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; projections regarding the size of the addressable patient population for *omecamtiv mecarbil*; Cytokinetics' commercial readiness for *omecamtiv mecarbil*; the likelihood of approval and timing for approval of *omecamtiv mecarbil* or any of our other drug candidates; the submission of a new drug application (NDA) for *omecamtiv mecarbil* in 2H 2021; the timing and results of clinical trials of CK-274, including the expectation of results of REDWOOD-HCM in mid-2021; the commencement of a phase 3 clinical trial of reldesemtiv by year end; 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*, CK-136 (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' 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

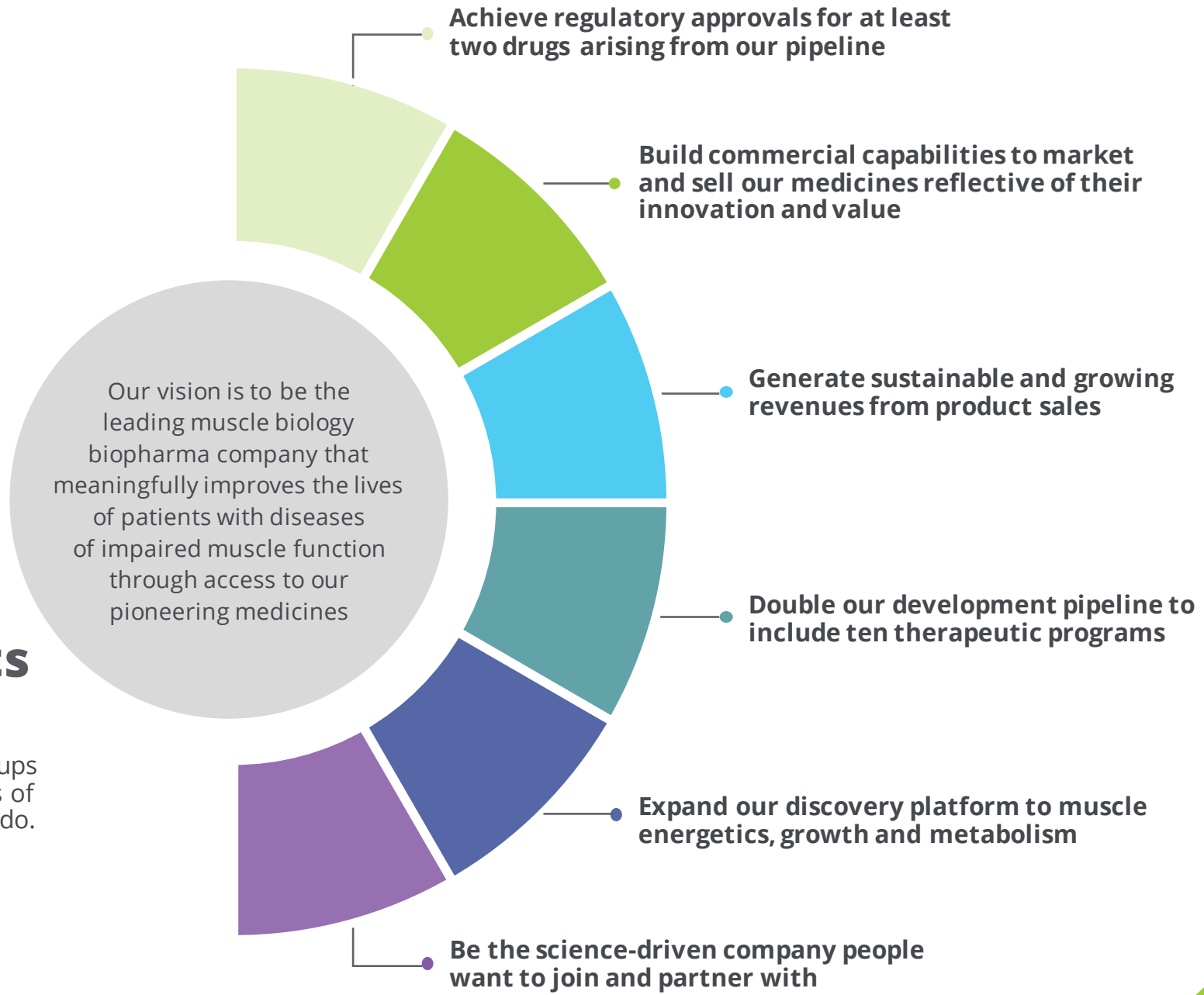
To bring forward new medicines to improve the healthspan of people with devastating cardiovascular and neuromuscular diseases of impaired muscle function.

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.



How Do We Get There?

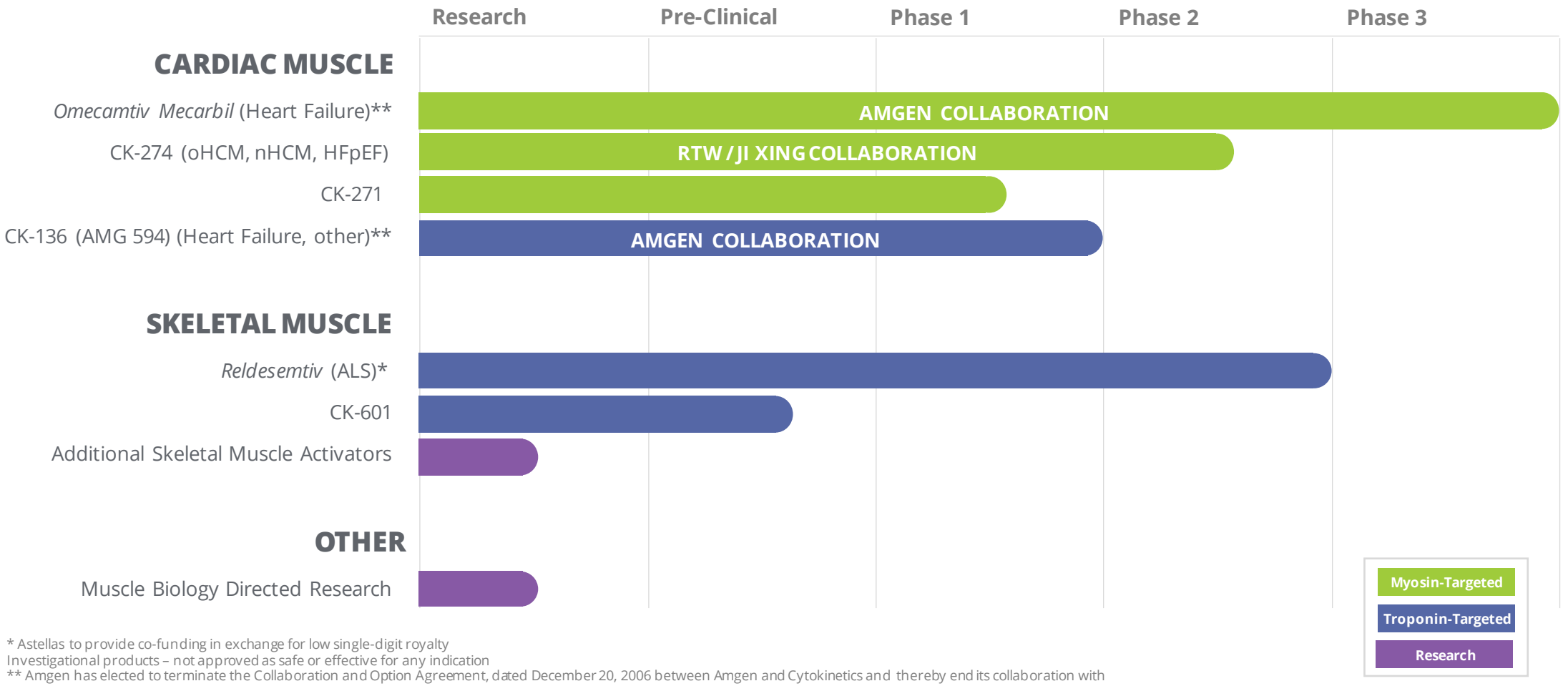
- Exploit muscle biology roots
- Measure pharmacodynamics of muscle function
- Develop first-in-class, next-in class, best-in-class compounds
- Expand contractility focus to muscle energetics, metabolism

- Adopt customer-centric approach to portfolio management
- Pioneer and lead: innovate, integrate and scale
- Extend and expand through lifecycle management
- Continually pursue back-ups, follow-ons, next-gen drug candidates

- Conduct rigorous, step-wise clinical research
- De-risk development programs to increase POS
- Optimize PK/PD relationships
- Maintain continuity of engagement with leading KOLs

- Engage early and often for input and guidance
- Elevate patient voice
- Improve function, performance and healthspan
- Adapt trial design to facilitate participation

Pipeline of Novel Muscle-Directed Drug Candidates



* Astellas to provide co-funding in exchange for low single-digit royalty
Investigational products – not approved as safe or effective for any indication
** Amgen has elected to terminate the Collaboration and Option Agreement, dated December 20, 2006 between Amgen and Cytokinetics and thereby end its collaboration with Cytokinetics, effective May 20, 2021, Upon termination all development and commercialization rights for *omecamtiv mecarbil* and CK-136 (AMG 594) will revert to Cytokinetics.
*** 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 (AMG 594)

CK-274, CK-271

Cytokinetics

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)*

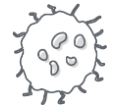
#4 Endocrine *($227B)*

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**

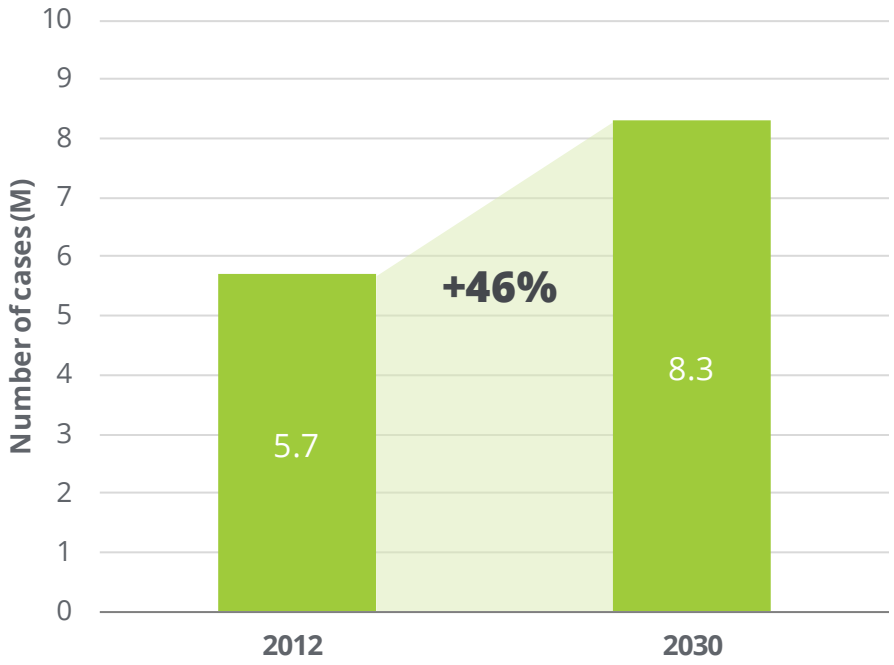
# of Approved Drugs since 2010

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

Heart Failure: Growing Prevalence and Low Survival Rates

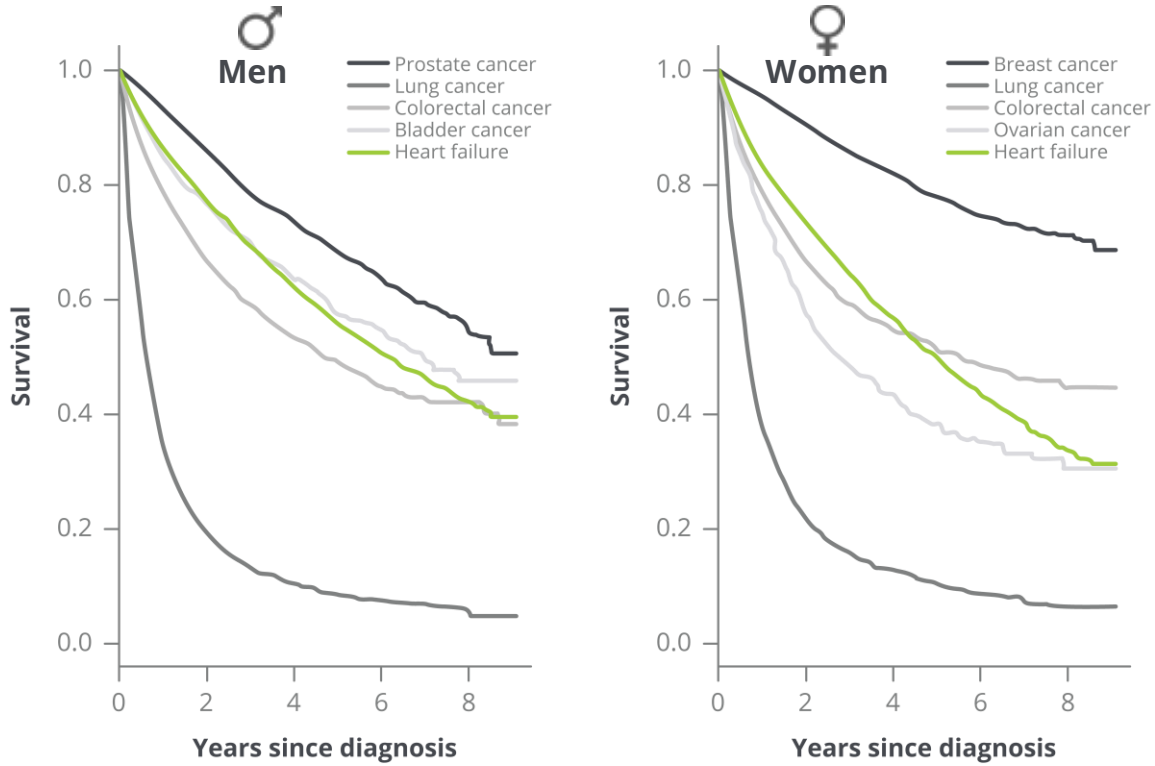
6 million people have heart failure in the United States

