Cytokinetics

Sarcomere Directed Therapies

EMPOWERING MUSCLE EMPOWERING LIVES

Nefertari, *diagnosed with heart failure*

Jillian, *diagnosed with HCM*

Chuck, *diagnosed with ALS*

Actual patients who consented to use of their name, image, and condition.

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 or acceptance of filing of a new drug application (NDA) to or by the FDA for *omecamtiv mecarbil* in 2021; the timing of an interim analysis of COURAGE-ALS, a phase 3 clinical trial of *reldesemtiv* or the timing of commencement of SEQUOIA-HCM, a phase 3 clinical trial of *aficamten*; our ability to fully enroll COURAGE-ALS or SEQUOIA-HCM; Cytokinetics' cash expenditures or runway; the timing or availability of additional sale proceeds or loan disbursements from Royalty Pharma; interactions with the FDA; the properties, potential benefits and commercial potential of *aficamten*, *omecamtiv mecarbil*, *reldesemtiv* and Cytokinetics' other drug candidates; the activities of Ji Xing under our collaboration agreements therewith or our ability to earn any additional milestone payments or royalties pursuant thereto. 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

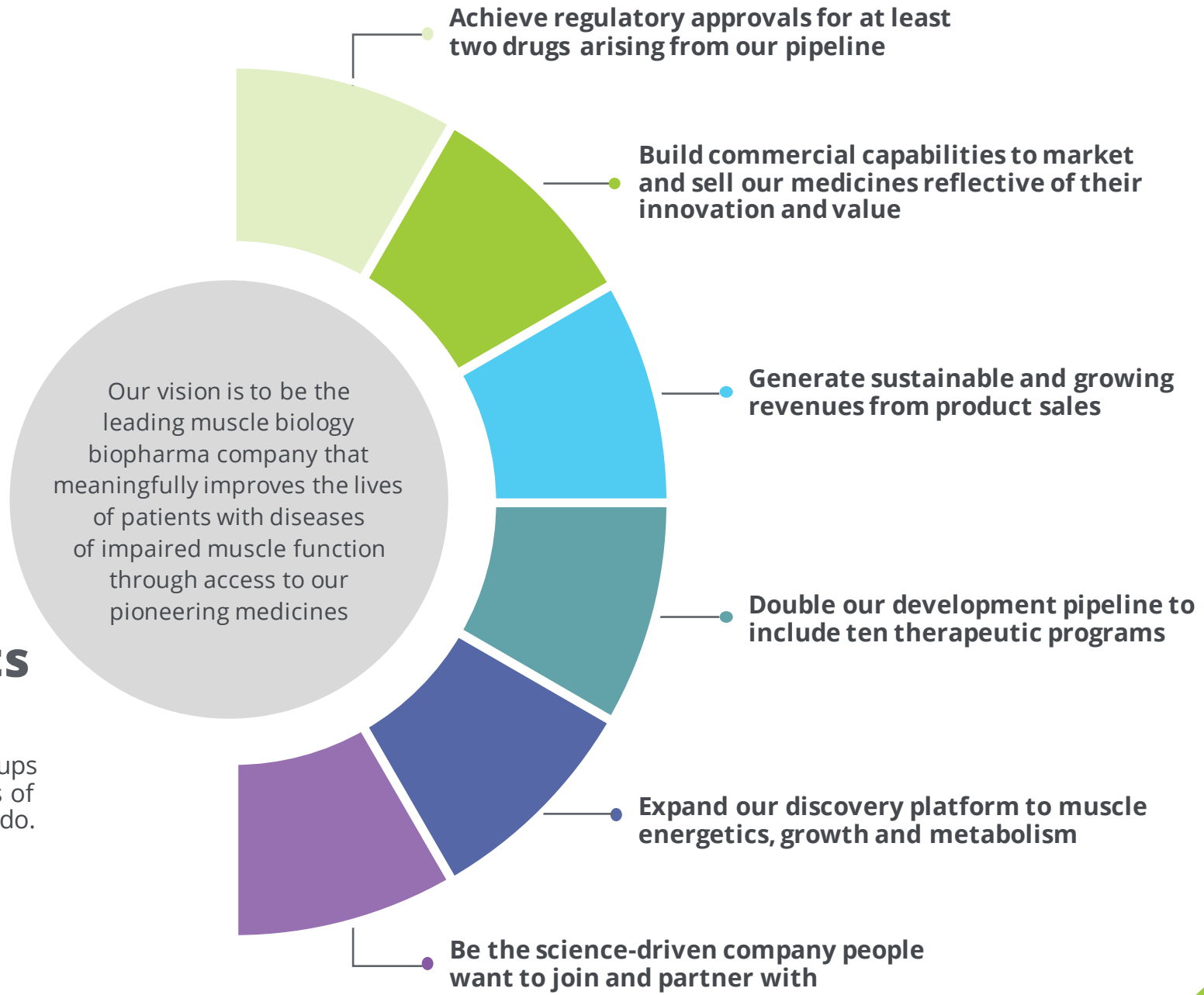
To bring forward new medicines to improve the healthspan of people with devastating cardiovascular and neuromuscular diseases of impaired muscle function.

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

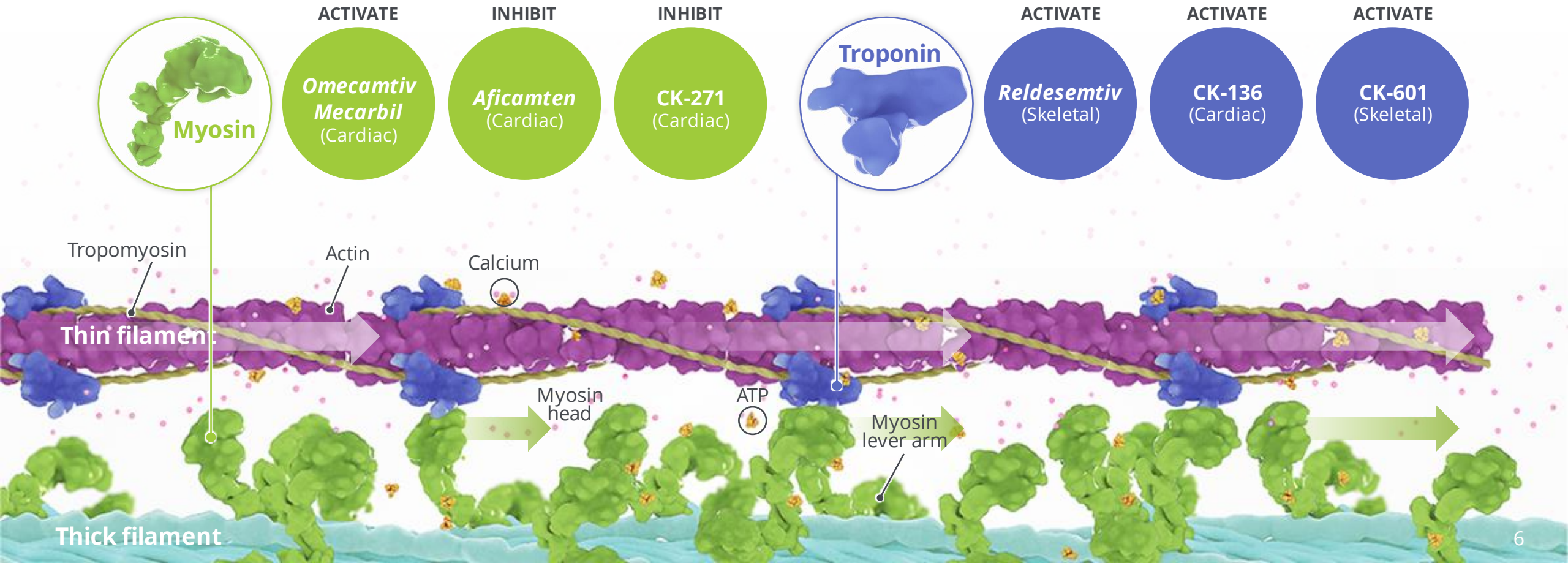
- Positive Phase 3 results from GALACTIC-HF
- Phase 3 trial, SEQUOIA-HCM, enrolling patients with oHCM
- Cohort 4 of Phase 2 trial, REDWOOD-HCM, enrolling patients with nHCM
- Phase 3 trial, COURAGE-ALS, enrolling patients with ALS

- 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

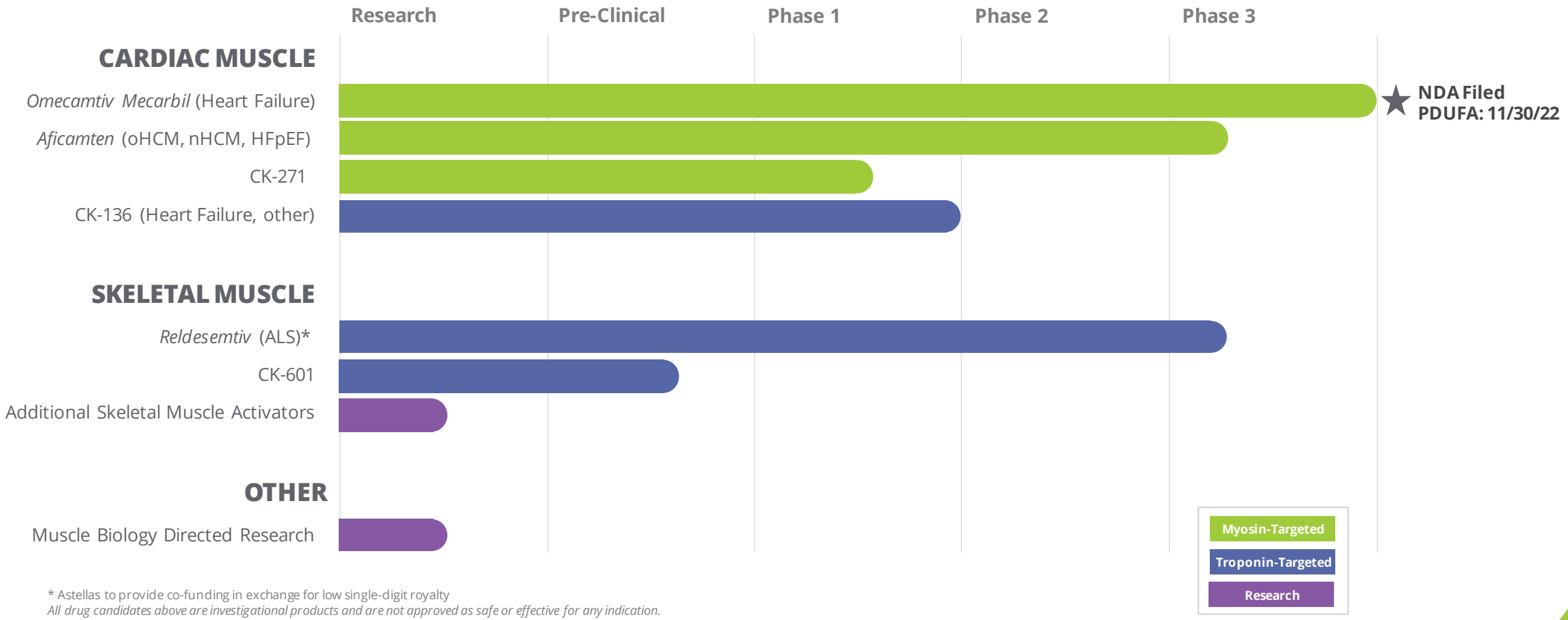
- Regular input, collaboration and guidance
- Elevate patient voice
- Improve function, performance and healthspan

Sarcomere Directed Drug Development

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



Pipeline of Novel Muscle-Directed Drug Candidates



* Astellas to provide co-funding in exchange for low single-digit royalty

All drug candidates above are investigational products and are not approved as safe or effective for any indication.

