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

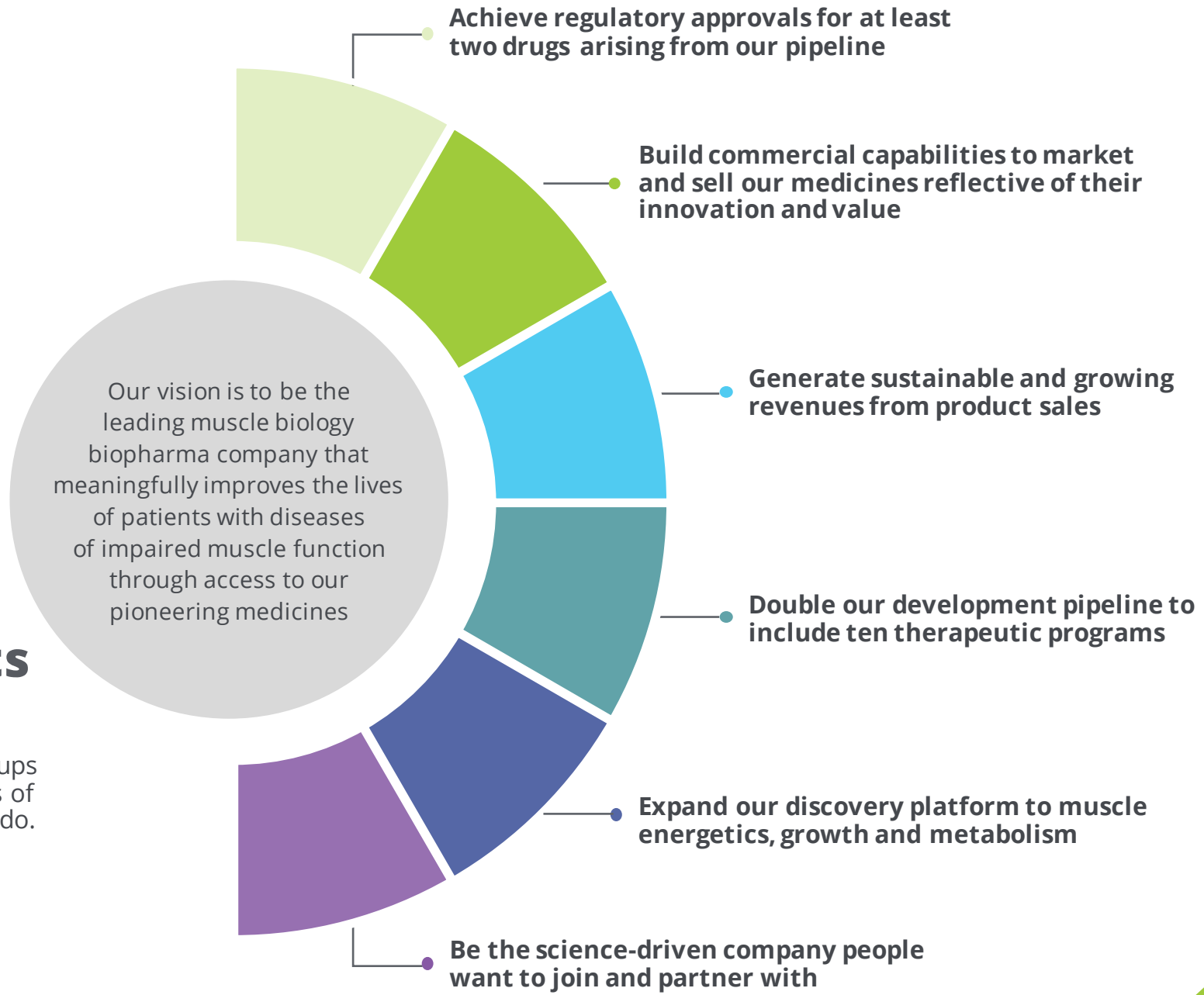
To bring forward new medicines to improve the healthspan of people with devastating cardiovascular and neuromuscular diseases of impaired muscle function.

Cytokinetics

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.



Executing On Our Vision

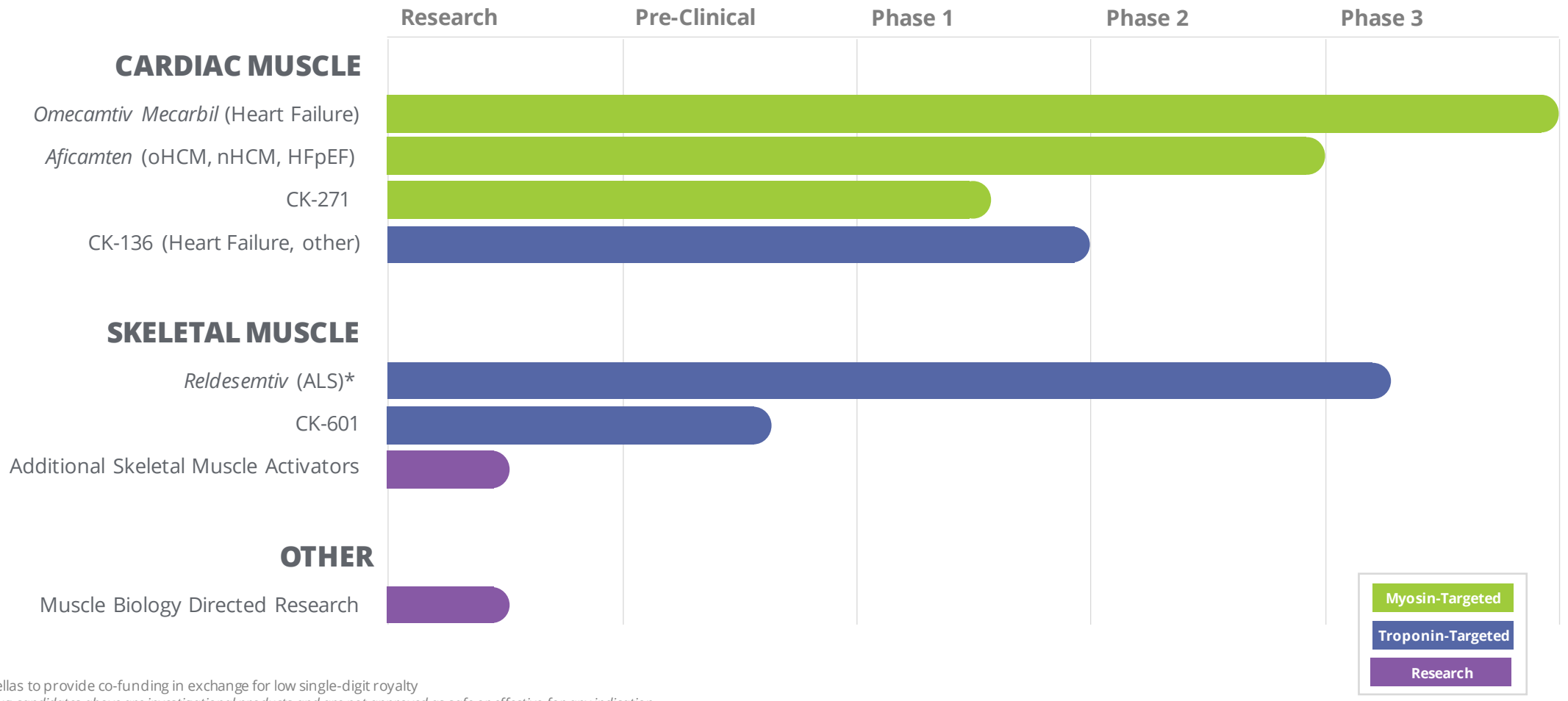
- Scientific innovation driven by modulating cardiac myosin
- First-in-class myosin activator
- Next-in-class myosin inhibitor
- Expansion beyond contractility to muscle energetics, metabolism

- 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.

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Sarcomere Directed Drug Development

CARDIAC MUSCLE

Omecamtiv Mecarbil

CK-136

Aficamten, CK-271

Cytokinetics

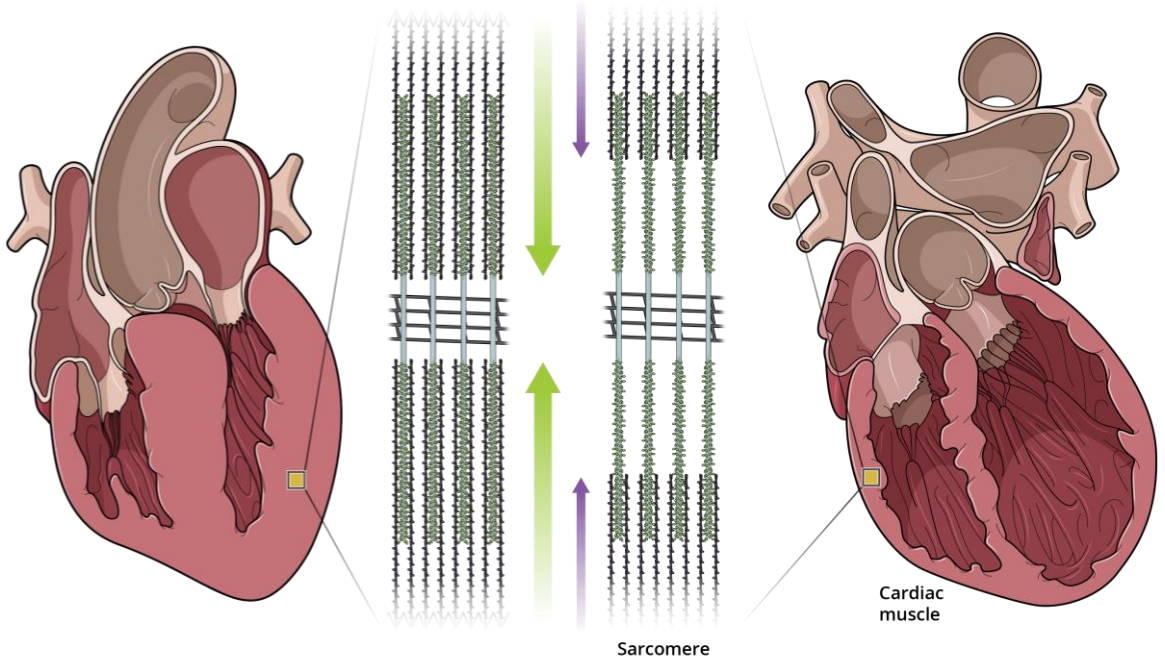
Omecamtiv Mecarbil

Cytokinetics

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)