Prevalence Expected to Increase by 46% from 2012 – 2030



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

HF Survival Rates Worse than Some Prevalent Cancers

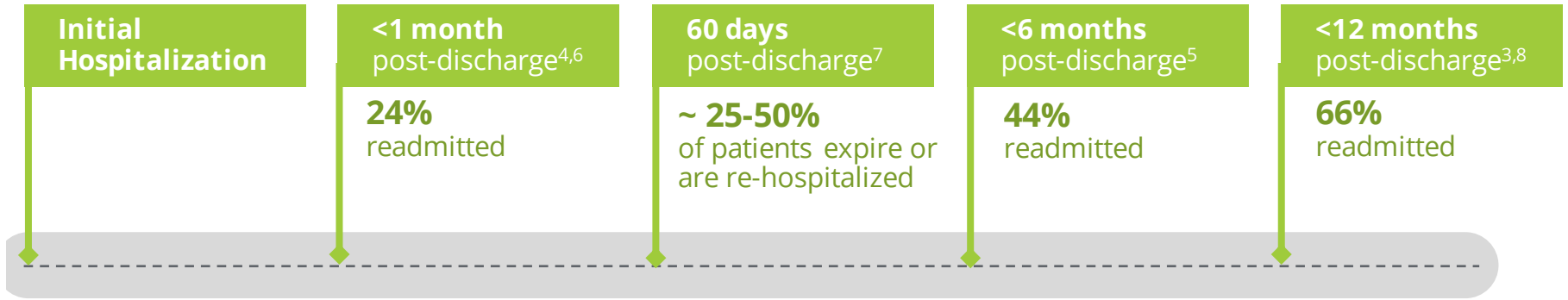


Mamas et al. *Eur J Heart Fail.* 2017 Sep;19(9):1095-104

High Hospital Readmission Rates

Heart failure is one of the most frequent causes of hospitalization in people > 65[1,2]

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



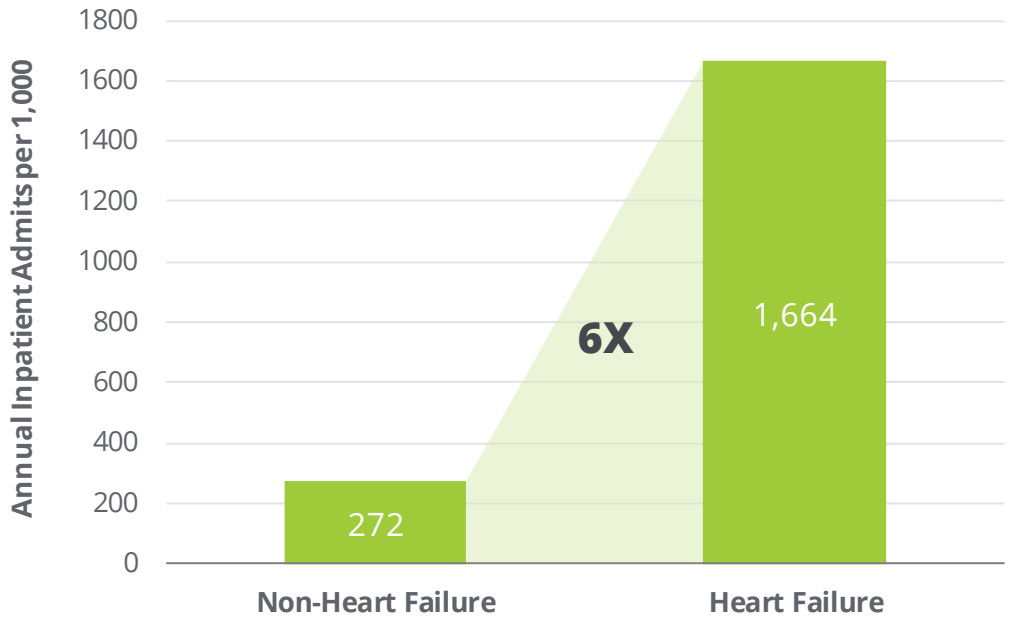
1, Adams et al. *Am Heart J* 2006; 149:209-16
2. Chen et al. *JAMA* 2011;306:1669-78
3. Dickstein et al. *Eur Heart J* 2008;29:2388-442
4. Korda,, et al. *BMC Health Serv Res*. 2017;21;17(1):220.
5. Krumholz et al. *Arch Intern Med* 1997;15799 – 105
6. Krumholz et al. *Circ Cardiovasc Qual Outcomes* 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

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**

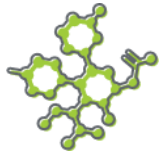
Drugs that do not affect renal function

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

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

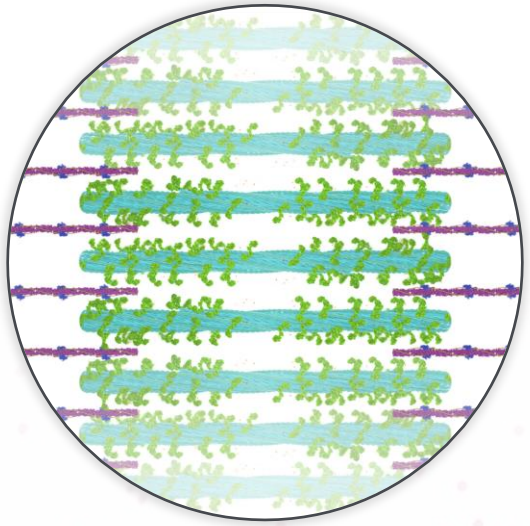
Current medical therapy does not target underlying disease

Indirect mechanisms of action with systemic side effects

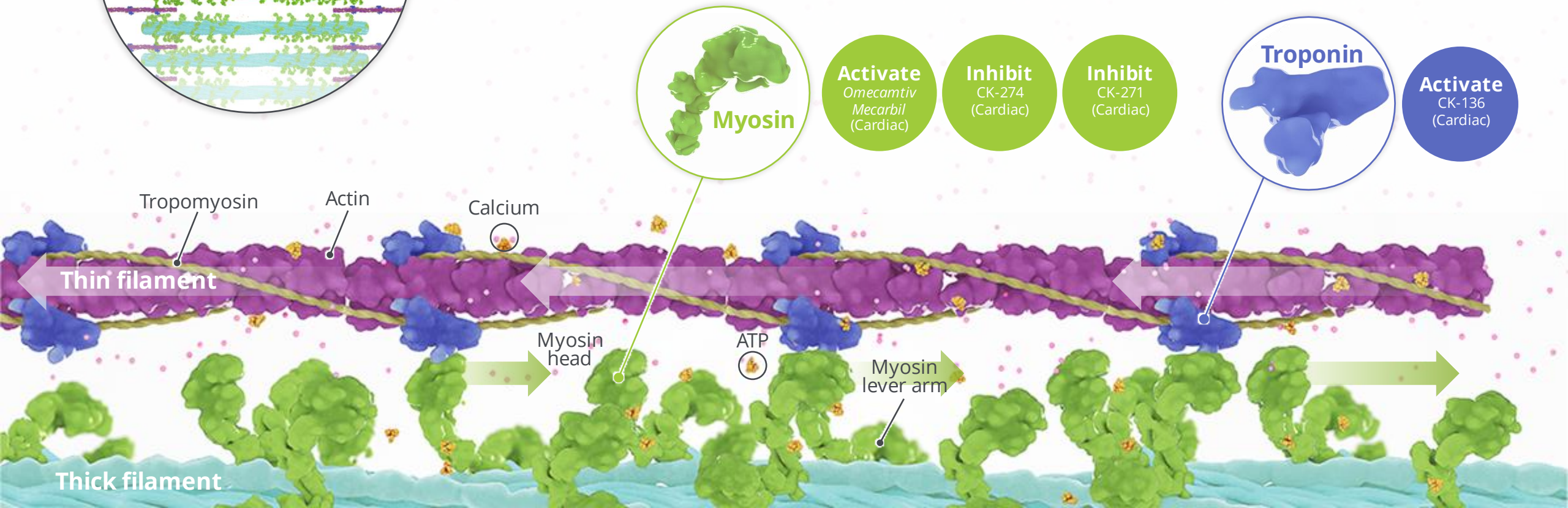
Variable efficacy, often inadequate

Sarcomere Directed Drug Development

Cardiac muscle

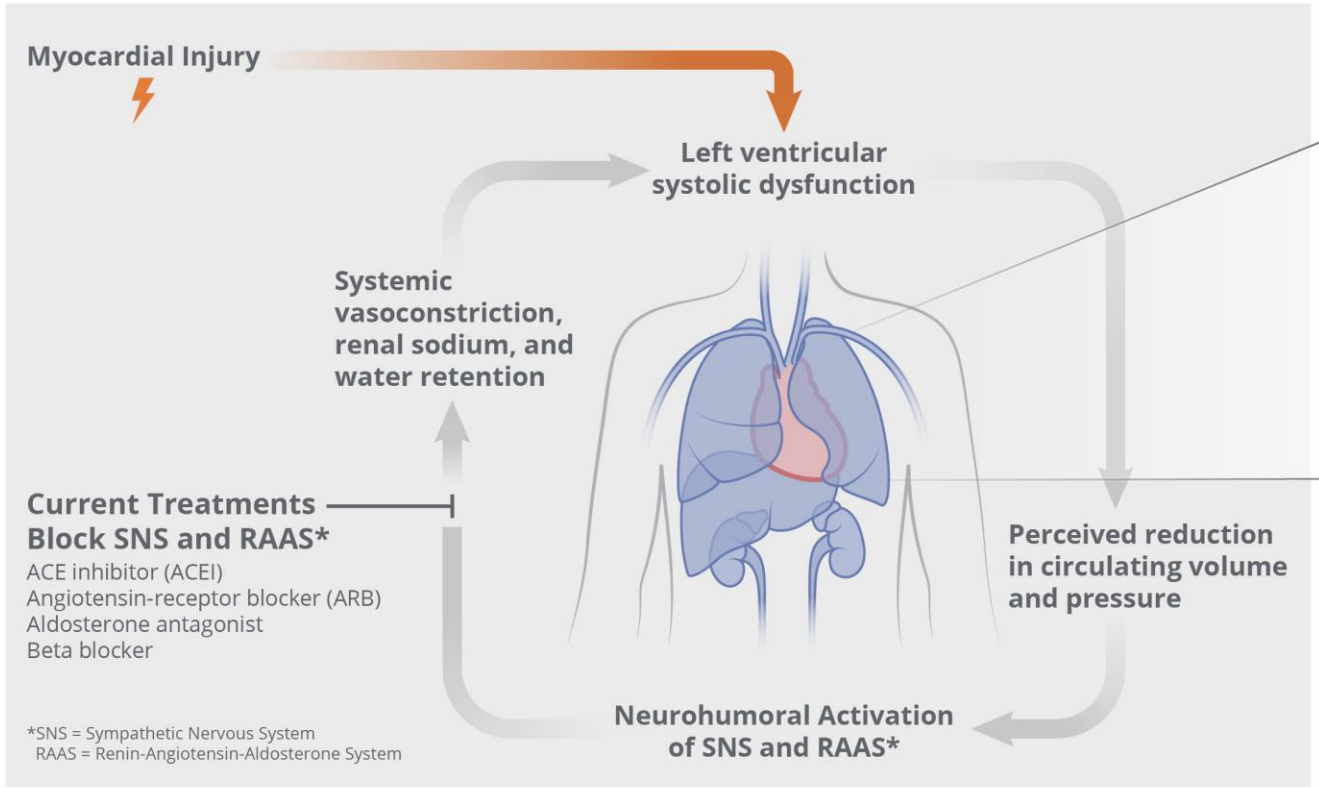


The sarcomere is a molecular structure found in skeletal and cardiac muscle that enables cardiac myocytes to contract and generate force

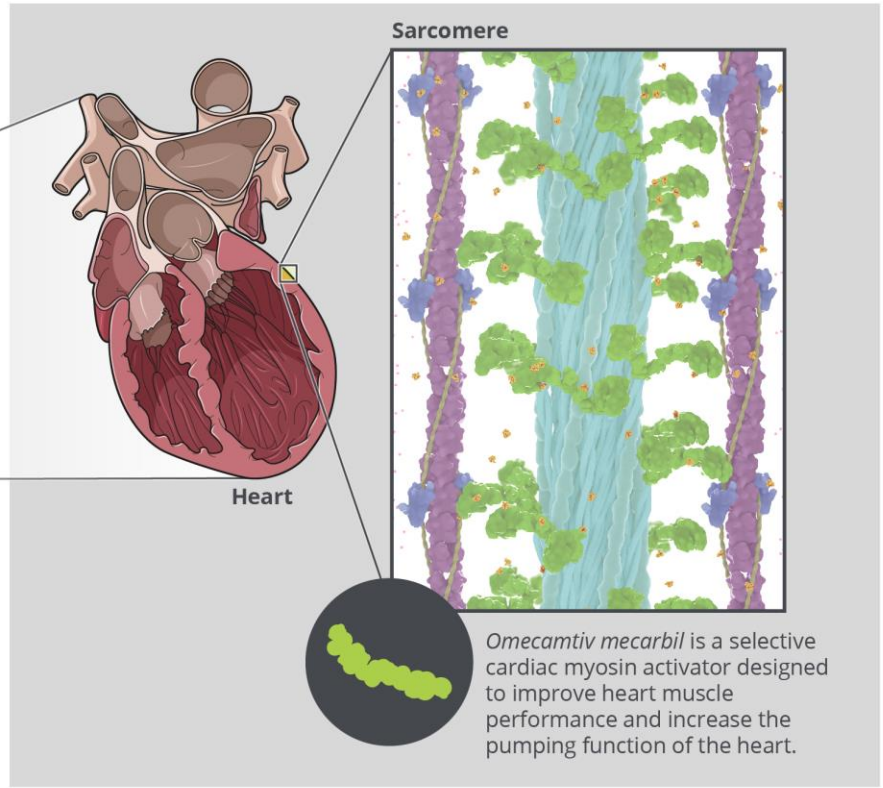


Omecamtiv Mecarbil: Novel Mechanism Approach

Current Treatments

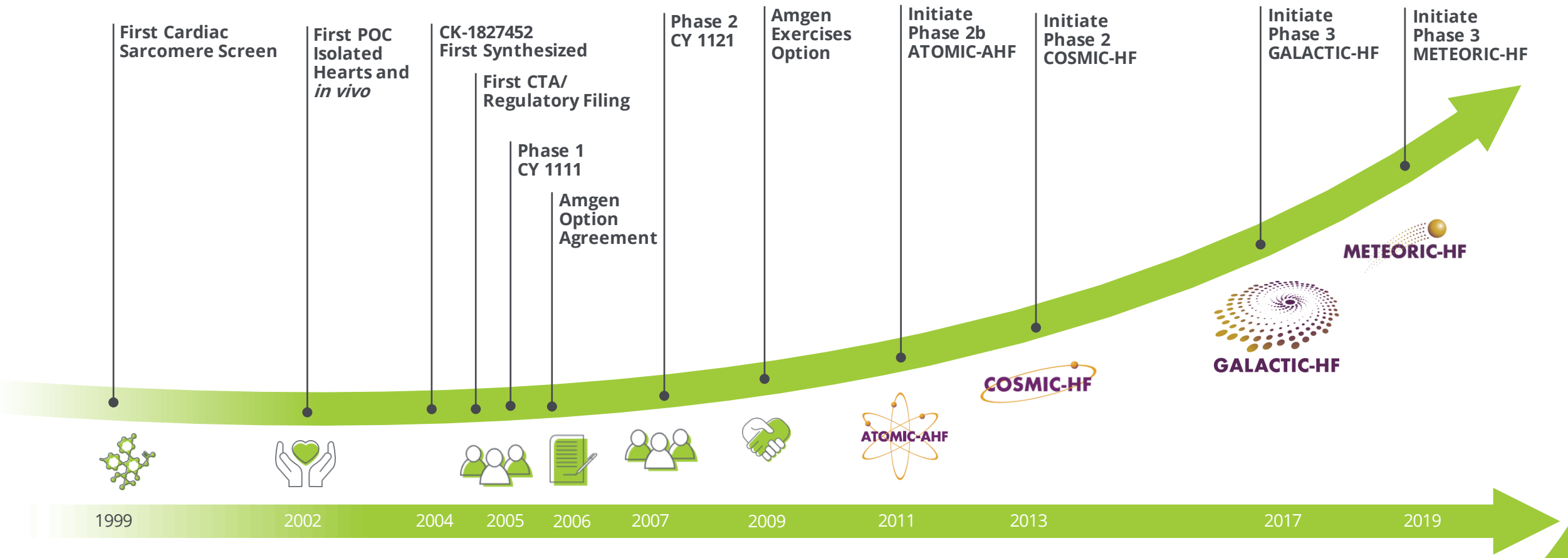


Omecamtiv mecarbil



Omecamtiv Mecarbil: Positive Phase 3 Trial Results

>30 trials: 23 Phase 1 studies with 600+ participants, 7 Phase 2 trials with 1,400+ patients, 2 Phase 3 trials with 8,000+ patients



