Medicare budget<sup>1,2</sup>

Heart failure is the most frequent diagnosis for hospitalized Medicare patients in the US<sup>1,2</sup>

## Inpatient Admission Rates for HF Patients 6X Higher than Non-HF Patients<sup>1</sup>



1. Milliman Analysis of Medicare 5% Sample 2011-2012 (2012 index year, 2011 look back year)

2. Milliman Analysis of Medicare 5% Sample (2014 index year, 2013 look back year) and Office of the Actuary 2016 Board of Trustees Report. The costs only include Part A & B costs

# Significant Unmet Need in HFrEF

## Proprietary market research suggests need for novel therapy



### Market research suggests need for novel therapy

Physicians say newly approved therapies have prolonged survival, decreased hospital visits, but still **see need for other therapies that reduce mortality**



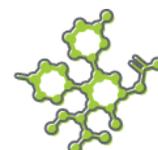
### Drugs that do not affect renal function

Most physicians recognize negative effect therapies such as aldosterone antagonists have **on renal function**



### Drugs that do not affect BP

BP often limiting factor for up titration and therapy initiation  
Need efficacious drugs **that do not result in hypotension**



### Drugs that enhance cardiac performance

Need drugs that target **novel/more specific molecular targets**  
Need targets other than the neurohormonal pathway



### Disease modifying therapies

Need drugs that safely enhance contractility  
Increased EF most frequently mentioned desired measure

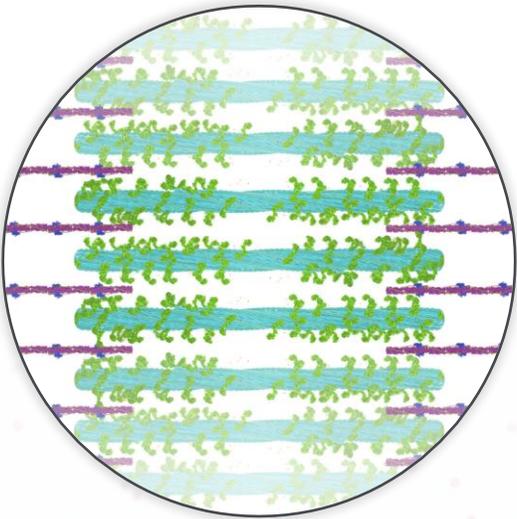


### Drugs that increase QoL

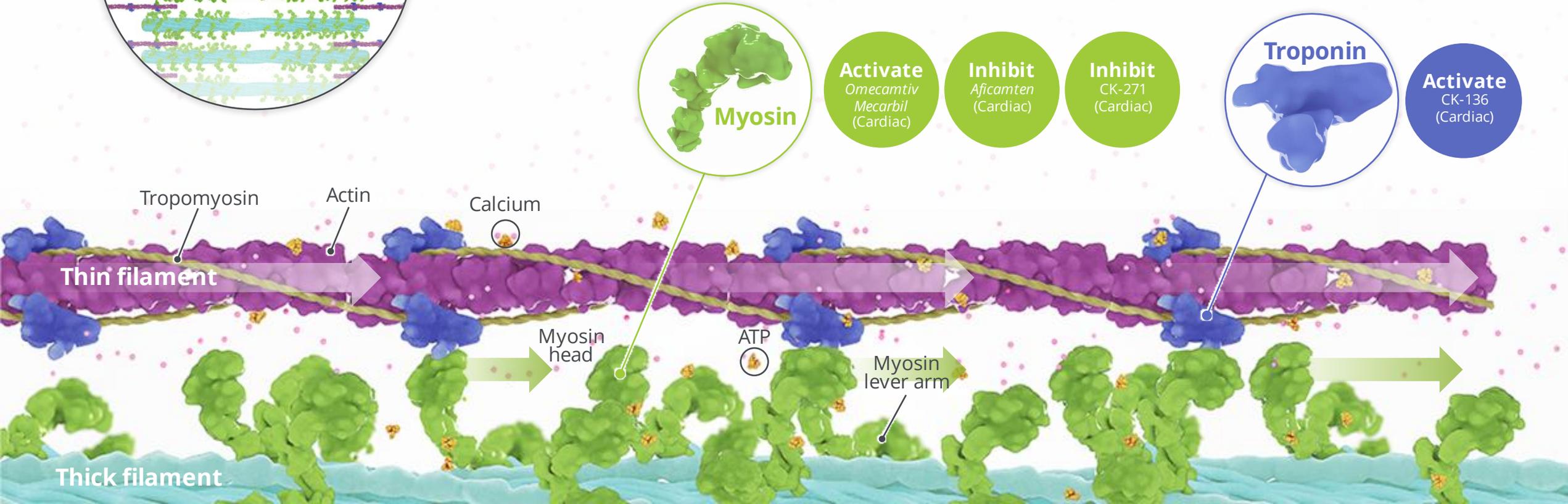
Patient management will improve **with drugs that increase QoL**  
Patient QoL decreases as they lose the ability to perform daily tasks

# Sarcomere Directed Drug Development

## Cardiac muscle



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



# Pivotal Phase 3 Trial Design



Landmark clinical trial results published in NEJM

## 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.

# Baseline Characteristics



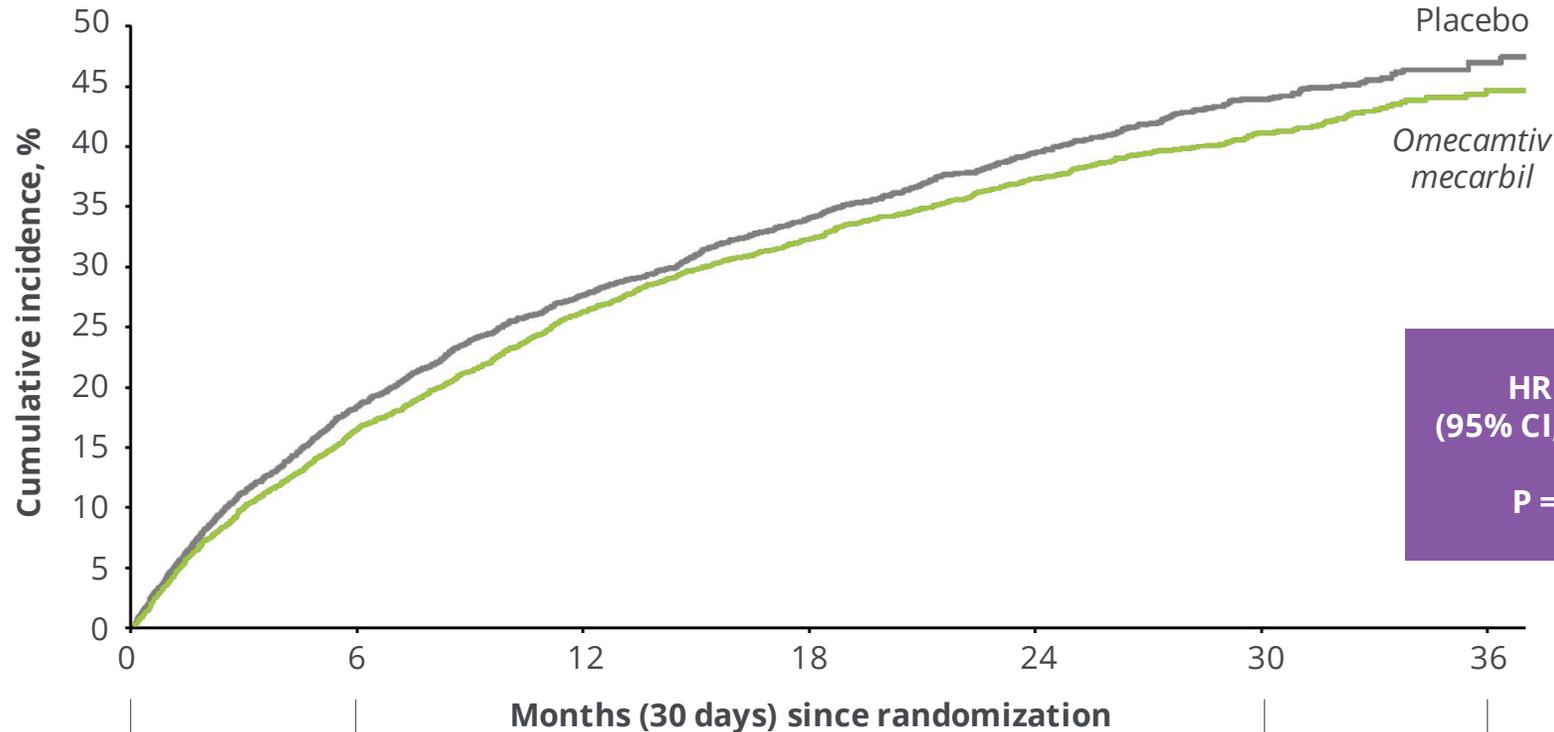
Characteristic	OM (N=4120)	Placebo (N=4112)
<i>Demographics</i>		
Age (years), median (Q1, Q3)	66 (58, 73)	66 (58, 73)
Sex, female, n (%)	875 (21.2)	874 (21.3)
White/Asian/Black/other, %	78/9/7/7	78/9/7/7
<i>Heart Failure History and Medical Conditions</i>		
LVEF (%), mean (SD)	26.6 (6.3)	26.5 (6.3)
NYHA class, II/III/IV, %	53/44/3	53/44/3
Ischemic etiology, %	53.2	54.0
Atrial fib/flutter at screening, %	27.8	26.7
Type 2 diabetes, %	40.1	40.3

Characteristic	OM (N=4120)	Placebo (N=4112)
<i>Vitals and Laboratory Parameters</i>		
NT-proBNP (pg/mL), median (Q1, Q3)	1977 (980, 4061)	2025 (1000, 4105)
SBP (mmHg), mean (SD)	116 (15)	117 (15)
Heart rate, mean (SD)	72 (12)	72 (12)
eGFR (mL/min/1.73m <sup>2</sup> ), median (Q1, Q3)	59 (44, 74)	59 (44, 74)
Cardiac TnI (ng/mL), median (Q3)	0.027 (0.052)	0.027 (0.052)
<i>Medications and Cardiac Devices</i>		
ACEI/ARB/ARNi, %	87	87
ARNi, %	20	19
BB, %	94	94
MRA, %	78	78
SGLT2i, %	2.5	2.8
CRT, %	14	14
ICD, %	32	31

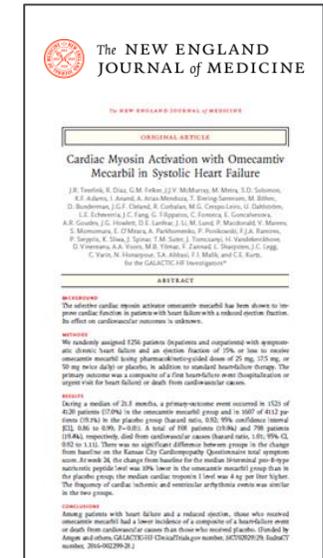
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; BB, beta blocker; CRT, cardiac resynchronization therapy; eGFR, estimated glomerular filtration rate; fib, fibrillation; hsTnI, high-sensitivity troponin I; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; Q, quartile; SBP, systolic blood pressure; SGLT2i, sodium-glucose co-transporter 2 inhibitor.

# Primary Composite Endpoint

## Time to first HF event or CV death



	0	6	12	18	24	30	36
Patients at risk, n							
Placebo	4112	3310	2889	2102	1349	647	141
OM	4120	3391	2953	2158	1430	700	164



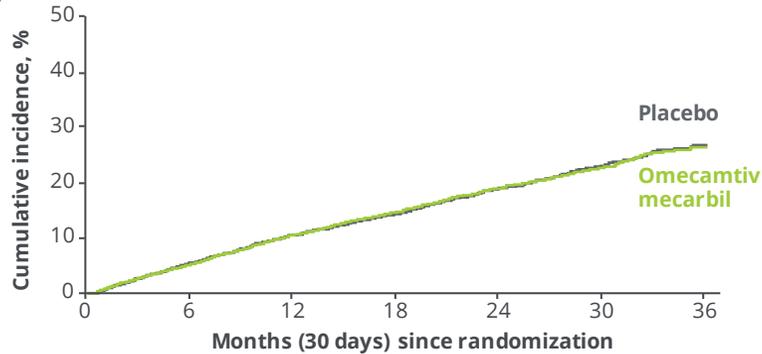
# Primary Composite Components and KCCQ TSS



## CV Death

HR = 1.01 (95% CI, 0.92–1.11)