Sarcomere Directed Drug Development

CARDIAC MUSCLE

Omecamtiv Mecarbil

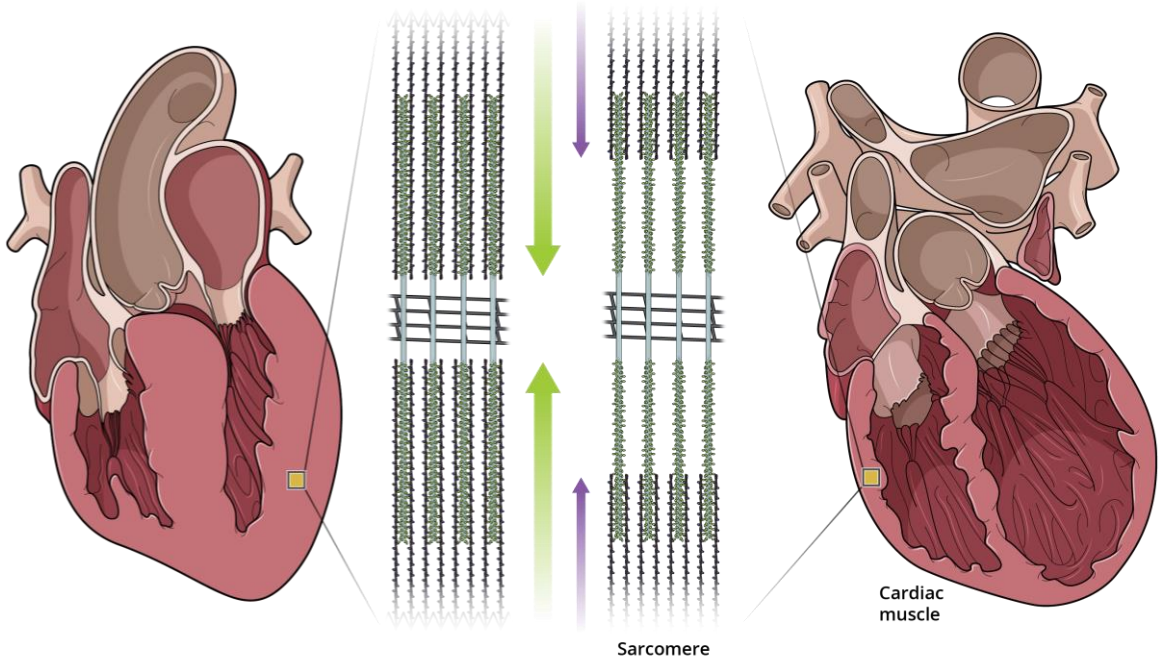
Aficamten

Cytokinetics

Contractile Dysfunction Underlies Cardiac Diseases

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

Omecamtiv Mecarbil

Cytokinetics

Omecamtiv mecarbil is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.

Heart Failure Is a Public Health Epidemic

~6.5M Americans ≥20 years of age have HF; 1M new HF cases occur annually[1]

High cost burden driven by hospitalizations; mean cost for each hospital stay ~$17K[2]

46%

Increase in Americans living with HF through 2030[1]

127%

Cost increase of HF through 2030 (increasing from $43.6[3] billion to $69.7 billion)[4]

50%

HF patients who will die within 5 years[1]

~900,000

Annual HF hospitalizations in the US[5]

24%

Patients readmitted to hospital within 30 days[6,a]

49%

Patients readmitted to hospital within 5 years[7,b]

HF: heart failure

1. Benjamin EJ, et al. *Circulation*. 2018;137:e67-e492;
2. Gaziano et al, AMA Cardiol. 2016;1(6):666-672. doi:10.1001/jamacardio.2016.1747
3. Urbich, M., Globe, G., Pantiri, K. et al. A Systematic Review of Medical Costs Associated with Heart Failure in the USA (2014–2020). PharmacoEconomics 38, 1219–1236 (2020). https://doi.org/10.1007/s40273-020-00952-0
3. Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail. 2013;6(3):606–19. https://doi.org/10.1161/HHF.0b013e318291329a.
4. Benjamin EJ, et al. *Circulation*. 2019;139:e56-e528;
5. Davis JD, et al. *Am J Med*. 2017;130:93.e9-93.e28. (a) In an investigational study of patients with an index hospitalization for HF from California, New York, and Florida from 2007–2011 (N=547,088).
6. Shah KS, et al. *J Am Coll Cardiol*. 2017;70:2476-2486. (b) Among HFrEF patients (n=18,398), HFbEF patients (n=3285), and HFpEF patients (n=18,299) in the GWTG-HF registry, a study of patients on Medicare and Medicaid services (N=39,982). GWTG-HF, Get With the Guidelines®-Heart Failure

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**

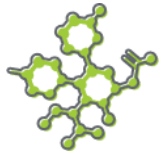
Drugs that do not affect renal function

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**

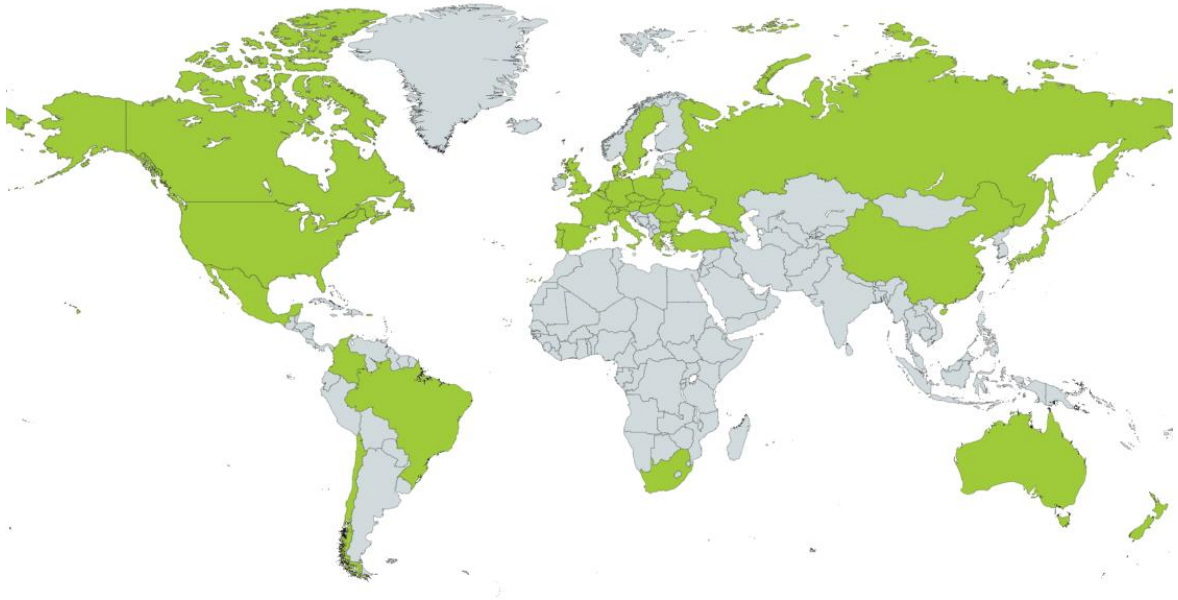
Patient QoL decreases as they lose the ability to perform daily tasks

Pivotal Phase 3 Trial Design

GALACTIC-HF

Second largest clinical trial ever conducted in heart failure

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



*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

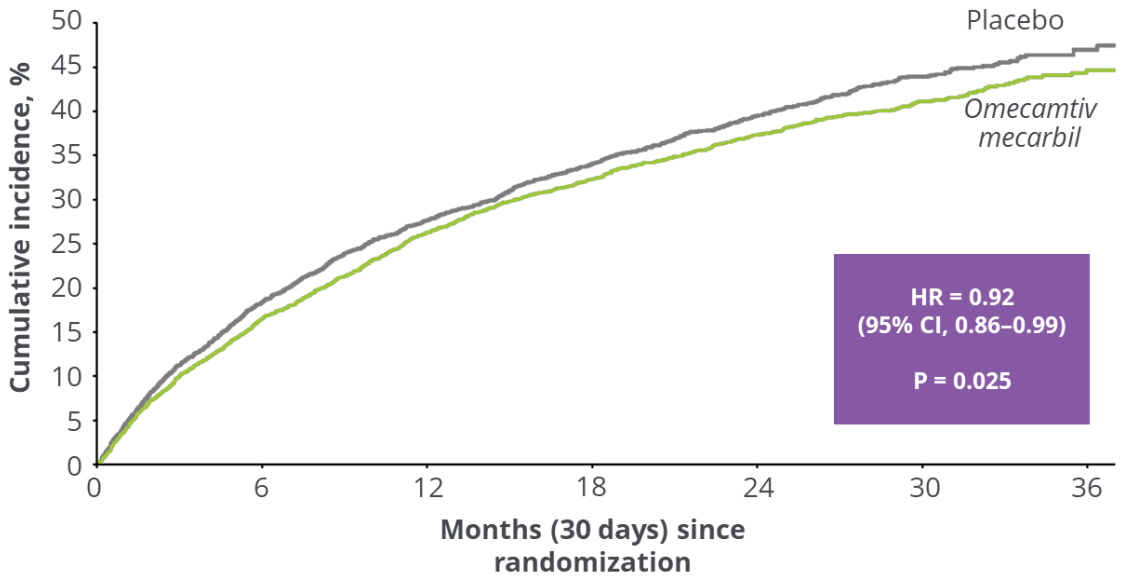
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; BB, beta blocker; CRT, cardiac resynchronization therapy; eGFR, estimated glomerular filtration rate; fib, fibrillation; hsTnI, high-sensitivity troponin I; ICD, implantable 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.

Positive Primary Composite Endpoint

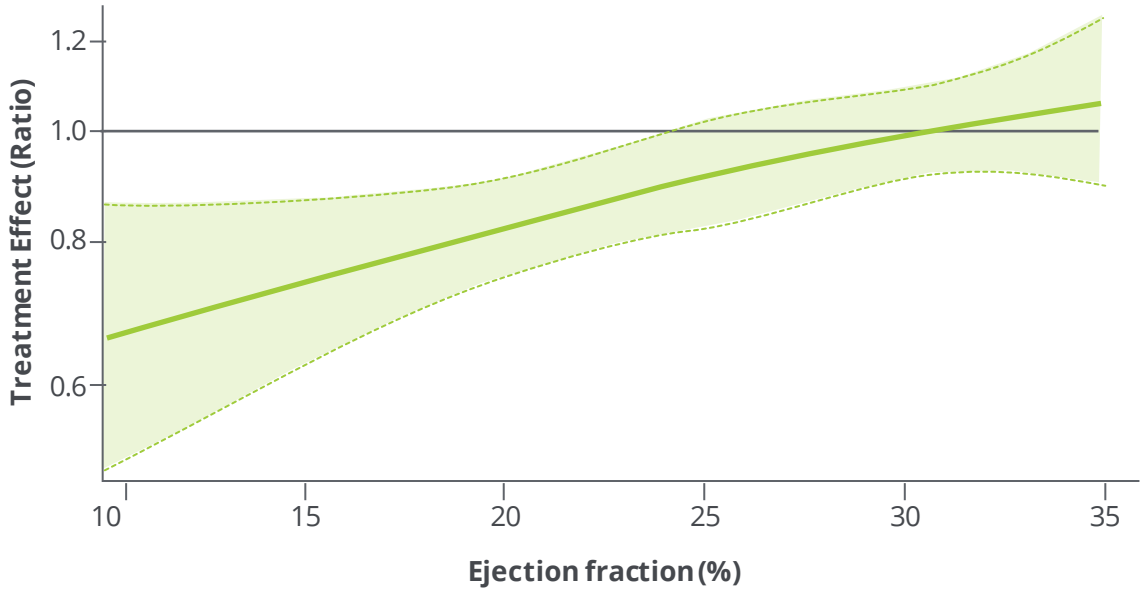
Treatment effect increased in more advanced patients

GALACTIC-HF

8% Relative Risk Reduction in Primary Composite Endpoint
(Time to First Heart Failure Event or CV Death)[1]



Treatment Effect Increased Progressively As Baseline LVEF Decreased[2]