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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

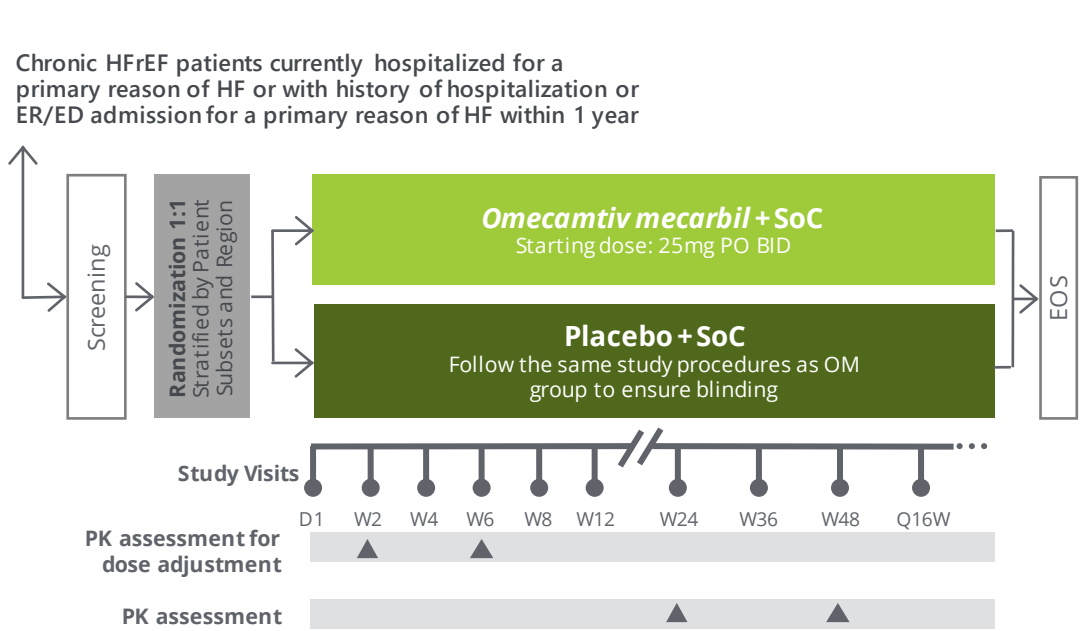
*An HF event defined as the presentation of the subject for an urgent, unscheduled clinic/office/ED visit, or hospital admission, with a primary diagnosis of HF, where the patient exhibits new or worsening symptoms of HF on presentation, has objective evidence of new or worsening HF, and receives initiation 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.

Clinical Trial Overview

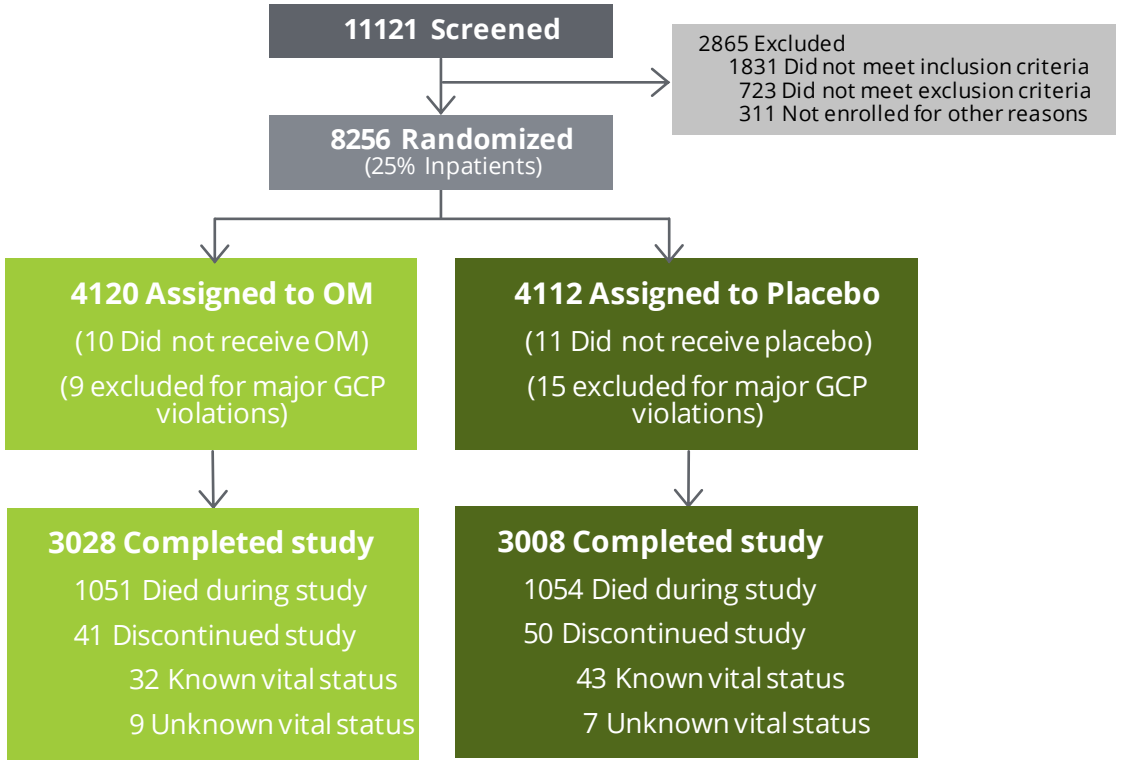
Overall median study exposure was 21.8 months

GALACTIC-HF

Clinical Trial Schema



Patient Disposition



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

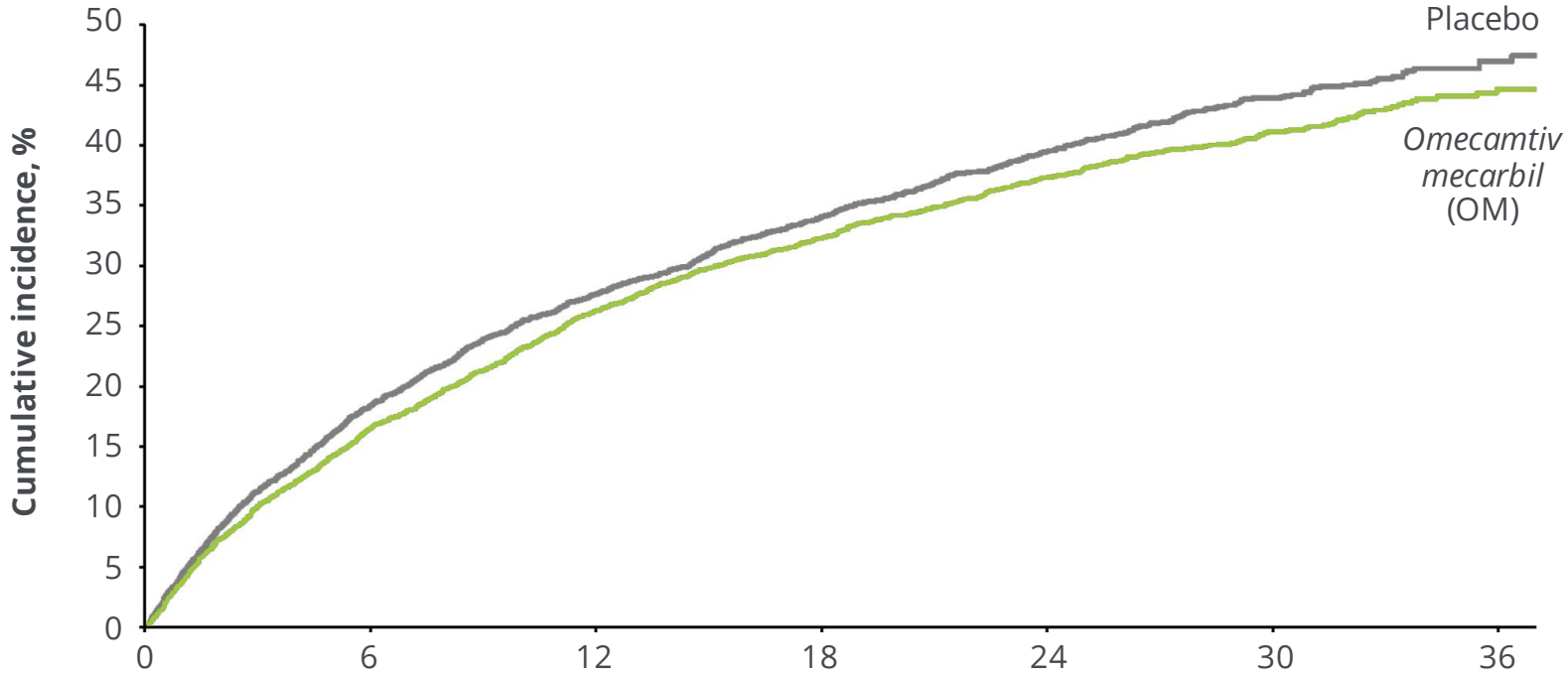
Characteristic	OM (N=4120)	Placebo (N=4112)
Vitals and Laboratory Parameters		
NT-proBNP (pg/mL), median (Q1, Q3)	1977 (980, 4061)	2025 (1000, 4105)
SBP (mmHg), mean (SD)	116 (15)	117 (15)
Heart rate, mean (SD)	72 (12)	72 (12)
eGFR (mL/min/1.73m^2), median (Q1, Q3)	59 (44, 74)	59 (44, 74)
Cardiac TnI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



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

HR = 0.92
(95% CI, 0.86–0.99)

P = 0.025

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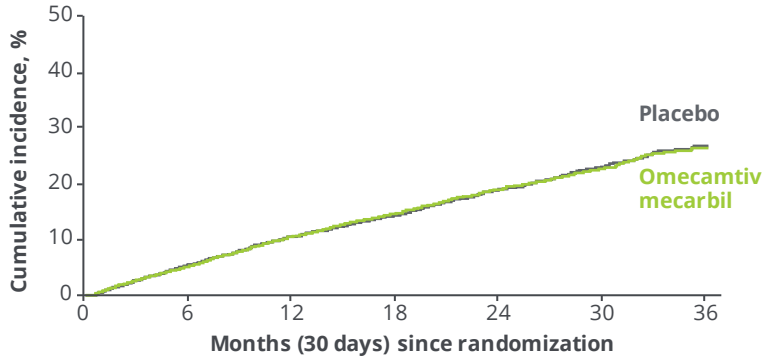
Primary Composite Components and KCCQ TSS