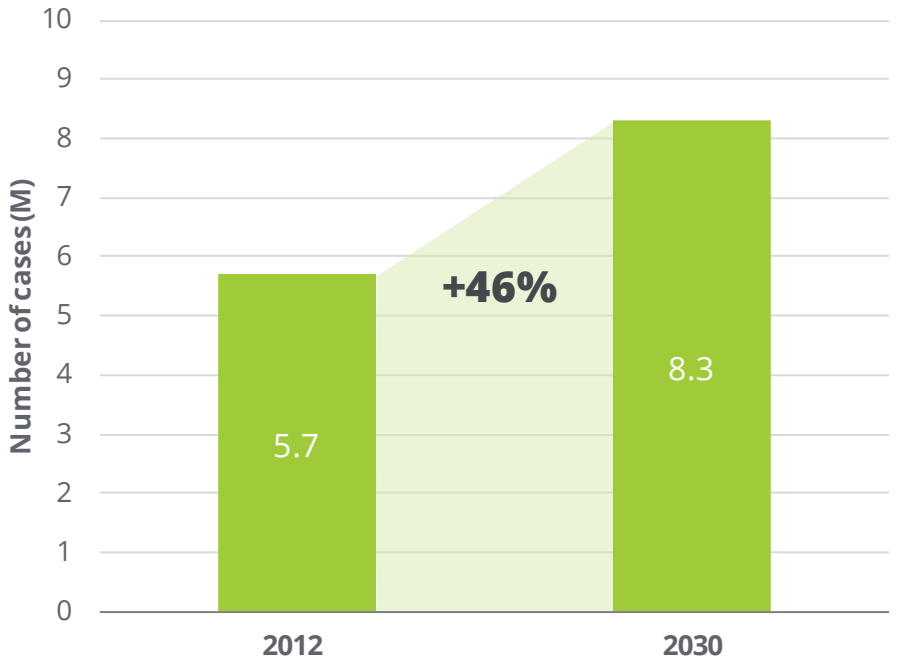
Decreased Cardiac Contractility

- **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

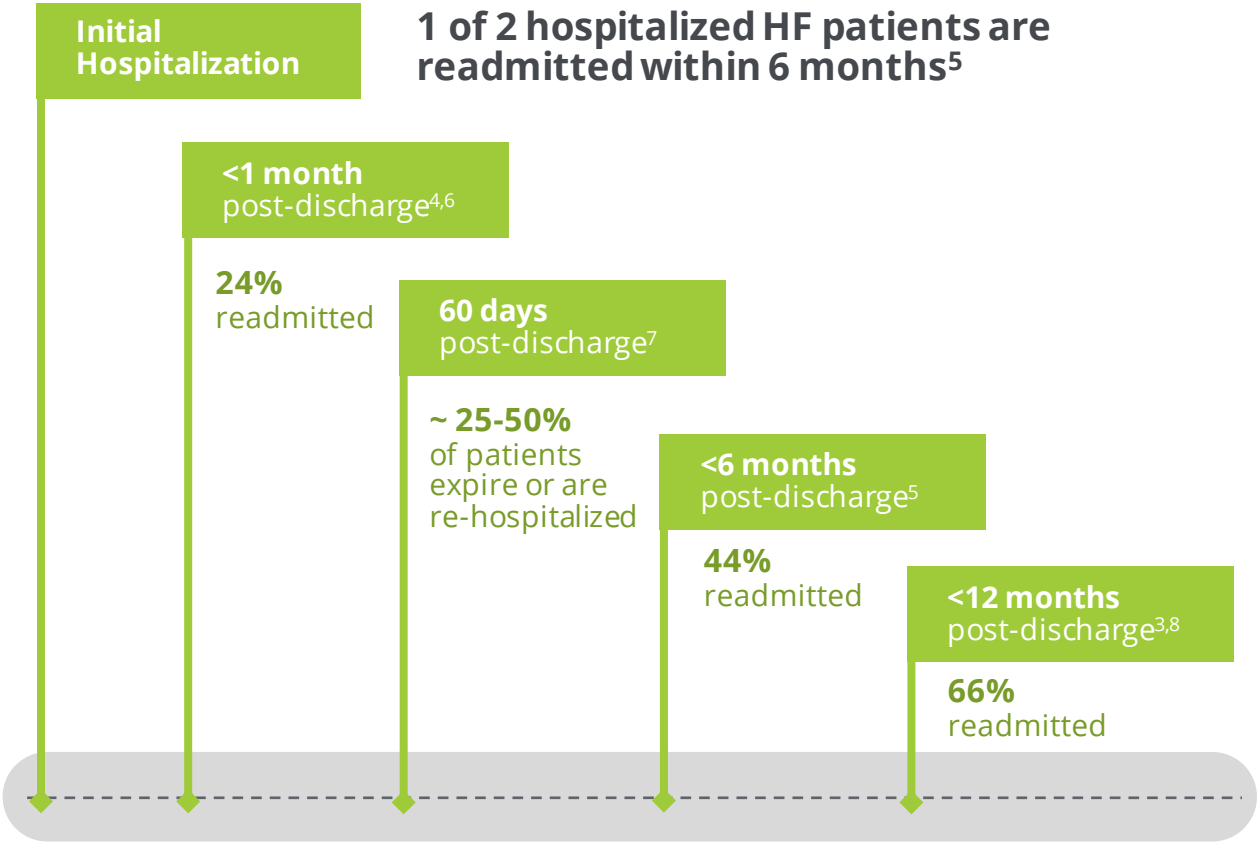
6 million people have heart failure in the United States

Prevalence Expected to Increase by 46% from 2012 – 2030



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

1 of 2 hospitalized HF patients are readmitted within 6 months[5]



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

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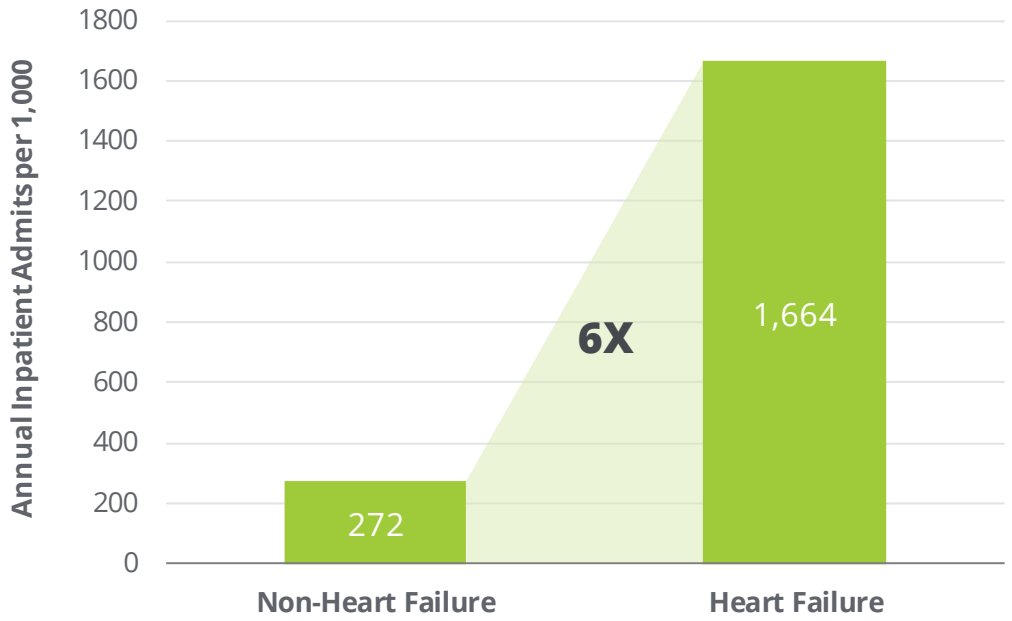
High Economic Burden of Heart Failure

Heart failure costs ~$123 billion annually, representing 33% of total Medicare budget[1,2]

Heart failure is the most frequent diagnosis for hospitalized Medicare patients in the US[1,2]

Inpatient Admission Rates for HF Patients 6X Higher than Non-HF Patients[1]



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**

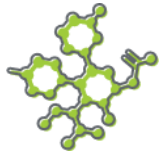
Drugs that do not affect renal function

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

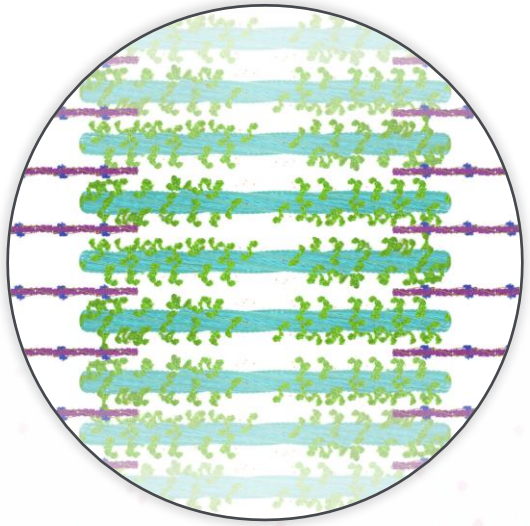
Drugs that increase QoL

Patient management will improve **with drugs that increase QoL**

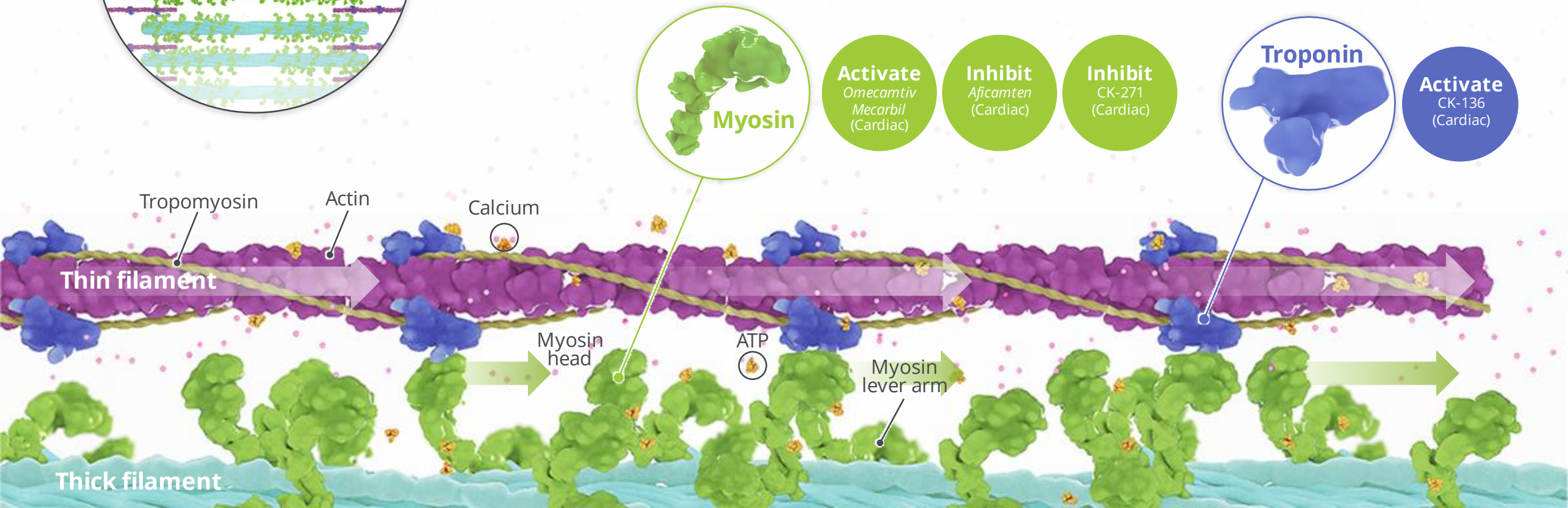
Patient QoL decreases as they lose the ability to perform daily tasks

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

GALACTIC-HF

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

GALACTIC-HF

Characteristic	OM (N=4120)	Placebo (N=4112)
Demographics		
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
Heart Failure History and Medical Conditions		
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

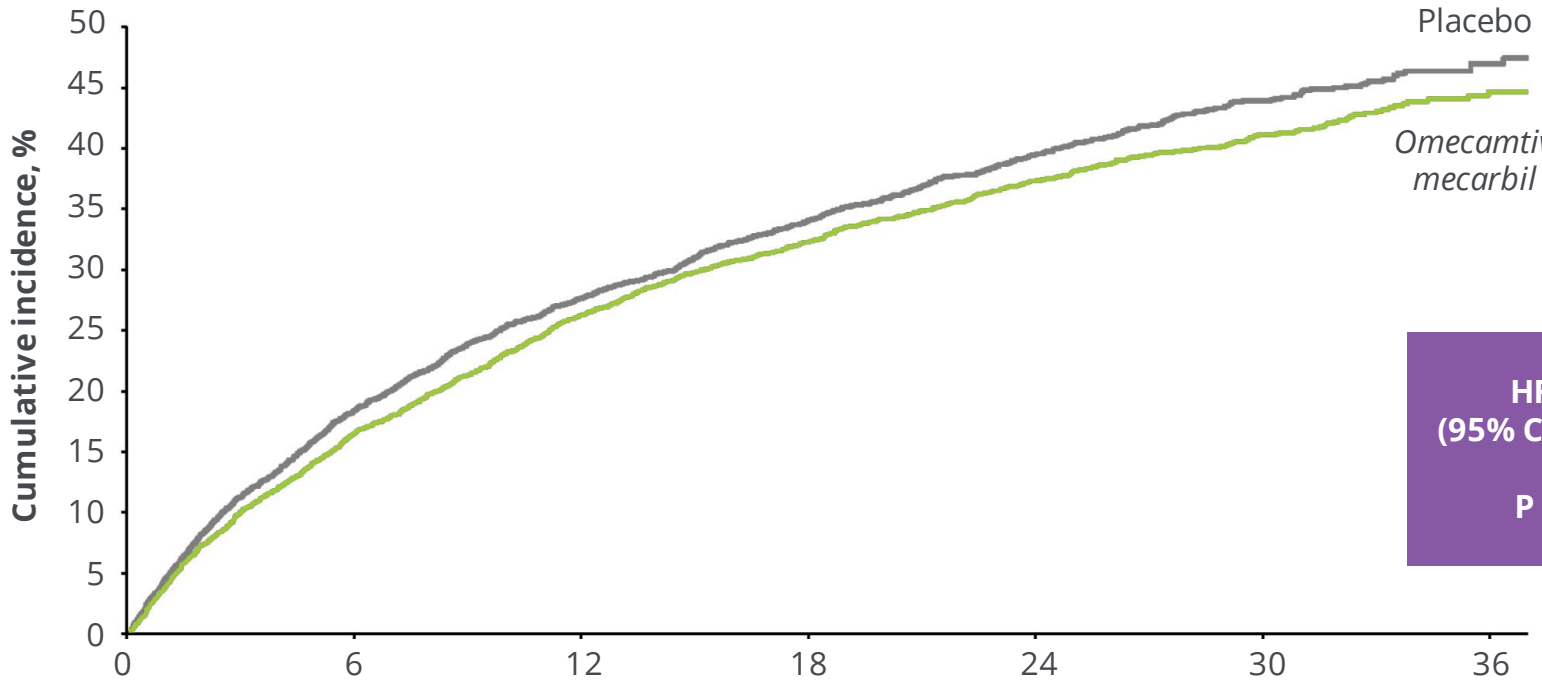
Characteristic	OM (N=4120)	Placebo (N=4112)
Vitals and Laboratory Parameters		
NT-proBNP (pg/mL), median (Q1, Q3)	1977 (980, 4061)	2025 (1000, 4105)
SBP (mmHg), mean (SD)	116 (15)	117 (15)
Heart rate, mean (SD)	72 (12)	72 (12)
eGFR (mL/min/1.73m^2), median (Q1, Q3)	59 (44, 74)	59 (44, 74)
Cardiac TnI (ng/mL), median (Q3)	0.027 (0.052)	0.027 (0.052)
Medications and Cardiac Devices		
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

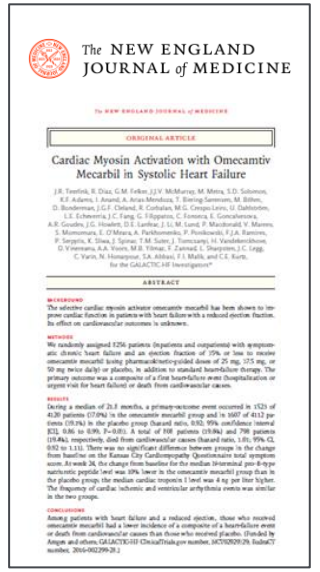
GALACTIC-HF



HR = 0.92
(95% CI, 0.86–0.99)

P = 0.025

Patients at risk, n							
Placebo	4112	3310	2889	2102	1349	647	141
OM	4120	3391	2953	2158	1430	700	164