AEs and treatment discontinuation balanced between treatment arms

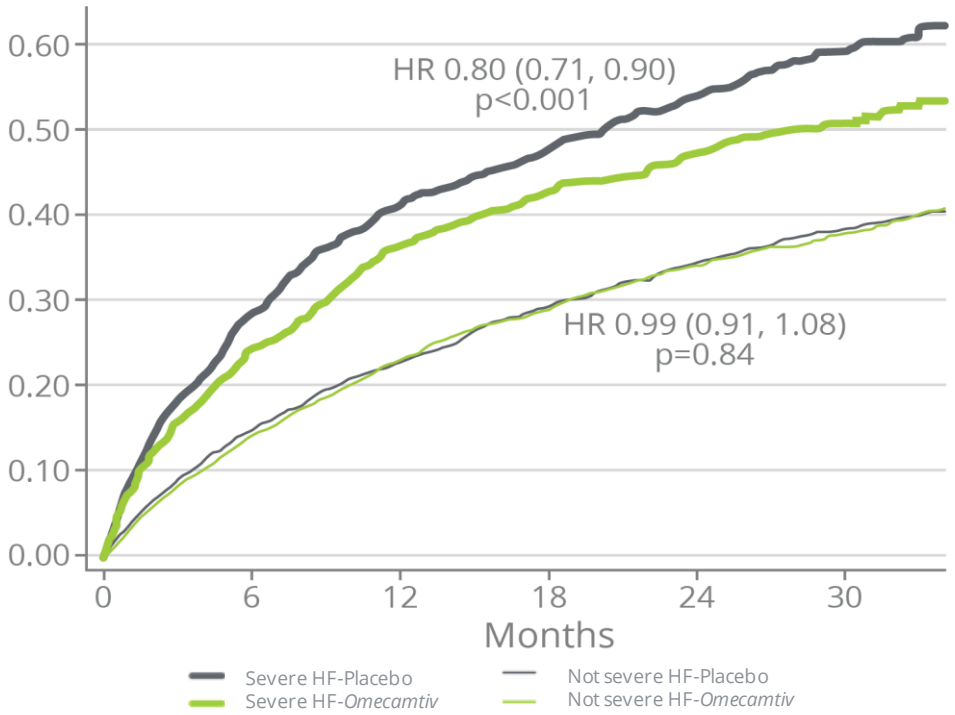
1. Teerlink JR et al., Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure; N Eng J Med 2020, 384:105-116.
2. Teerlink JR., Diaz R., Felker GM., et al. Effect of Ejection Fraction on Clinical Outcomes in Patients treated with Omecamtiv Mecarbil in GALACTIC-HF. JACC. 2021

Greater Treatment Effect in Worsening HF

GALACTIC-HF

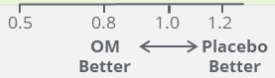
Primary Outcome in Severe HF: HR = 0.80 (0.71, 0.90)

(Severe HF defined as NYHA III-IV, EF ≤30%, HF hosp <6 mos)[1,2]



Primary Outcome in Patients with LVEF ≤28%: 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%



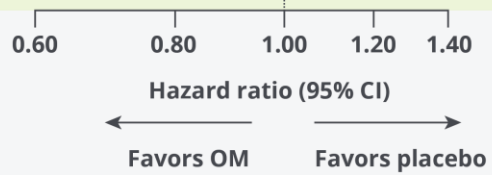
1. Felker GM, Omecamtiv Mecarbil in Patients with Severe Heart Failure: An Analysis from GALACTIC-HF, ESC Heart Failure 2021, June 2021
2. Felker GM, et al. Assessment of Omecamtiv Mecarbil for the Treatment of Patients With Severe Heart Failure. JAMA Cardiology, October 2021.

Similar Risk Reduction in Hospitalized Patients vs. Outpatients

Initiating *omecamtiv mecarbil* in hospitalized patients safe, well-tolerated

GALACTIC-HF

	Omecamtiv mecarbil Rate/100PY	Placebo Rate/100PY	HR (95% CI)	Interaction p-value
Primary Outcome				
All patients	24.2	26.3	0.92 (0.86, 0.99)	
Inpatient	34.1	38.3	0.89 (0.78, 1.01)	0.51
Outpatient	21.5	23.1	0.94 (0.86,1.02)	
First Heart Failure Event				
All patients	18.7	20.3	0.93 (0.86, 1.00)	
Inpatient	28.7	30.2	0.95 (0.82, 1.09)	0.64
Outpatient	15.9	17.6	0.91 (0.83, 1.01)	
Heart Failure Hospitalization				
All patients	18.0	19.1	0.95 (0.87, 1.03)	
Inpatient	27.8	28.7	0.97 (0.84, 1.12)	0.66
Outpatient	15.3	16.5	0.93 (0.85, 1.03)	
Cardiovascular Death				
All patients	10.9	10.8	1.01 (0.92, 1.11)	
Inpatient	13.3	15.1	0.87 (0.73, 1.04)	0.055
Outpatient	10.2	9.5	1.08 (0.96, 1.21)	
All-Cause Death				
All patients	14.4	14.4	1.00 (0.92, 1.09)	
Inpatient	17.2	20.0	0.85 (0.73, 1.00)	0.02
Outpatient	13.5	12.8	1.07 (0.96, 1.18)	



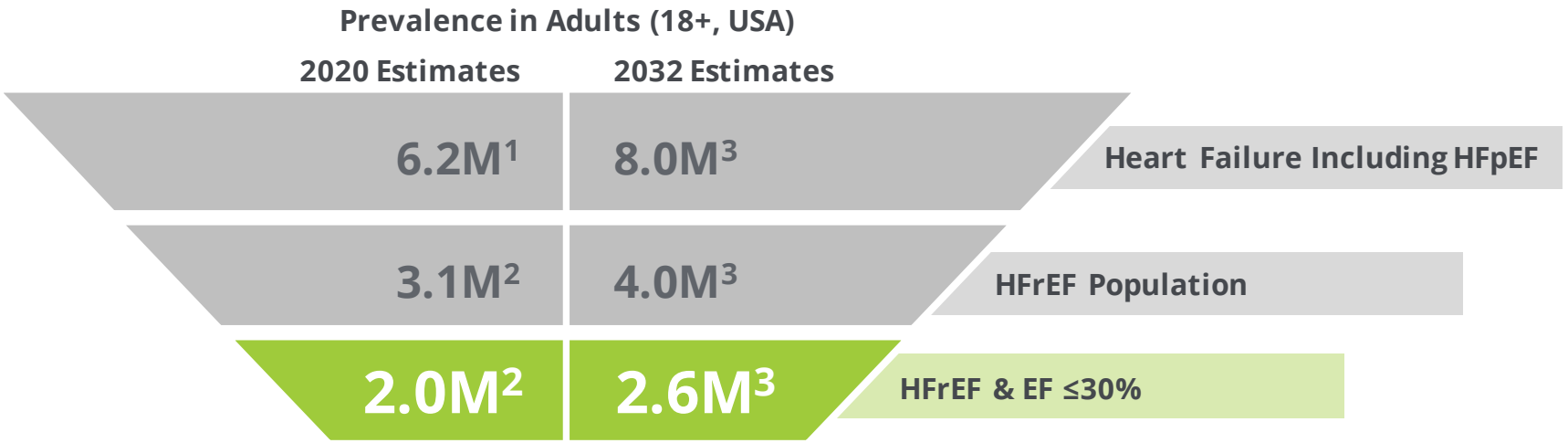
- Rate of primary outcome **higher in hospitalized patients** in the placebo group than in outpatients
- Effect of *omecamtiv mecarbil* versus placebo on the primary outcome **similar in hospitalized patients & outpatients**
- *Omecamtiv mecarbil* similarly reduced the risk of primary outcome both **when initiated in hospitalized patients and in outpatients**
- **Safe to initiate** treatment with *omecamtiv mecarbil* in hospitalized patients

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)

Large and Growing Heart Failure Patient Population



Proposed
Omecamtiv Mecarbil
Target Patient

Worsening signs and symptoms of heart failure requiring intensification of treatment despite periods of stabilization on GDMT

Cardiac Function

LVEF ≤ 30%

+

Recent Event

HF Event*
≤ 12 months

+ / -

GDMT Limitations

Co-morbidities and/or tolerability**

* HF Event: Urgent, unscheduled outpatient visit or hospitalization ** Due to renal impairment, low BP and/or hyperkalemia

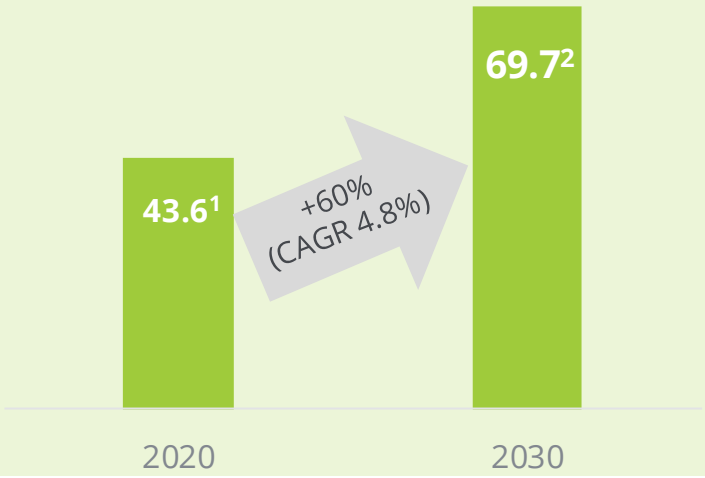
1. National Center for Health Statistics. National Health and Nutrition Examination Survey (NHANES) as accessed 4/1/2019 at website. https://www.cdc.gov/nchs/nhanes/. – data from 2013-2016 as quotes in Benjamin 2019 Circulation. 2019;139:e56–e528. DOI: 10.1161/
2. EF based on distribution as presented 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)

High Cost Burden Primarily Due to Hospitalizations

Omecamtiv mecarbil reduced clinical events, resource utilization & costs related to HF events

Over next decade, HF cost burden is expected to **increase over half**

US HF Burden ($B)



Mostly due to cycle of **hospitalizations** and re-admissions

Mean cost for **each** hospital stay of ~$17K[3]

HF-associated costs of initial hospitalization and 12 months following discharge ~$35K[4]

Of total lifetime HF cost burden, **~80% due to hospital stays**[5]

Outpatient HF-related **drug costs only ~2–3%** of the total HF-related costs[4]

Omecamtiv mecarbil **reduced costs** related to HF events in patient subgroup*

Treatment with *omecamtiv mecarbil* associated with significant reductions in risk of first HF event, **total HF events** and cumulative HF events

Estimated cost reductions related to HF events were **$3,085, a 19% reduction per patient**

Of the cost reductions, 99% due to HF **hospitalizations avoided**

* Subgroup of 5,369 patients (65%) of the 8,256 patients enrolled in GALACTIC-HF excluding those with digoxin & atrial fibrillation or with EF >30%

1. Urbich, M., Globe, G., Pantiri, K. et al. A Systematic Review of Medical Costs Associated with Heart Failure in the USA (2014–2020). PharmacoEconomics 38, 1219–1236 (2020). https://doi.org/10.1007/s40273-020-00952-0
2. Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail. 2013;6(3):606-19. https://doi.org/10.1161/HHF.0b013e318291329a.
3. Gaziano et al, AMA Cardiol. 2016;1(6):666-672. doi:10.1001/jamacardio.2016.1747
4. Givertz, M. M., Yang, M., Hess, G. P., Zhao, B., Rai, A., and Butler, J. (2021) Resource utilization and costs among patients with heart failure with reduced ejection fraction following a worsening heart failure event. ESC Heart Failure, 8: 1915 – 1923. https://doi.org/10.1002/ehf2.13155
5. Dunlay SM, Shah ND, Shi Q, Morlan B, VanHouten H, Long KH, Roger VL. Lifetime costs of medical care after heart failure diagnosis. Circ Cardiovasc Qual Outcomes. 2011 Jan 1;4(1):68-75. doi: 10.1161/CIRCOUTCOMES.110.957225. Epub 2010 Dec 7

Omecamtiv Mecarbil: Value Proposition

In HFrEF, patients with lower ejection fractions are hospitalized more often

In HFrEF, every 10 points lower EF, is proven to drive higher events and risk of increased hospitalizations[1]

Hospitalization reductions seen in clinical trial of *omecamtiv mecarbil*

Clinically meaningful and statistically significant hospitalization reductions seen among worsening HF patients with EF≤30[2]

Our access activities may demonstrate economic value of *omecamtiv mecarbil*

Partnering with key institutions to generate **real world evidence** of unmet needs in patients with lower ejection fractions