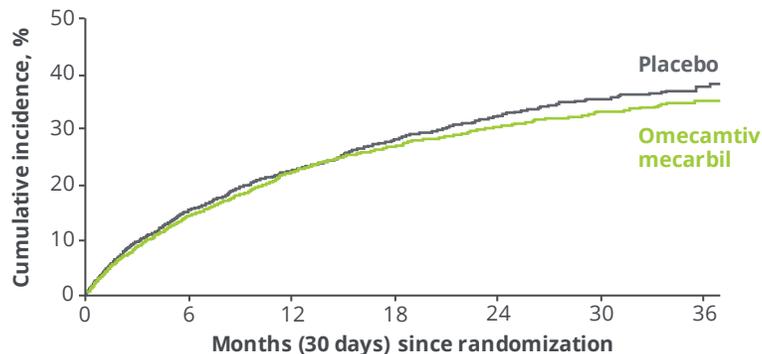
P = 0.86



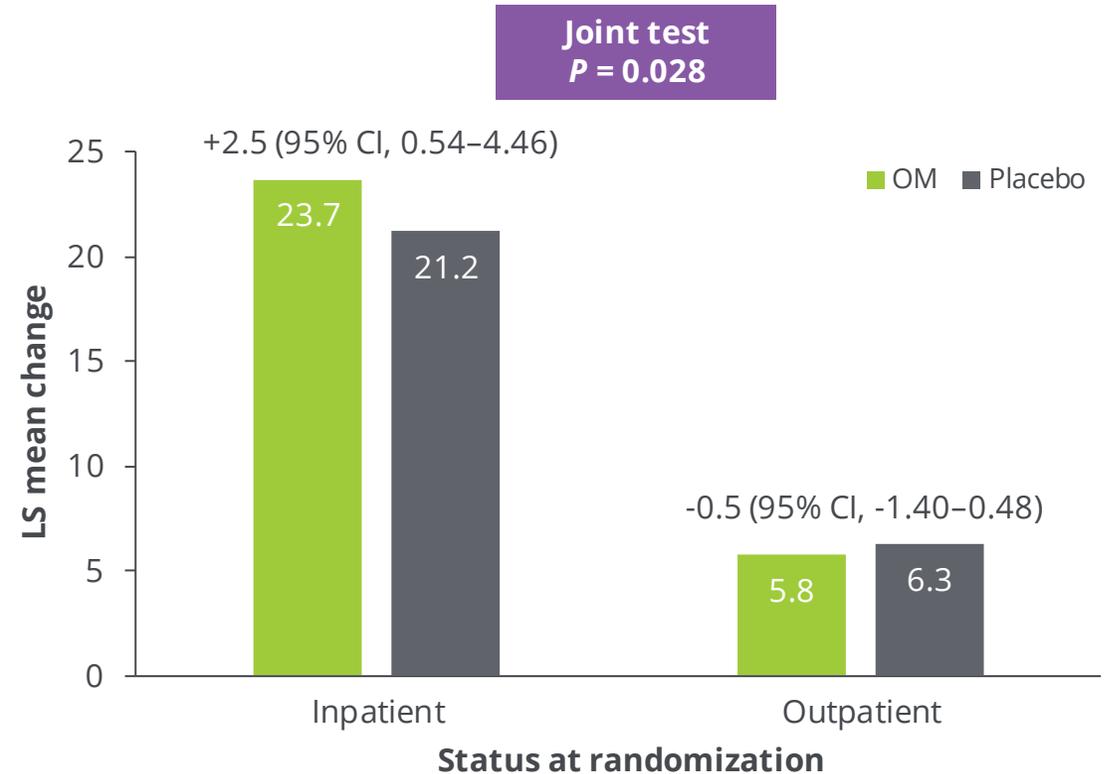
## Heart Failure Event

HR = 0.93 (95% CI, 0.86–1.00)

P = 0.063



## Change in KCCQ TSS from Baseline to Week 24



*No reduction in the secondary endpoint of time to CV death was observed*

# Laboratory and Safety Events



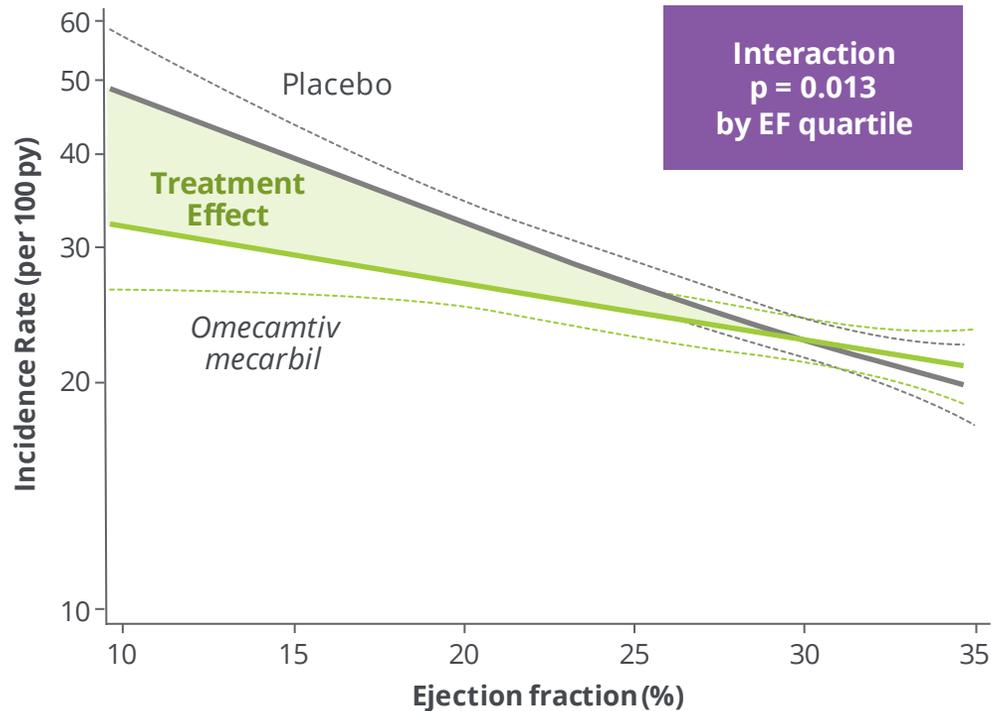
Variable	<i>Omeamtiv Mecarbil</i> (N=4110)	Placebo (N=4101)	Relative Risk or Difference (95% CI)
<i>Laboratory value change from baseline to Week 24</i>			
<b>Systolic blood pressure - mmHg, mean (SD)</b>	<b>1.4 (15.3)</b>	<b>1.5 (15.6)</b>	-0.1 (-0.9, 0.6)
<b>Heart rate, bpm, mean (SD)</b>	<b>-2.1 (12.6)</b>	-0.5 (12.8)	-1.6 (-2.2, -1.0)
<b>Cardiac Troponin I, ng/L, median (Q1, Q3)</b>	0.004 (-0.002, 0.021)	0.000 (-0.009, 0.008)	0.004 (0.003, 0.005)
<b>NT-proBNP, pg/mL, median (Q1, Q3)</b>	<b>-251 (-1180, 295)</b>	-180 (-915, 441)	0.90 (0.86, 0.94)
<i>Adverse events (AEs)</i>			
<b>Any serious AE, n (%)</b>	2373 (57.7)	2435 (59.4)	0.97 (0.94, 1.01)
<b>Drug discontinuation due to AE, n (%)</b>	371 (9.0)	382 (9.3)	0.97 (0.85, 1.11)
<b>Adverse events of interest</b>			
<b>Ventricular tachyarrhythmias</b>	290 (7.1)	304 (7.4)	0.95 (0.82, 1.11)
<b>Torsade de pointes/QT prolongation</b>	176 (4.3)	195 (4.8)	0.90 (0.74, 1.10)
<b>SAE of ventricular arrhythmia requiring treatment</b>	119 (2.9)	127 (3.1)	0.93 (0.73, 1.20)
<b>Adjudicated major cardiac ischemic events, n (%)</b>	200 (4.9)	188 (4.6)	1.06 (0.87, 1.29)
<b>Myocardial infarction</b>	122 (3.0)	118 (2.9)	
<b>Hospitalized for unstable angina</b>	25 (0.6)	12 (0.3)	
<b>Coronary revascularization</b>	115 (2.8)	117 (2.9)	
<b>Adjudicated Strokes</b>	76 (1.8)	112 (2.7)	0.68 (0.51, 0.91)

# Treatment Effect Increased Progressively As Baseline EF Decreased

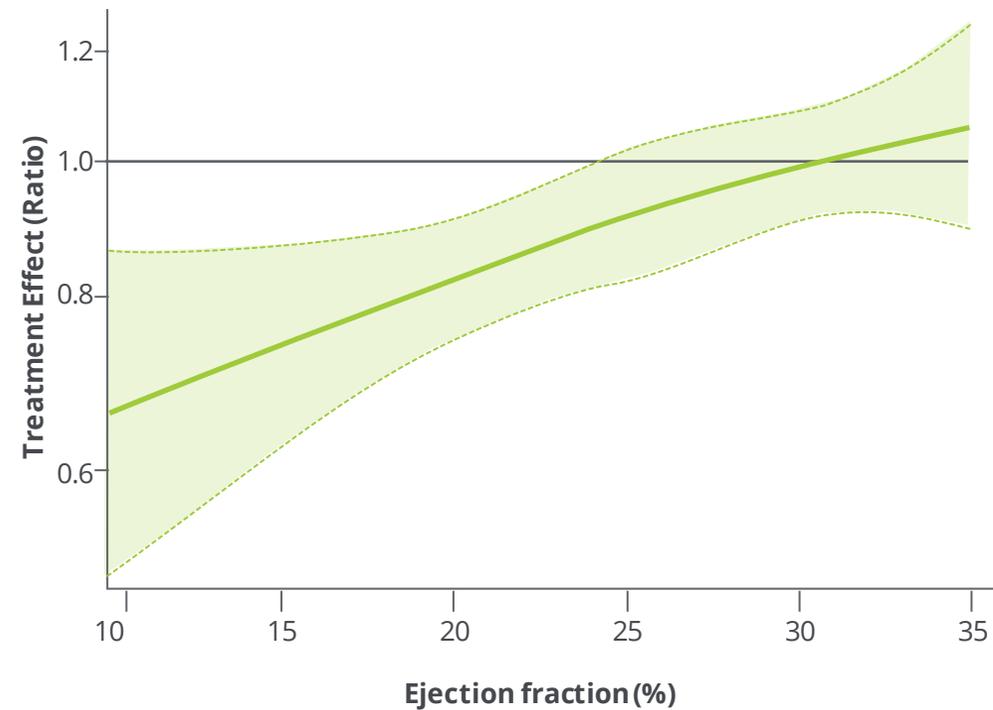
## In EF ≤22%, 11.8 needed-to-treat to prevent 1 event over 3 years



### Incidence of Primary Composite Endpoint



### Relative Treatment Effect on Primary Composite Endpoint



# Greater Treatment Effect in More Severe HF



Results of the primary outcome in pre-specified subgroups showed greater treatment effect in patients with markers of more severe heart failure, including patients with LVEF  $\leq 28\%$ : (n=4,456) HR 0.84; 95% CI 0.77, 0.92

Subgroup	No. of Events/ No. of Patients		Hazard Ratio (95% CI)	Norm p-value	ARR
All Patients	3103/8232		0.92 (0.86, 0.99)	0.025	2.1%
<b>LVEF <math>\leq 28\%</math></b>	<b>1821/4456</b>		<b>0.84 (0.77, 0.92)</b>	<b>&lt;0.001</b>	<b>4.9%</b>
Outpatients	1255/3304		0.83 (0.75, 0.93)	0.001	5.0%
Inpatients	566/1152		0.86 (0.73, 1.02)	0.084	3.9%
Hosp <3 mos	1200/2688		0.83 (0.74, 0.93)	0.001	5.2%
Class III/IV	1055/2132		0.80 (0.71, 0.90)	<0.001	7.0%
NT-proBNP >2000	1249/2431		0.77 (0.69, 0.87)	<0.001	8.1%
SBP <110	843/1820		0.81 (0.70, 0.92)	0.002	7.4%

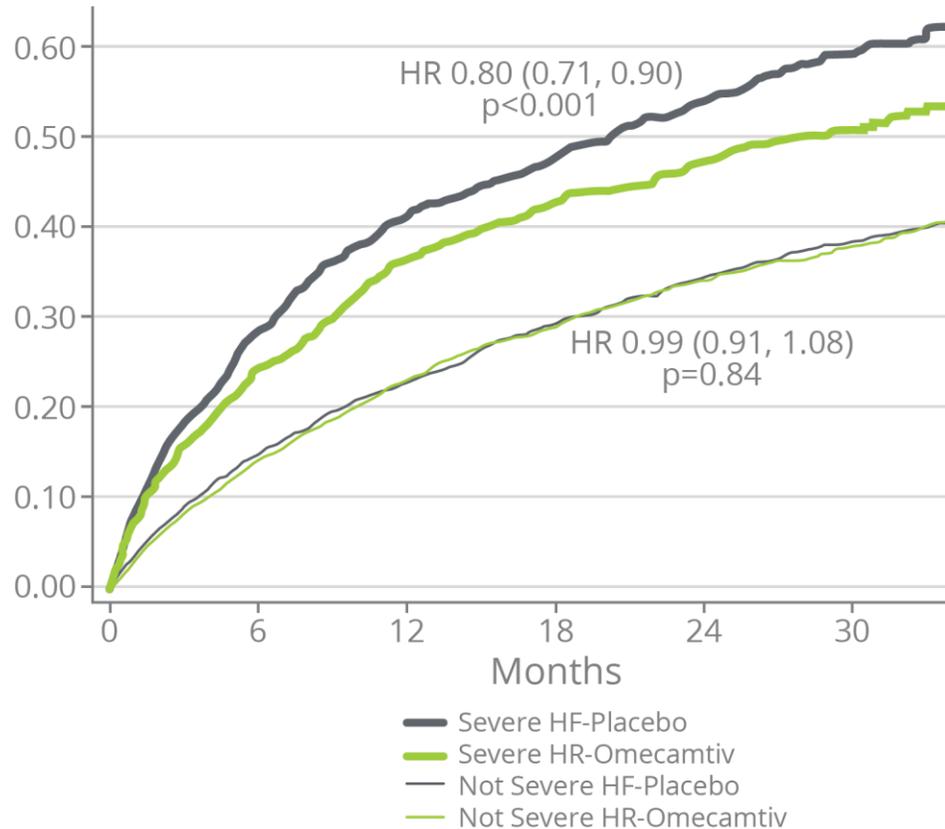
0.5      0.8      1.0      1.2  
 OM Better      ←      →      Placebo Better

# Increased Treatment Effect with Severe HF

Severe HF defined as NYHA III-IV, EF  $\leq$  30%, HF hospitalization in last 6 months