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure

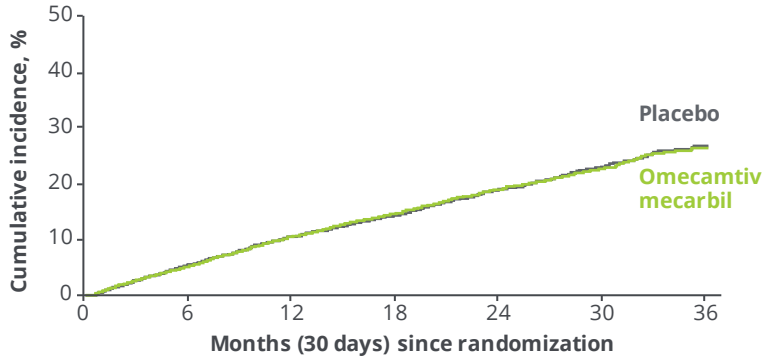
ABSTRACT

Cytokinetics

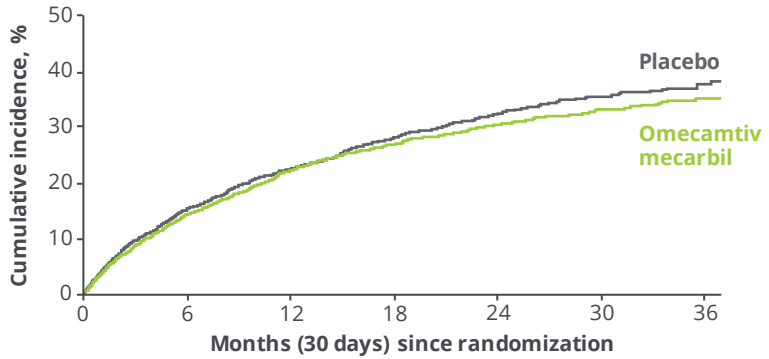
Primary Composite Components and KCCQ TSS

GALACTIC-HF

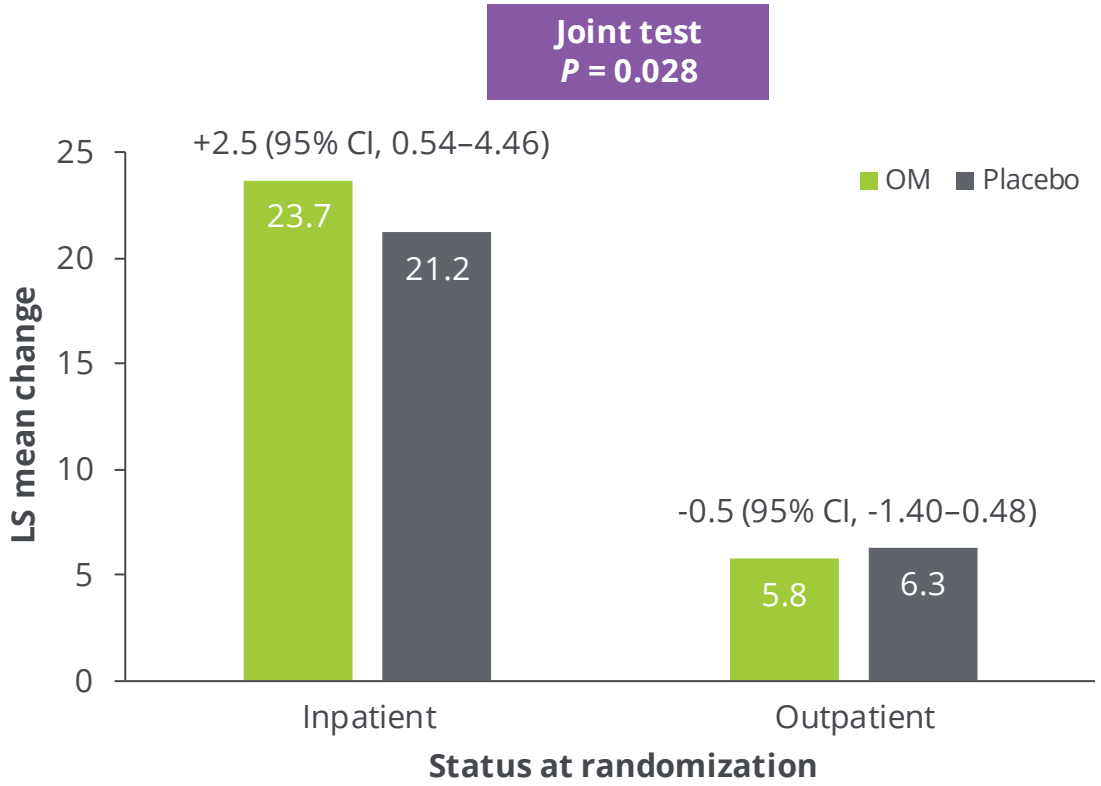
CV Death
HR = 1.01 (95% CI, 0.92–1.11)
***P* = 0.86**



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

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Laboratory and Safety Events

GALACTIC-HF

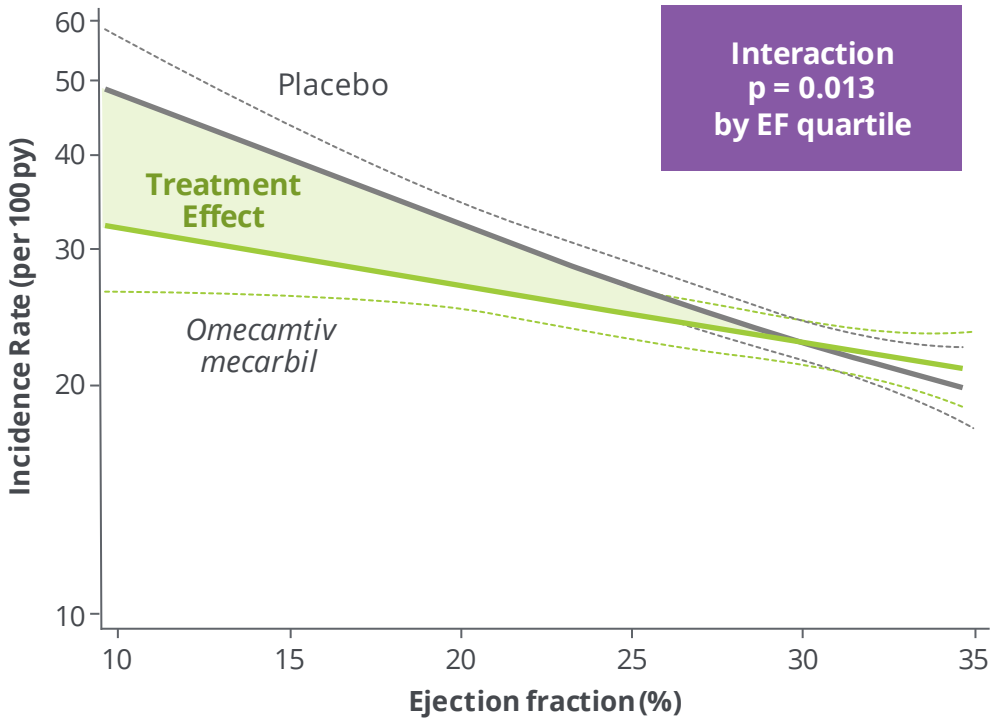
Variable	*Omecamtiv Mecarbil* (N=4110)	Placebo (N=4101)	Relative Risk or Difference (95% CI)
Laboratory value change from baseline to Week 24			
Systolic blood pressure – mmHg, mean (SD)	**1.4 (15.3)**	**1.5 (15.6)**	-0.1 (-0.9, 0.6)
Heart rate, bpm, mean (SD)	**-2.1 (12.6)**	-0.5 (12.8)	-1.6 (-2.2,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

Treatment Effect Increased Progressively As Baseline EF Decreased

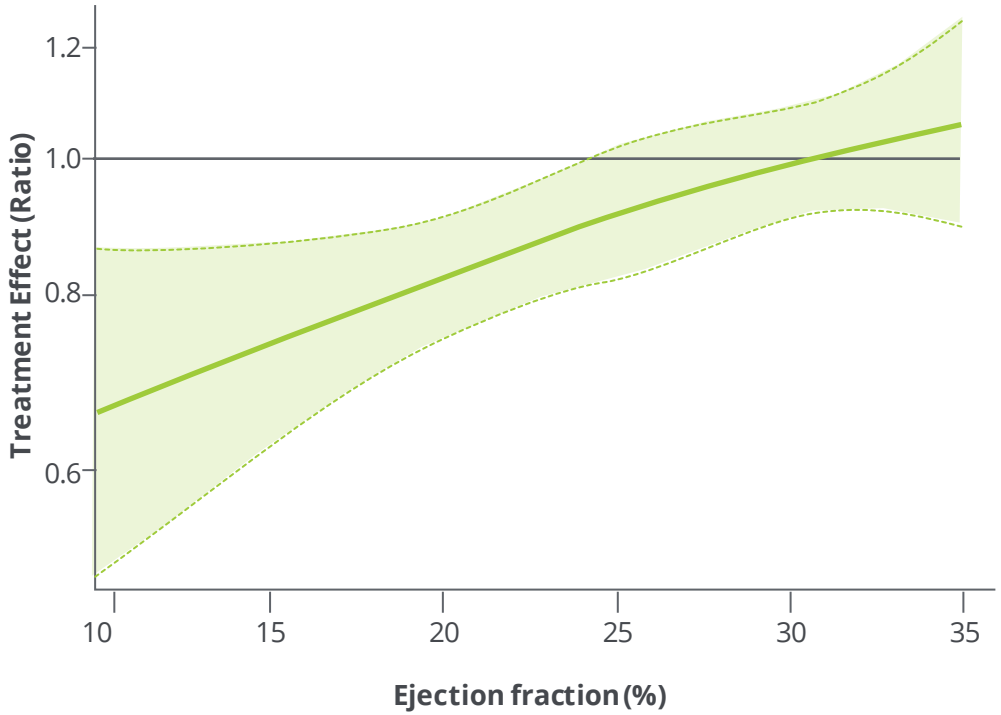
In EF ≤22%, 11.8 needed-to-treat to prevent 1 event over 3 years

GALACTIC-HF

Incidence of Primary Composite Endpoint



Relative Treatment Effect on Primary Composite Endpoint




JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Effect of Ejection Fraction on Clinical Outcomes in Patients treated with Omecamtiv Mecarbil in GALACTIC-HF

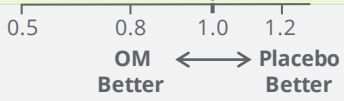
Brief title: Ejection Fraction and Clinical Outcomes in GALACTIC-HF

Greater Treatment Effect in More Severe HF

GALACTIC-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 ≤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%
LVEF ≤28%	**1821/4456**	**0.84 (0.77, 0.92)**	**<0.001**	**4.9%**
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%



Increased Treatment Effect with Severe HF

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

GALACTIC-HF

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

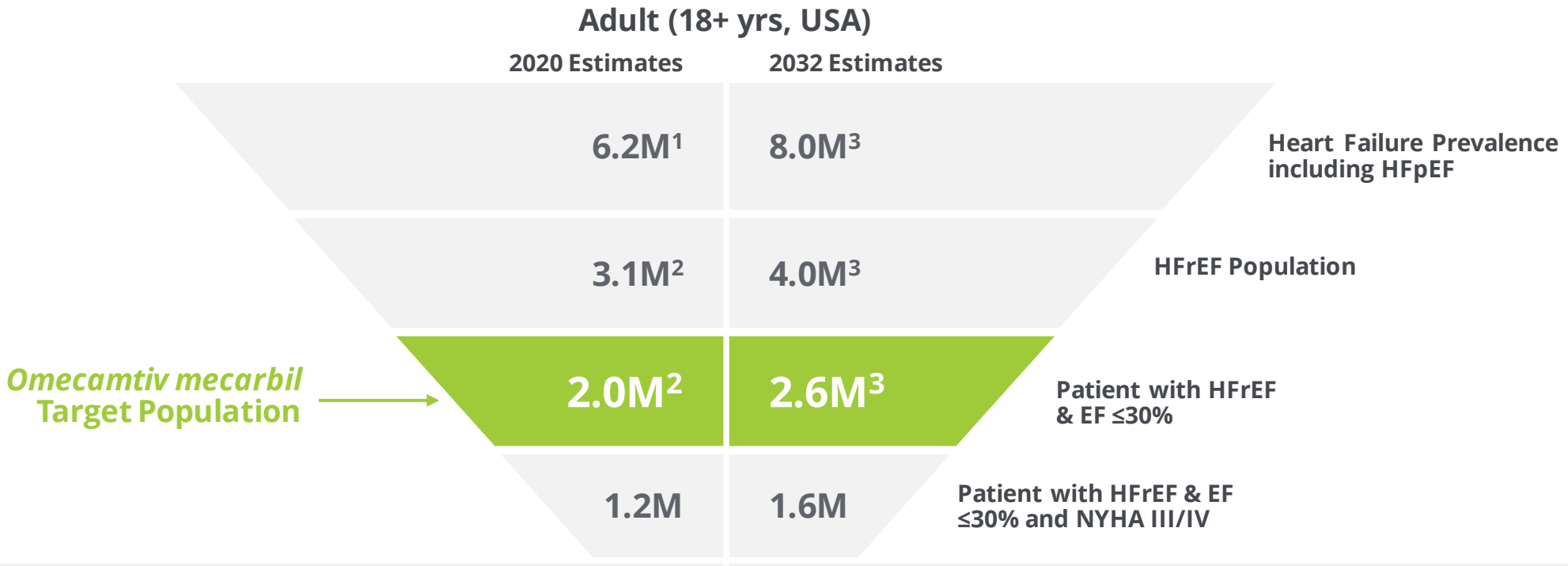
Increased Treatment Effect with Higher NT-proBNP