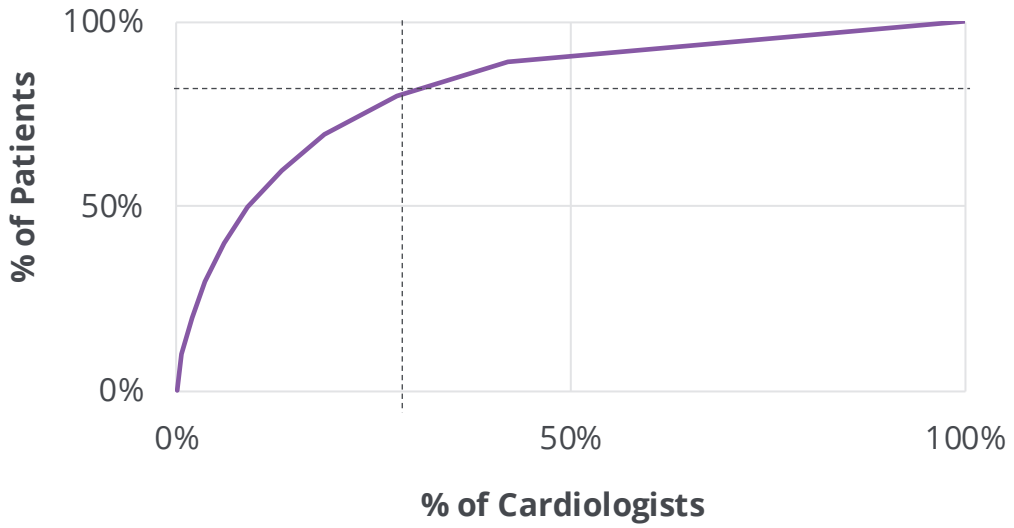
Using **HEOR** and clinical results to demonstrate the economic impact and value

Building Market Access team holding early discussions with **payers**

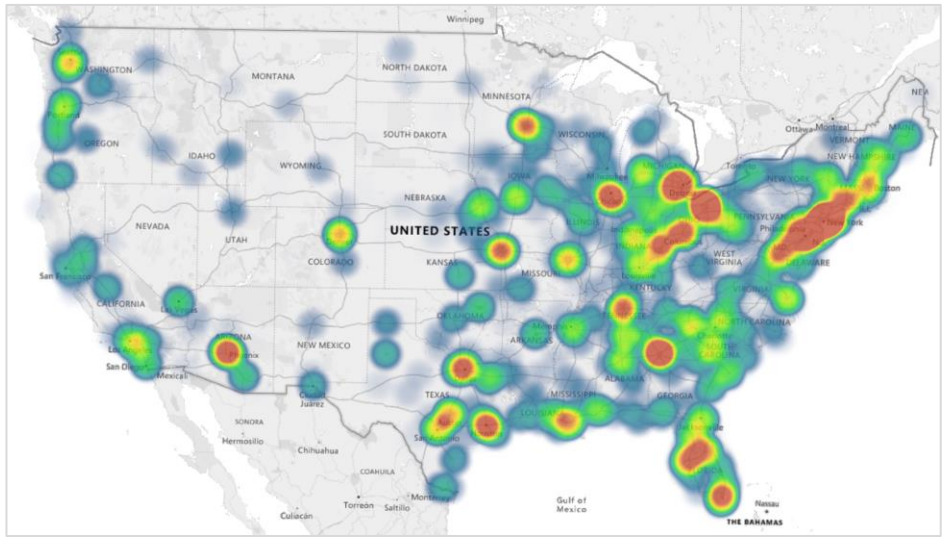
1. Based on Solomon S, Influence of Ejection Fraction on Cardiovascular Outcomes in a Broad Spectrum of Heart Failure Patients, Circulation 2005
2. Felker GM. *ESC Heart Fail* 2021 Oral Presentation. Data based on post hoc analyses.

Small Subset of Cardiologists Manage Majority of Patients

HFrEF Patient Concentration in Cardiologists



Distribution of High-Volume Cardiologists



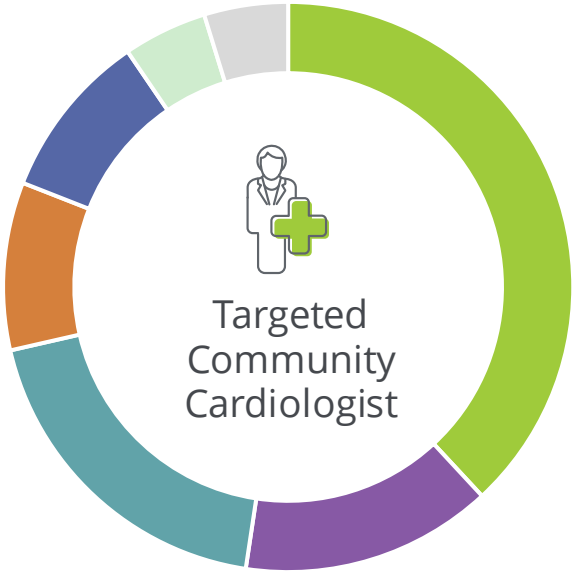
Allows for more targeted field team approach, focusing on <10,000 HCPs

Symphony APLD (1/1/2019 – 12/31/2020); Physician Interviews; *Analysis includes **n = 25,510 cardiologists** and **n = 110,114 PCPs** who see **at least 1 HFrEF patient** during the two-year market map period*

Engagement Approach Allows Customizing and Broadening

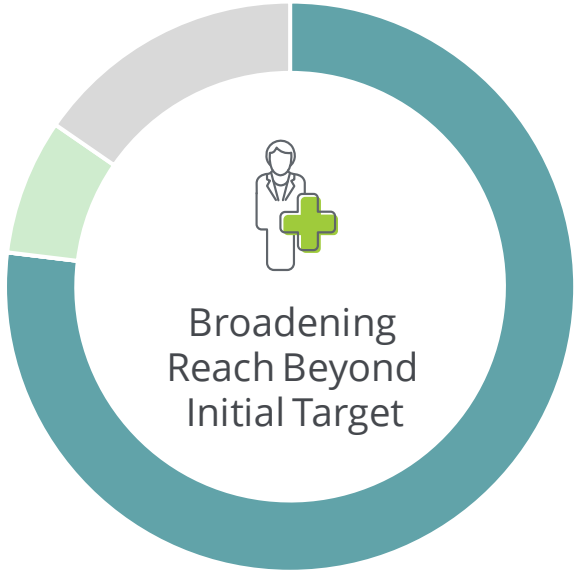
Customizing engagement by different types of customers

~~ illustrative ~~



Digital allows broader reach

~~ illustrative ~~




Field &
Account Reps

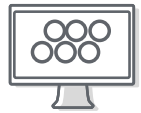

Inside
Sales


Digital
Engagement


Reimbursement
Specialists

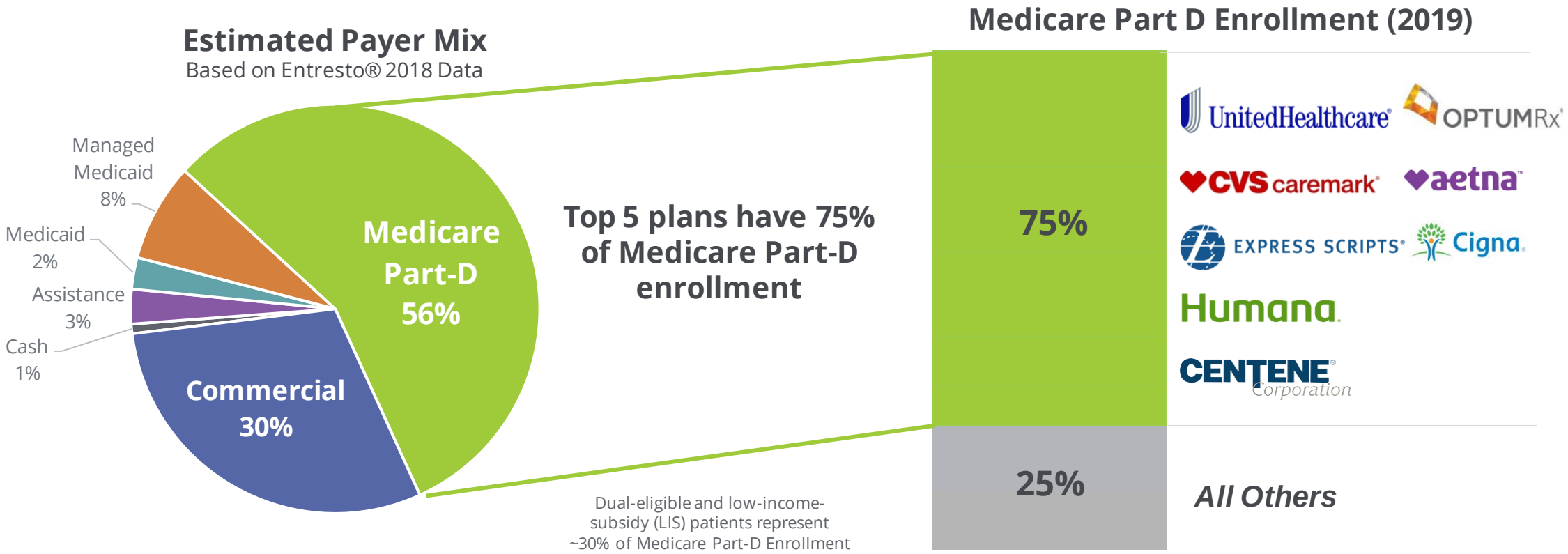

MSLs


Patient
Services


Online
communities

Medicare Is Major Payer with Select Key Players

Medicare is largest payer; enrollment highly concentrated with nearly 3 of 4 patients in only 5 plans

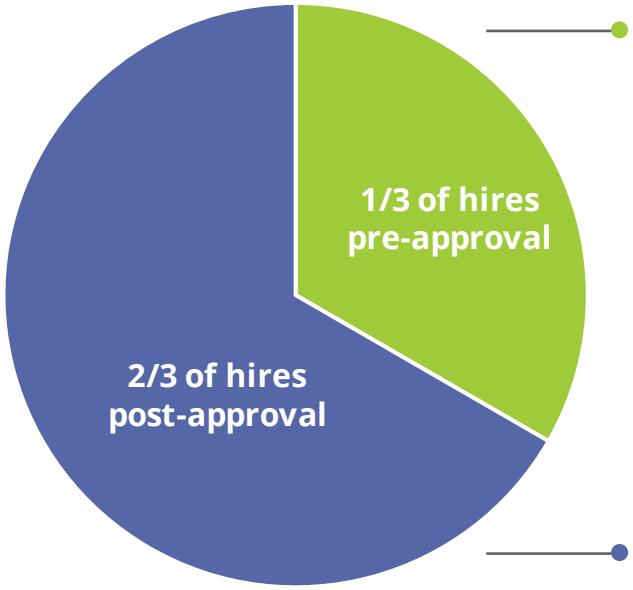


Sources: National Trends in Heart Failure Hospitalizations and Readmissions From 2010 to 2017; Agarwal, Fanarow, and Ziaeian; JAMA Cardiol, Feb 10, 2021 (Table 2 Payer Status); https://www.kff.org/medicare/issue-brief/10-things-to-know-about-medicare-part-d-coverage-and-costs-in-2019; IQVIA LAAD data. SGLT-2 US Market Access Assessment, IQVIA. 1/7/2020

Gated Build of Commercial Infrastructure

Majority of spending to occur post-approval

2/3 of hiring to occur post-approval



Commercial leadership
Marketing
HEOR
Patient services
Access & distribution
Sales team leads
First line field managers
Sales operations
Commercial learning & development