GALACTIC-HF

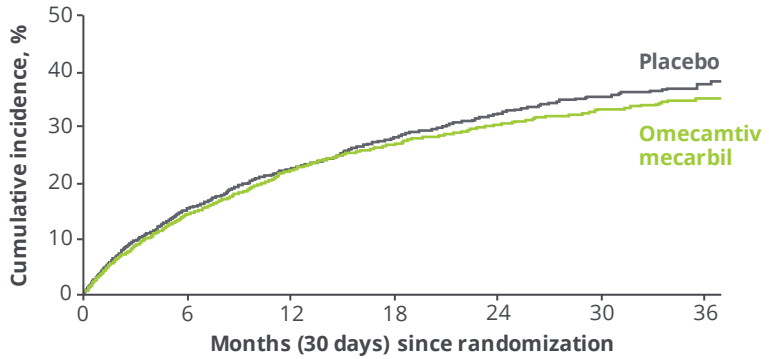
CV Death

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

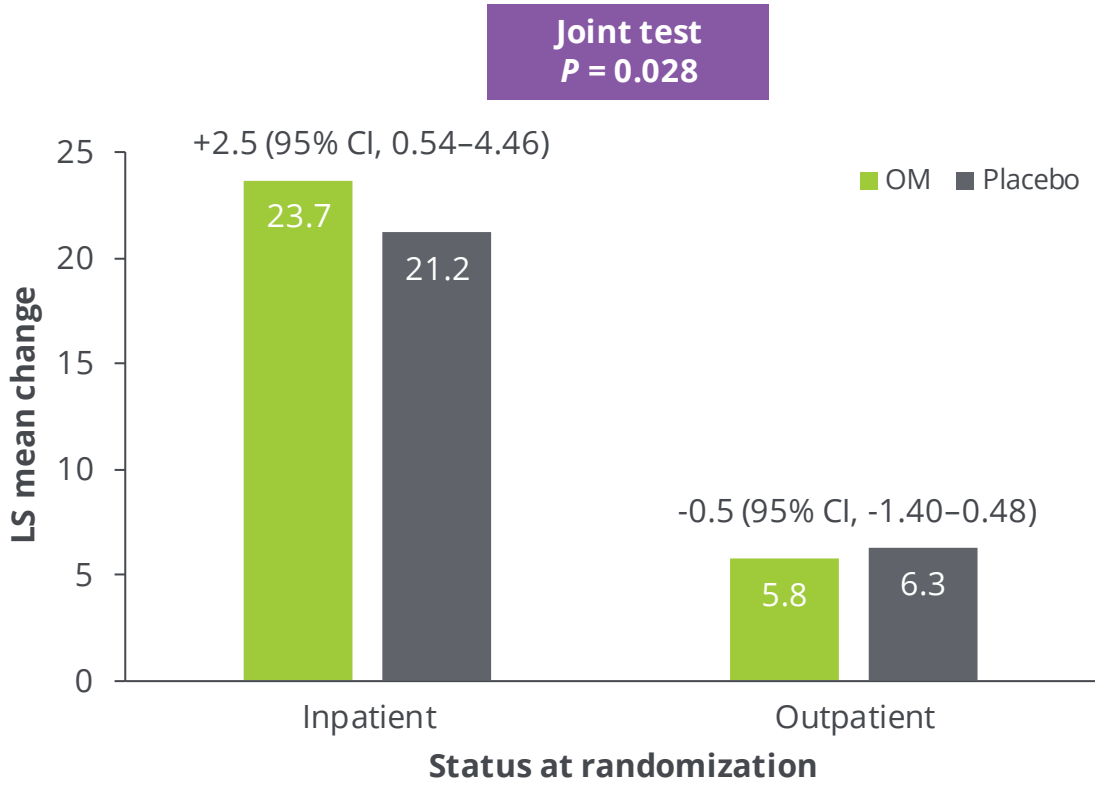


Heart Failure Event

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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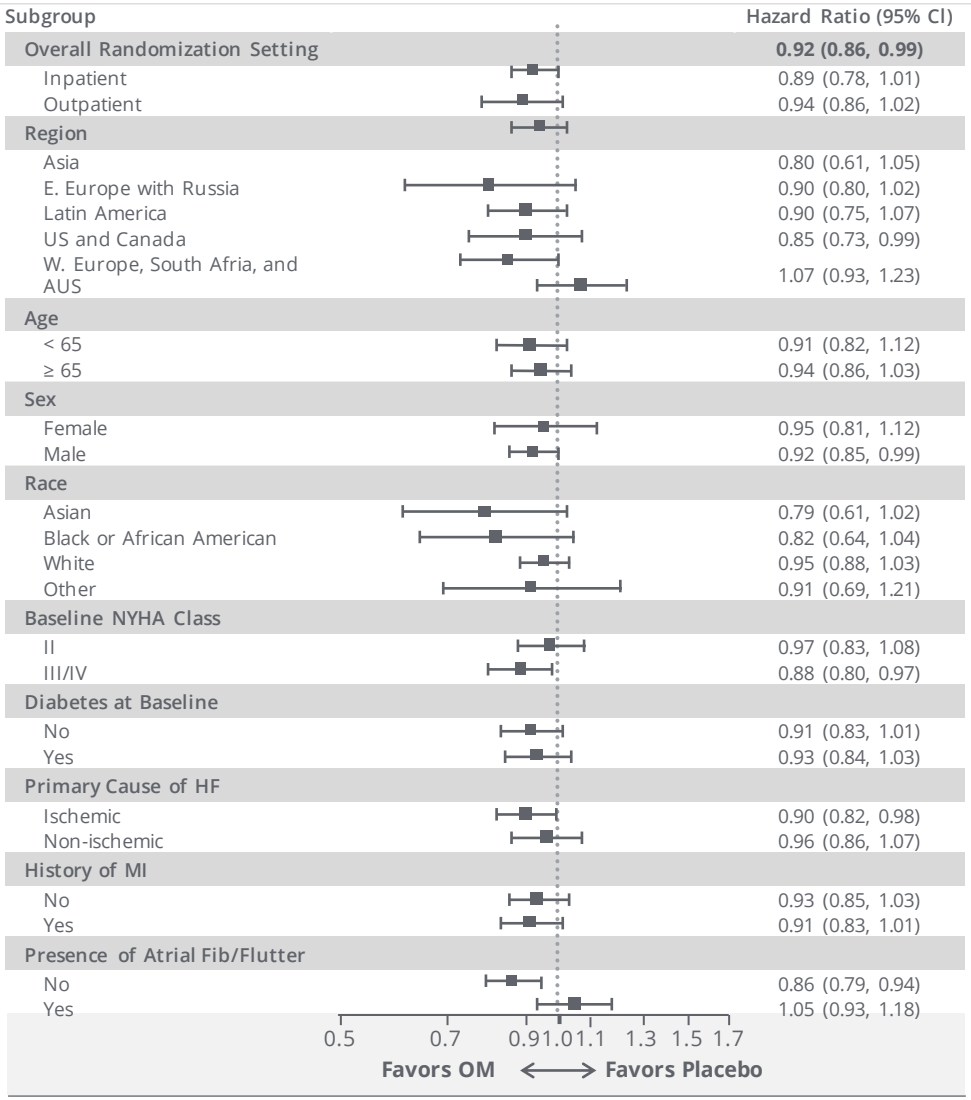
Laboratory and Safety Events

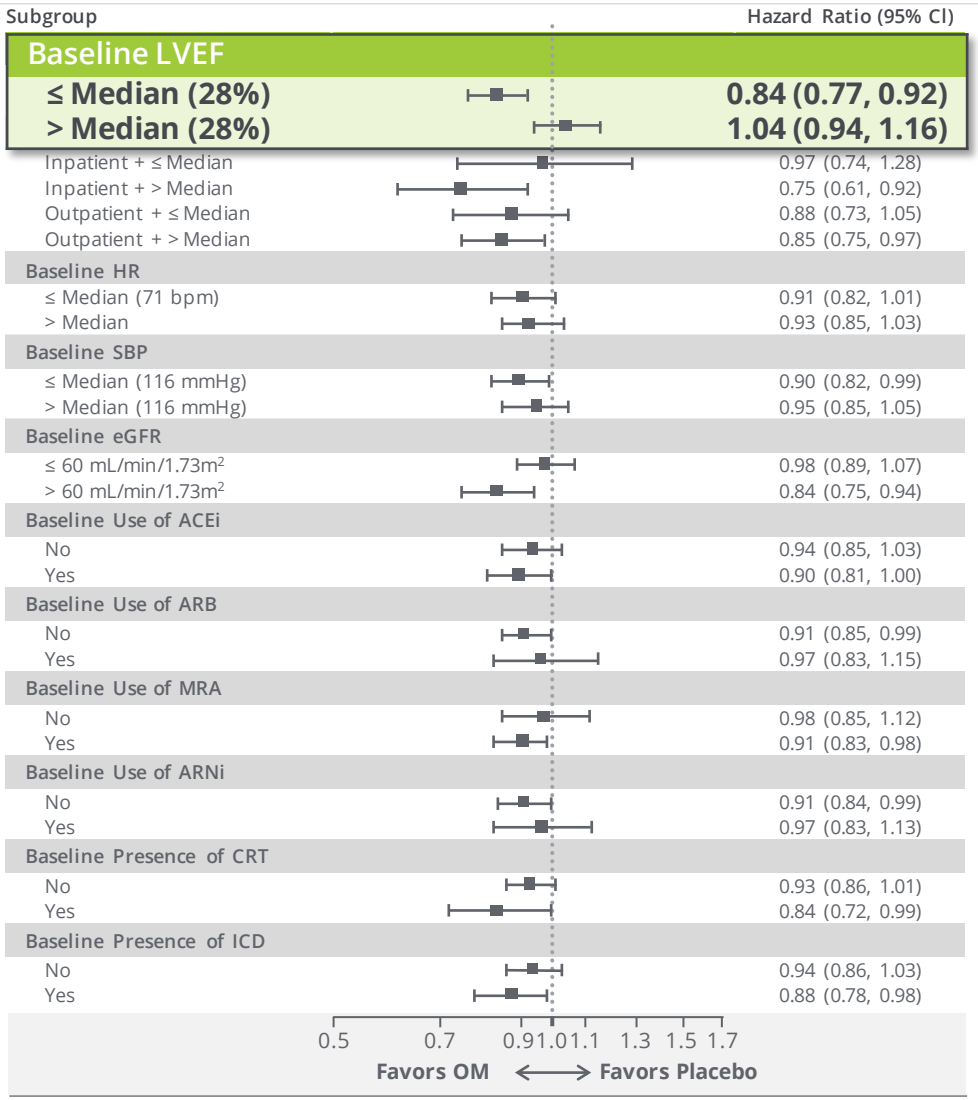
GALACTIC-HF

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)

Primary Outcome: Subgroup Results

GALACTIC-HF





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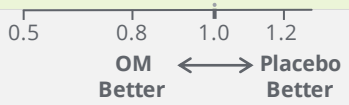
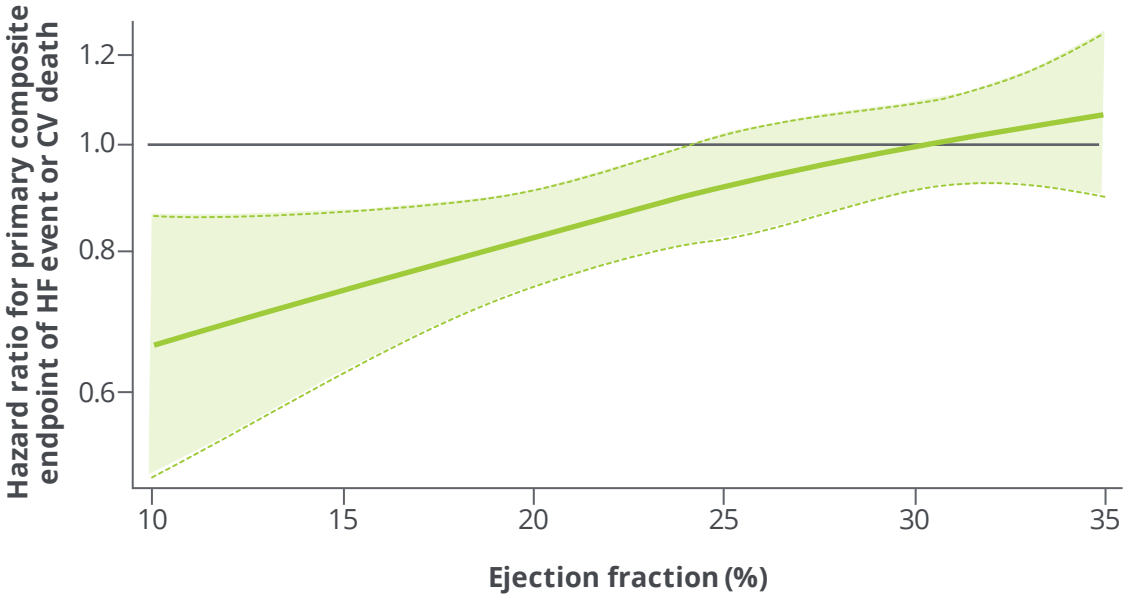
Greater Treatment Effect in Advanced HF Patients

GALACTIC-HF

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%



- **Greater treatment effect in prespecified subgroup of patients with LVEF ≤28%: (n=4,456) HR 0.84; 95% CI 0.77, 0.92**



- Continuous relationship between ejection fraction and hazard ratio for the primary composite endpoint in GALACTIC-HF suggested potentially **stronger treatment effect of *omecamtiv mecarbil* in patients with increasingly lower ejection fractions**

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Secondary Analysis: ACC 2021 Late Breaker

Secondary analysis assesses effect of *omecamtiv mecarbil* on clinical outcomes in relationship to patient baseline ejection fraction

Late-Breaking Clinical Trials IV

May 17, 2021, 9:00 – 9:10 AM ET

Impact Of Ejection Fraction On The Therapeutic Effect Of *Omecamtiv Mecarbil* In Patients With Heart Failure And Reduced Ejection Fraction: A Secondary Analysis From GALACTIC-HF

John Teerlink, M.D., Professor of Medicine, University of California San Francisco, Director of Heart Failure, San Francisco Veterans Affairs Medical Center and Executive Committee Chair, GALACTIC-HF

Comparable Results Supported Recent FDA Approval

Approval of Verquvo Reflects Unmet Need in Advanced HF Patients

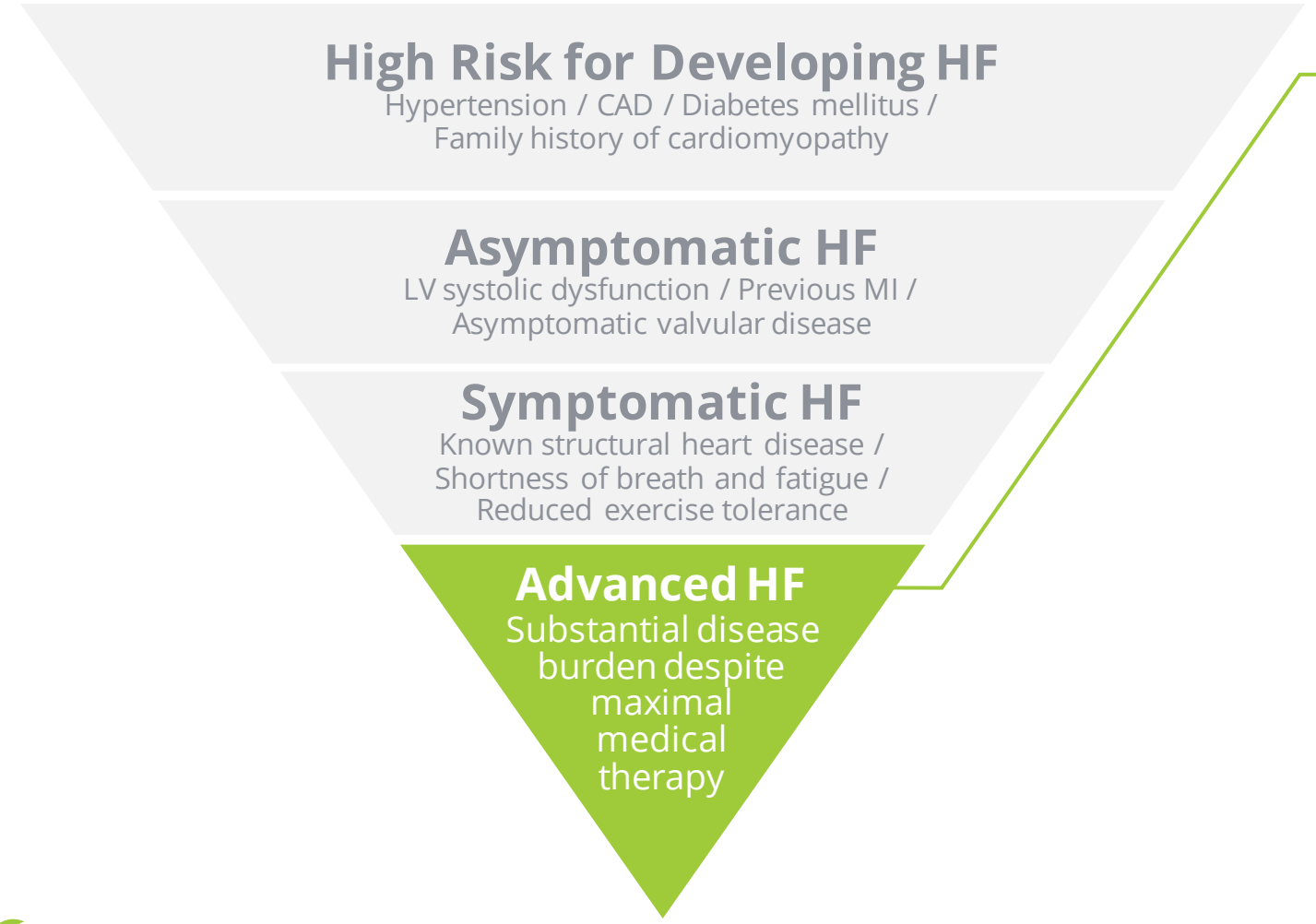
	Primary Endpoint	Key Secondary Endpoints		Hosp. Patients	Patient Baseline Characteristics		
Trial	**Composite: CV Death or First HFH**	**CVD**	**KCCQ**	**Inclusion Criteria**	**Mean LVEF**	**NYHA Class**	**Median NT-proBNP**
GALACTIC-HF 8,256 patients	**8% RRR** (p = 0.025)	*No effect*	**2.5-point change***	Hosp required w/in past 12 mos = 75% Currently hospitalized = 25%	26.6	II = 53% III = 44% IV = 3%	1,998
VICTORIA 5,050 patients	**10% RRR** (p = 0.02)	*No effect*	N/A**	Hosp <3 mos = 67% Hosp 3-6 mos = 17% IV Diuretic (w/o hosp) <3 mos = 16%	28.9	II = 59% III = 40% IV = 1%	2,816