GALACTIC-HF

Heart Failure & World Congress on Acute Heart Failure 2021

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[1]

- 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[2]

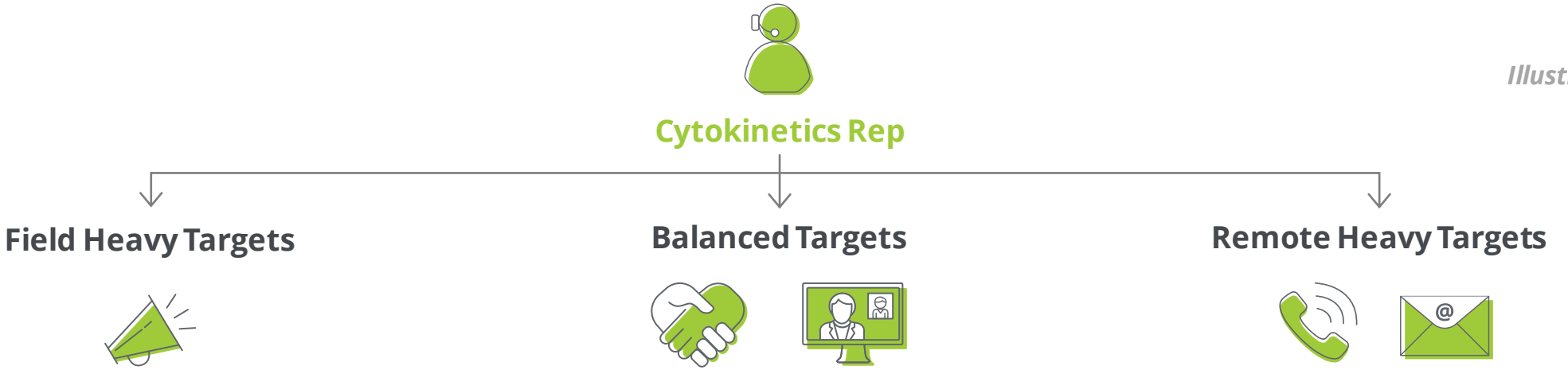
Decrease in number of hospital admissions per year

Reduction in 30-day re-admissions

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

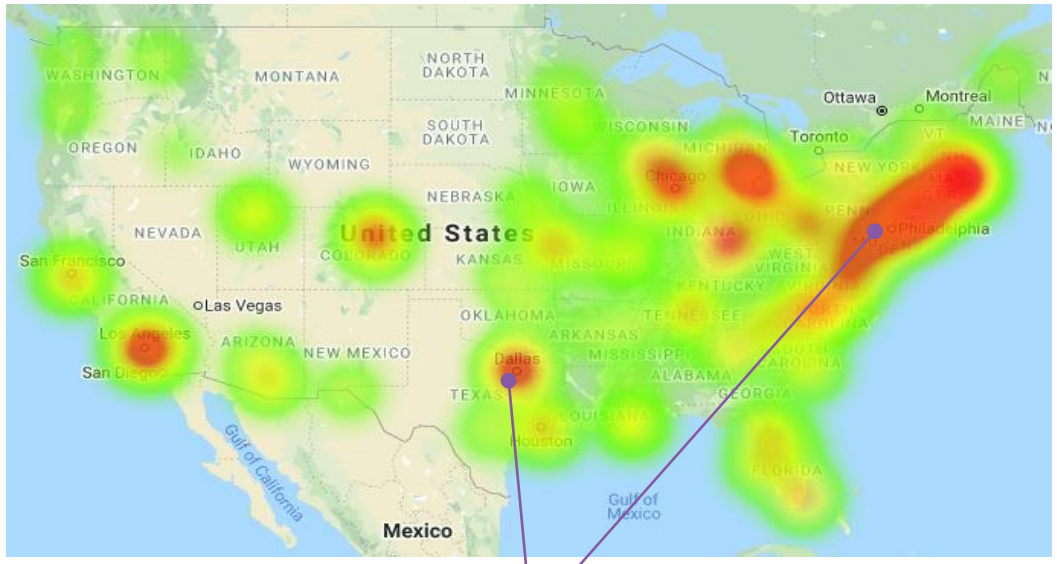


% of Face-to-Face Visits		
Heavy face-to-face	Mix of face-to-face and remote	Minimum face-to-face
Engagement Description		
Similar to traditional engagement – rep spends most of the time in face-to-face interaction	Hybrid engagement – mix of face-to-face and virtual visits to sequence interactions depending 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

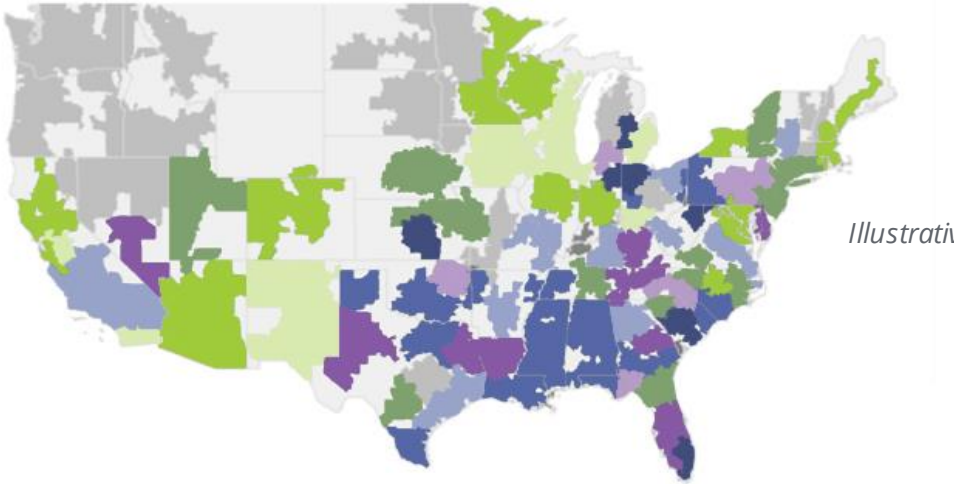
Applied Analytics Will Inform Channel Mix and Deployment

Patient and HCP Heat Map in HFrEF



Deploy to Hot Spots

Physician Engagement Type by Geography



Illustrative

	Example Cities
High PFF High DP	Miami, FL Wichita, KS
High PFF Low DP	Montgomery, AL Las Vegas, NV
Low PFF High DP	Boston, MA Minneapolis, MN
Low PFF Low DP	Austin, TX Grand Rapids, MI

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

METEORIC-HF

Enrollment complete; results expected in 2H 2022

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**

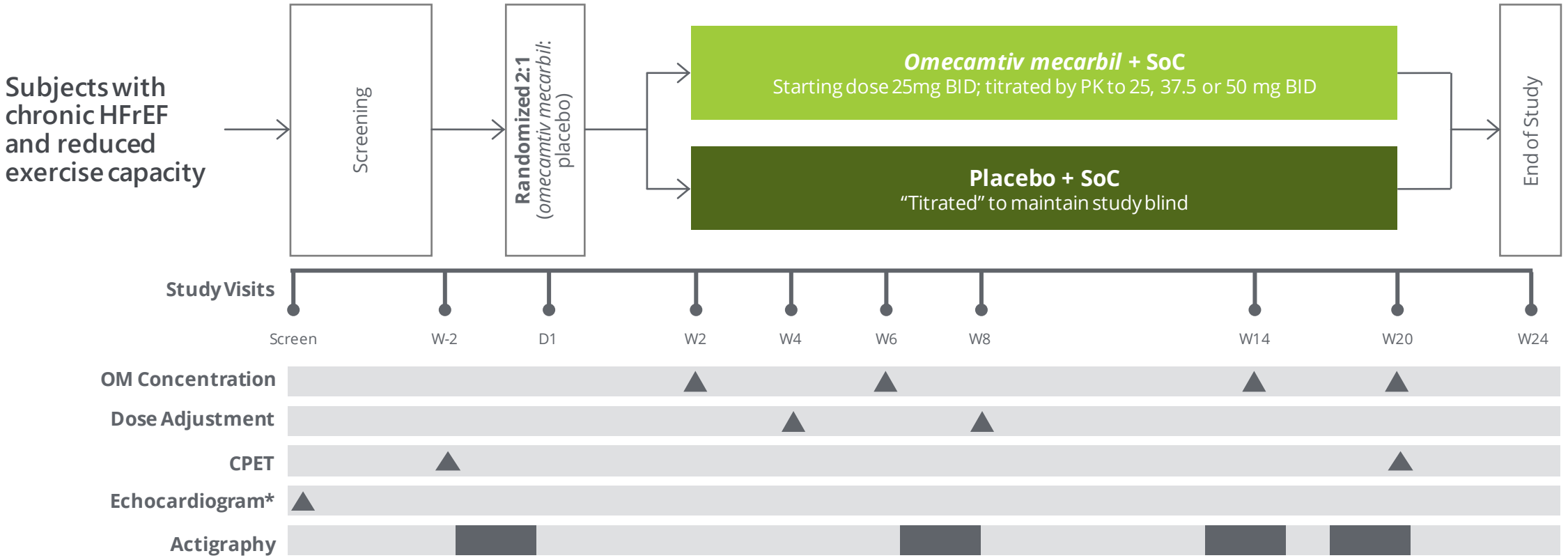
Key Design Points

- 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

METEORIC-HF



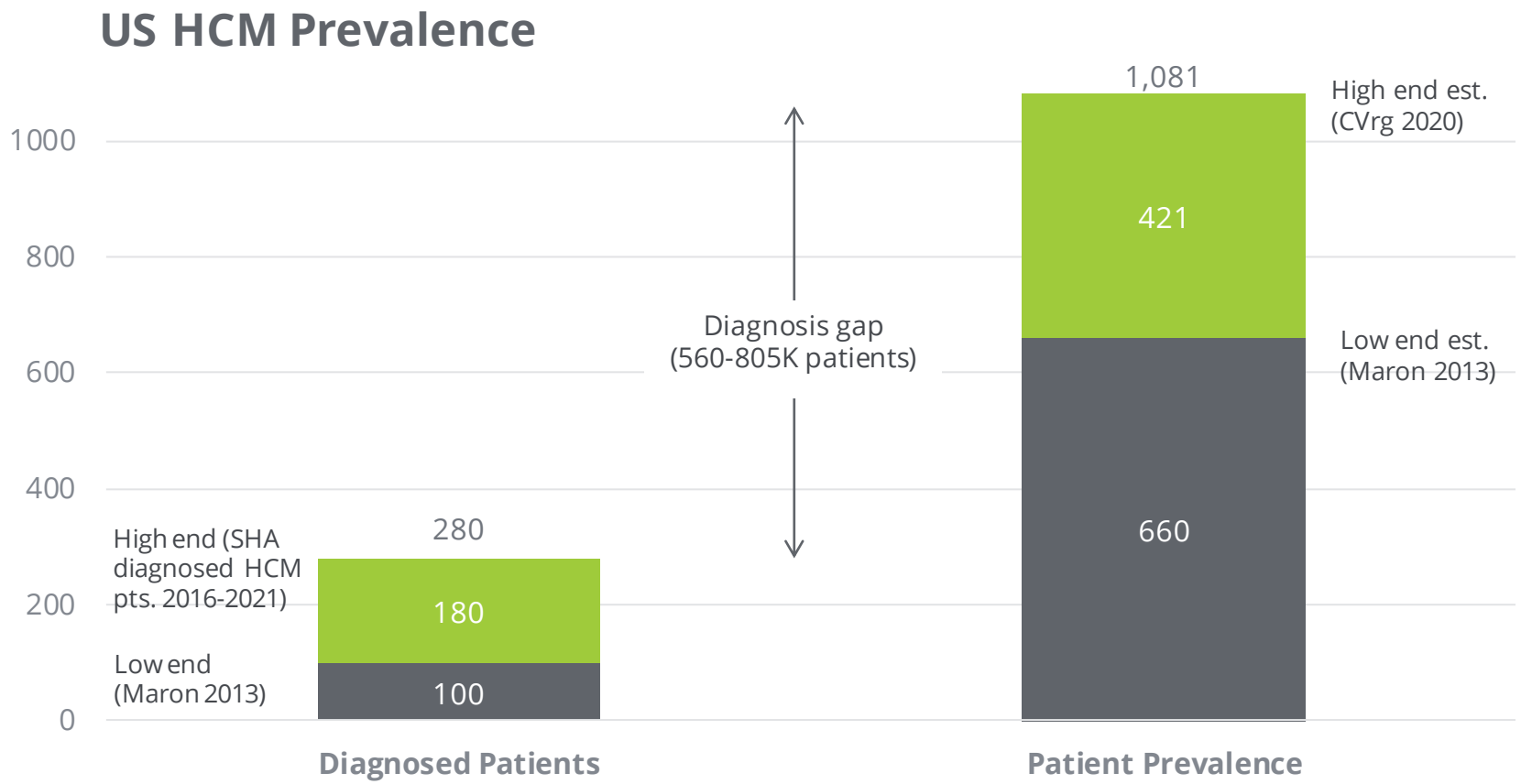
*Screening echocardiogram is not required if an appropriate LVEF assessment has been performed within one year