Sales representatives

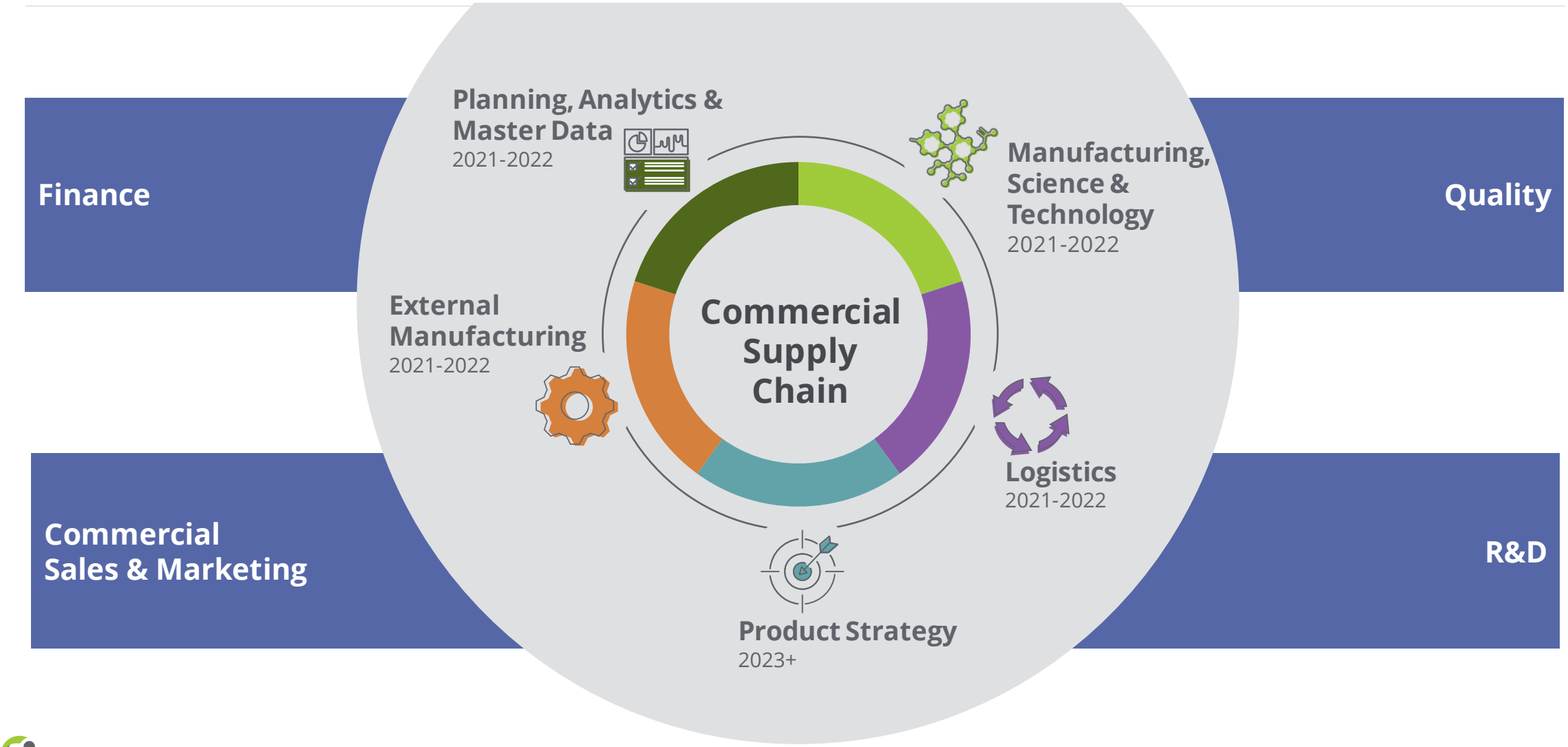
Activities initiated upon key de-risking events

Underway Pre-NDA filing
Market access
Pricing strategy
Distribution approach
Payer engagement
Brand strategy
Sales force planning

Initiated upon NDA acceptance
Launch campaign
Commercial training
PIE deployment (payers)
Technology build
Omnichannel execution

Initiated upon FDA approval
Media purchases
Patient support programs

Commercial Supply Chain Operating Model



Aficamten

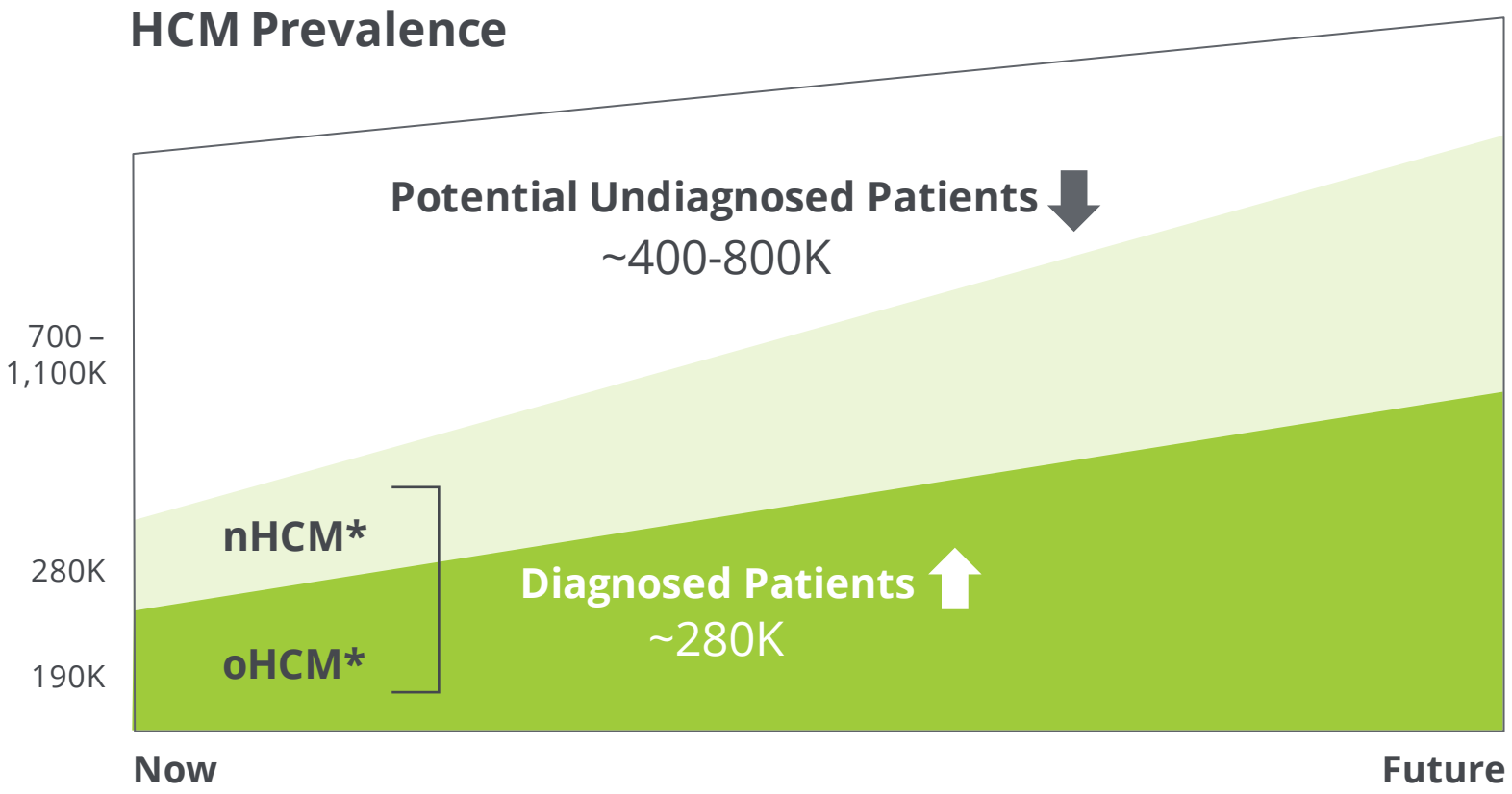
Cytokinetics

Aficamten is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.

In US, Large HCM Population With Many Undiagnosed

Currently
~280K diagnosed,
~190K oHCM
symptomatic patients

Estimated ~400-800K
un-diagnosed patients



nHCM: non-obstructive HCM; oHCM: obstructive HCM
CVRG market strategies heart failure 2Q 2021 and other sources on file

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: Aspirational Target Profile

Potential next-in-class cardiac myosin inhibitor

Efficacy

Functional Improvement: Improved exercise capacity

Symptom Improvement: One or two class improvement in **NYHA class**

Quality of Life: KCCQ improvement

Safety and Tolerability

Minimal drug-drug interactions

Maintain LVEF: >50% on vast majority of patients

Reversibility: Quickly reversible with titration down

Dosing

Titration: Time to optimal dose, ~2-week titration intervals using echocardiography

No monitoring of plasma concentrations

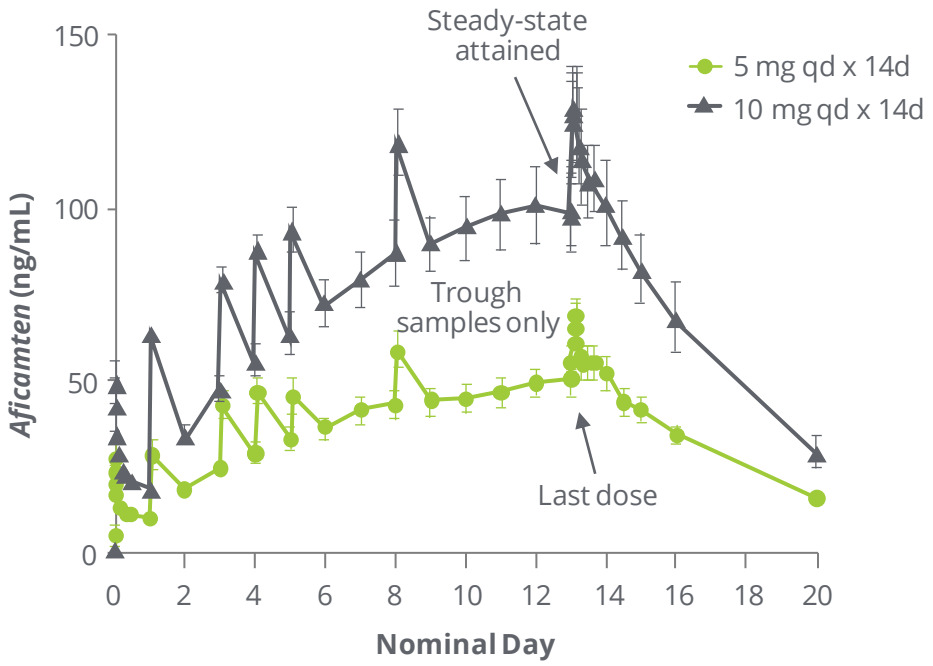
Product not FDA approved, aspirational profile dependent on phase 3 data

Aficamten is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.

SAD & MAD Results Support Progression to Phase 2

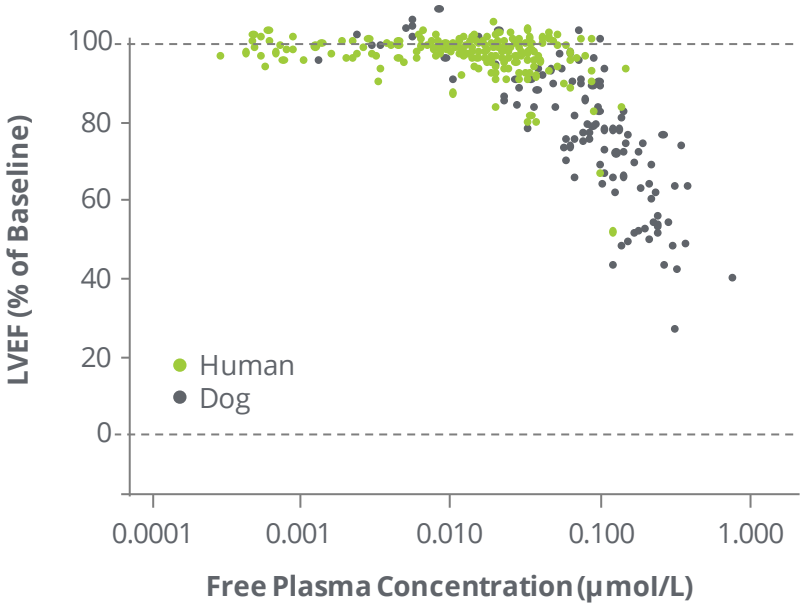
Preclinical data translated to healthy participants

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.