Heart Failure  
World Congress on  
Acute Heart Failure  
**2021**



Treatment effect for primary endpoint in severe HF

**HR = 0.80 (0.71, 0.90)**

Absolute risk reduction 8.3 events/100 pt-years

**NNT = 12**

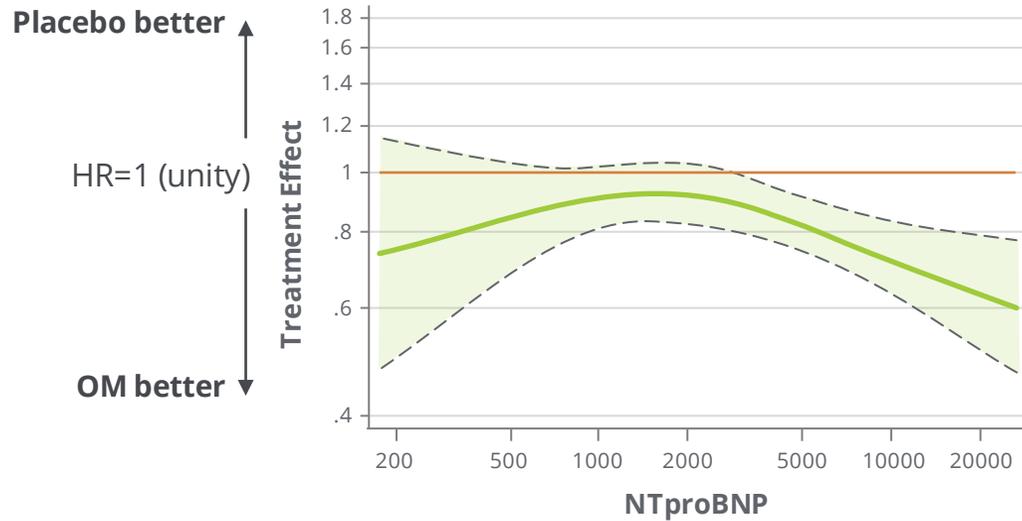
Source: Felker GM, Omecamtiv Mecarbil in Patients with Severe Heart Failure: An Analysis from GALACTIC-HF, ESC Heart Failure 2021, June 2021

# Increased Treatment Effect with Higher NT-proBNP

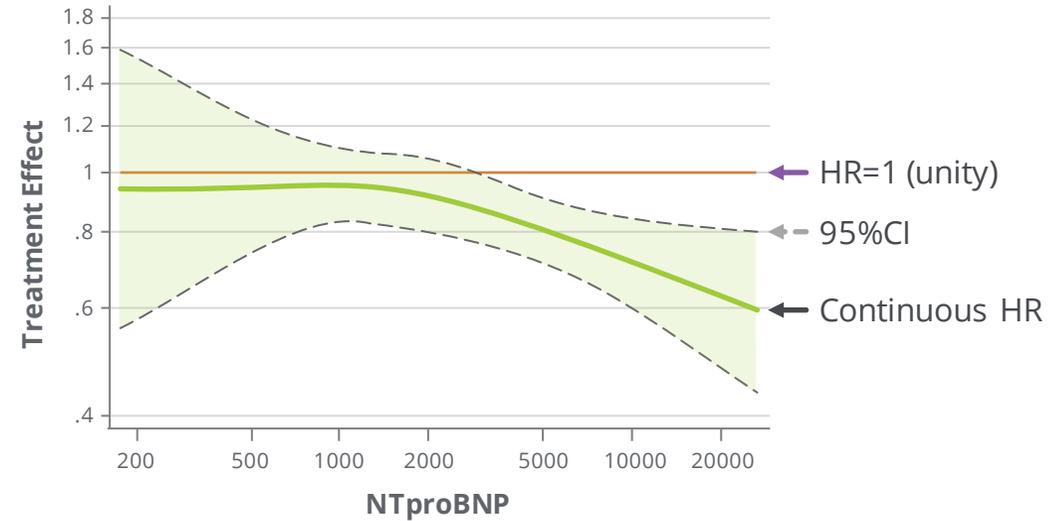


Heart Failure  
 & World Congress on  
 Acute Heart Failure 2021

Primary Composite Outcome

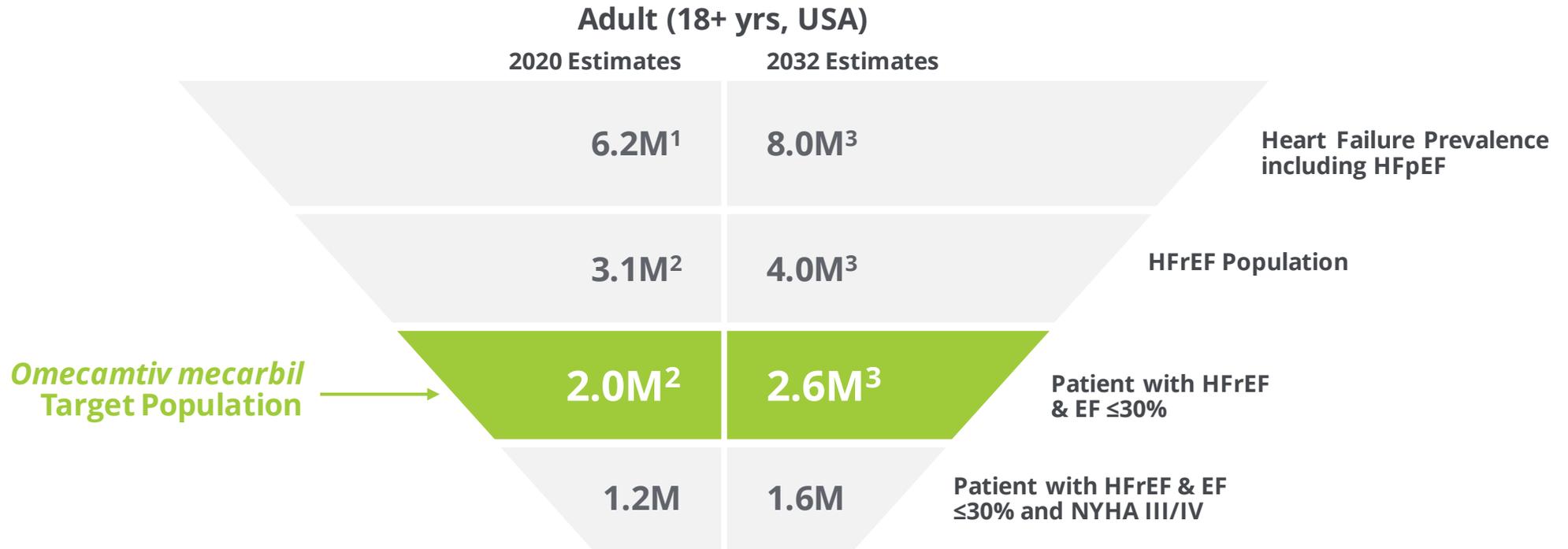


HF Hospitalization



Source: McMurray JM, Efficacy of omecamtiv mecarbil in HFrEF according to NT-proBNP level: Insights from the GALACTIC-HF trial, ESC Heart Failure 2021, June 2021

# Large Number of Patients At Potential US Launch Of *Omecamtiv Mecarbil*



**1.2 – 2.0M patients at potential launch**

1) National Center for Health Statistics. National Health and Nutrition Examination Survey (NHANES) as accessed 4/1/2019 at website. <https://www.cdc.gov/nchs/nhanes/>. – data from 2013-2016 as quotes in Benjamin 2019 Circulation. 2019;139:e56–e528.

DOI: 10.1161/

2) EF based on distribution as presented in Dunlay et al Circ Heart Fail. 2012;5:720-726,

3) 2.1% annual growth rate:1.9% annual growth rate of patient population 65+ (UN World Populations Prospects Nov 2019) and a 0.2% mortality impact of HF treatment (doi: 10.1136/bmj.l223 | BMJ 2019;364:l223)

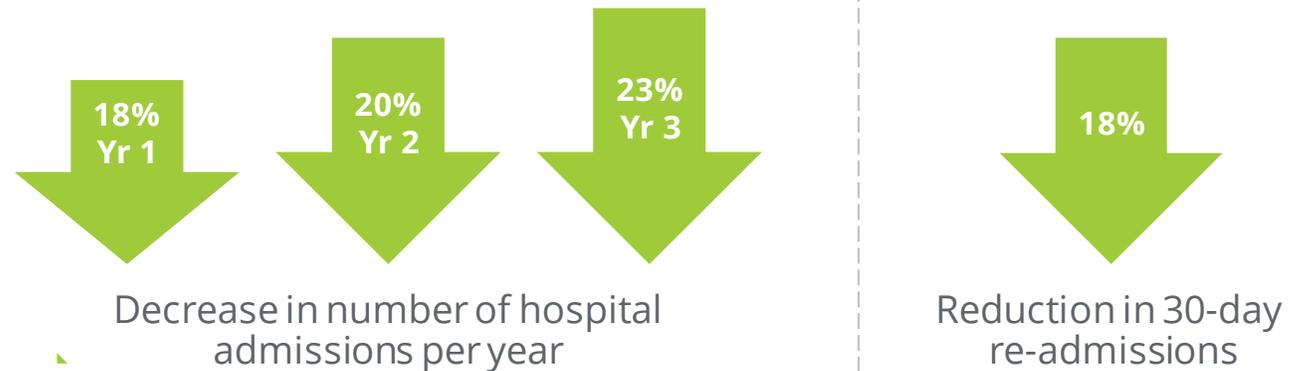
# Potential to Offset Medicare Hospitalization Costs

Outcomes from GALACTIC-HF may translate into economic benefits to payers and IDNs

## Hospitalization drives cost for Medicare patients<sup>1</sup>

- Mean cost per HFrEF hospitalization: **\$10,735**
- Mean cost for 30-day post-hospitalization care: **\$7,060**
- **Total 30-day cost for HFrEF hospitalization & post-hospitalization care: \$17,795**

## Patients on *omecamtiv mecarbil* showed reductions in both hospital admissions and re-admissions<sup>2</sup>

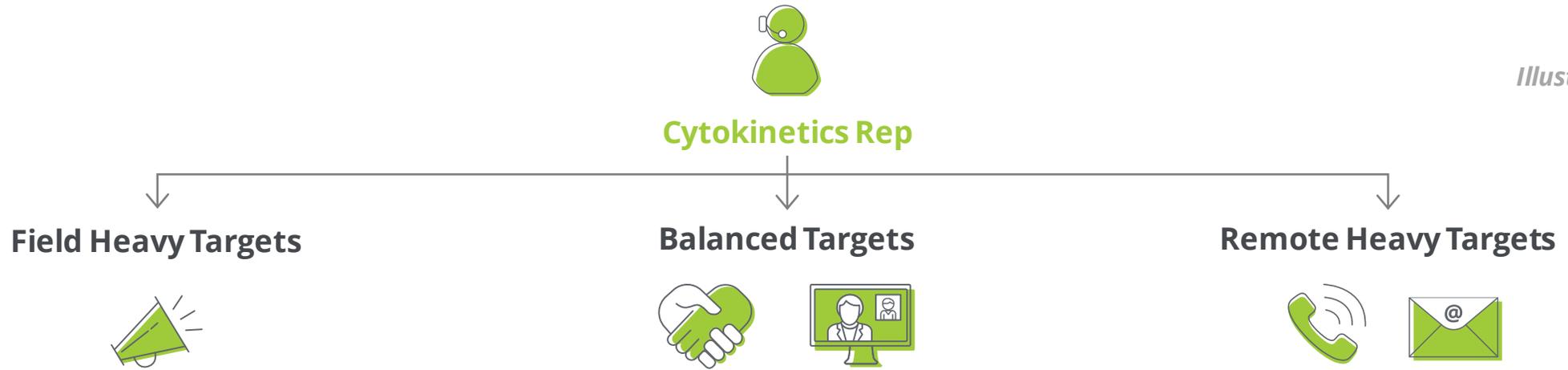


1. Desai et al, Yale University School of Medicine, AHA 2020; Congest Heart Fail. 2011 Jul-Aug; 17(4): 10.1111/j.1751-7133.2011.00246.x.

2. GALACTIC-HF

# Fit-for-Purpose Sales Team: Face-to-Face & Virtual Visits

Illustration

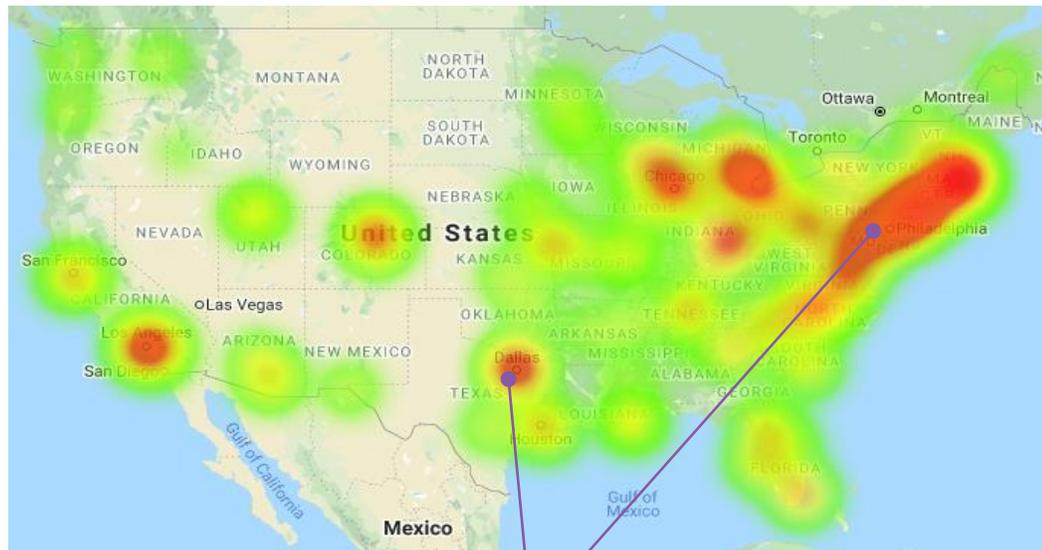


% of Face-to-Face Visits		
Heavy face-to-face	Mix of face-to-face and remote	Minimum face-to-face
Engagement Description		
Similar to traditional engagement – rep spends most of the time in face-to-face interaction	Hybrid engagement – mix of face-to-face and virtual visits to sequence interactions depending on customer needs and constraints. Remote resources deployed (i.e., samples, speakers, literature)	Dominant use of virtual platforms. Interaction is primarily over scheduled virtual visits or phone calls in response to office queries. Remote resources deployed (i.e., samples, speakers, literature)

Note: Sep'20 Access Monitor stats indicate the growing preference for face-face visits. Based on Access Monitor and Voice of Patient & Provider surveys