* Inpatient population only
** Data from the VITALITY-HFpEF trial showed that vericiguat did not improve the KCCQ physical limitation score at 24 weeks

Verquvo™ (vericiguat) tablets 2.5 mg, 5 mg, 10 mg

Approved for Reduction of Risk of CV Death and Heart Failure Hospitalization Following a Hospitalization for Heart Failure or Need for Outpatient Intravenous Diuretics in Adults with Symptomatic Chronic Heart Failure and Ejection Fraction Less than 45%

Focusing to the Advanced Heart Failure Patient

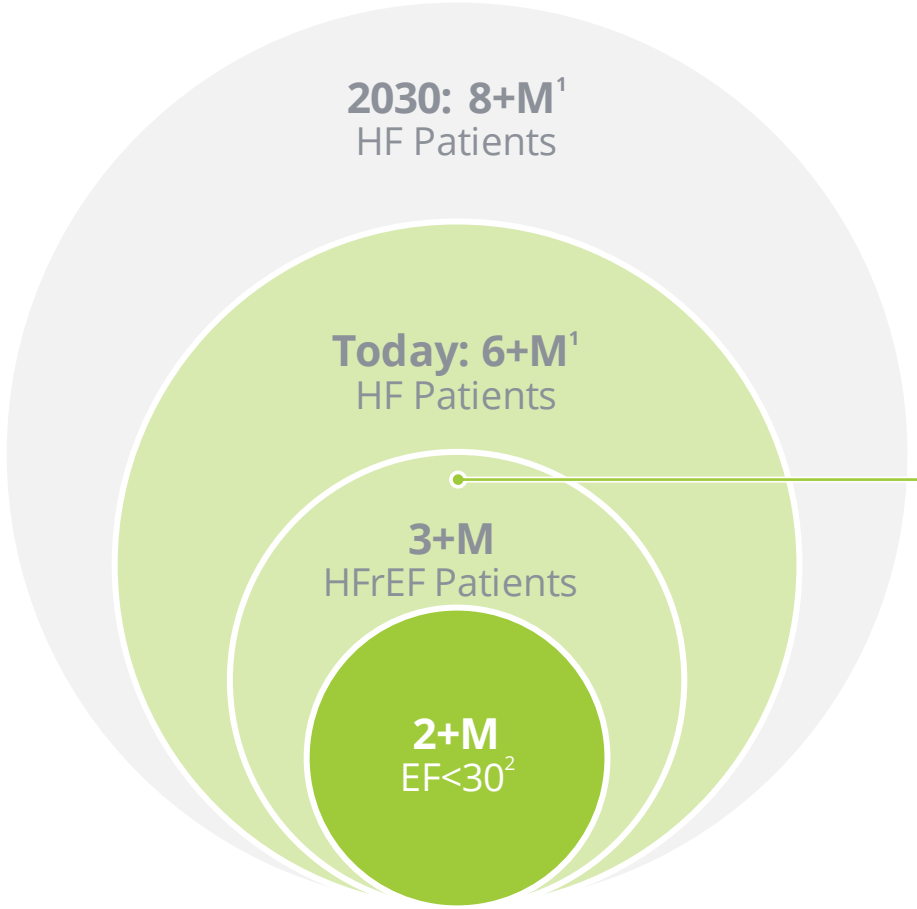


Advanced heart failure is defined as:

- Significant persistent symptoms
- Objective evidence of severe impairment of cardiac performance
  - EF < 30%
  - Impaired invasive or non-invasive hemodynamics
- Recurrent hospitalizations
- Severe impairment of functional capacity (6MWD < 300 m, peak VO_2 < 12 mg/kg/min)

Despite optimal medical and device treatment

Addressable U.S. Patient Population: Up to 2M Patients



Comorbidities may limit ability to tolerate SOC therapy

- 75% Hypertension[2]
- 80% eGFR<90[2]
- 25–30% Afib[2]
- 20–30% Chronic Lung Disease[2]
- 20% Diabetes[2]

Sources:
1. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics—2020 update: a report from the American Heart Association Circulation. 2020;141(9):e139-596. p e509
2. Shannon M. Dunlay, Véronique L. Roger, Susan A. Weston, Ruoxiang Jiang, and Margaret M. Redfield (Circ Heart Fail. 2012;5:720-726.); Olmsted County community cohort of HF patients (1984 to 2009).

Clinical and Economic Burden of Advanced HF

High rates of hospitalization and high costs of care

Among patients with HFrEF who experienced a worsening heart failure event (HF hospitalization or ER visit) in last 12 months[1]

- **63.5% had LVEF ≤25%,** despite statistically significantly higher use of guideline-directed medical therapy compared to patients without a worsening heart failure event
- Statistically significant greater rate of HF hospitalizations, all-cause hospitalizations and mortality

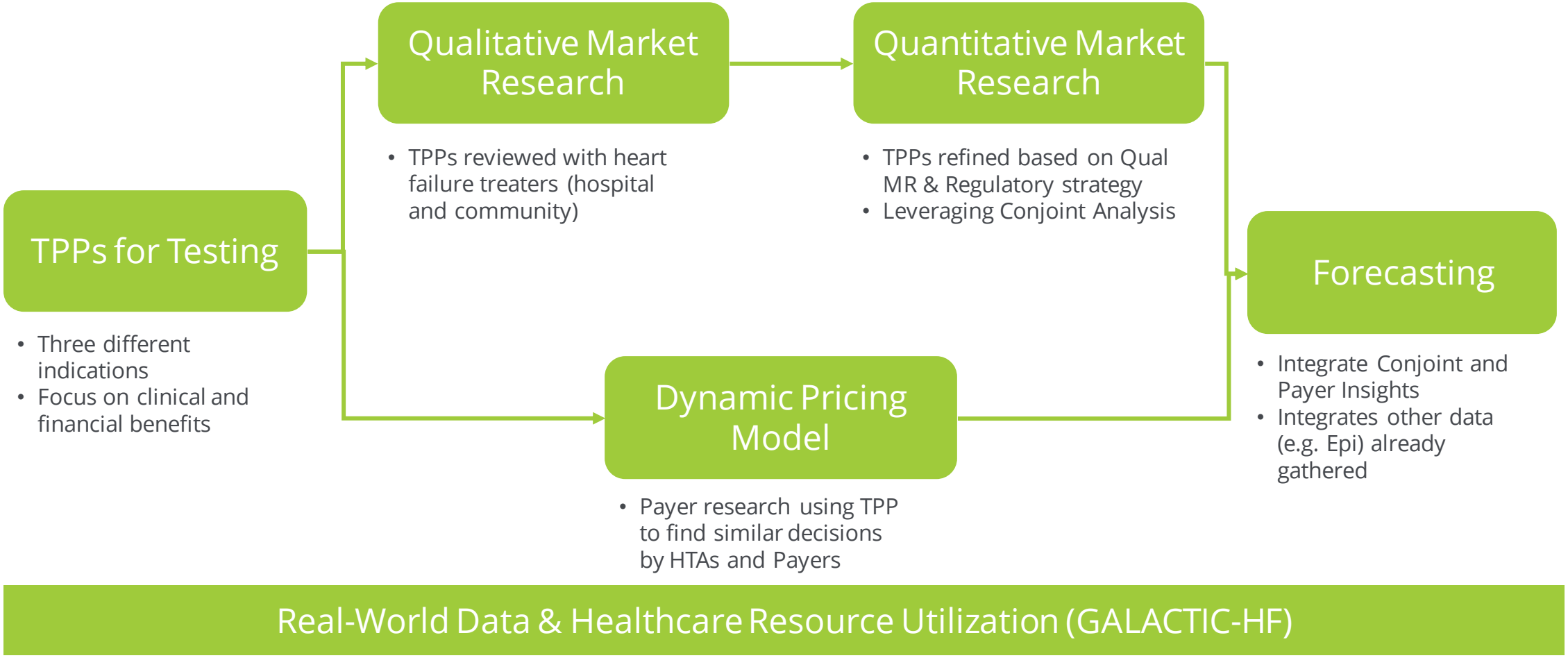
For Medicare patients hospitalized for heart failure between 2016-2018[2]

- 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**

1. Carnicelli et al. Duke Clinical Research Institute, AHA 2020
2. Desai et al, Yale University School of Medicine, AHA 2020

Refining the Market Opportunity

Current Workstreams: 1H 2021



Go-To-Market Strategy: Customer Facing Deployment

Key Considerations

Strategic Importance of the Hospital/IDN Channel

- ~45% of patients diagnosed for HF in hospitals and **treated by physicians primarily affiliated with strategic hospitals** – home of HF COEs, KOLs
- **Advanced HF patients more likely to be treated in hospitals** - a critical capture point and discharge treatment opportunity

Array of Weighted Metrics

- Targeting institutions and high prescribing community physicians based on a weighted blend of
  - Patient claims
  - Entresto® uptake
  - Advanced HF medicine usage
  - Access tiers

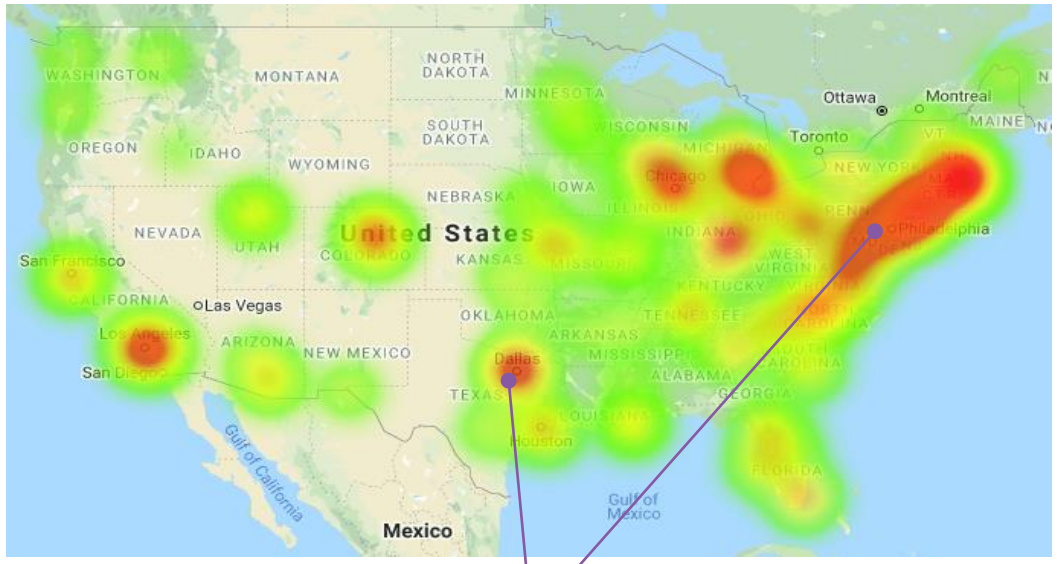
Applied Analytics

- Deployment of customer facing teams informed by claims data, Rx data, "communities of practice," rep access and digital affinity
- Non-personal promotion leveraged to address "no see" physicians, restricted hospitals, especially post COVID-19

Top 1,100 Hospitals Represent 70% of HFrEF Admissions

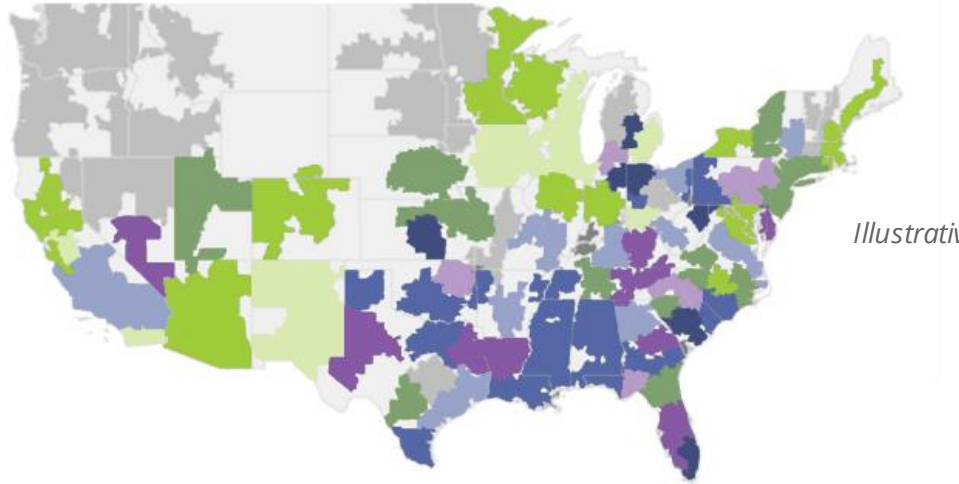
“Future Ready” Deployment & Promotion Enables Customization