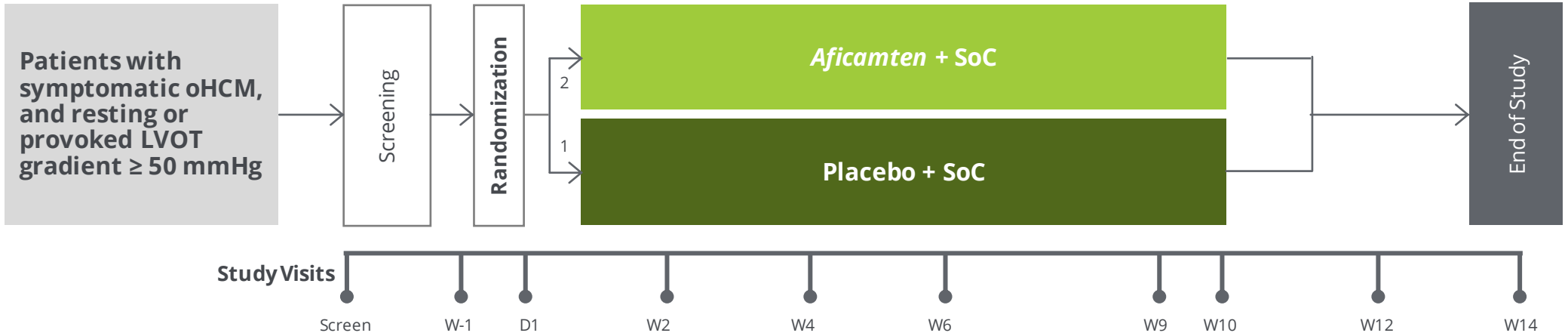
Decrease in LVEF as function of exposure is similar in humans and dogs.

REDWOOD-HCM: Cohorts 1 & 2

Patients with symptomatic oHCM on background therapy excluding *disopyramide*

REDWOOD HCM

Two sequential dose-finding cohorts



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

Patient Enrollment and Dosing

Cohorts 1 & 2

41 Total Enrolled Patients

		Final Dose Achieved (N)				
		5 mg	10 mg	15 mg	20 mg	30 mg
N = 14	**Cohort 1**	4	5	5		
N = 14	**Cohort 2**		9		4	1

Baseline Characteristics

Cohorts 1 & 2

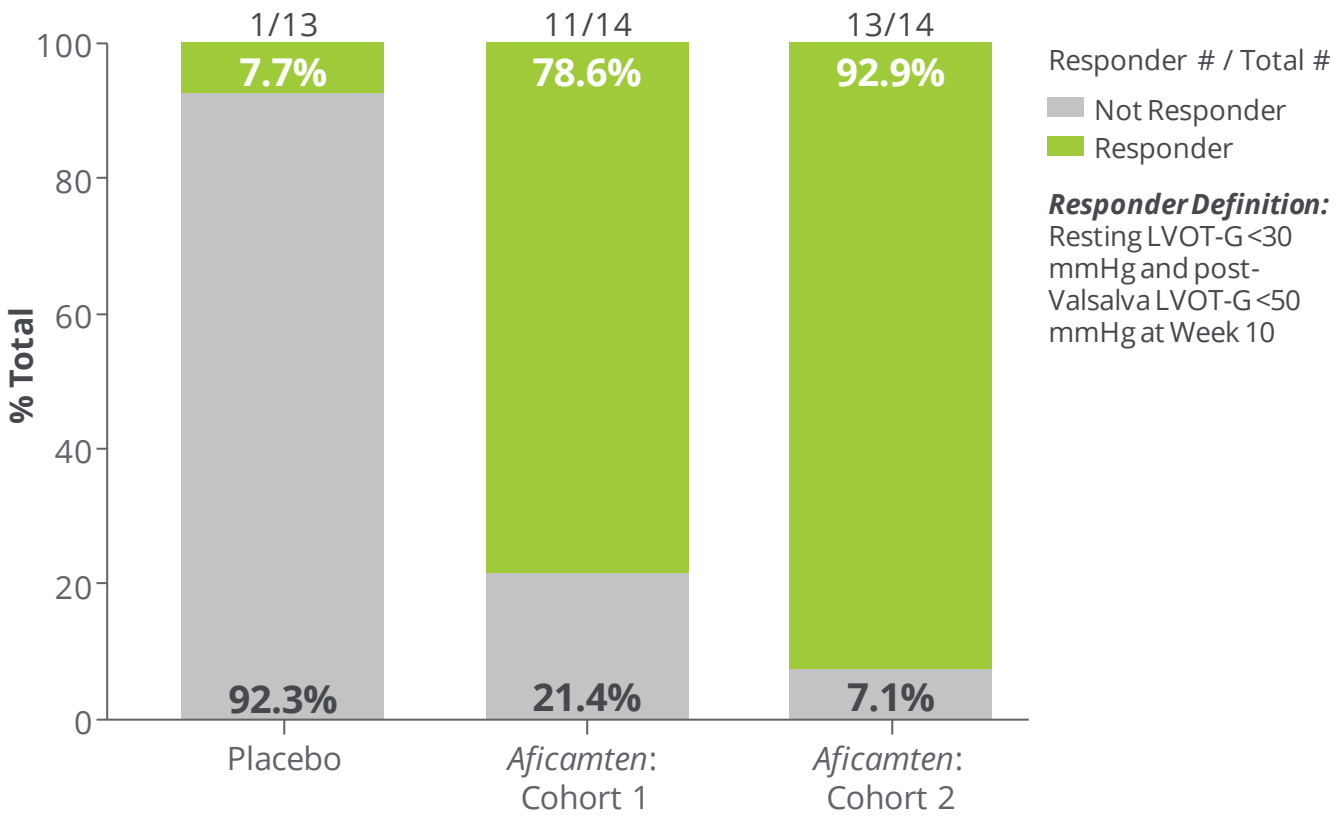
Characteristic	Placebo (n = 13)	*Aficamten* (n = 28)
Age (Years), Mean (SD) [Range]	57.2 (9.6) [36,69]	56.6 (13.6) [33,78]
< 65 Years	10 (77%)	17 (61%)
Sex, n (%)		
Female	8 (62%)	15 (54%)
Race = White, n (%)	12 (92%)	28 (100%)
NYHA Class, n (%)		
Class II	11 (85%)	17 (61%)
Class III	2 (15%)	11 (39%)
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

Maron M, Abraham T, Masri A, et al. "REDWOOD-HCM: A Randomized, Double-blind, Placebo-controlled, Dose-finding Trial of the Cardiac Myosin Inhibitor, *Aficamten*, In Obstructive Hypertrophic Cardiomyopathy"

Response Rates on Treatment with *Aficamten*

Cohorts 1 & 2



- Consistent, **clinically meaningful reductions in LVOT gradients** within two weeks
- **No treatment interruptions** or discontinuations
- No treatment-related SAEs
- **Reversibility of drug effect** demonstrated
- Statistically significant reductions in NT-proBNP
- Improvement in NYHA class

Maron M, Abraham T, Masri A, et al. "REDWOOD-HCM: A Randomized, Double-blind, Placebo-controlled, Dose-finding Trial of the Cardiac Myosin Inhibitor, *Aficamten*, In Obstructive Hypertrophic Cardiomyopathy"
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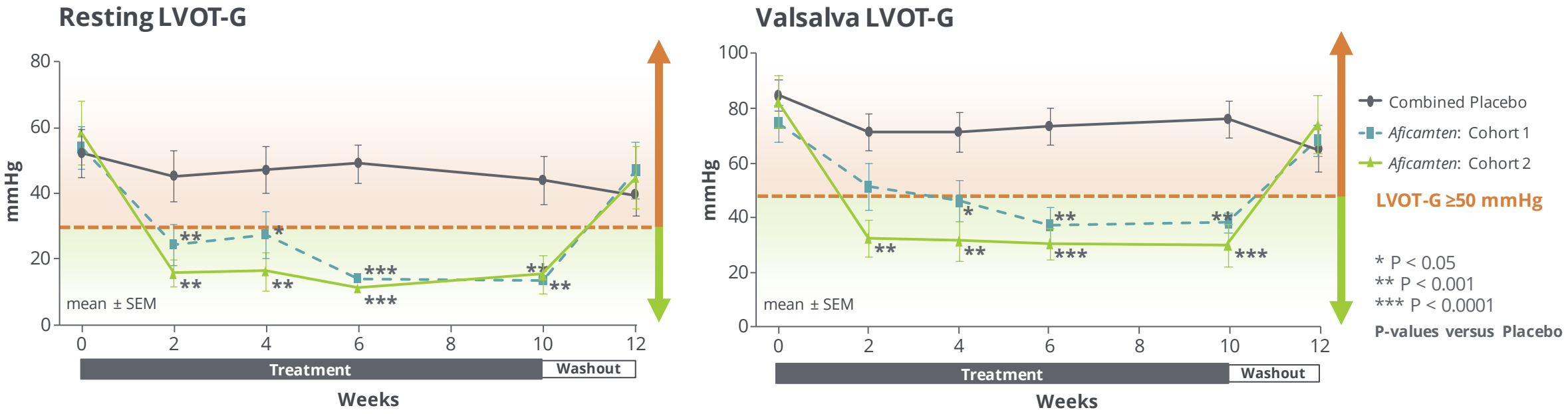
REDWOOD-HCM: Efficacy

Cohorts 1 & 2

Reductions in LVOT gradients



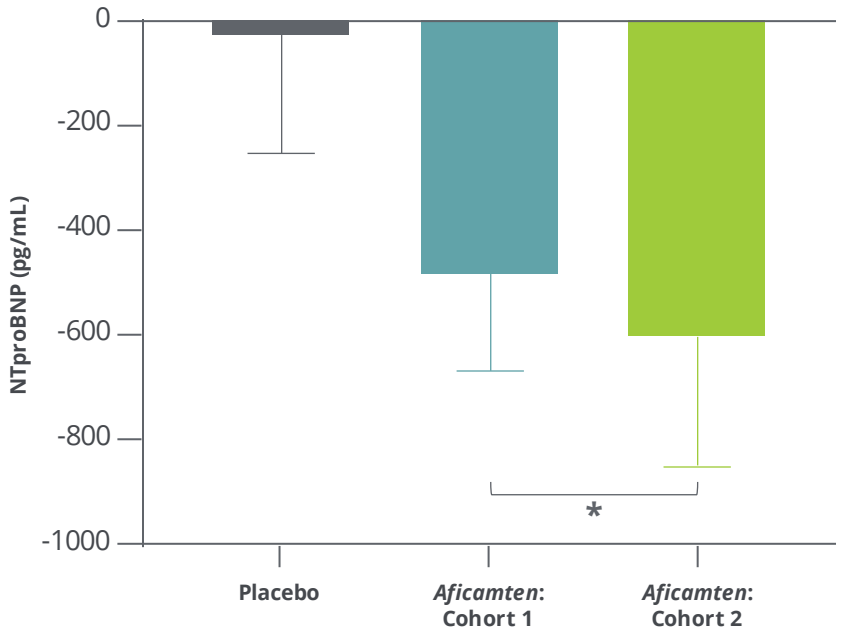
Dose finding study
Cohort 1 (n=21), Cohort 2 (n=20)

Maron M, Abraham T, Masri A, et al. "REDWOOD-HCM: A Randomized, Double-blind, Placebo-controlled, Dose-finding Trial of the Cardiac Myosin Inhibitor, *Aficamten*, In Obstructive Hypertrophic Cardiomyopathy"