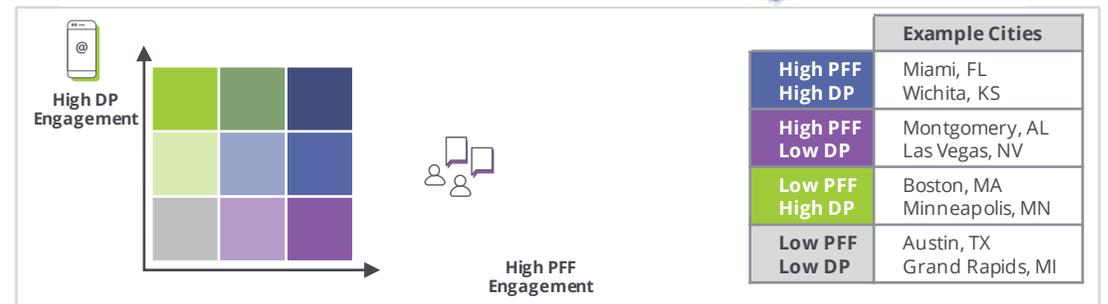
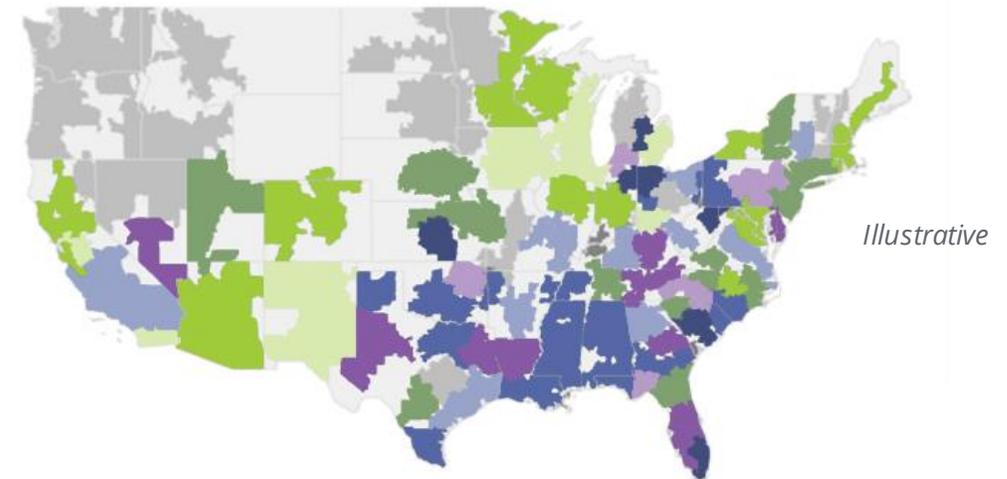
# Applied Analytics Will Inform Channel Mix and Deployment

## Patient and HCP Heat Map in HFReF



**Deploy to Hot Spots**

## Physician Engagement Type by Geography



Note: Based on 2020 cycle 1 AffinityMonitor™ metrics for LHMs; LHM engagement was considered to be the average engagement of rated HCPs within each LHMs; LHMs are ZS designed market which are homogeneous market within LHM boundaries

# Second Phase 3 Clinical Trial Underway

Investigating effect of *omecamtiv mecarbil* on exercise tolerance

Enrollment complete; results expected in 2H 2022

Primary Endpoint
Change in peak VO2 on CPET from baseline to Week 20
Second Endpoints
<ul style="list-style-type: none"> <li>Change in total workload during CPET from baseline to Week 20</li> <li>Change in ventilatory efficiency (VE/VCO2 slope) during CPET from baseline to Week 20</li> <li>Change in average daily activity units measured over 2 weeks from baseline to Week 18-20 by accelerometry</li> </ul>

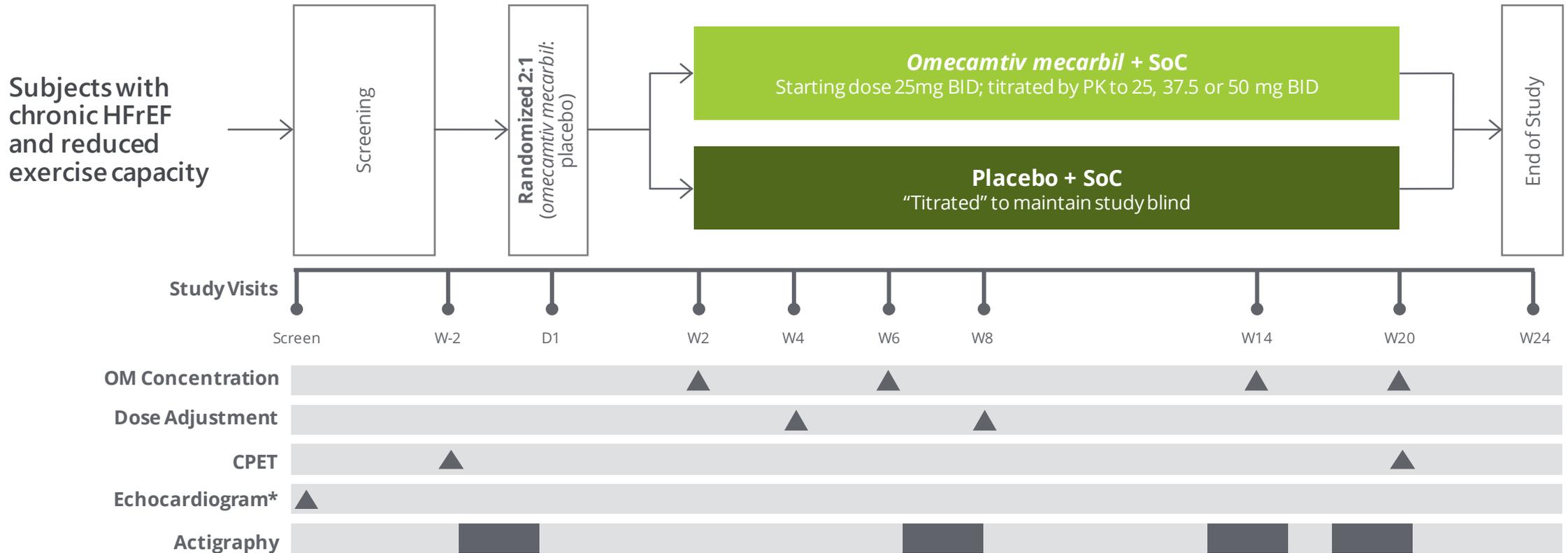
Study Plan	
Total Countries Planned	9
Active Countries	4
Total Sites Planned	92
Activated Sites	69
Total Patients Planned	270

### 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

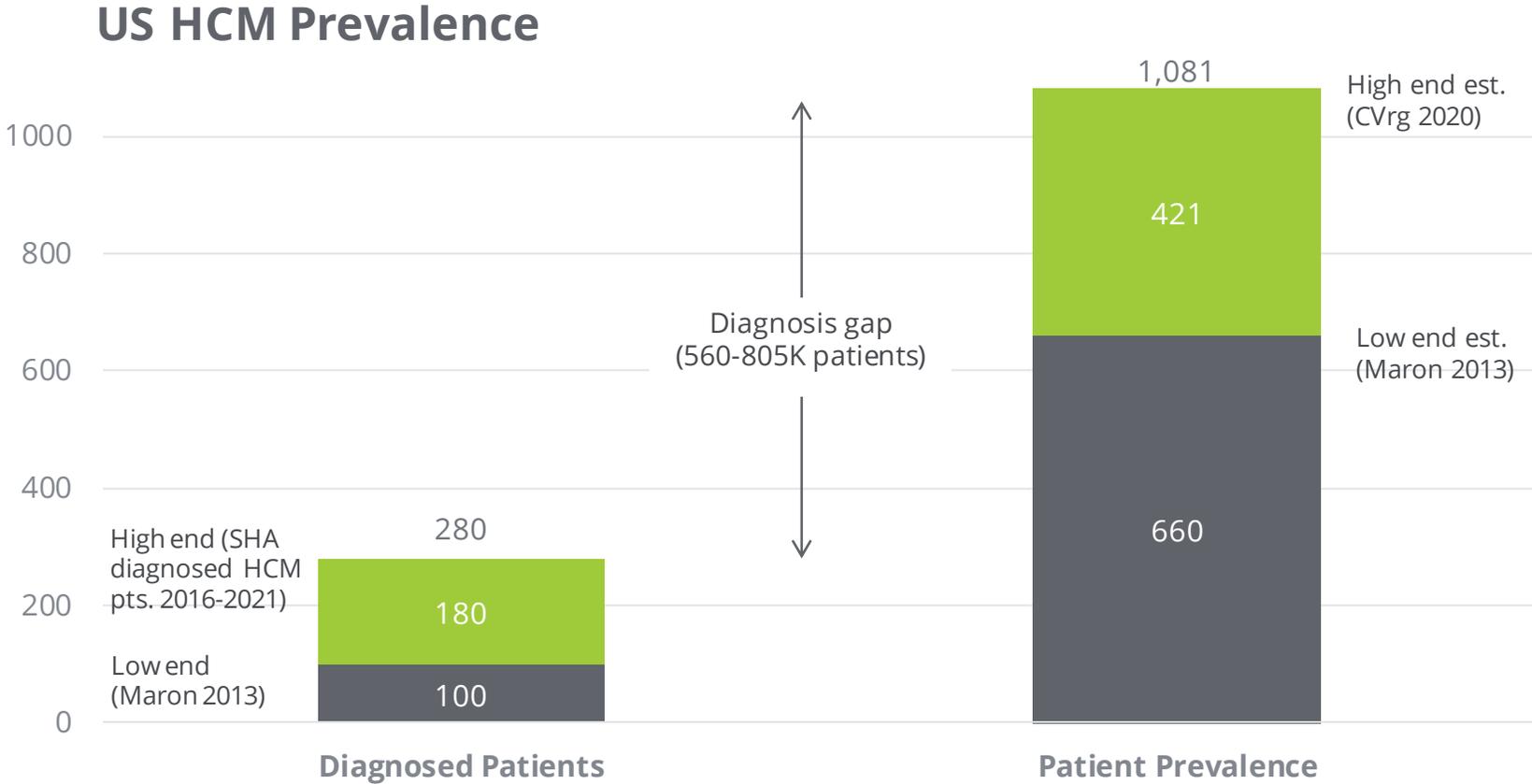
# Clinical Trial Overview



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

# ***Aficamten***

# Symptomatic HCM: Orphan Indication



Source: #26 SHA 2016-2021 Patient Claims Data; #20 Cogent HC 2020 DoF

# Significant Unmet Need in HCM

## Current therapies do not target underlying disease



### HCM is an inherited cardiovascular disease

1 in 500 have genetic mutation  
1 in 3200 have HCM  
Subset of patients have progressive symptoms, atrial fibrillation, stroke, sudden death



### Surgical intervention not permanent solution

Invasive therapy to reduce septal thickness is effective  
Surgical myectomy or percutaneous ablation



### Current medical therapy does not target underlying disease

Indirect mechanisms of action with systemic side effects  
Variable efficacy, often inadequate

# Aficamten: Next-In-Class Cardiac Myosin Inhibitor

Potential treatment for patients with HCM

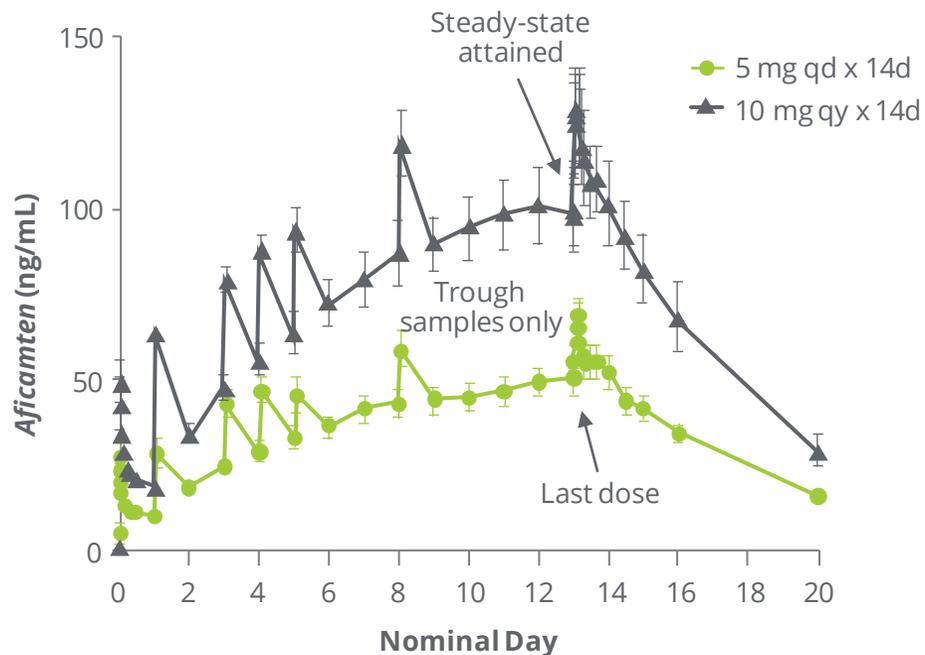


- Selective allosteric inhibitor of cardiac myosin discovered by company scientists independent of collaborations
- Potential *in vivo* pharmacodynamic advantages related to distinctive binding site
- Optimized for
  - Onset of action (reach steady state within two weeks)
  - Rapid reversibility of effect
  - Minimal drug-drug interactions
  - Favorable tolerability
  - Ease of titration for personalized dosing
- Clear pharmacokinetic/pharmacodynamic (PK/PD) relationship observed
- Shallow exposure-response relationship