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

Expect enrollment to complete in 1H 2021

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**

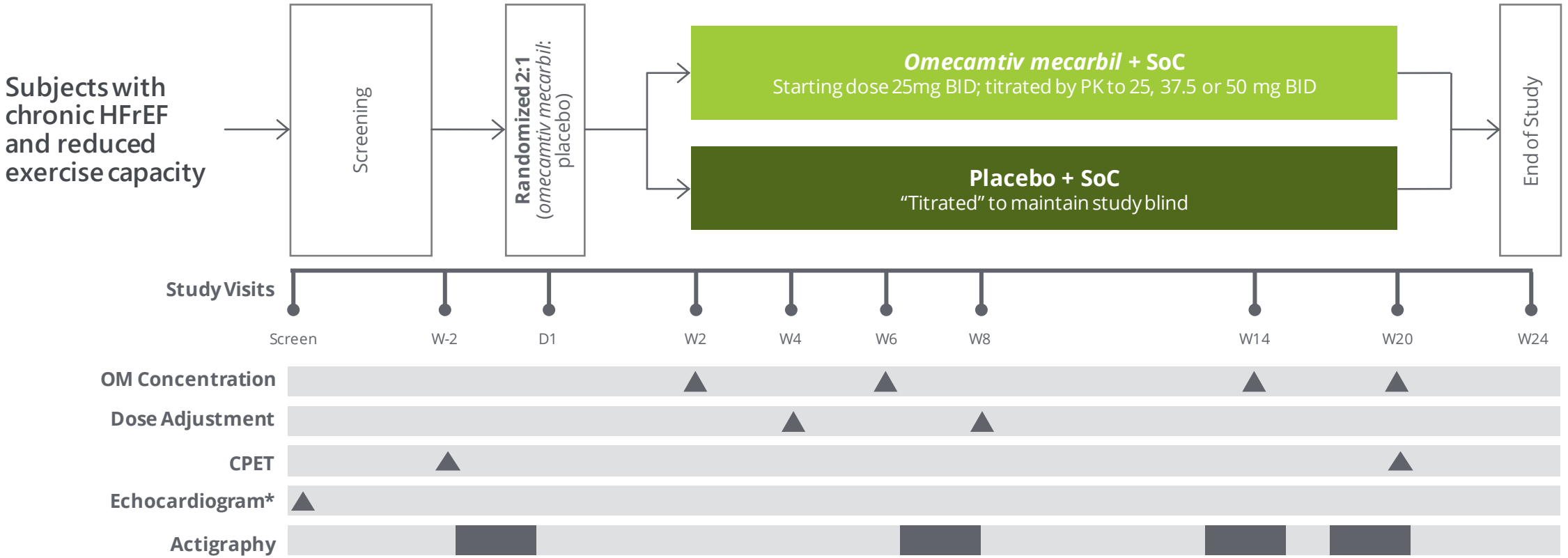
Key Design Points

- 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

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

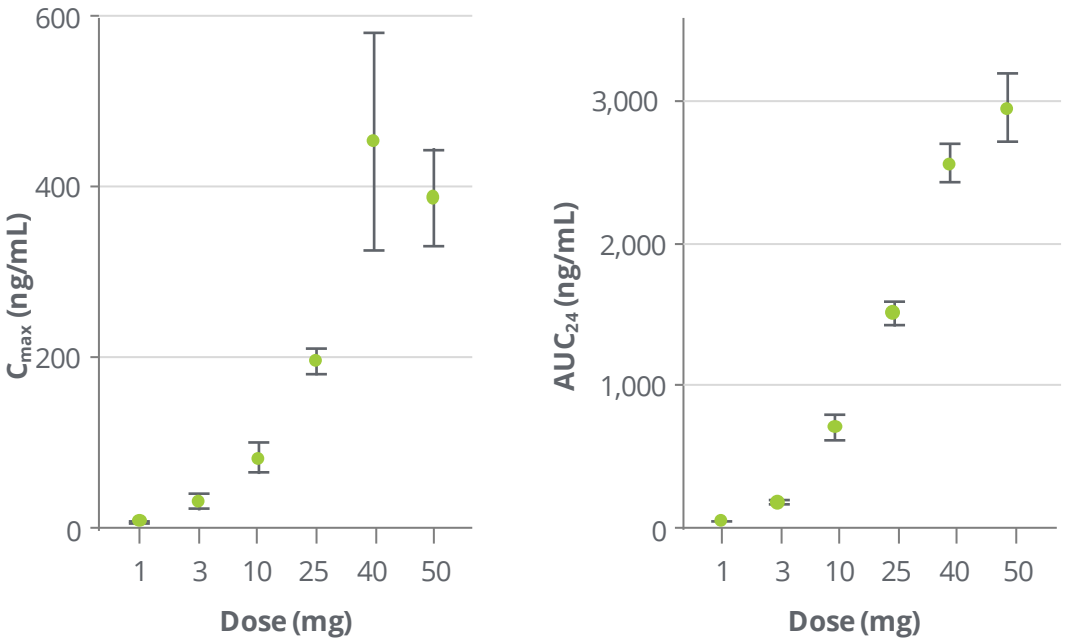
Potential treatments for patients with HCM

- 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 dose optimization in humans as may contribute to its efficacy and safety profile**

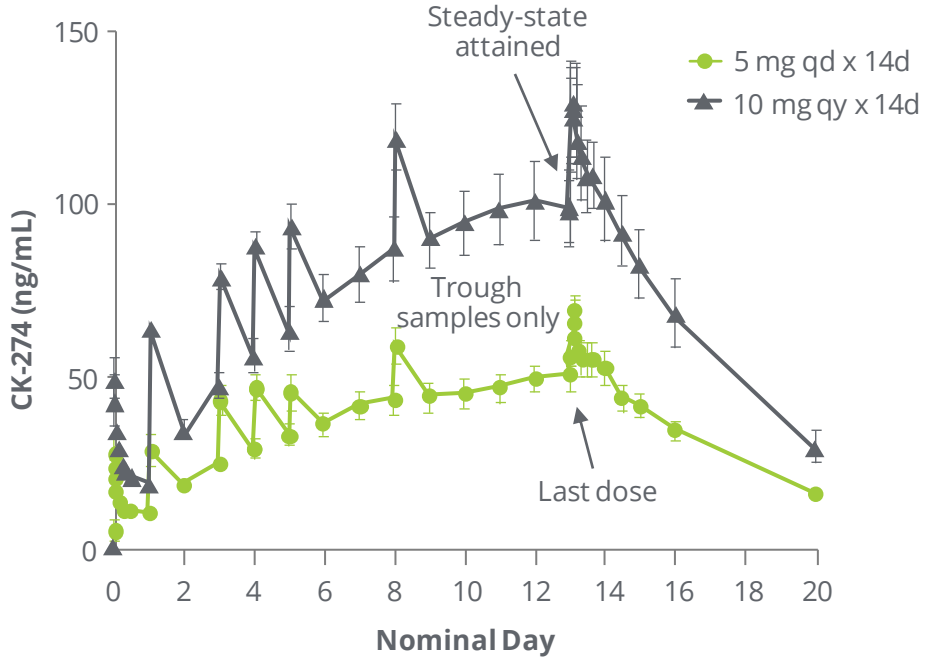
SAD & MAD Results Support Progression to Phase 2

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 ± standard error of the mean
Cmax = maximum drug plasma concentration; AUC = area under the plasma concentration curve; SAD = single ascending dose; d = day; qd = once daily

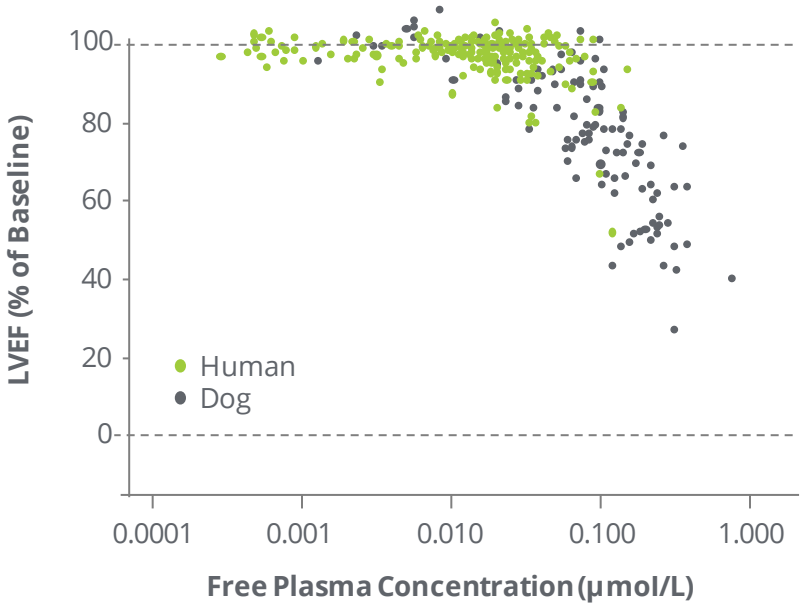
CY 6011: MAD Pharmacokinetic Parameters

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

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

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



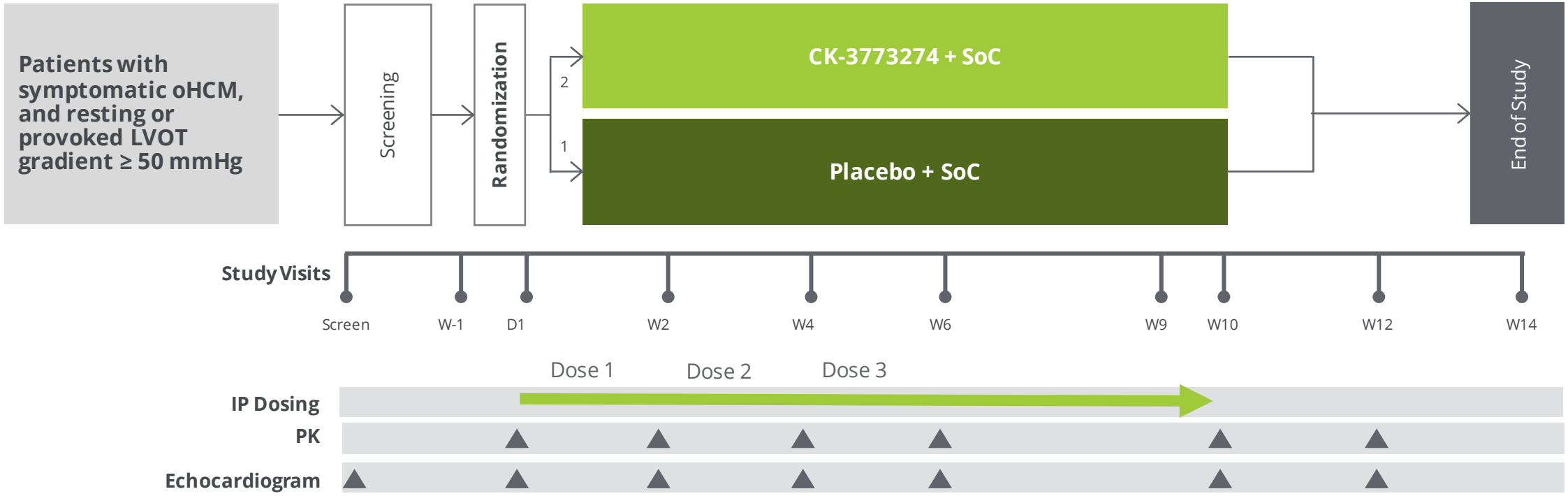
Graphs show LVEF as a function of exposure; data points represent observed values in dogs and humans.

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

*Except data for tmax shown as median (minimum-maximum), and t½ 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; Cmax = maximum plasma concentration; AUC24 = area under the plasma concentration curve;
MAD = multiple ascending dose; t½ = apparent plasma terminal elimination half-life; tmax = time to maximum observed plasma concentration.

Phase 2 Clinical Trial Design

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



Interim Analysis Informed Progression to Cohort 2

Cohort 2 Enrollment Complete; Cohort 3 Enrolling Patients on Disopyramide

REDWOOD HCM

Topline results for Cohort 1 and 2 expected mid-year 2021

- **Interim analysis of data from Cohort 1 demonstrated:**
  - Substantial reductions in average resting LVOT-G & post-Valsalva LVOT-G
  - Only modest decreases in average LVEF and no dose interruptions due to LVEF falling below 50% (prespecified safety threshold)
  - No serious adverse events attributed to study treatment

Cohort 1: Escalating doses of 5, 10, 15 mg once daily

Cohort 2: Escalating doses of 10, 20, 30 mg once daily

Cohort 3: Escalating doses of 5, 10, 15 mg once daily
For patients taking disopyramide

Open Label Extension Trial

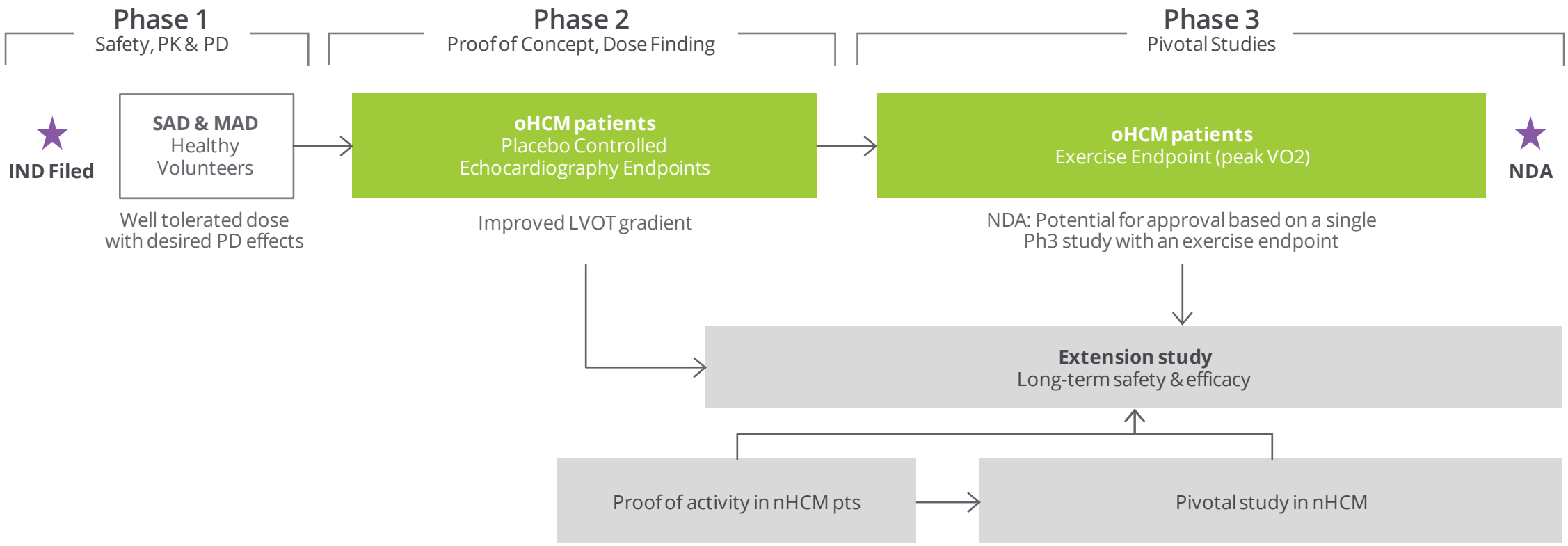
REDWOOD HCM OLE

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 CK-274 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