Cytokinetics

Aficamten

Cytokinetics

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

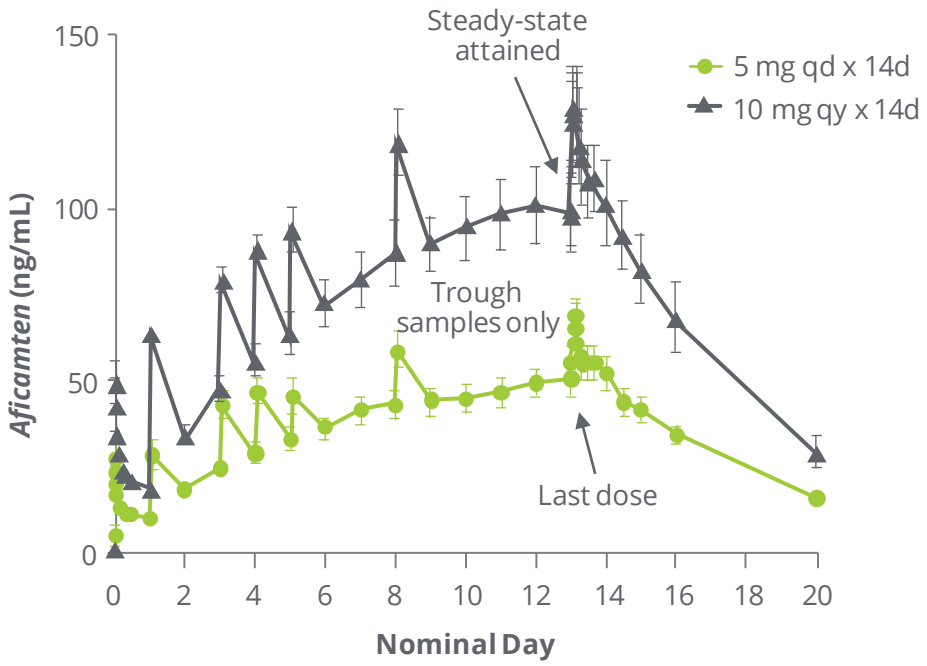
Potential treatment for patients with HCM

- 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

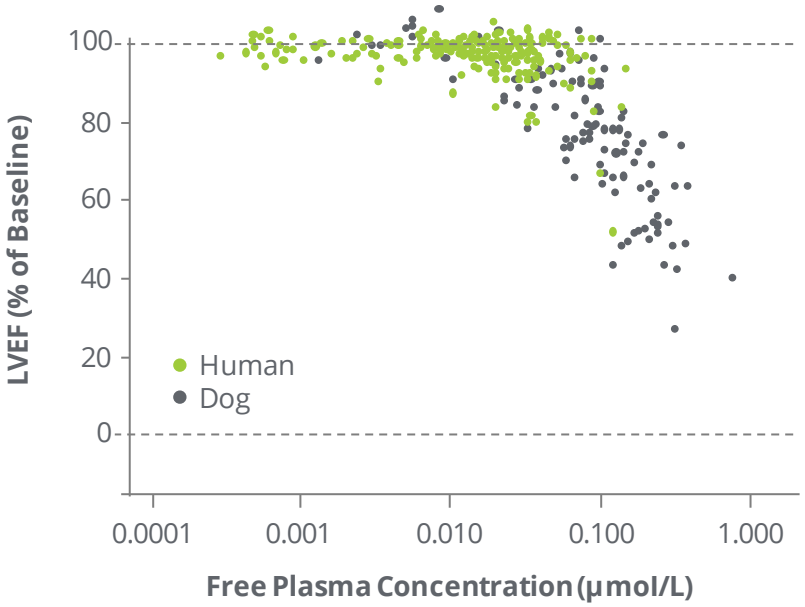
Preclinical data translated to healthy participants

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)



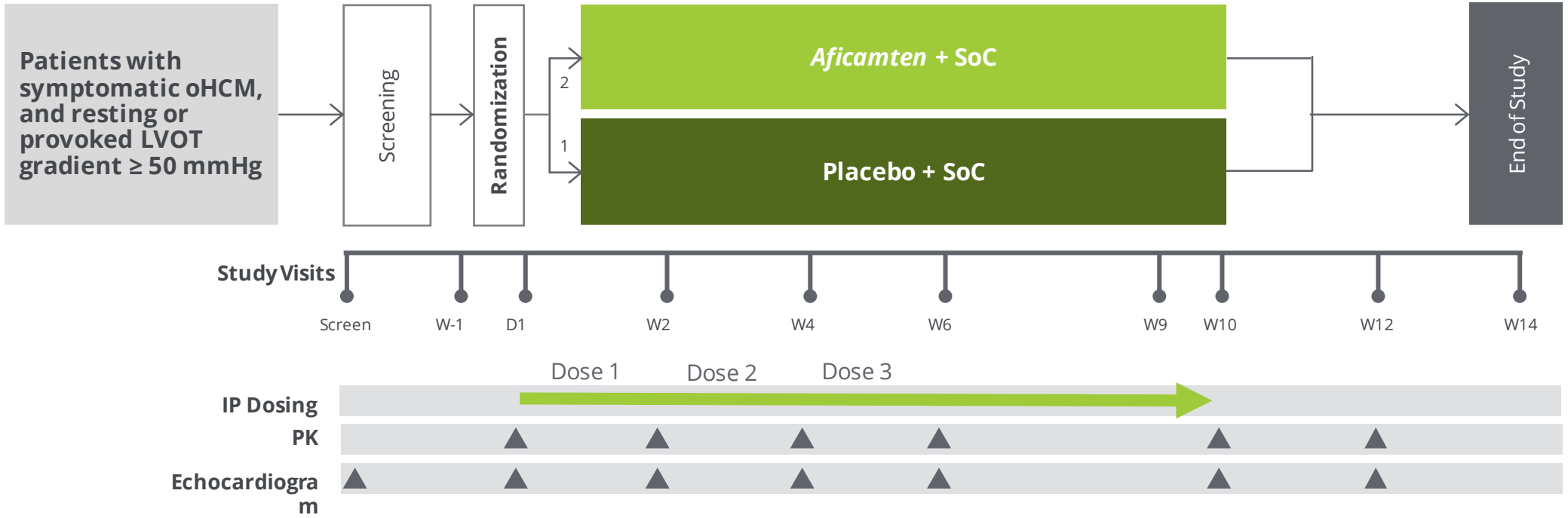
Graphs show LVEF as a function of exposure; data points represent observed values in dogs and humans.

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

Phase 2 Clinical Trial Design

REDWOOD HCM

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



	Dose 1	Dose 2	Dose 3
Cohort 1	5 mg	10 mg	15 mg
Cohort 2	10 mg	20 mg	30 mg

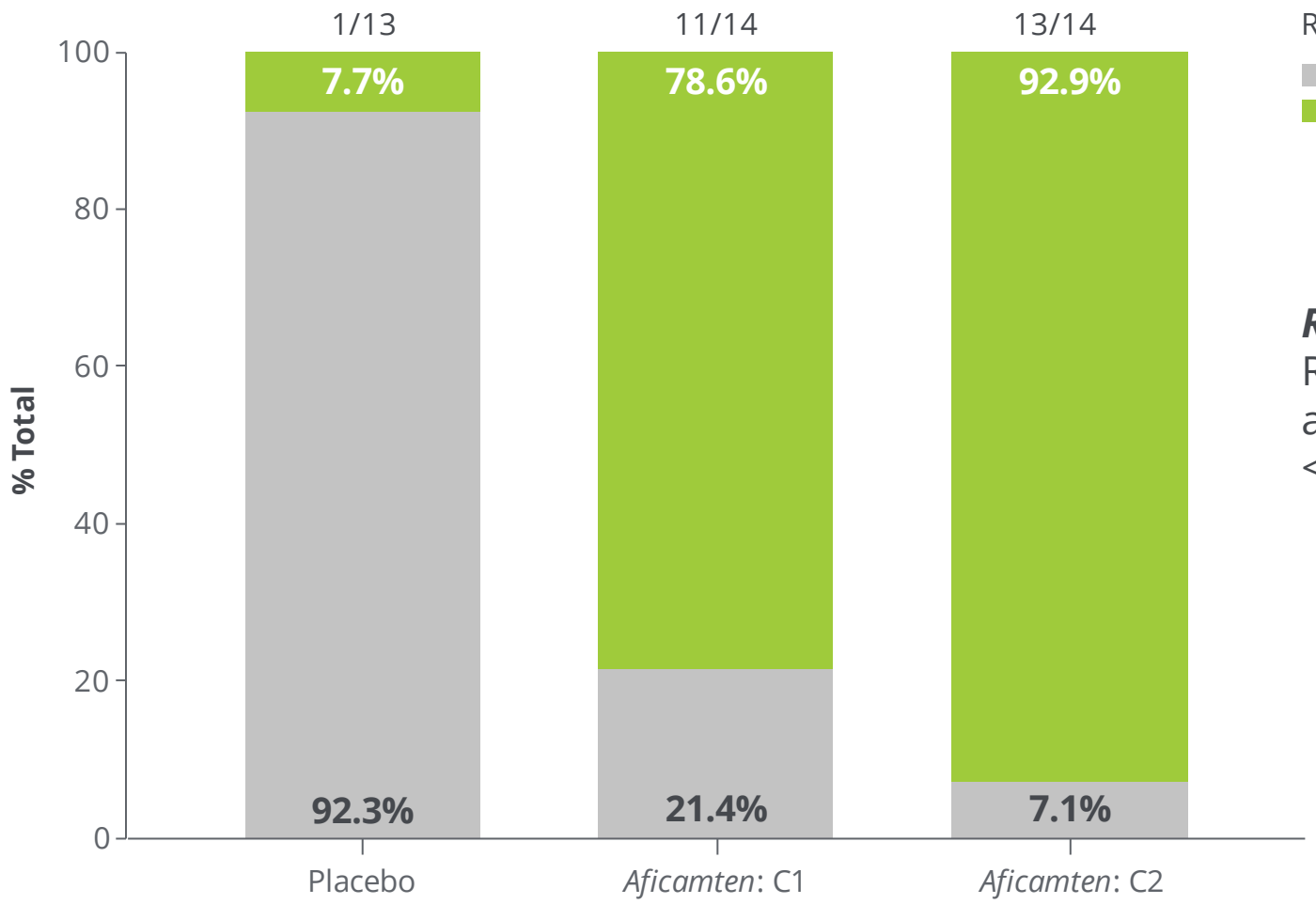
Cytokinetics

Baseline Characteristics

Characteristic	Placebo (n = 13)	*Aficamten* (n = 28)
Age (Years), Mean (SD) [Range]	57.2 (9.6) [36,69]	56.6 (13.6) [33,78]
< 65 Years	10 (77%)	17 (61%)
Sex, n (%)		
Female	8 (62%)	15 (54%)
Race = White, n (%)	12 (92%)	28 (100%)
NYHA Class, n (%)		
Class II	11 (85%)	17 (61%)
Class III	2 (15%)	11 (39%)
Maximal LV Wall Thickness (mm) Mean (SD)	16 (3)	17 (3)
LVEF* at Screening (%), Mean (SD)	73.6 (5.9)	71.7 (8.0)
LVOT-G*, Rest at Screening (mmHg), Mean (SD)	70.0 (28.0)	61.1 (29.8)
LVOT-G*, Valsalva at Screening (mmHg), Mean (SD)	93.3 (27.2)	89.3 (31.5)

* Site-read echocardiogram

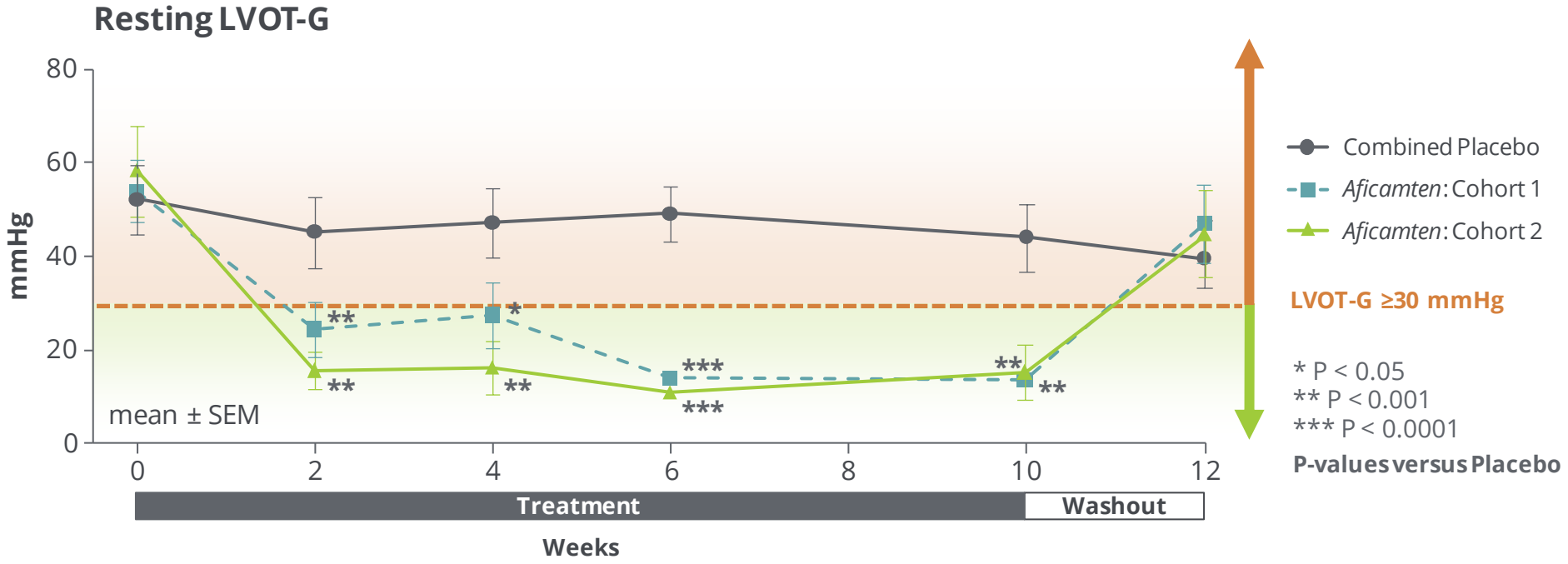
High Response Rates on Treatment with *Aficamten*