# SAD & MAD Results Support Progression to Phase 2

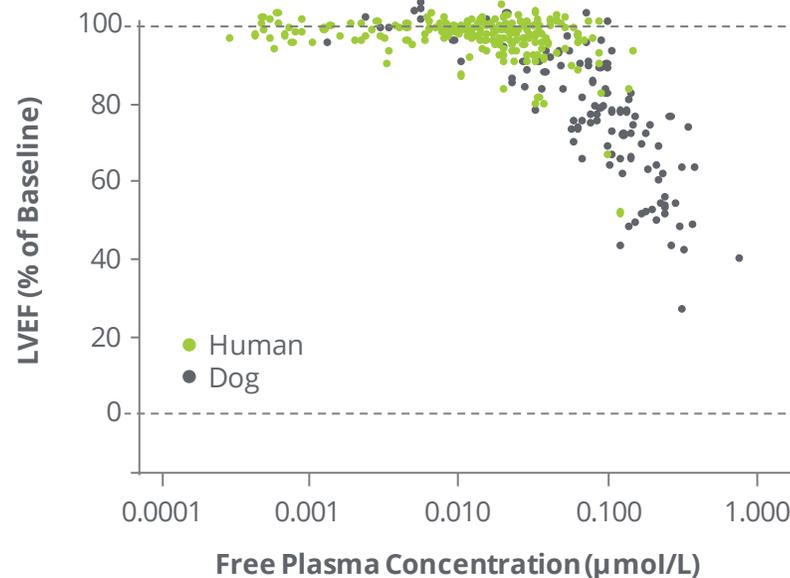
## Preclinical data translated to healthy participants

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



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

#### PK/PD Relationship of *Aficamten* for Ejection Fraction (LVEF)



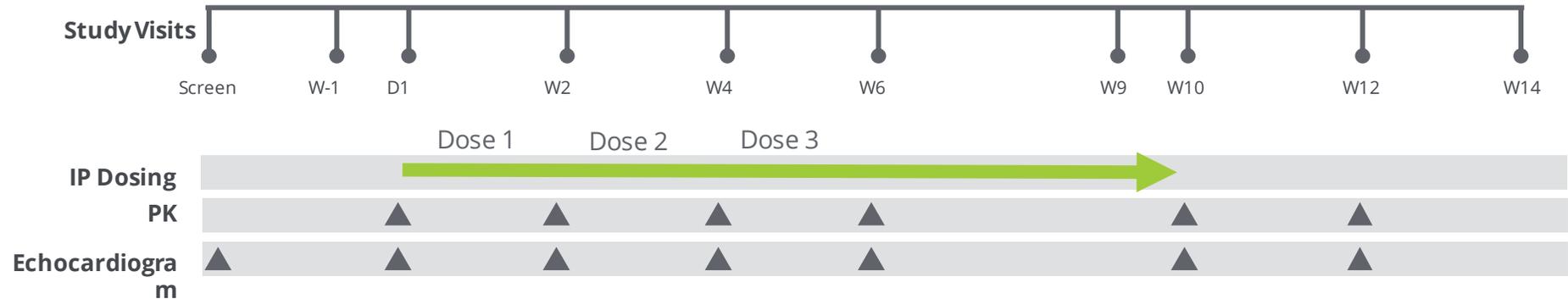
Graphs show LVEF as a function of exposure; data points represent observed values in dogs and humans.

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

# Phase 2 Clinical Trial Design



Two sequential dose-finding cohorts (with third cohort assessing patients on *disopyramide*)



	Dose 1	Dose 2	Dose 3
<b>Cohort 1</b>	5 mg	10 mg	15 mg
<b>Cohort 2</b>	10 mg	20 mg	30 mg

# Patient Enrollment and Dosing



41 Total Enrolled Patients

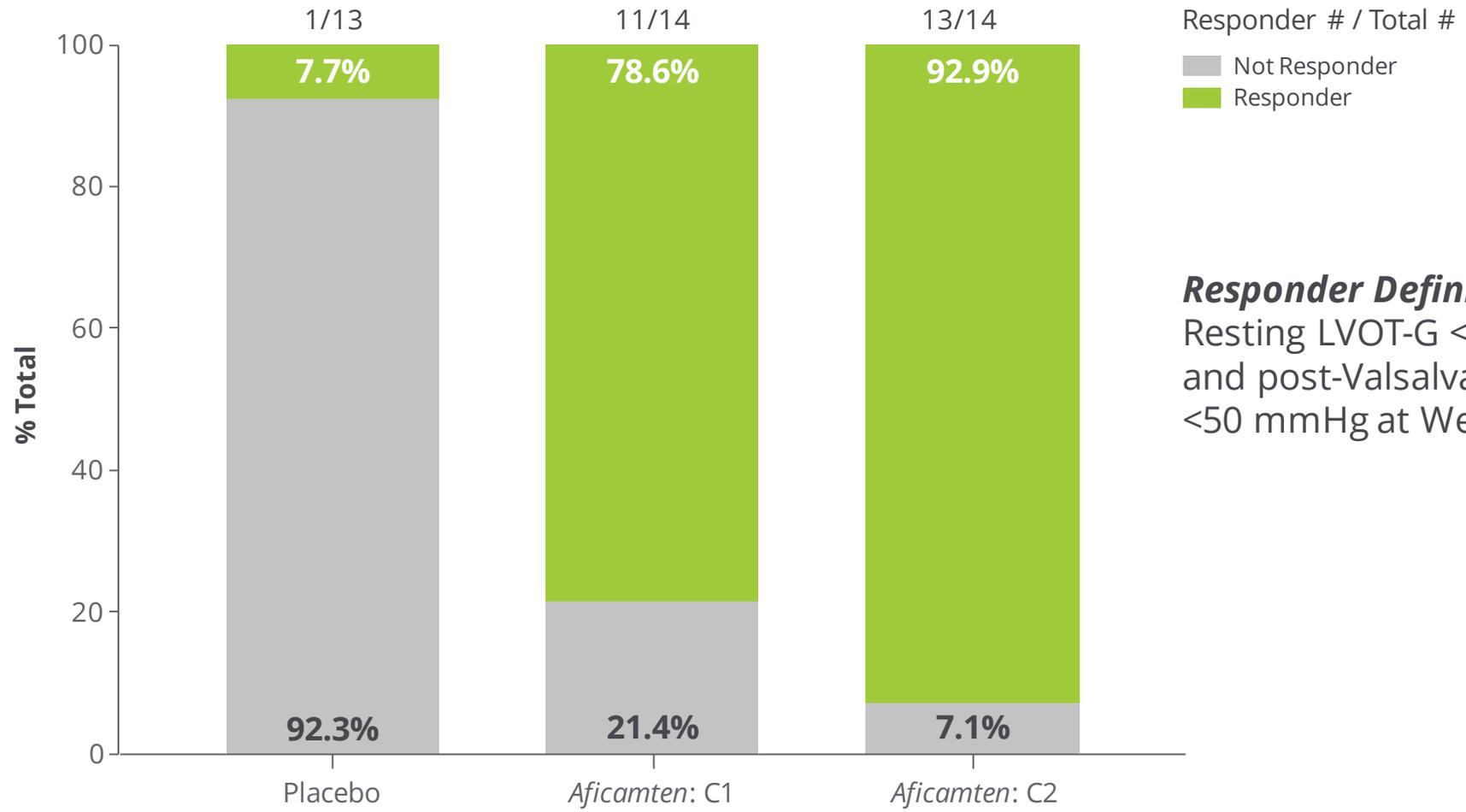
Final Dose Achieved (N)						
	Cohort 1			Cohort 2		
Placebo	5 mg	10 mg	15 mg	10 mg	20 mg	30 mg
13	4	5	5	9	4	1

# Baseline Echocardiographic Data



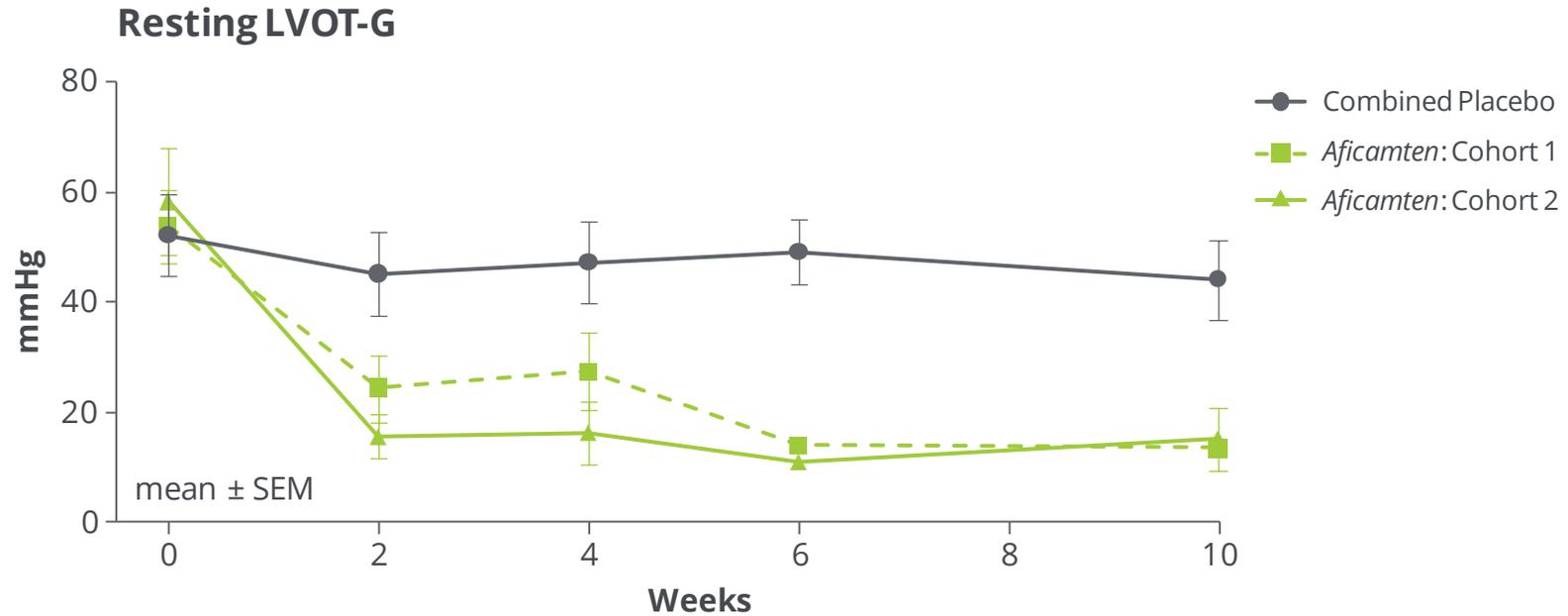
Characteristic, mean	Baseline (Day 1 Pre-dose)		
	Placebo C1 + C2 Combined (N = 13)	<i>Aficamten</i>	
		Cohort 1 (N = 14)	Cohort 2 (N = 14)
LVEF (%)	74.5	73.2	75.4
LVOT-G, Rest (mmHg)	52.1	53.8	58.2
LVOT-G, Valsalva (mmHg)	84.6	74.4	82.3

# High Response Rates on Treatment with *Aficamten*



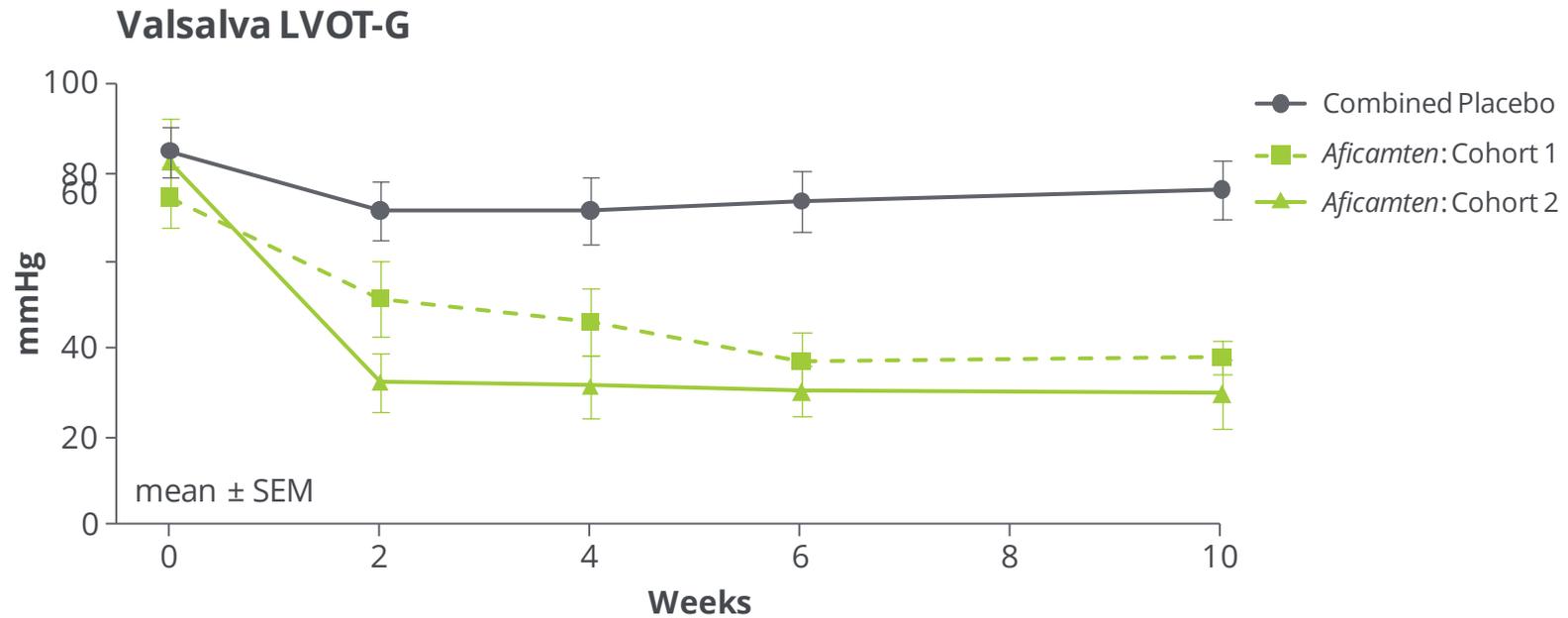
**Responder Definition:**  
Resting LVOT-G <30 mmHg  
and post-Valsalva LVOT-G  
<50 mmHg at Week 10

# Resting Left Ventricular Outflow Tract Gradient



Mean ± SEM	Valsalva LVOT-G (mmHg)				
	Baseline	Week 2	Week 4	Week 6	Week 10
Placebo (n=13)	52.1	45.0	47.1	49.0	44.0
Cohort 1 (n = 14)	53.8	24.3	27.3	13.9	13.4
p-value vs placebo	-	0.007	0.025	<0.0001	0.0003
Cohort 2 (n = 14)	58.2	15.5	16.1	10.9	15.1
p-value vs placebo	-	0.0002	0.0006	<0.0001	0.0004