CK-274: Clinical Development Plan for HCM

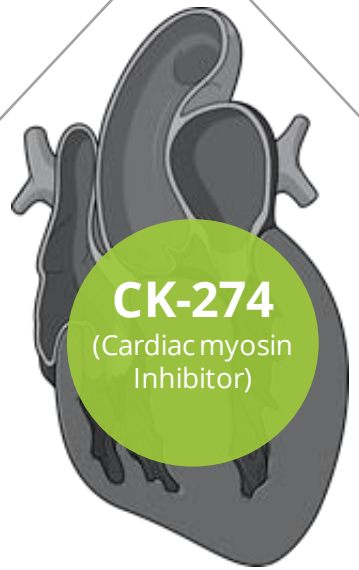


Novel Approach May Address Multiple Unmet Patient Needs

No FDA Approved Therapies

Obstructive HCM

oHCM



nHCM

Non-Obstructive HCM

HFpEF

Heart Failure with Preserved Ejection Fraction

Cytokinetics

CK-274: 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 purchased equity and 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:

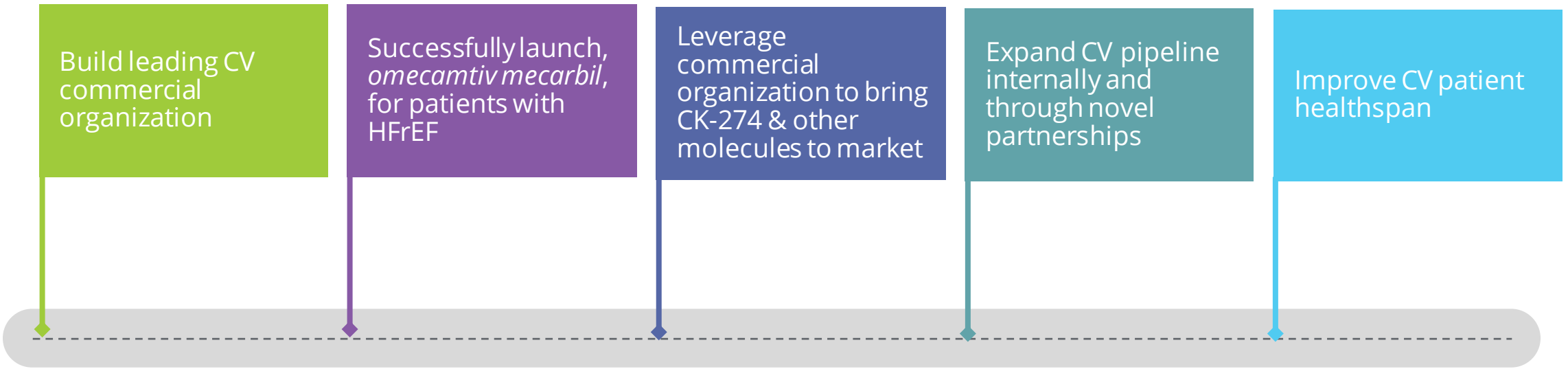
- Eligible for **$45M** in each of 2 tranches (upon initiation of global registration programs in oHCM and nHCM) in exchange for 2% royalty on sales in U.S. & certain European countries
- If **full $90M** received, Cytokinetics pays RTW 4% royalty on sales of CK-274 in U.S. & certain European countries,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

RTW: Other Purchases

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

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

CV Franchise: Building to Improve Patient Healthspan



Today → **Tomorrow**

Leverage deep **leadership in cardiac muscle biology,** to develop and commercialize innovative medicines for CV disease

Meaningfully **improve the healthspan of CV patients** with an initial focus on HFrEF and HCM

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

Cytokinetics

Sarcomere Directed Drug Development

SKELETAL MUSCLE

Reldesemtiv

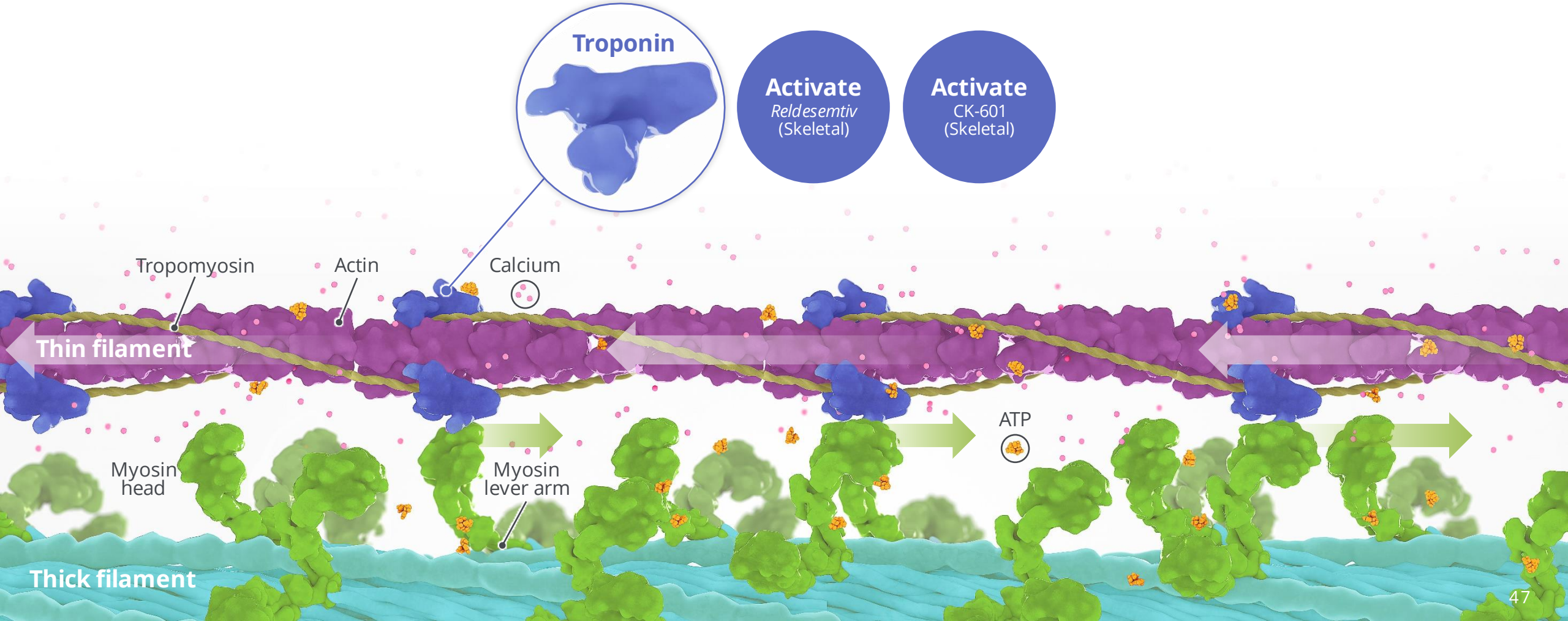
CK-601

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

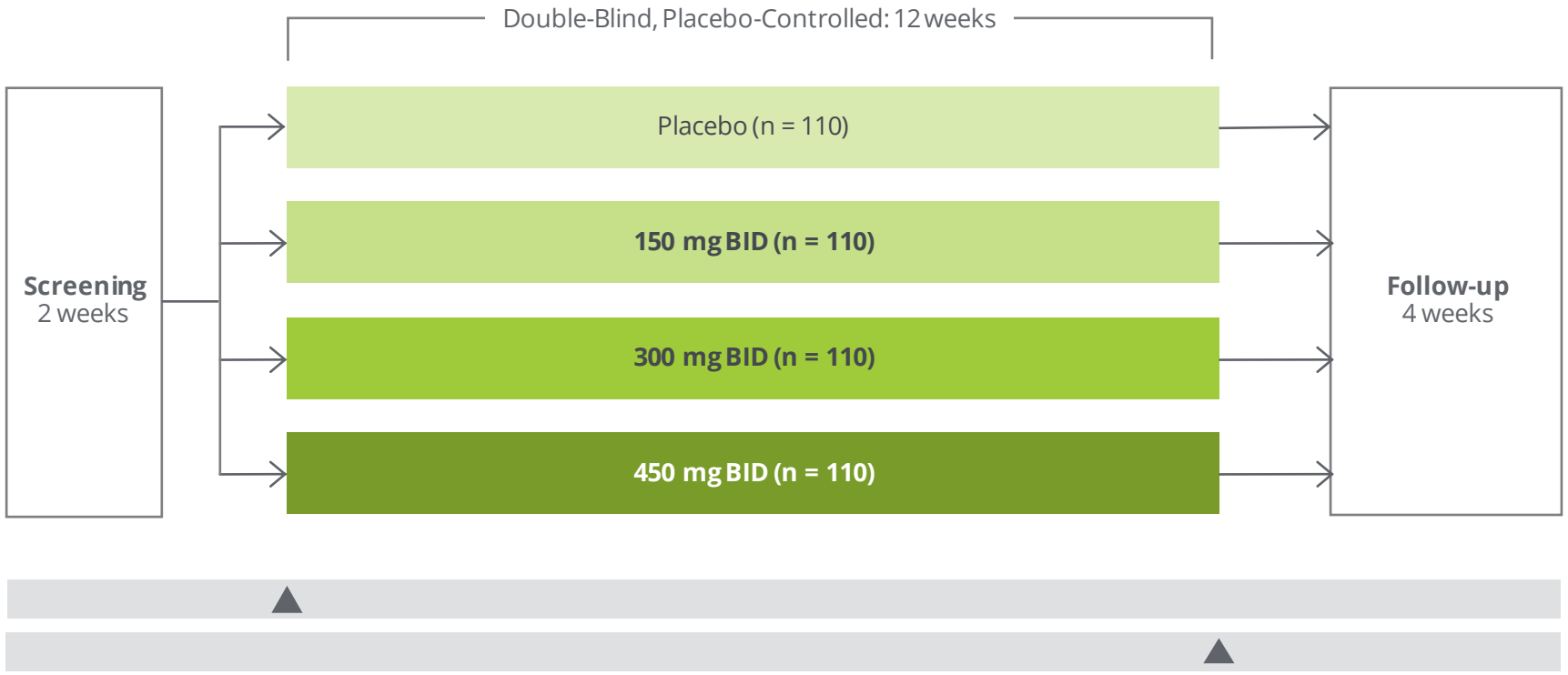


Phase 2 Clinical Trial in ALS

FORTITUDE ALS

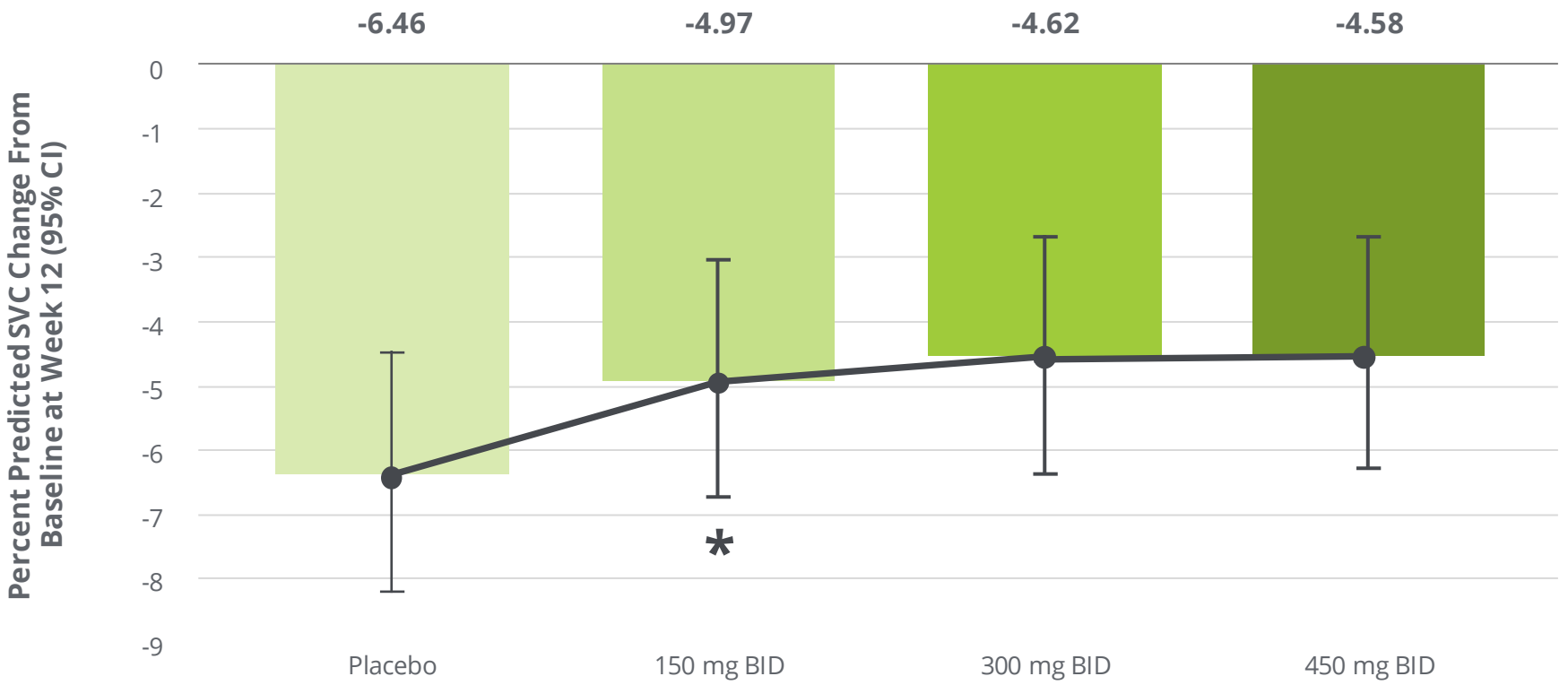
Results presented at American Academy of Neurology 2019