Change from Baseline in NT-proBNP & NYHA Class

Cohorts 1 & 2

Change from Baseline NT-proBNP to Week 10

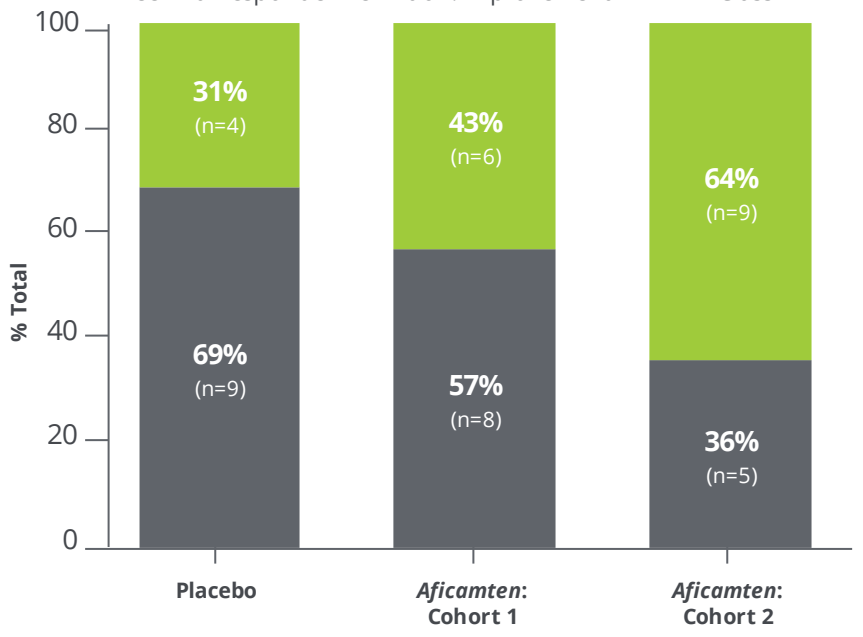


*** p = 0.003 for Pooled Cohort 1 & 2 vs. Placebo**

- 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

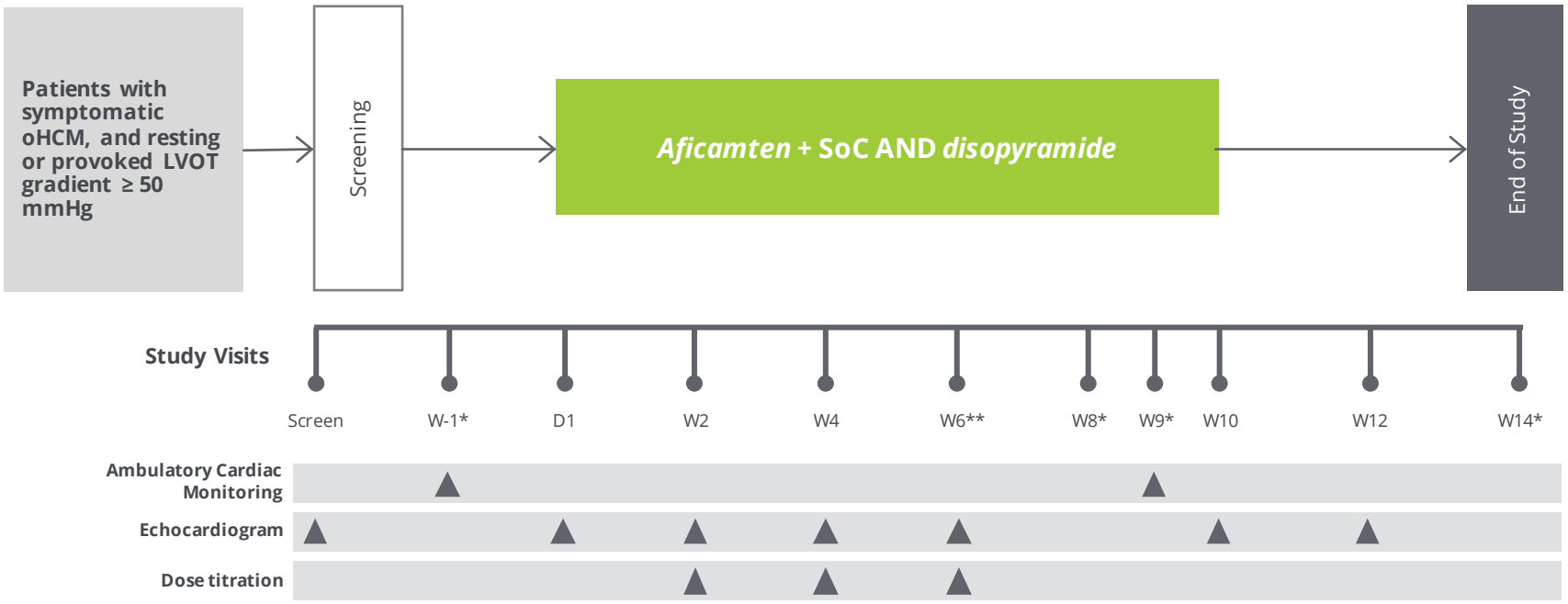
- No Improvement in NYHA Class
- ≥1 NYHA Class Improvement

Maron M, Abraham T, Masri A, et al. "REDWOOD-HCM: A Randomized, Double-blind, Placebo-controlled, Dose-finding Trial of the Cardiac Myosin Inhibitor, *Aficamten*, In Obstructive Hypertrophic Cardiomyopathy"

REDWOOD-HCM: Cohort 3

Patients with symptomatic oHCM on background therapy of *disopyramide*

Same doses used in Cohort 3 as in Cohort 1



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

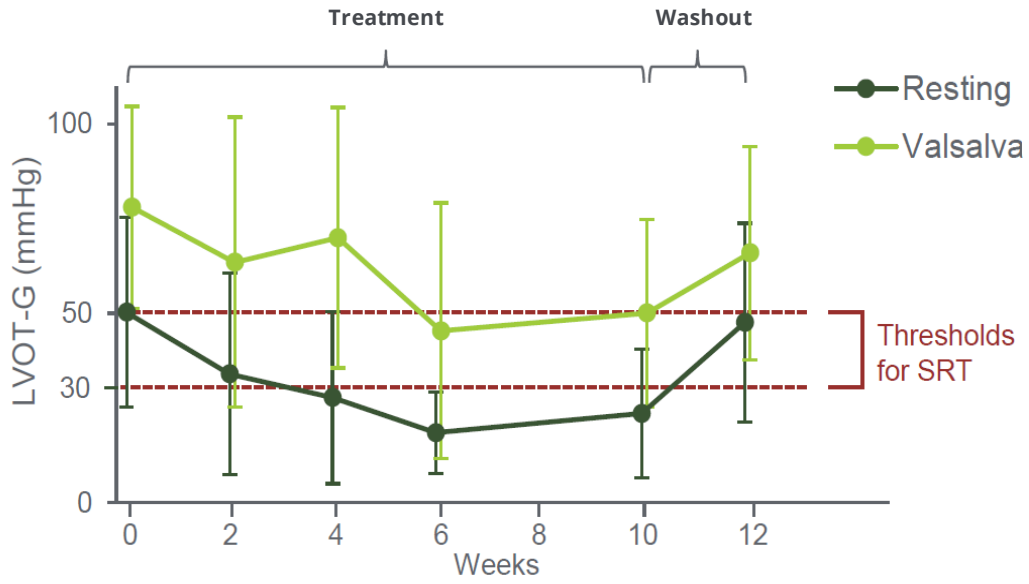
*Telephone visits
**Patient can only be down-titrated at Week 6

REDWOOD-HCM: Efficacy in Patients on *Disopyramide*

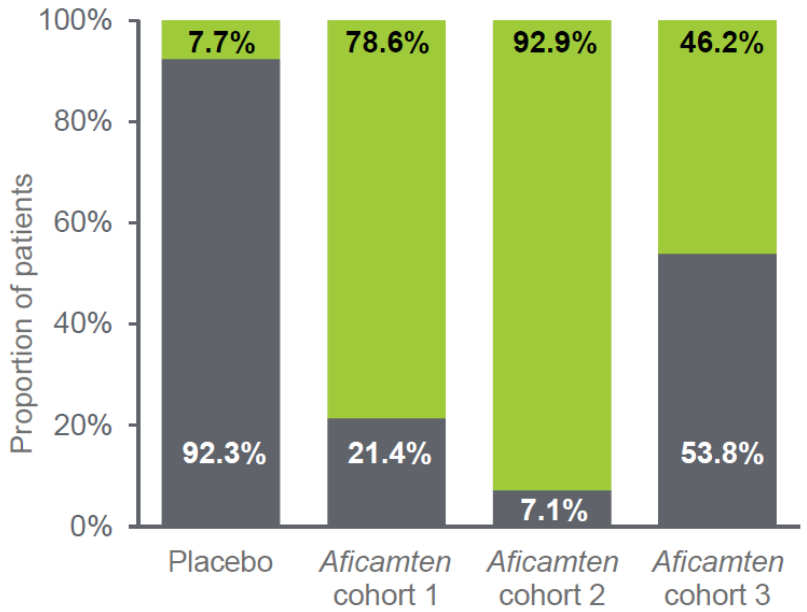
Cohort 3

Reductions in LVOT gradients; no patients whose LVEF dropped below safety threshold

LVOT Gradients



Response Rates



For 53.8% with incomplete response, opportunity for dose escalation in SEQUOIA-HCM

Complete Response:

Resting LVOT-G <30 mmHg
AND Valsalva LVOT-G <50 mmHg

Values are mean ± SD. Core-lab read echocardiograms. SRT, septal reduction therapy

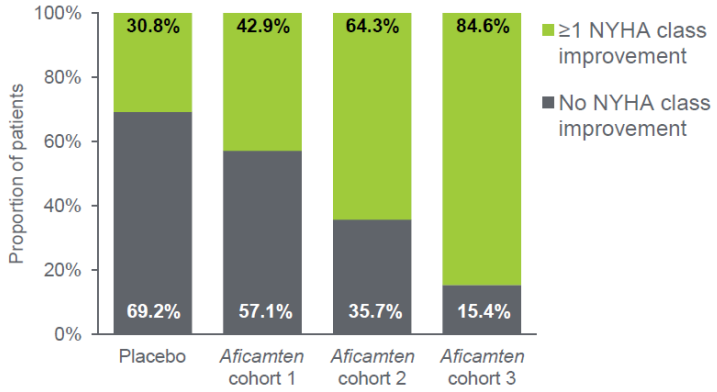
REDWOOD-HCM: Efficacy in Patients on *Disopyramide*

Cohort 3

REDWOOD HCM

Improvement in functional class and cardiac biomarkers

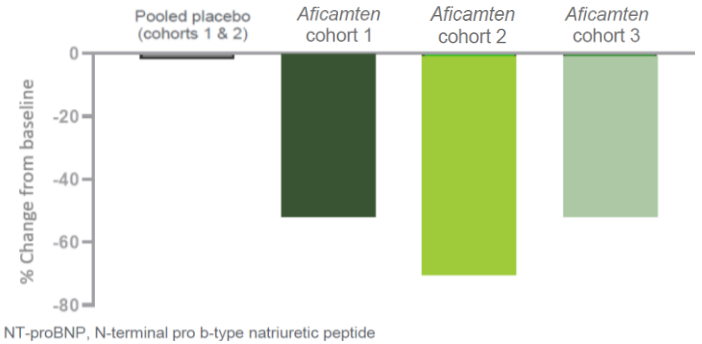
NYHA Response



NYHA, New York Heart Association

NT-proBNP

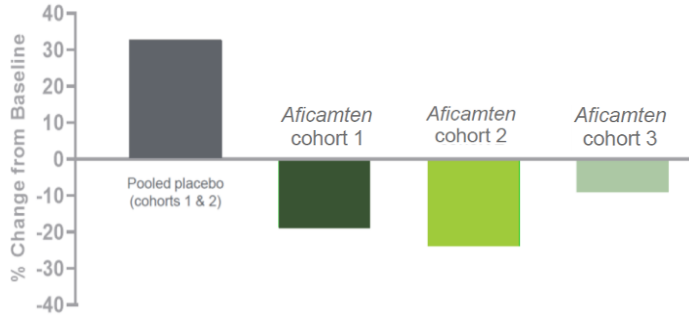
Geometric mean change from baseline to Week 10



NT-proBNP, N-terminal pro b-type natriuretic peptide

Hs-Troponin I

Mean change from baseline to Week 10



hs, high sensitivity

REDWOOD-HCM: Cohort 4

Patients with symptomatic nHCM on background therapy

Opened to enrollment in Q1 2022

	Dose 1	Dose 2	Dose 3
Cohort 4	5 mg	10 mg	15 mg

hs-cTnI: high- sensitivity cardiac troponin
*Telephone visits
**Patient can only be down-titrated at Week 6