# Post-Valsalva Left Ventricular Outflow Tract Gradient



Mean ± SEM	Valsalva LVOT-G (mmHg)				
	Baseline	Week 2	Week 4	Week 6	Week 10
Placebo (n=13)	84.6	71.3	71.3	73.4	76
Cohort 1 (n = 14)	74.4	51.3	46.1	37.1	38.1
p-value vs placebo	-	0.097	0.038	0.0003	0.001
Cohort 2 (n = 14)	82.3	32.3	31.5	30.3	29.8
p-value vs placebo	-	0.0005	0.0005	<0.0001	<0.0001

# Safety Data



- Incidence of adverse events on *aficamten* similar to placebo and mild or moderate
- There were no treatment related serious adverse events reported by investigators
- No patients who received *aficamten* in Cohort 1 had an LVEF <50%
- In Cohort 2, one patient with LVEF at baseline of 58% was up titrated to 20 mg and experienced transient LVEF reduction to <50% (remaining above 40%) requiring down titration
- No interruptions or discontinuations of treatment with *aficamten* occurred across both cohorts

# Open Label Extension Trial



REDWOOD-HCM OLE open for eligible patients who completed REDWOOD-HCM

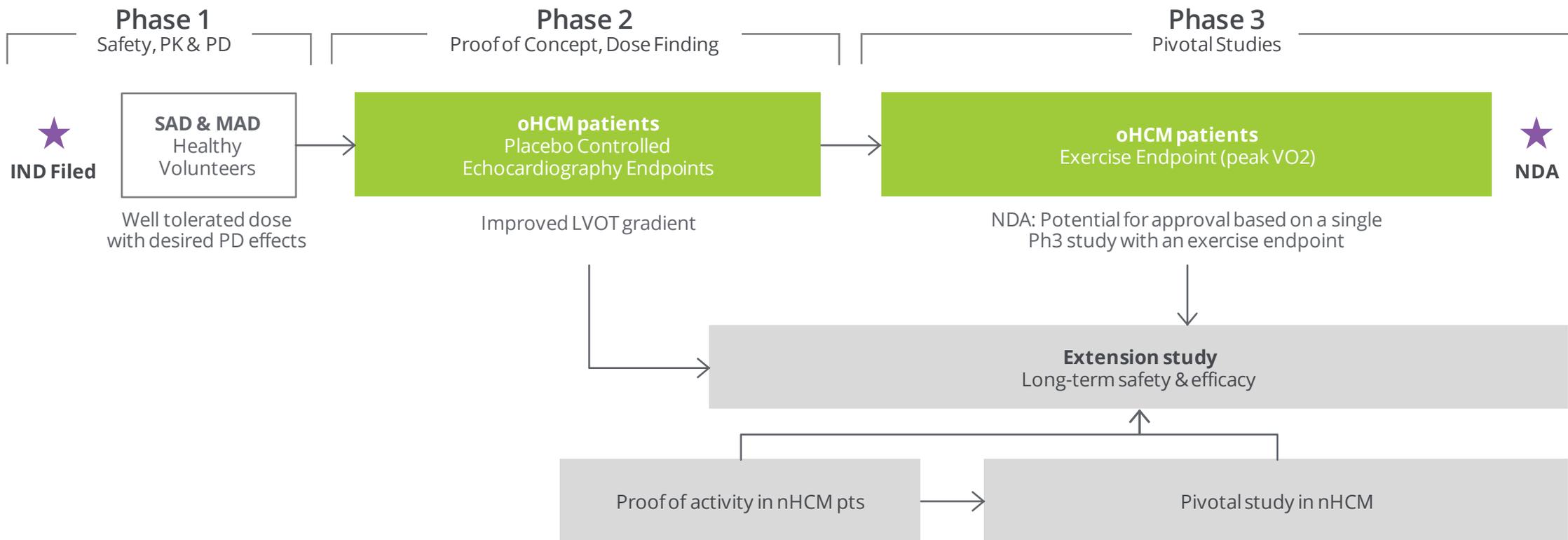
- Primary endpoint: incidence of AEs & LVEF <50
- Secondary endpoints: measures of long-term effects of *aficamten* on LVOT-G; assessments of steady-state pharmacokinetics.
  - Cardiac MRI sub-study to assess changes in cardiac morphology, function and fibrosis
- Individually optimized dose starts at lowest dose in prespecified range with echo-guided dose titration
- Initial dose and highest target dose informed by interim analyses from REDWOOD-HCM

**OLE:** Escalating doses based on echo-guided dose titration

# Aficamten: Clinical Development Plan for HCM

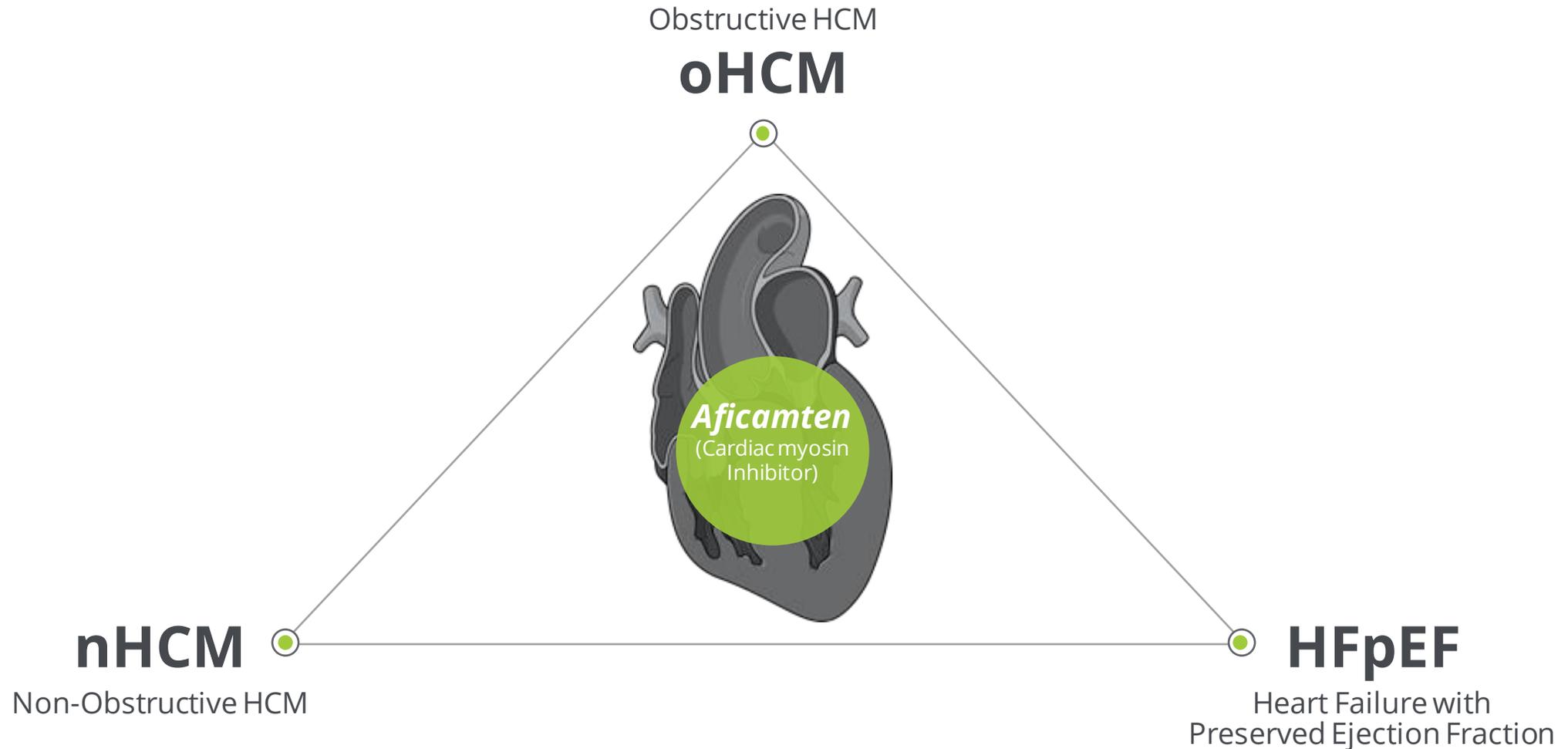
## Engaging regulatory authorities to inform Phase 3

Type C meeting with FDA to review Phase 3 design; End-of-Phase 2 meeting to review dose selection rationale for Phase 3



# Novel Approach May Address Multiple Unmet Patient Needs

**No FDA-approved therapies**



# Aficamten: 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 *aficamten* in China, subject to royalties and up to \$200M in milestone payments

RTW Investments purchased equity and royalty; provides access to capital for development of *aficamten*

#### Ji Xing Pharma

Ji Xing to develop & commercialize *aficamten* in Greater China & Taiwan

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

#### RTW: Funding for Development of *Aficamten*

Cytokinetics receives options for additional funding for further development of *aficamten* 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 *aficamten* in U.S. & certain European countries, subject to royalty reductions for potential other indications