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

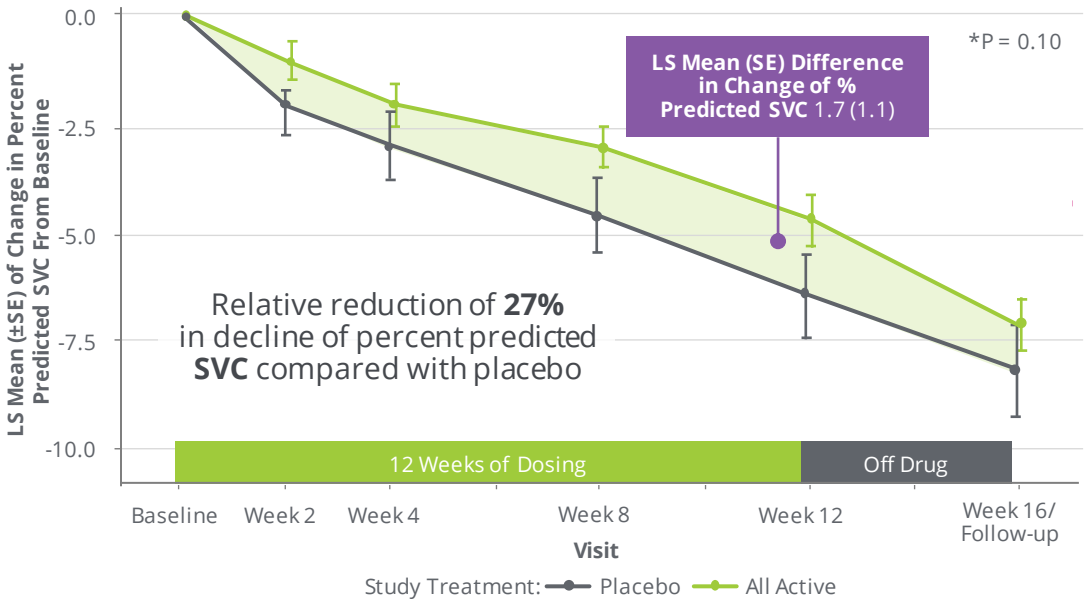
*Based on Mixed Model for Repeated Measures (MMRM) with the contrasts of (-5, -1, 3, 3) for placebo, *reldesemtiv* 150 mg, 300 mg and 450 mg BID, respectively

Change From Baseline: All Active vs Placebo*

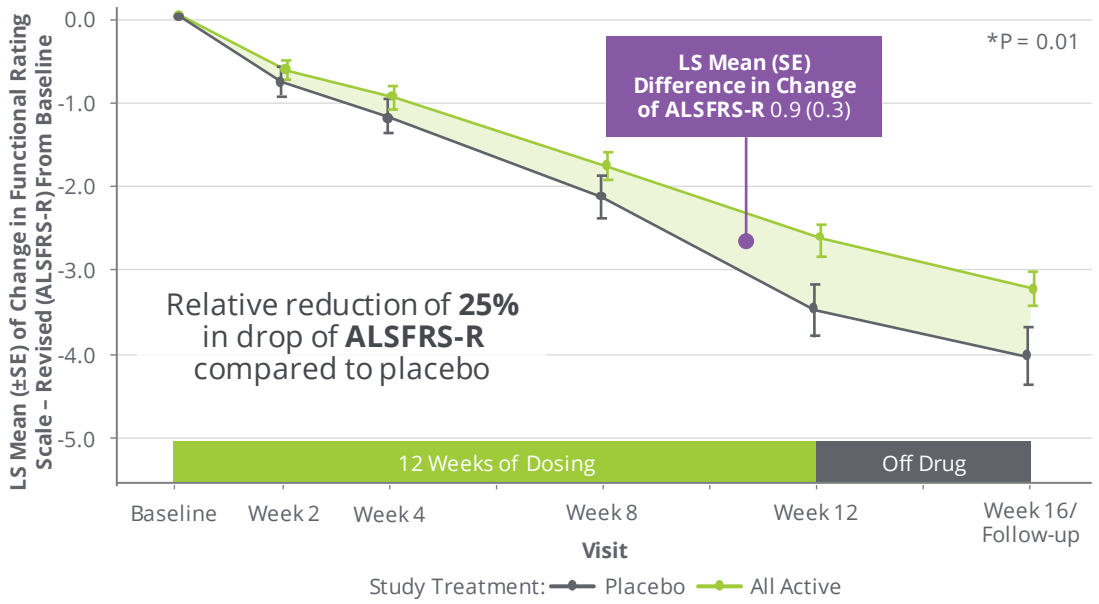
FORTITUDE ALS

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

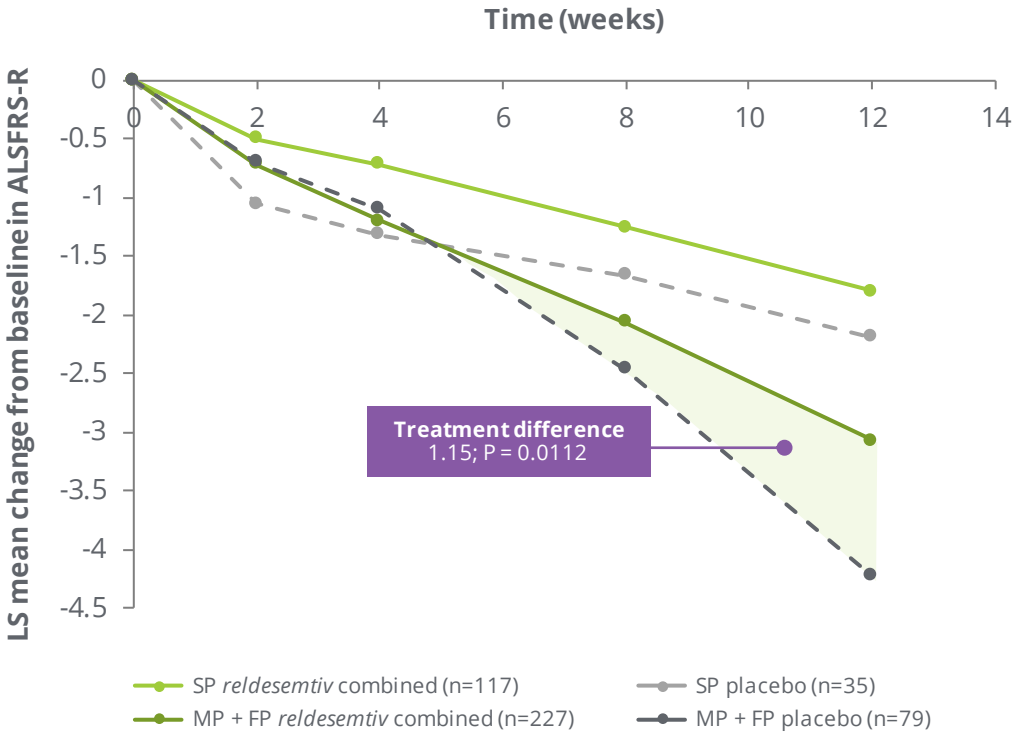
	No. of Patients (pbo/ *reldesemtiv*)	LSM Difference (95% CI)	Estimate	*P* value
Percent predicted SVC at baseline				
<80	43/109		1.588	0.0089
≥80	57/196		0.264	0.5296
ALSFRS-R total score at baseline				
<Median (38.0)	48/129		1.107	0.0585
≥Median (38.0)	52/176		0.685	0.0987
ALSAQ-5 total score at baseline				
<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

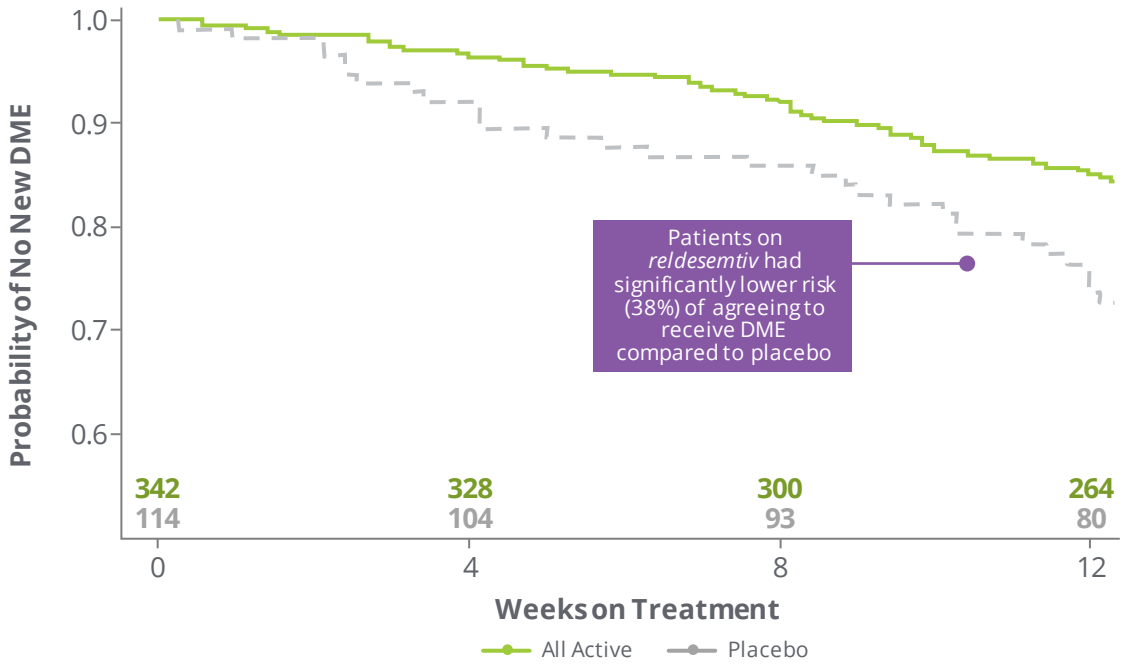
FORTITUDE ALS

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



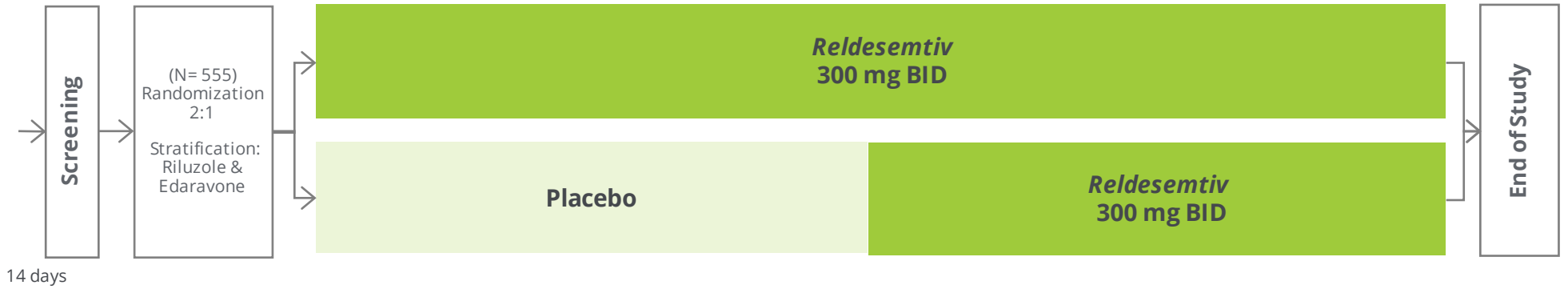
Cytokinetics

Planned Phase 3 Clinical Trial Design

COURAGE ALS

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

Reldesemtiv: Collaborations & Agreements

Astellas Collaboration

Cytokinetics has exclusive rights to *reldesemtiv*, CK-601 and other FSRAs

Cytokinetics has exclusive control and responsibility for development and commercialization of *reldesemtiv*, CK-601 and other fast skeletal regulatory activators

Astellas to pay certain costs up to $12M for potential Phase 3 clinical trial of *reldesemtiv* in ALS

Cytokinetics to pay Astellas low- to mid- single digit **royalty on sales** of *reldesemtiv* in certain countries

Astellas has funded **joint research program** with 15 Cytokinetics employees through 2020

Sarcomere Directed Therapies

CORPORATE PROFILE

Cytokinetics

Robust Pipeline, Solid Financial Position

Pipeline*

1 Positive 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

Omecamtiv mecarbil

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

CK-136

- Phase 1

HCM

CK-274

- Phase 2 trial results from REDWOOD-HCM mid-year 2021

ALS

Reldesemtiv

- Prepare for COURAGE-ALS, potential Phase 3 trial

Ongoing R&D

Additional research in muscle biology, energetics & metabolism

Foundations

185

Full time employees

$460M

At Q1 2021

More than two years of cash runway

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

Cytokinetics Financing History

in millions

	Financing	Equity	Upfront Cash, Option, & Milestones	R&D Reimbursement	Total
Investors					
Private Investors (VCs)		$116			$116
IPO		$94			$94
Public Post-IPO/Other		$609			$609
Term Loan	$45				$45
Convertible Debt (net)*	$120.5				$120.5
	$165.5	**$819**			**$984.5**
Strategic Partners & Grants					
RTW/Ji Xing		$50	$113		$163
Astellas		$10	$130	$103	$243
Amgen		$43	$145	$58	$246
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
		$137	**$506**	**$200**	**$843**

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

Capital raised: combination of strategic partners and investors

Balance Sheet & Financial Guidance

Ended Q1 with 2+ years cash runway based on 2021 guidance

2021 Condensed Balance Sheet

As of 3/31/2021

in millions

	Total
Cash and investments	$460.2
Leased assets	$86.1
Other assets	$30.8
Total Assets	**$577.1**
Debt	$134.0
Liability related to sale of future royalties	$168.9
Deferred Revenue	$87.0
Lease liability	$85.6
Other liabilities	$33.7
Total Liabilities	**$509.2**
Working capital	$397.2
Accumulated deficit	($1,039.4)
Stockholders' equity	$67.8
Wtd Avg Basic Shares Outstanding	**71.2**

2021 Financial Guidance

in millions

	Total
Cash Revenue	$23 – 28
Cash Operating Expenses*	$195 – 205
Net	**~ $160-170**

*We expect to revise our financial guidance mid-year once we finalize strategies and potential commercial launch plans for *omecamtiv mecarbil*. Executing on those strategies and plans may result in our incurring significant additional expenses that were not included in our current financial guidance.

Upcoming 2021 Milestones

Continue to Engage Regulatory Authorities for ***Omecamtiv Mecarbil*** in Q2 2021; Submit US NDA in 2H 2021

Develop Go-To-Market Strategy and Launch Plan for ***Omecamtiv Mecarbil*** in 1H 2021

Expect to Complete Enrollment in **METEORIC-HF** in 1H 2021

Expect Results from **REDWOOD-HCM** in mid-2021

Expect to Begin **Phase 3 Trial of CK-274** by Year End

Conduct Start-Up Activities for COURAGE-ALS, Phase 3 Clinical Trial of ***Reldesemtiv*** in Patients with ALS

Cytokinetics

Sarcomere Directed Therapies

THANK YOU

John, *diagnosed with heart failure*

Jillian, *diagnosed with HCM*

Chuck, *diagnosed with ALS*