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

REDWOOD-HCM: Efficacy

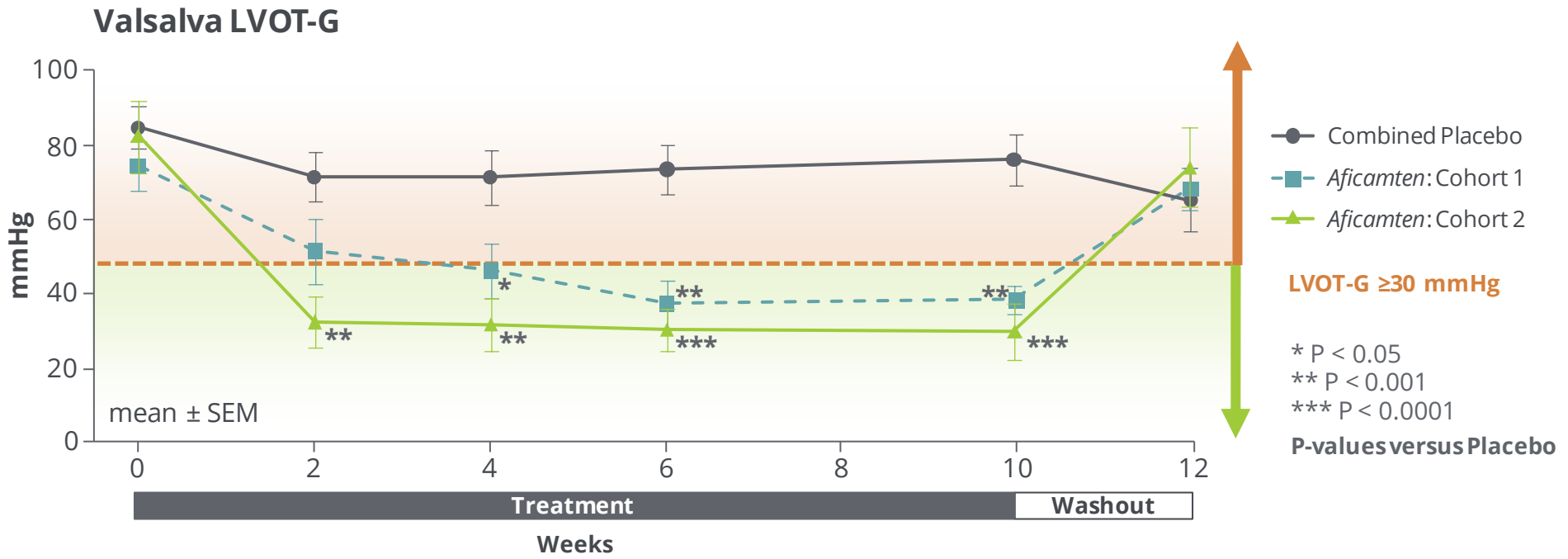
Resting Left Ventricular Outflow Tract Gradient (LVOT-G)



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

REDWOOD-HCM: Efficacy

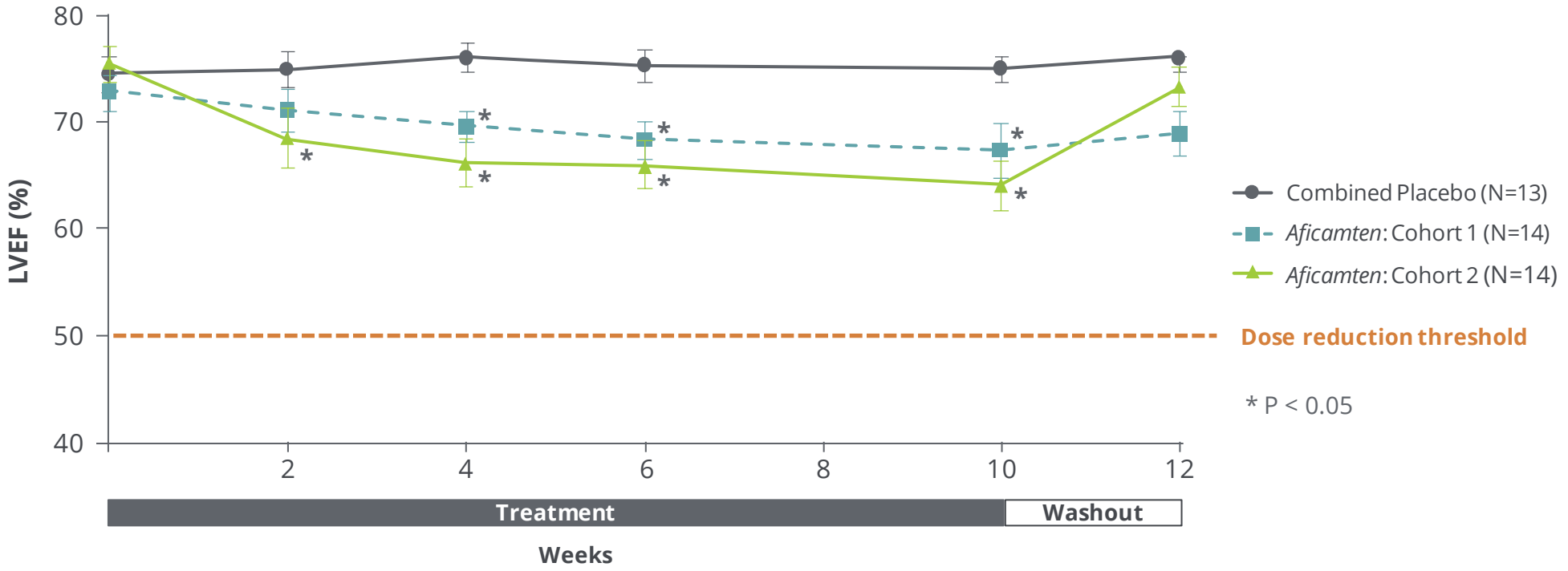
Valsalva LVOT-G



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

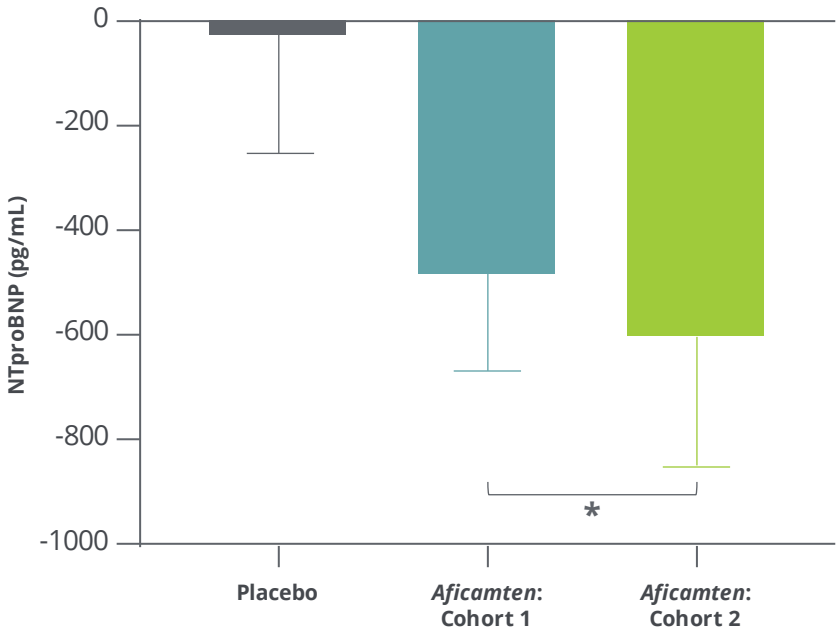
REDWOOD-HCM: Efficacy

Changes in Left Ventricular Ejection Fraction over Study Period



Change from Baseline in NT-proBNP & NYHA Class

Change from Baseline NT-proBNP to Week 10

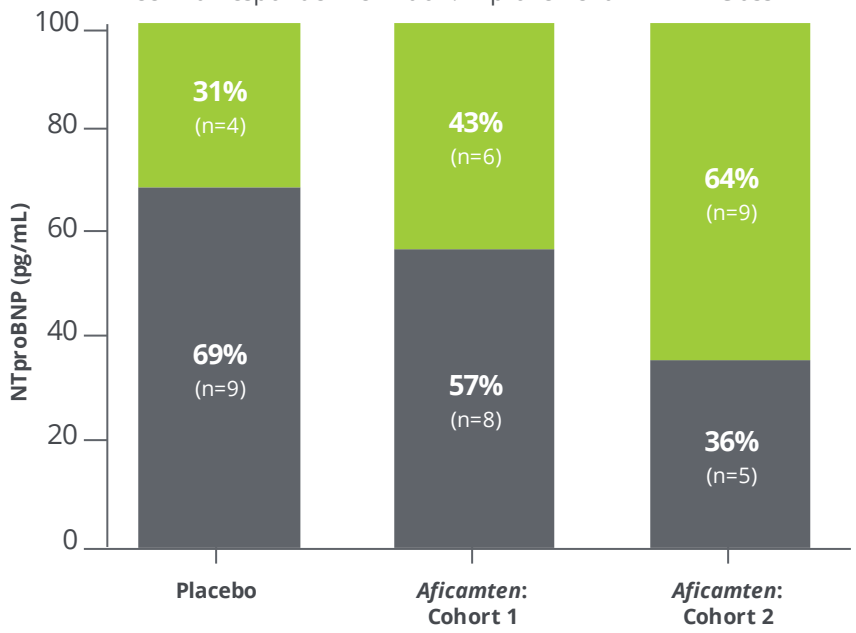


*** P = 0.003 for Pooled Cohort 1 & 2 vs. Placebo**

- Combined Placebo (N=13)
- *Aficamten*: Cohort 1 (N=14)
- *Aficamten*: Cohort 2 (N=14)

Improvement in Heart Failure Symptoms (NYHA Class)

Week 10 Responder Definition: Improvement in NYHA Class ≥1



Cohort 1 vs Placebo: p>0.1
Cohort 2 vs Placebo: p = 0.08

- No Improvement in NYHA Class
- ≥1 NYHA Class Improvement

Safety Data

- **2 SAEs reported in Cohort 1 and none in Cohort 2**
  - Stress Cardiomyopathy: 55-year-old female assigned to Placebo, with associated cardiogenic shock after IP discontinuation at end of treatment (Week 10).
  - Back Pain: 50-year-old male assigned to *aficamten* (dose 5 mg at the time of SAE, and max dose 15 mg) visited Emergency Room for exacerbation of preexisting musculoskeletal back pain.
- **No SAEs reported that resulted in early termination**
- **No treatment-related serious adverse events**
- **No imbalance in adverse events between *aficamten* and placebo treated arms**

- **No patients met the "stopping criteria" of LVEF < 40%**
- **No treatment interruptions or discontinuations**
- **Treatment Emergent Adverse Events**
  - Placebo 85% of participants
  - *Aficamten* 88% of participants
- **LVEF < 50% (Cohort 2 only)**
  - 1 patient (baseline EF = 58%) underwent per-protocol dose reduction at Week 4 and had LVEF return above 50% (max dose 20 mg)
  - 1 patient (baseline EF = 70%) had LVEF 49.3% at Week 10 (max dose 20 mg; no dose changes) and LVEF returned to baseline at the end of study (Week 12)

Open Label Extension Trial

REDWOOD HCM OLE

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

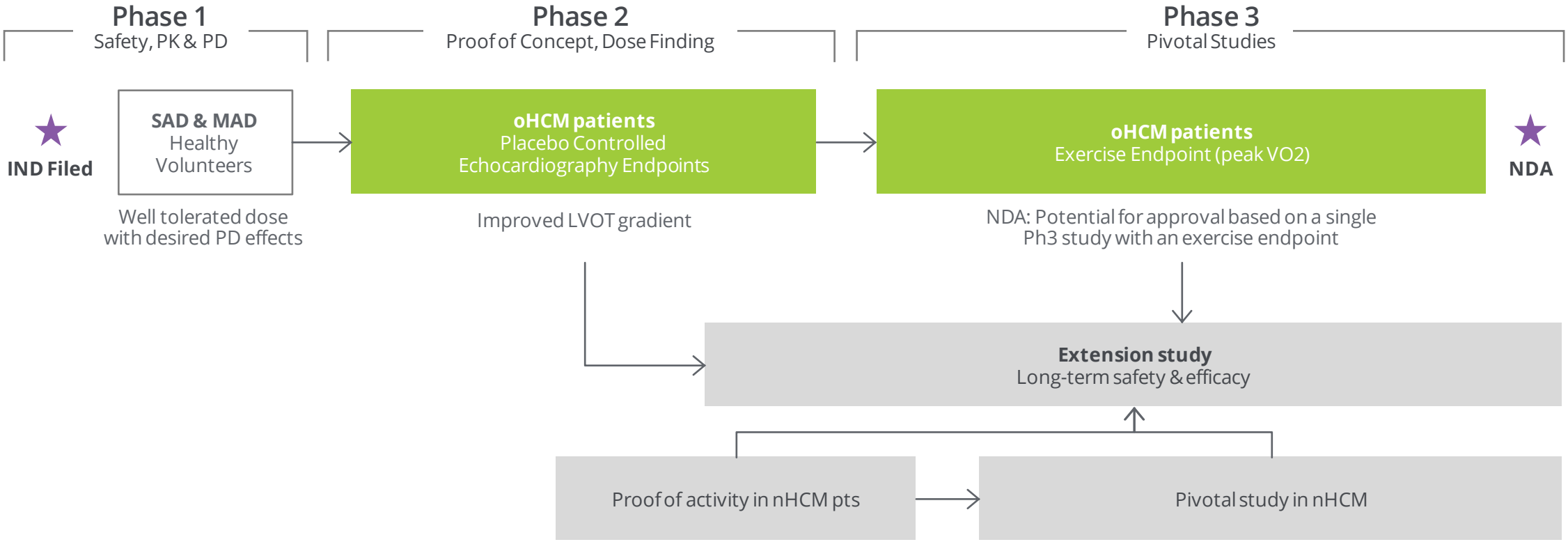
- Primary endpoint: incidence of AEs & LVEF <50
- Secondary endpoints: measures of long-term effects of *aficamten* on LVOT-G; assessments of steady-state pharmacokinetics.
  - Cardiac MRI sub-study to assess changes in cardiac morphology, function and fibrosis
- Individually optimized dose starts at 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