#### RTW: Other Purchases

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

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

# Building Synergistic Commercial Capabilities

## Building Today...

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

- 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



**6,000+**

Hospitals and  
CoEs in US



**1,100**

Highest Value  
Hospitals & CoEs



**~75% HFrEF Patients**

**~78% HCM Patients**

IQVIA HPD - Q3'18 - Q2'19

*Sarcomere Directed Drug Development*

# **SKELETAL MUSCLE**

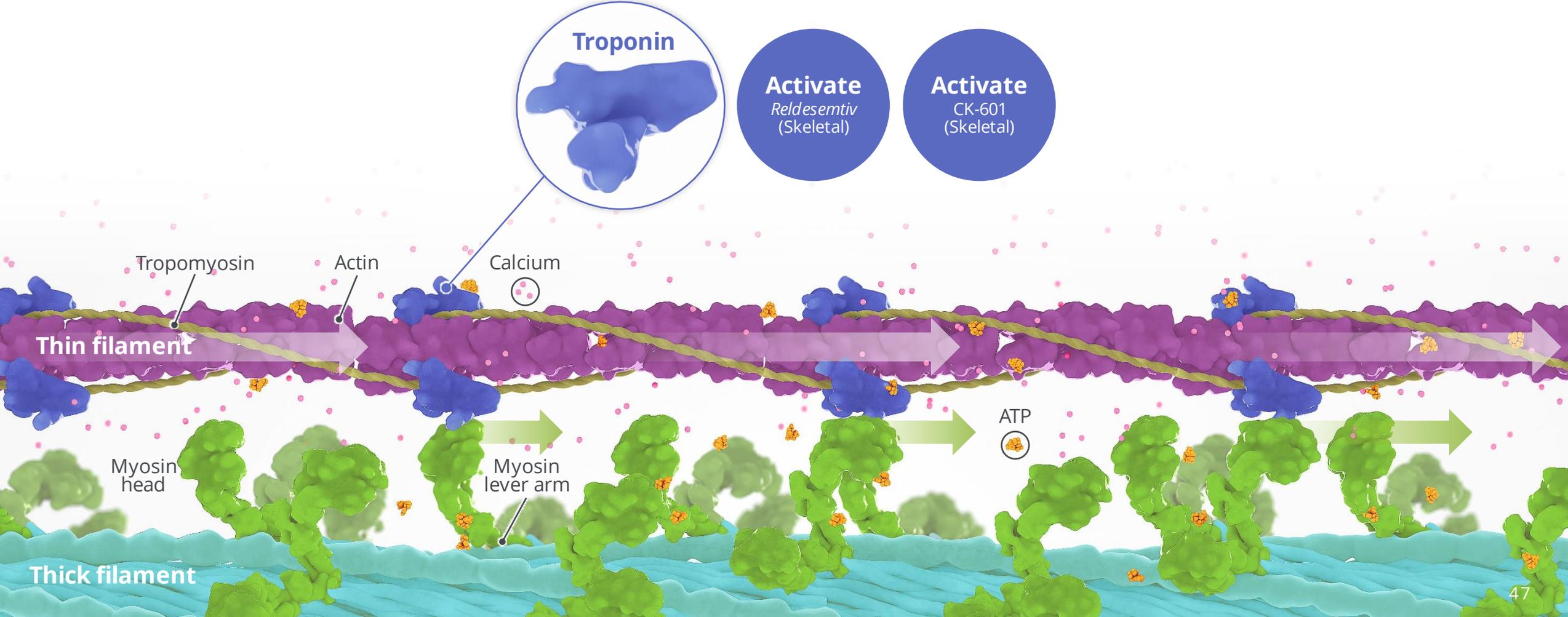
*Reldesemtiv*

CK-601

# Sarcomere Directed Drug Development

## Skeletal muscle

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

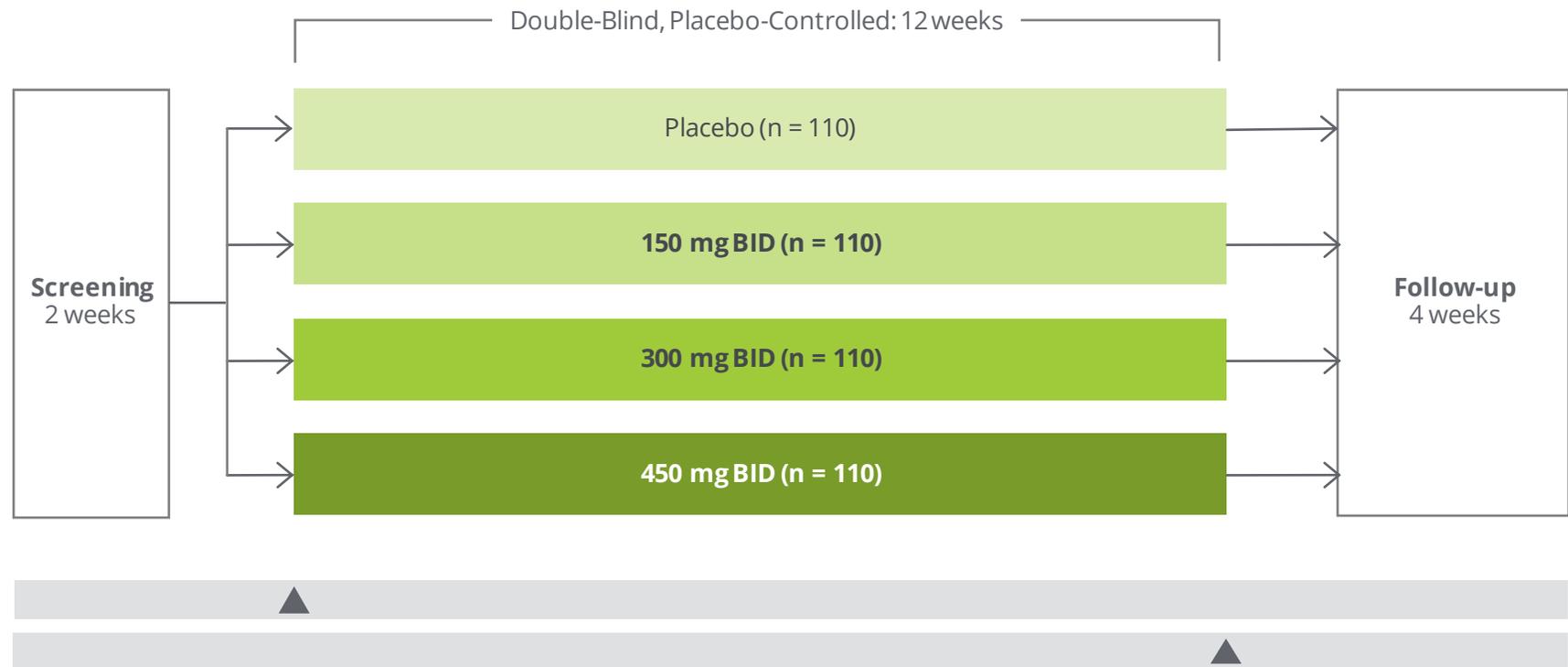


# ***Reldesemtiv***

# Phase 2 Clinical Trial in ALS

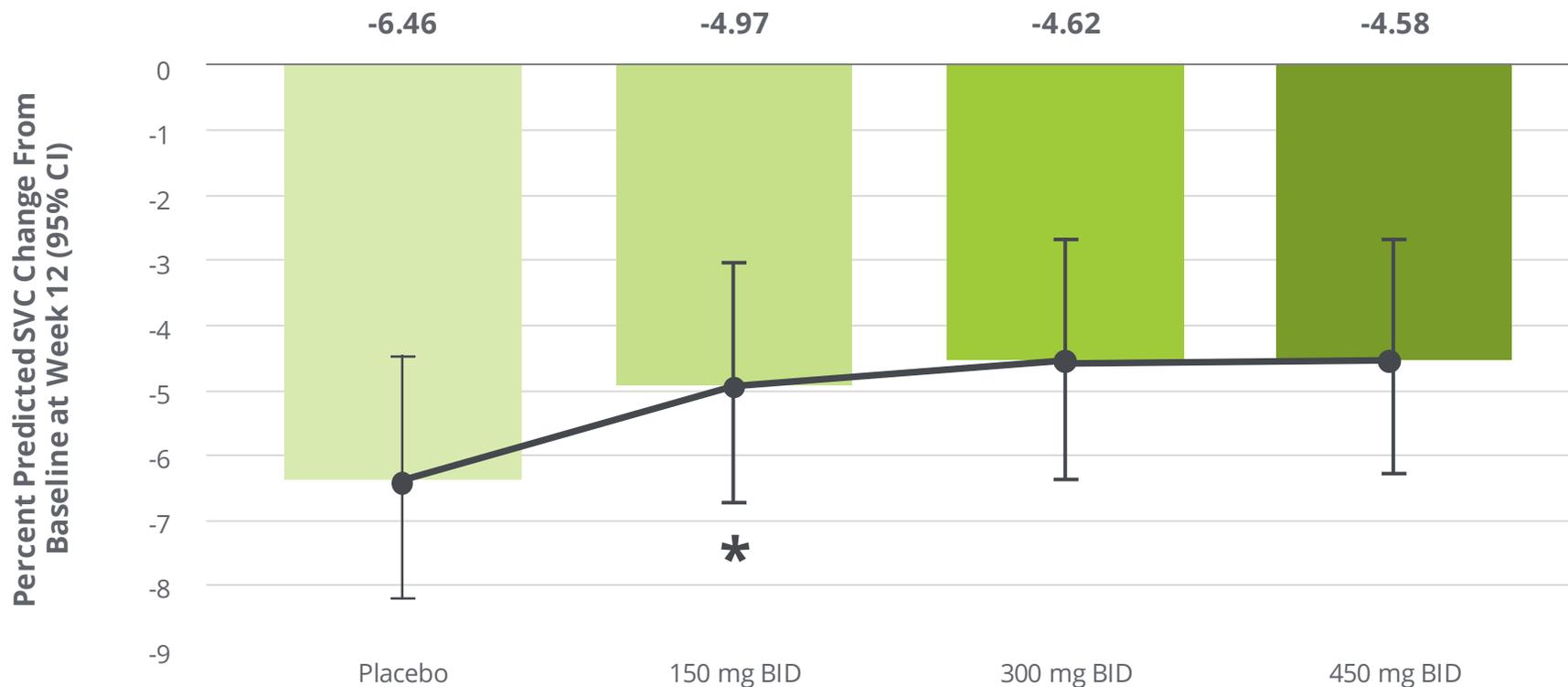
Results presented at American Academy of Neurology 2019

Parallel group, dose ranging study enrolled 458 patients with ALS in the US, Canada, Australia and Europe evaluating change from baseline in the percent predicted slow vital capacity (SVC) at 12 weeks of treatment with *reldesemtiv* or placebo



# Primary Endpoint: SVC

## Change from baseline in percent predicted SVC at week 12



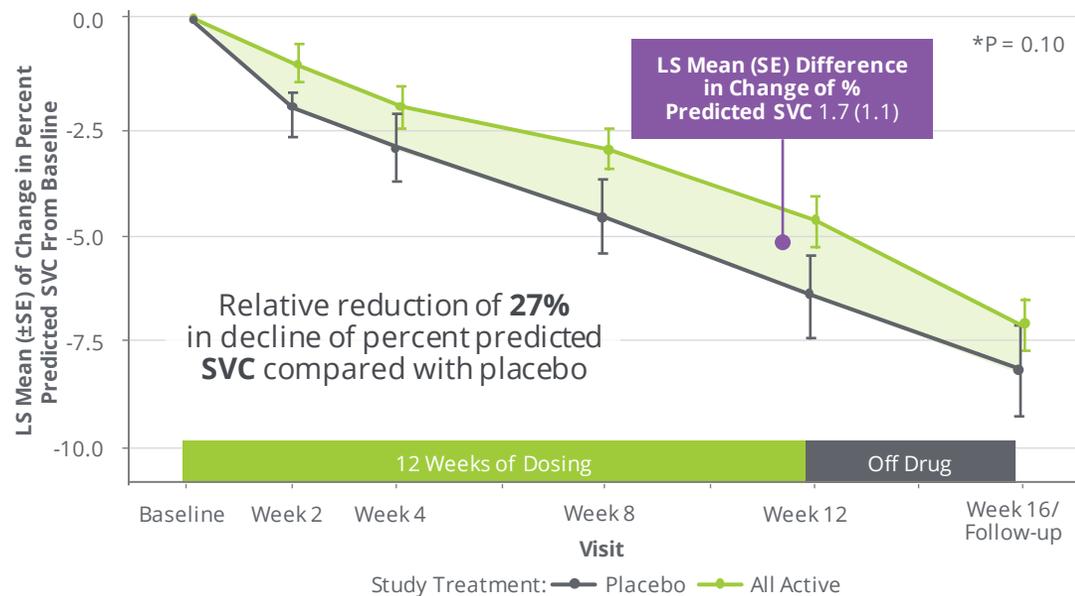
**Primary Analysis\***  
P = 0.11  
for weighted  
dose-response  
relationship

\*Based on Mixed Model for Repeated Measures (MMRM) with the contrasts of (-5, -1, 3, 3) for placebo, *reldesemtiv* 150 mg, 300 mg and 450 mg BID, respectively

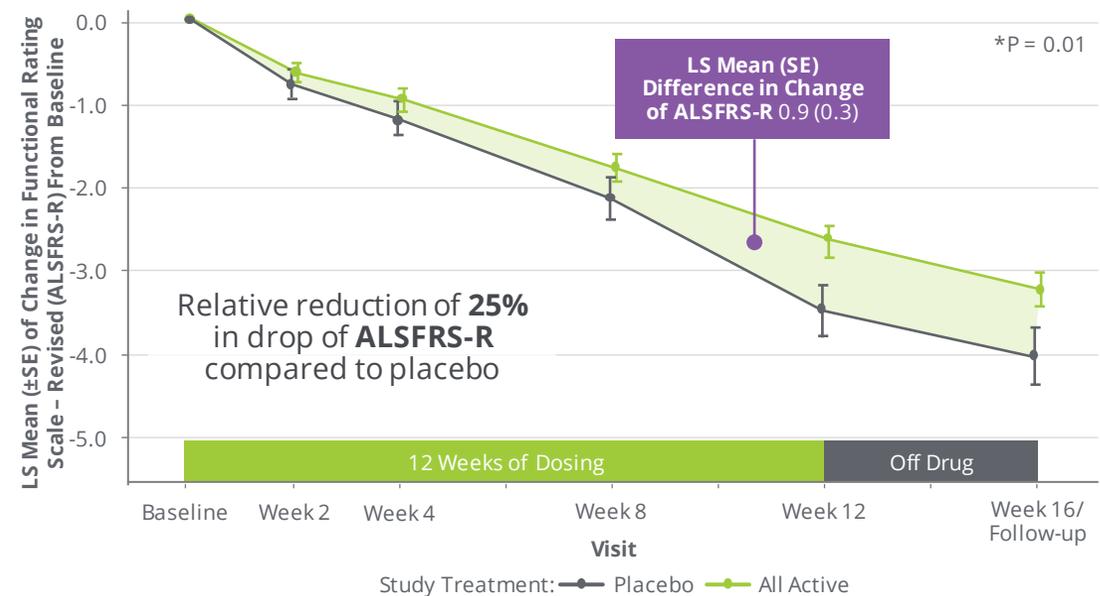
# Change From Baseline: All Active vs Placebo\*

Results support progression to potential Phase 3 clinical trial

### SVC Change From Baseline (All Active vs Placebo)



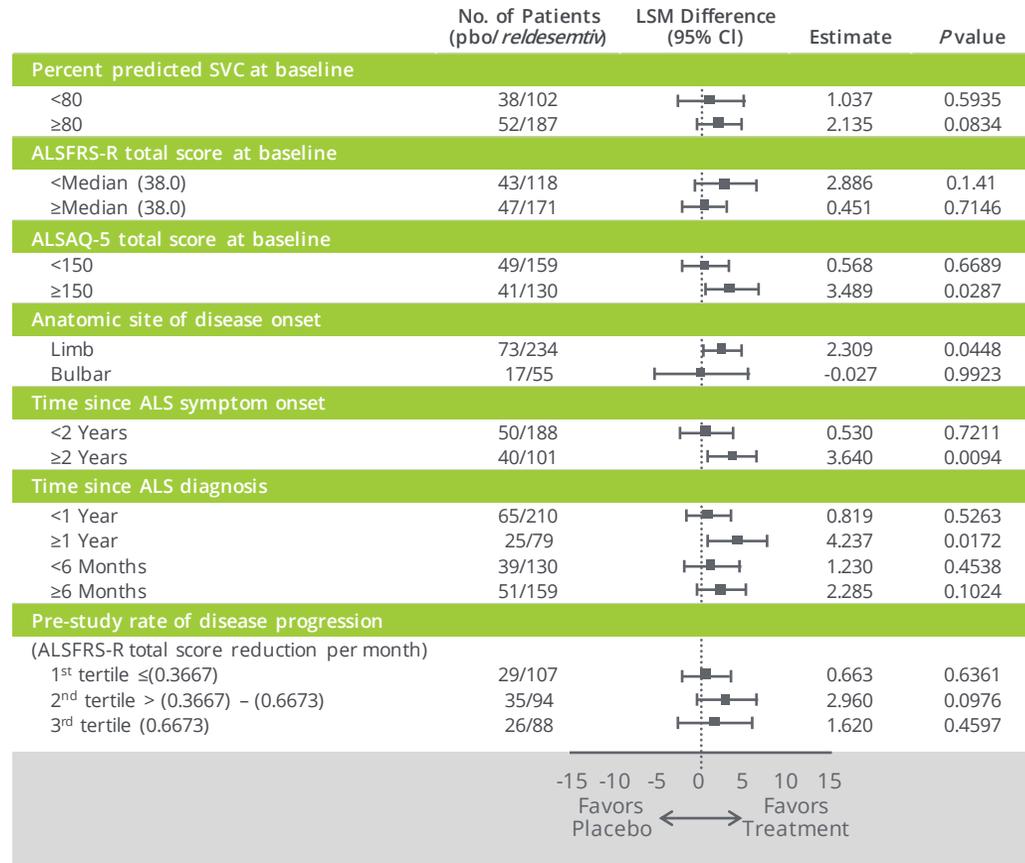
### ALSFRS-R Change From Baseline (All Active vs Placebo)



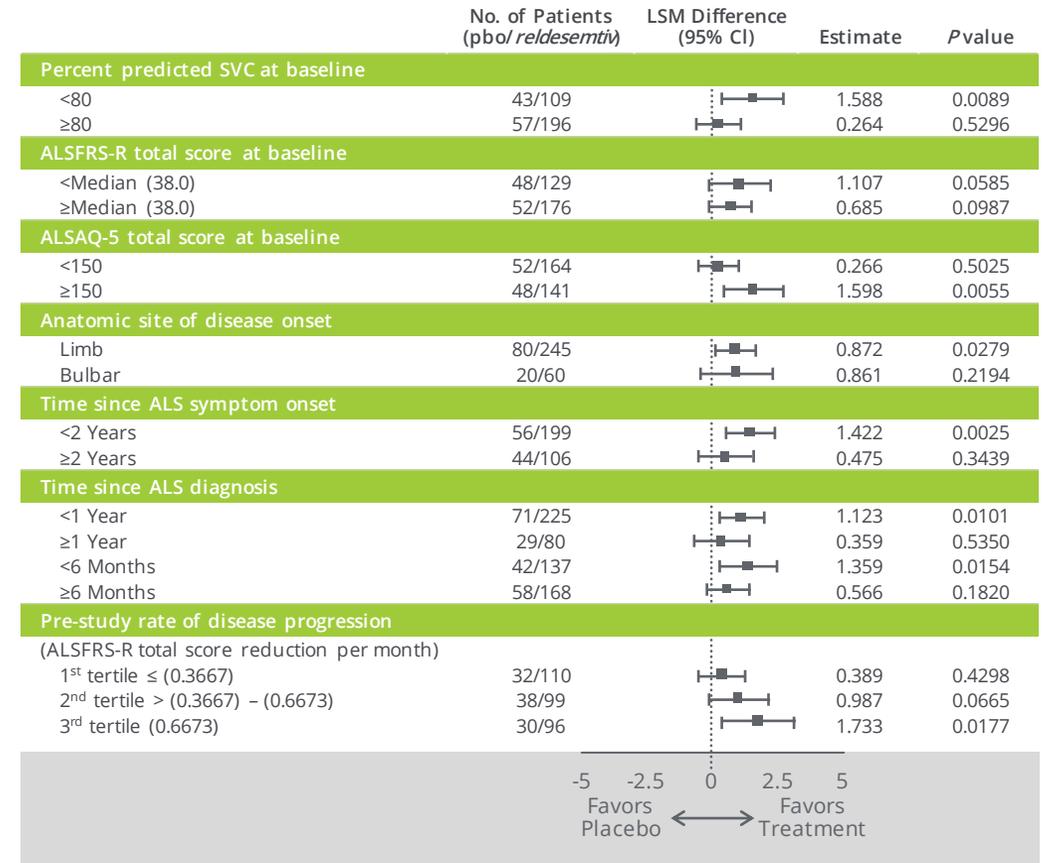
\*post hoc analysis  
FORTITUDE-ALS did not achieve statistical significance, but patients on all dose groups of *reldecentiv* declined less than patients on placebo

# Subgroup Analyses\*

## Percent Predicted SVC



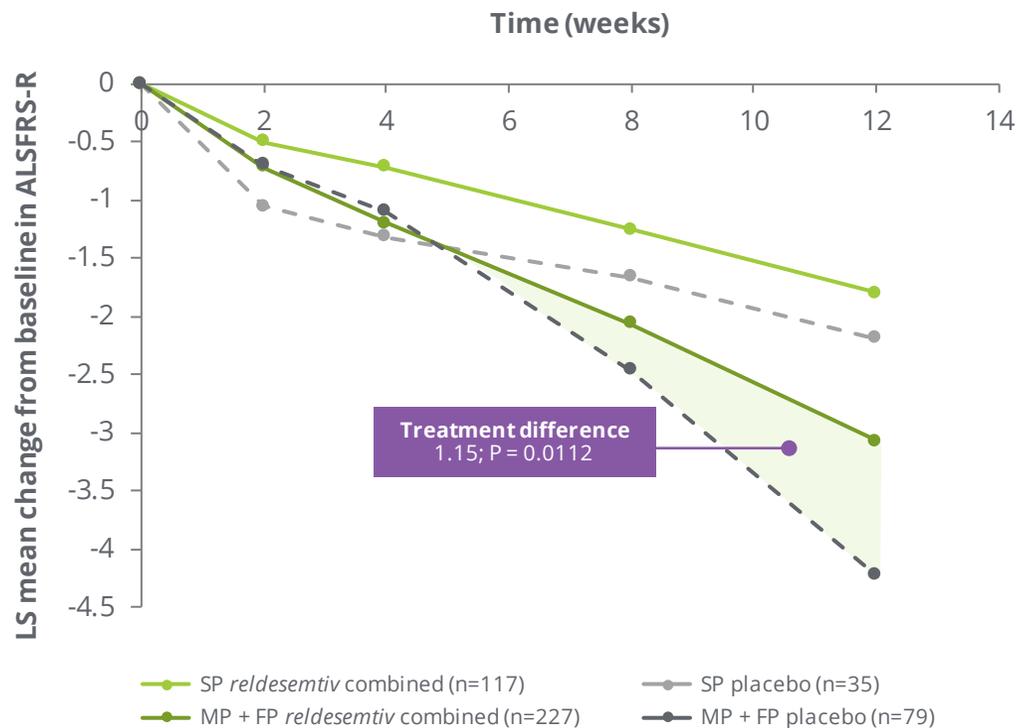
## ALSFERS-R Total Score



\*FORTITUDE-ALS did not achieve statistical significance, but patients on all dose groups of *reldesemtiv* declined less than patients on placebo

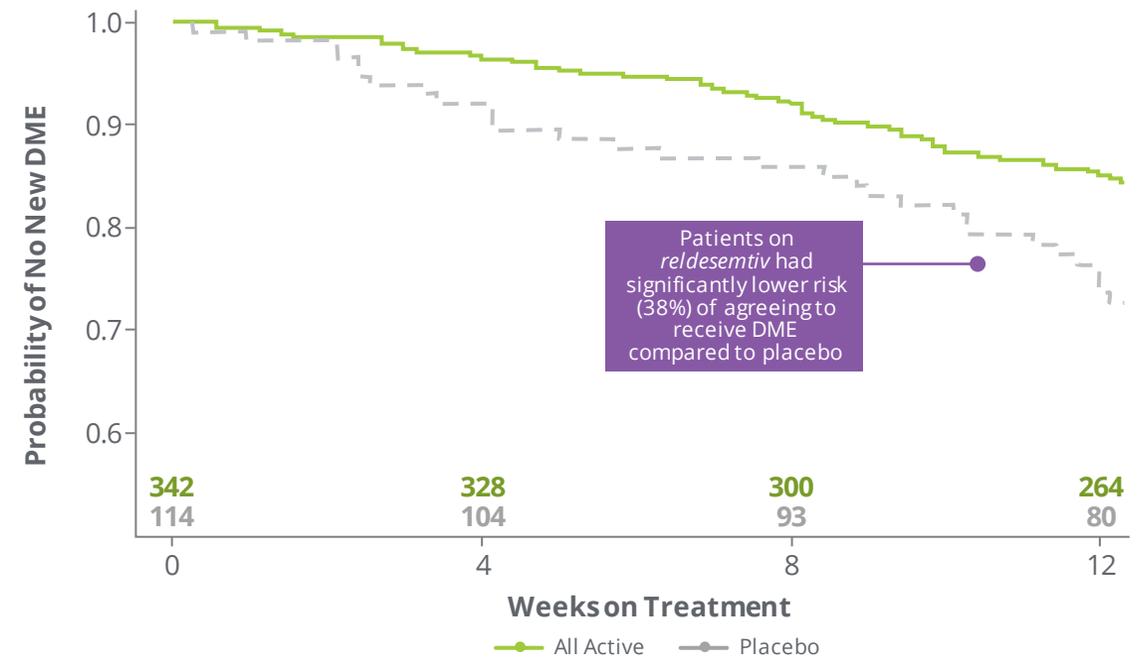
# Post-Hoc Analyses Inform Potential Path Forward

## Change From Baseline in ALSFRS-R by Progressor Tertiles



## Probability of No New DME\* Over Time With Treatment With *Reldesemtiv*

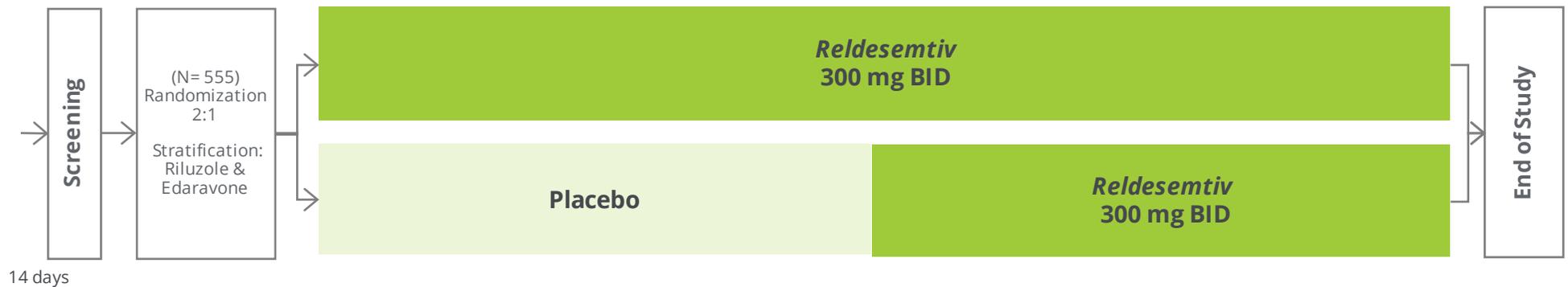
DME (Durable Medical Equipment): Manual wheelchair, power wheelchair, NIV, Augmentative Language Device, PEG



# Planned Phase 3 Clinical Trial Design

Trial to open for enrollment in 2021

Enrolling 555 patients with ALS in the US, Canada, Australia and Europe evaluating change from baseline ALSFRS-R at 24 weeks of treatment with *reldesemtiv* or placebo



Study Visits	Screen	D1	W2	W4	W8	W12	W16	W20	W24	W26	W28	W32	W36	W40	W44	W48	W52 FU
ALSFRS-R	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑
FVC	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑
Lab	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑
Muscle Strength	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑

↑ In-Clinic    ↑ Remote    ↑ Both In-Clinic & Remote

*Sarcomere Directed Therapies*

# **CORPORATE PROFILE**

# Robust Pipeline, Solid Financial Position

<b>Pipeline*</b>	<b>1</b> Positive trial readout in 2021	<b>2</b> Pivotal trials in 2021	<b>3</b> Potential FDA approvals by 2025	<b>5</b> Clinical stage programs	<b>10</b> Development programs by 2025
<b>Programs*</b>	<b>Heart Failure</b> <i>Omecamtiv mecarbil</i> <ul style="list-style-type: none"> <li>Positive trial results from GALACTIC-HF</li> <li>Phase 3 exercise capacity trial results early 2022</li> </ul>	 <b>CK-136</b> <ul style="list-style-type: none"> <li>Phase 1</li> </ul>	<b>HCM</b> <i>Aficamten</i> <ul style="list-style-type: none"> <li>Positive results from REDWOOD-HCM</li> <li>Expect to begin Phase 3 trial by Q4</li> </ul>	<b>ALS</b> <i>Reldesemtiv</i> <ul style="list-style-type: none"> <li>COURAGE-ALS, Phase 3 trial ongoing</li> </ul>	<b>Ongoing R&amp;D</b>  <p>Additional research in muscle biology, energetics &amp; metabolism</p>
<b>Foundations</b>	 <b>214</b> Full time employees		<b>\$424M*</b> At Q2 2021		

\* In July 2021, Cytokinetics raised \$275 million through a public offering of common stock. Timelines and milestones reflect Cytokinetics' current expectations and beliefs

# Cytokinetics Financing History

As of 6/30/2021, with proceeds from 7/23/21 offering

*in millions*

	<i>As of 6/30/2021</i>	<b>Financing</b>	<b>Equity</b>	<b>Upfront Cash, Option, &amp; Milestones Reimbursement</b>	<b>R&amp;D</b>	<b>Total</b>
<b>Investors</b>	Private Investors (VCs)		\$116			\$116
	IPO		\$94			\$94
	Public Post-IPO/Other		\$906			\$906
	Term Loan	\$45				\$45
	Convertible Debt (net)*	\$120.5				\$120.5
			<b>\$165.5</b>	<b>\$1,116</b>		
<b>Strategic Partners &amp; Grants</b>	RTW/Ji Xing		\$50	\$113		\$163
	Astellas		\$10	\$130	\$103	\$243
	Amgen		\$43	\$145	\$60	\$248
	Royalty Pharma		\$10	\$90	-	\$100
	GSK		\$24	\$22	\$33	\$79
	AstraZeneca		-	-	\$2	\$2
	MyoKardia		-	-	\$2	\$2
	Global Blood		-	-	\$2	\$2
	Grants (ALS Assoc/NINDS/other)		-	\$6	-	\$6
				<b>\$137</b>	<b>\$506</b>	<b>\$202</b>

Capital raised:  
combination of  
strategic partners  
and investors

\*Net of fees and expenses, and Capped Call costs

# Balance Sheet & Financial Guidance

Cash plus financing gives 3+ years cash runway based on 2021 updated guidance

## 2021 Condensed Balance Sheet

As of 6/30/2021

	<i>in millions</i>
	<b>Total</b>
Cash and investments	\$424.0
Leased assets	\$83.0
Other assets	\$57.3
<b>Total Assets</b>	<b>\$564.3</b>
Debt	\$134.0
Liability related to sale of future royalties	\$171.8
Deferred Revenue	\$87.0
Lease liability	\$111.6
Other liabilities	\$43.4
<b>Total Liabilities</b>	<b>\$547.8</b>
Working capital	\$302.5
Accumulated deficit	(\$1,101.0)
Stockholders' equity	\$16.4
<b>Wtd Avg Basic Shares Outstanding</b>	<b>71.2</b>

## 2021 Financial Guidance

	<i>in millions</i>
	<b>Total</b>
Cash Revenue	\$23 – 28
Cash Operating Expenses	\$230 – 250
<b>Net</b>	<b>~\$195-215</b>

# Expected Upcoming 2021 Milestones

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Submit US NDA for *omecamtiv mecarbil* in 2H 2021

Expect to Begin **Phase 3 Trial of Aficamten** by Q4

Expect to complete **METEORIC-HF** by year end

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Cytokinetics

*Sarcomere Directed Therapies*

**THANK  
YOU**



*John, diagnosed with heart failure*



*Jillian, diagnosed with HCM*



*Chuck, diagnosed with ALS*