Advancing to Phase 3 following regulatory engagement

Type C and end-of-phase 2 meetings with FDA occurred in Q3; Plans underway to start Phase 3 trial in Q4

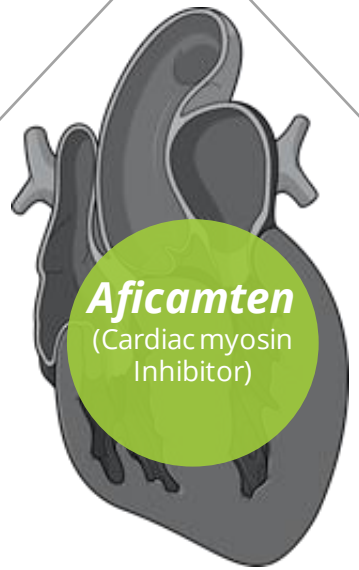


Novel Approach May Address Multiple Unmet Patient Needs

No FDA-approved therapies

Obstructive HCM

oHCM



Aficamten
(Cardiac myosin Inhibitor)

nHCM

Non-Obstructive HCM

HFpEF

Heart Failure with Preserved Ejection Fraction

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

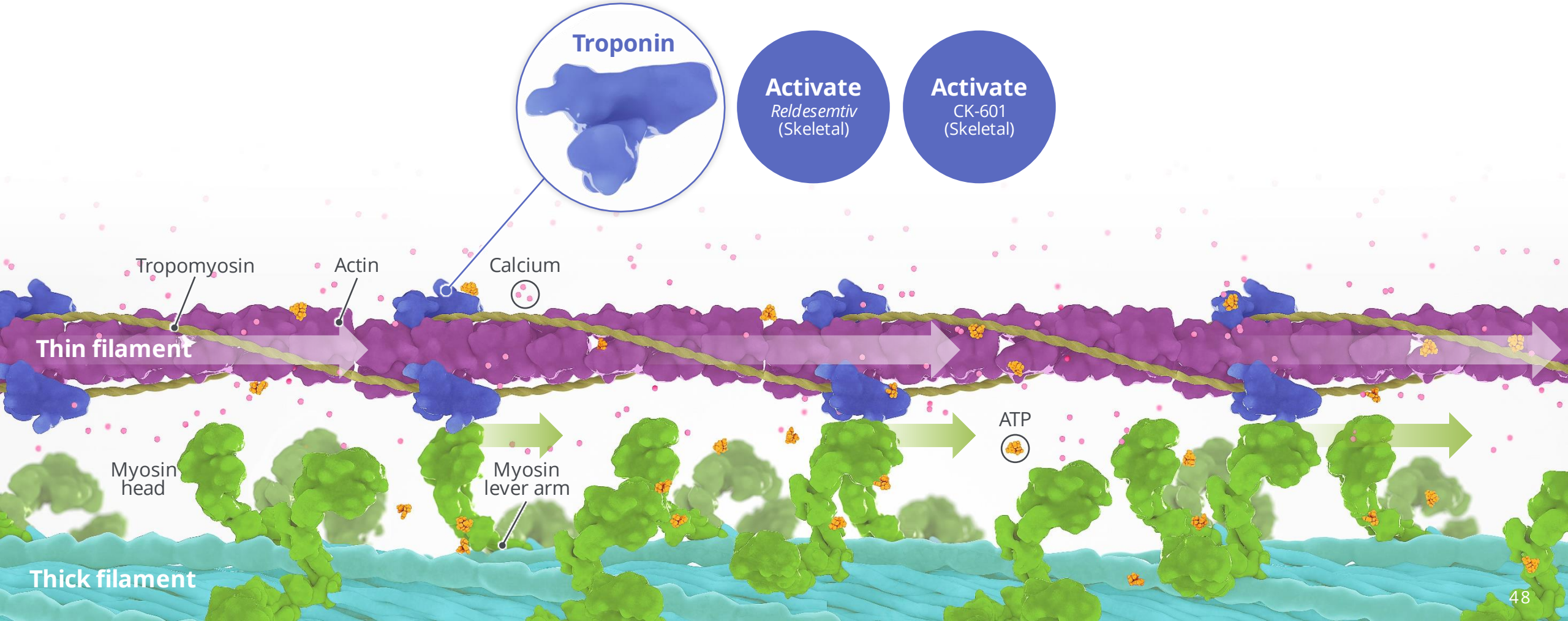
CK-601

Cytokinetics

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

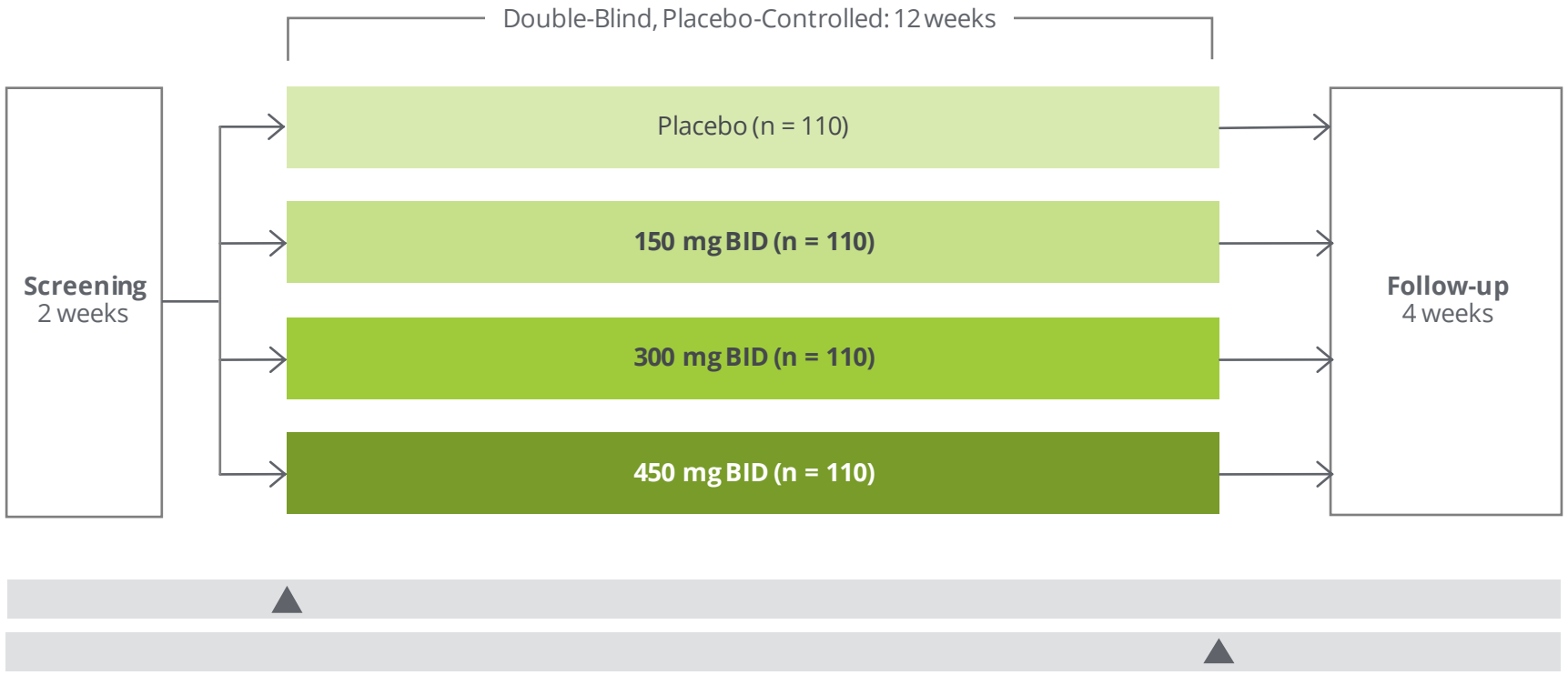
Cytokinetics

Phase 2 Clinical Trial in ALS

FORTITUDE ALS

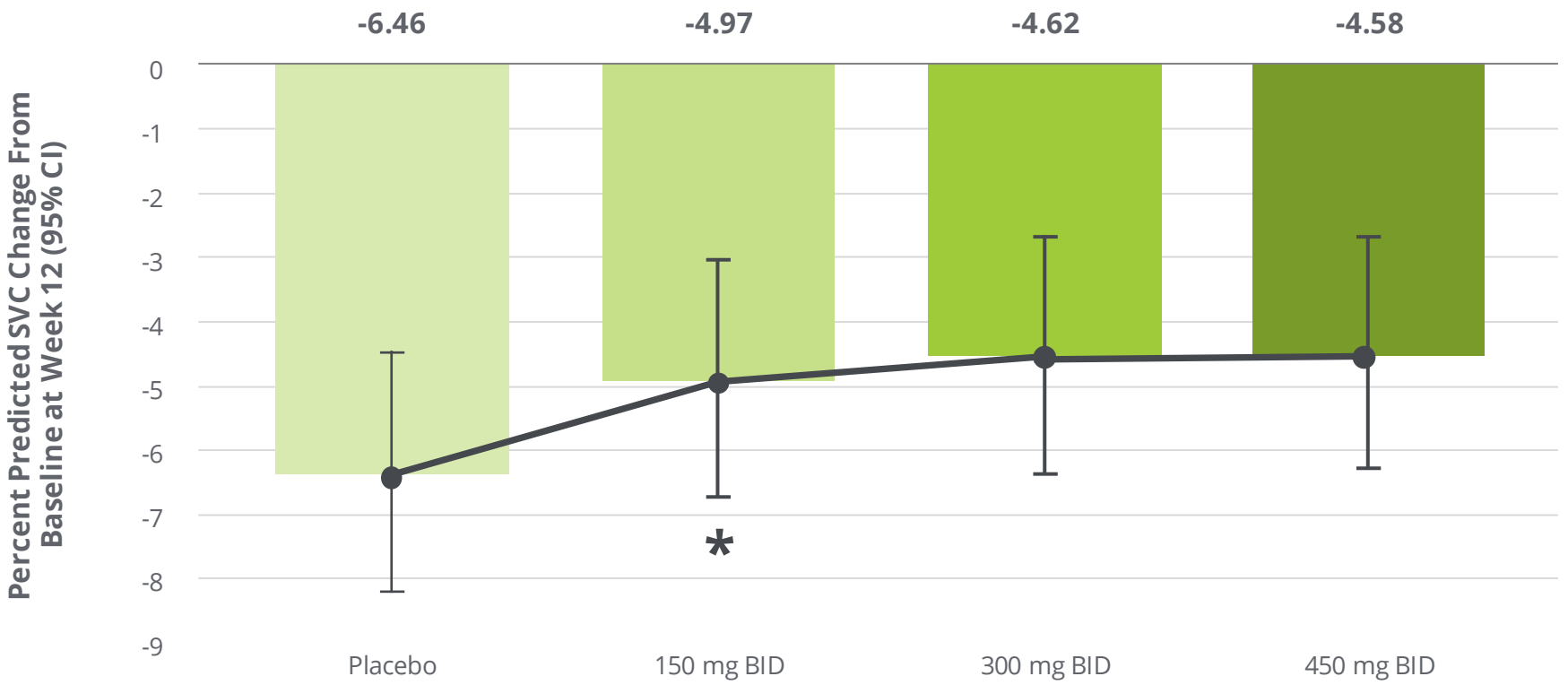
Results presented at American Academy of Neurology 2019

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

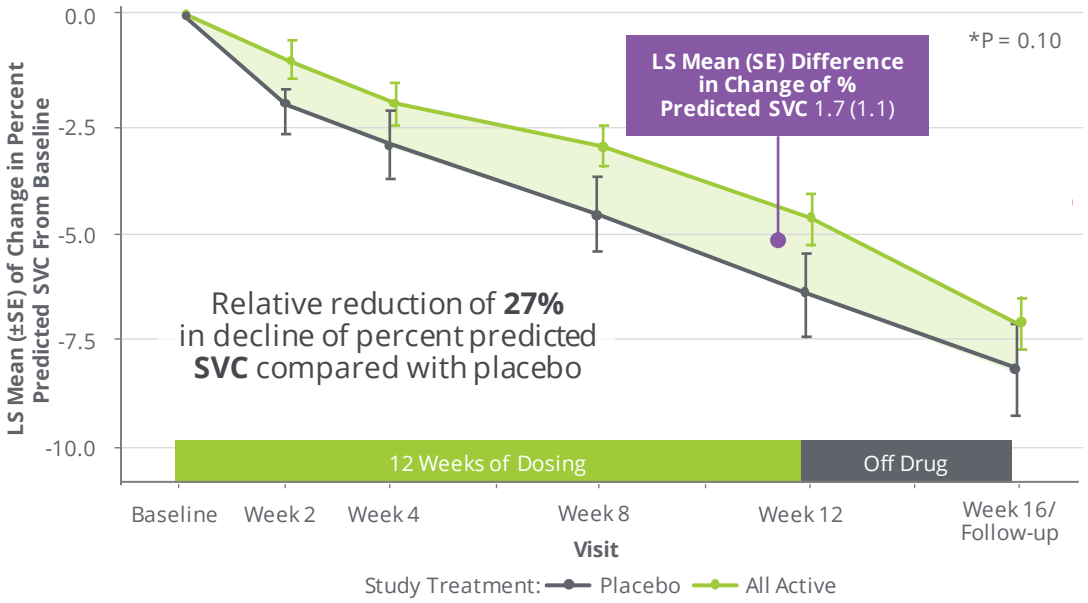
*Based on Mixed Model for Repeated Measures (MMRM) with the contrasts of (-5, -1, 3, 3) for placebo, *reldesemtiv* 150 mg, 300 mg and 450 mg BID, respectively

Change From Baseline: All Active vs Placebo*

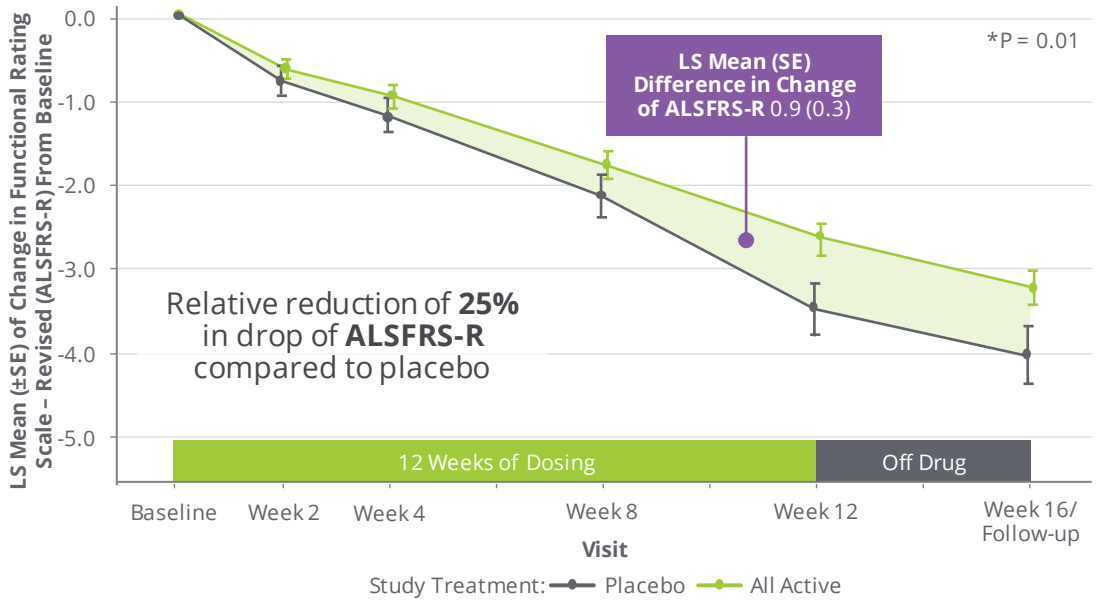
FORTITUDE ALS

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 *reldesemtiv* declined less than patients on placebo

Subgroup Analyses*

FORTITUDE ALS

Percent Predicted SVC

	No. of Patients (pbo/ *reldesemtiv*)	LSM Difference (95% CI)	Estimate	*P* value
Percent predicted SVC at baseline				
<80	38/102		1.037	0.5935
≥80	52/187		2.135	0.0834
ALSFRS-R total score at baseline				
<Median (38.0)	43/118		2.886	0.1.41
≥Median (38.0)	47/171		0.451	0.7146
ALSAQ-5 total score at baseline				
<150	49/159		0.568	0.6689
≥150	41/130		3.489	0.0287
Anatomic site of disease onset				
Limb	73/234		2.309	0.0448
Bulbar	17/55		-0.027	0.9923
Time since ALS symptom onset				
<2 Years	50/188		0.530	0.7211
≥2 Years	40/101		3.640	0.0094
Time since ALS diagnosis				
<1 Year	65/210		0.819	0.5263
≥1 Year	25/79		4.237	0.0172
<6 Months	39/130		1.230	0.4538
≥6 Months	51/159		2.285	0.1024
Pre-study rate of disease progression				
(ALSFRS-R total score reduction per month)				
1st tertile ≤(0.3667)	29/107		0.663	0.6361
2nd tertile > (0.3667) – (0.6673)	35/94		2.960	0.0976
3rd tertile (0.6673)	26/88		1.620	0.4597

ALSFRS-R Total Score

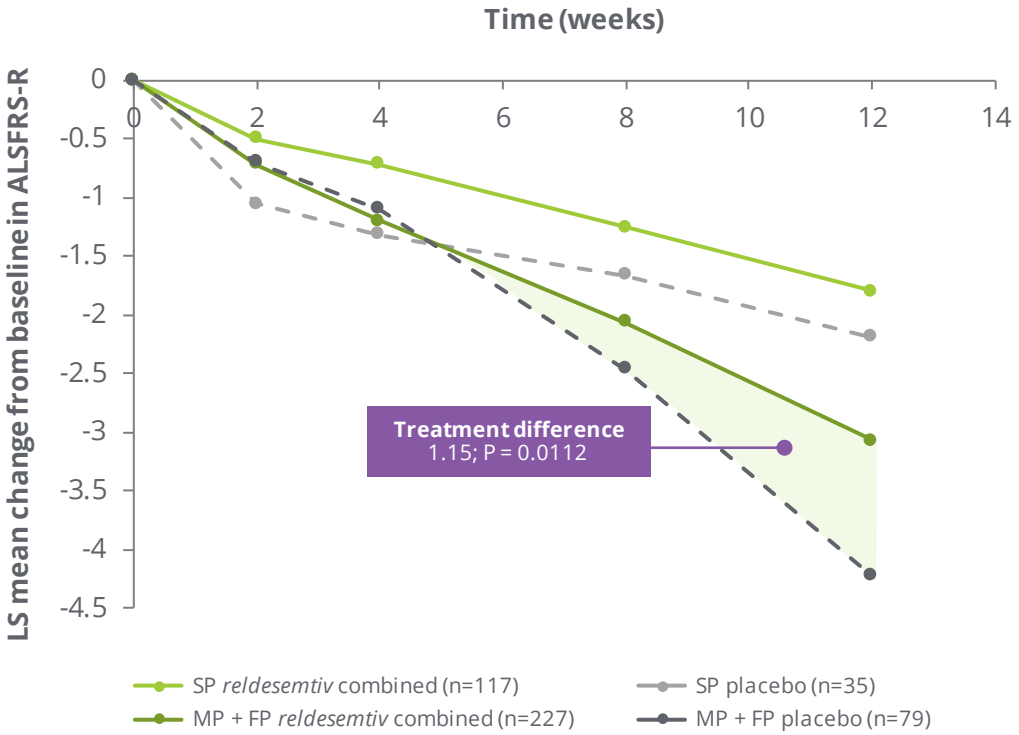
	No. of Patients (pbo/ *reldesemtiv*)	LSM Difference (95% CI)	Estimate	*P* value
Percent predicted SVC at baseline				
<80	43/109		1.588	0.0089
≥80	57/196		0.264	0.5296
ALSFRS-R total score at baseline				
<Median (38.0)	48/129		1.107	0.0585
≥Median (38.0)	52/176		0.685	0.0987
ALSAQ-5 total score at baseline				
<150	52/164		0.266	0.5025
≥150	48/141		1.598	0.0055
Anatomic site of disease onset				
Limb	80/245		0.872	0.0279
Bulbar	20/60		0.861	0.2194
Time since ALS symptom onset				
<2 Years	56/199		1.422	0.0025
≥2 Years	44/106		0.475	0.3439
Time since ALS diagnosis				
<1 Year	71/225		1.123	0.0101
≥1 Year	29/80		0.359	0.5350
<6 Months	42/137		1.359	0.0154
≥6 Months	58/168		0.566	0.1820
Pre-study rate of disease progression				
(ALSFRS-R total score reduction per month)				
1st tertile ≤ (0.3667)	32/110		0.389	0.4298
2nd tertile > (0.3667) – (0.6673)	38/99		0.987	0.0665
3rd tertile (0.6673)	30/96		1.733	0.0177

*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

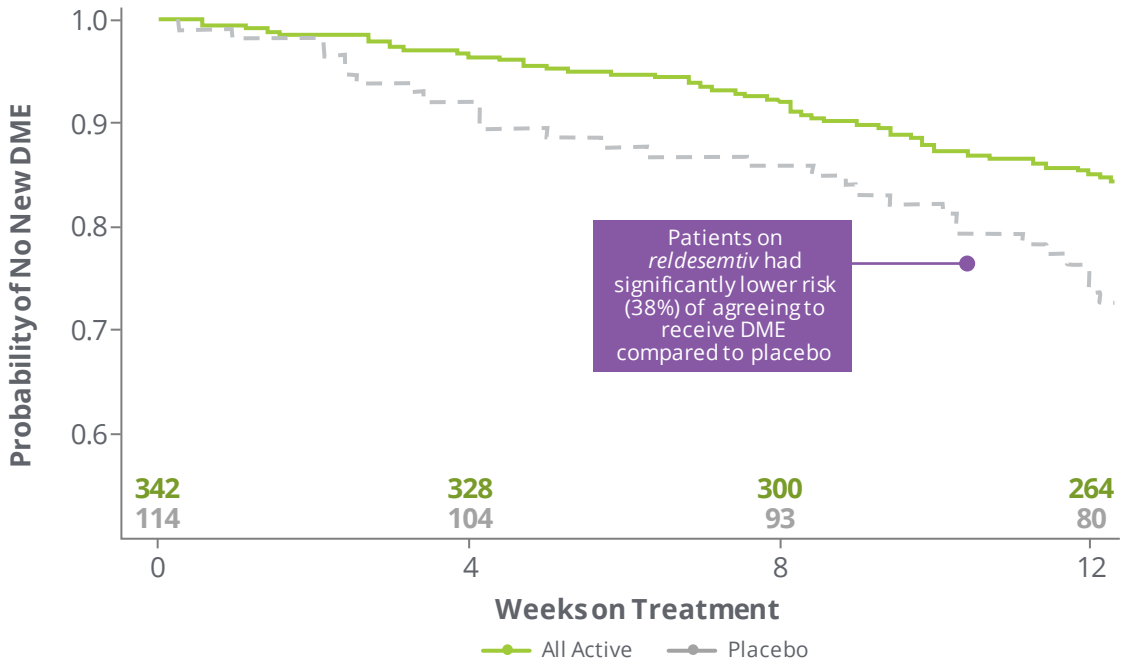
FORTITUDE ALS

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

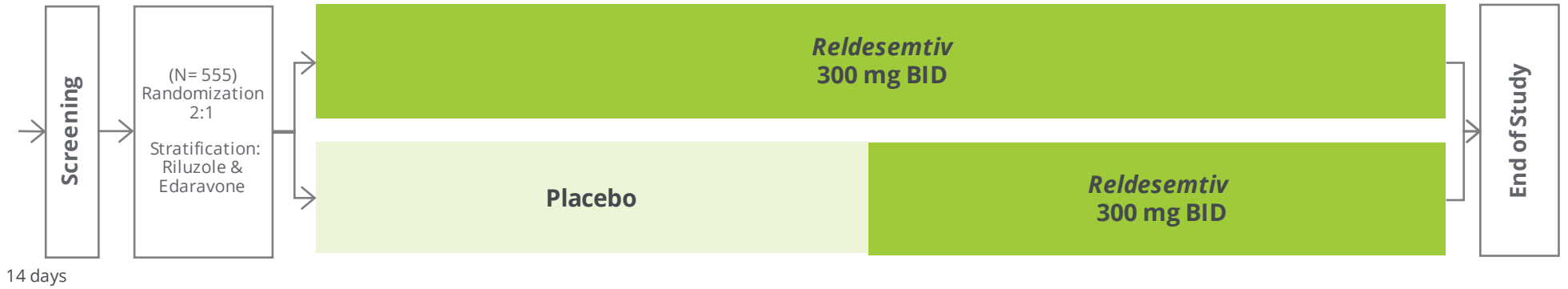


Phase 3 Clinical Trial Design

COURAGE ALS

Trial opened to 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

Cytokinetics

Sarcomere Directed Therapies

CORPORATE PROFILE

Cytokinetics

Robust Pipeline, Solid Financial Position

Pipeline*

1 Positive trial readout in 2021

2 Pivotal trials in 2021

3 Potential FDA approvals by 2025

5 Clinical stage programs

10 Development programs by 2025

Programs*

Heart Failure

Omecamtiv mecarbil

- Positive trial results from GALACTIC-HF
- Phase 3 exercise capacity trial results early 2022

CK-136

- Phase 1

HCM

Aficamten

- Positive results from REDWOOD-HCM
- Expect to begin Phase 3 trial by Q4

ALS

Reldesemtiv

- COURAGE-ALS, Phase 3 trial ongoing

Ongoing R&D

Additional research in muscle biology, energetics & metabolism

Foundations

214

Full time employees

$424M*

At Q2 2021

** In July 2021, Cytokinetics raised $297 million through a public offering of common stock.*
Timelines and milestones reflect Cytokinetics' current expectations and beliefs

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

in millions

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

2021 Financial Guidance

in millions

	Total
Cash Revenue	$23 – 28
Cash Operating Expenses	$230 – 250
Net	**~ $195-215**

** In July 2021, Cytokinetics raised $297 million through a public offering of common stock.*

Expected Upcoming 2021 Milestones

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

Cytokinetics

Sarcomere Directed Therapies

THANK YOU

John, *diagnosed with heart failure*

Jillian, *diagnosed with HCM*

Chuck, *diagnosed with ALS*