SEQUOIA-HCM: Phase 3 Trial

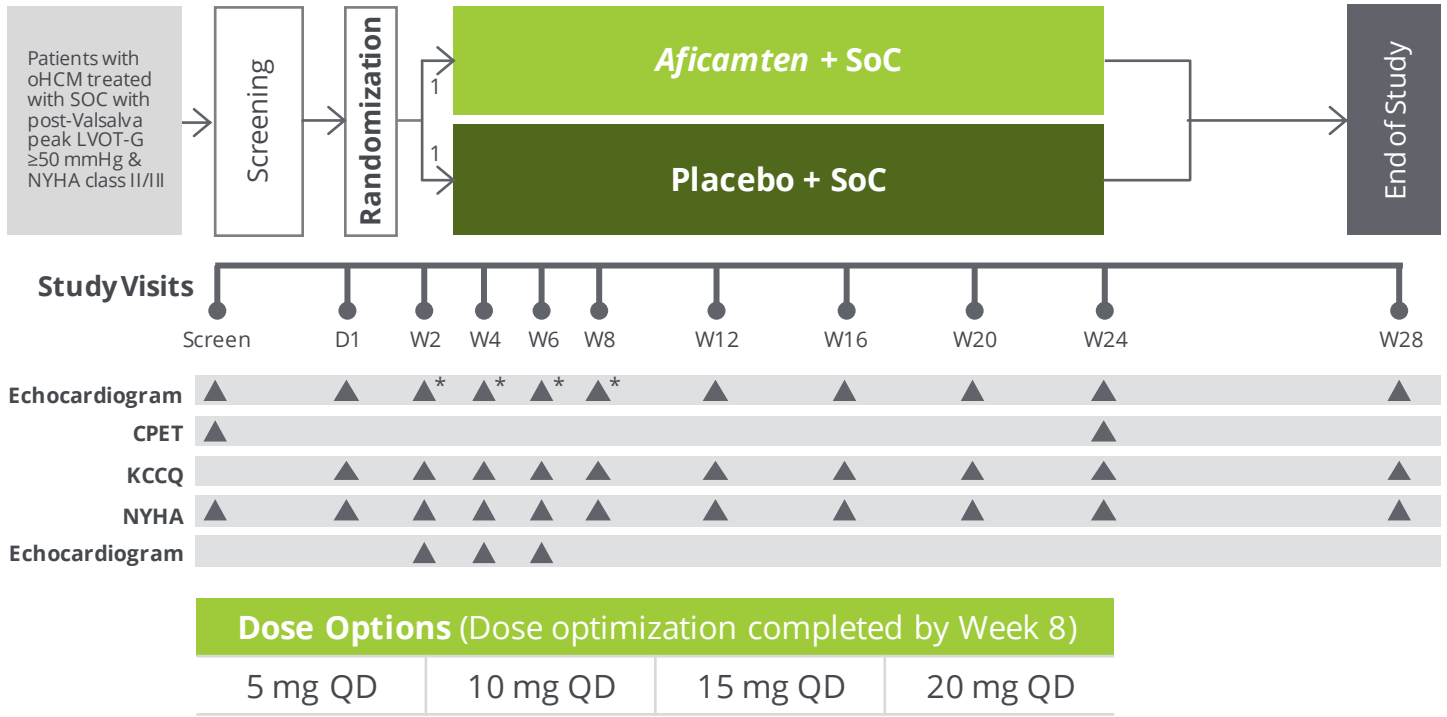
Plan to enroll at 115 sites in US, Europe and Asia**

Primary endpoint: **Change in pVO_2 by CPET from baseline to Week 24**

Secondary objectives include measuring **change in KCCQ & improvement in NYHA class at week 12 and 24**

Enrolling 270 patients treated with standard of care with:
- **resting LVOT-G ≥30 mmHg,**
- **post-Valsalva LVOT-G ≥50 mmHg,**
- **NYHA Class II or III,**
- **exercise performance <80% predicted**

Individualized dose up-titration based on echocardiography: LVEF ≥55%, post-Valsalva LVOT-G ≥30 mmHg



* Focused echocardiogram
** Plan to enroll in US, Italy, France, Germany, Czech Republic, Denmark, Hungary, Netherlands, Poland, Portugal, Spain, UK, Israel & China
SOC: standard of care

REDWOOD-HCM: Open Label Extension

Open for eligible patients who completed REDWOOD-HCM & SEQUOIA-HCM

REDWOOD HCM OLE

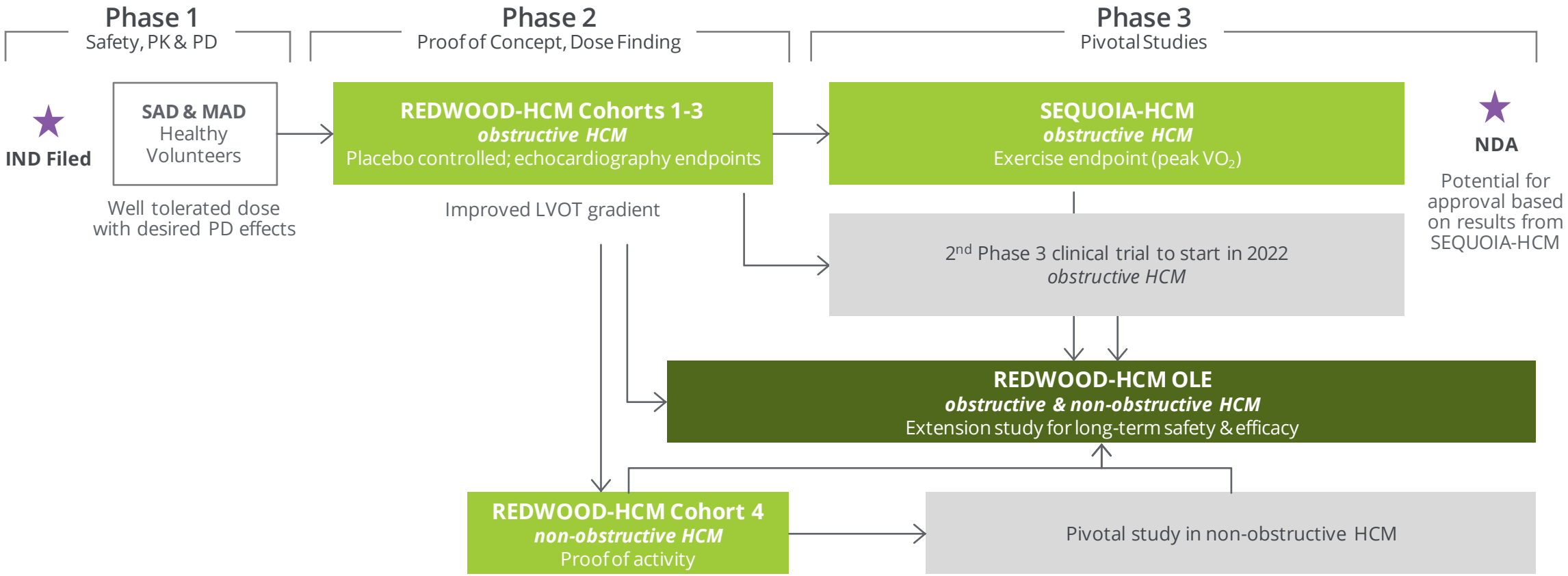
Expect to share data from REDWOOD-HCM OLE in 2022

- 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

OLE: Escalating doses based on echo-guided dose titration

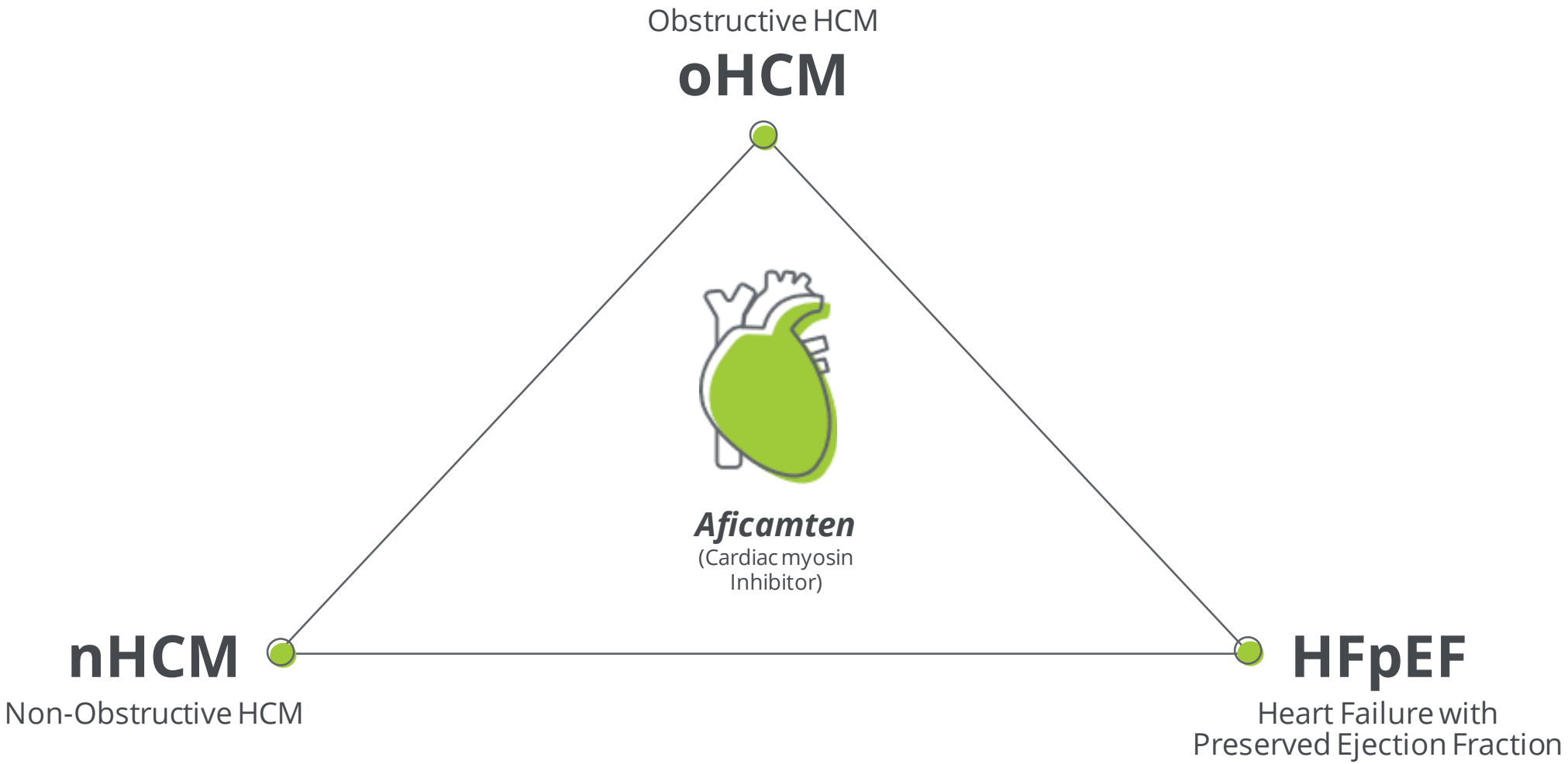
Aficamten: Clinical Development Plan for HCM

SEQUOIA-HCM enrolling patients with oHCM; REDWOOD-HCM Cohort 4 enrolling patients with nHCM



Novel Approach May Address Multiple Unmet Patient Needs

No FDA-approved therapies



Sarcomere Directed Drug Commercialization

FRANCHISE STRATEGY

Cytokinetics

Launch Guiding Principles Strengthen Franchise Build

Patient and customer centric	Creating **broad value for cardiac patients** and build long-term, **deep relationships with cardiologists** with multiple CV medicines
Cost-efficient	Leverage **Go-to-Market synergies** between multiple CV medicines, enabling **efficiencies** in both franchise functions and support functions
Scalable	Build and **develop core functional capabilities** while strategically outsourcing capabilities and processes that are non-core

Design commercial organization to optimize U.S. launch of *omecamtiv mecarbil*, enable geographic expansion & partnerships, and launch of *aficamten*

Limited Incremental Cost For Future U.S. CV Launches

Building Today …

To optimize value capture for potential launch of *omecamtiv mecarbil*

- Building deep, long-term relationships

… To Lead Tomorrow

To support future launches and establish Cytokinetics as a CV leader

- Significant overlap between HFrEF and HCM

<1,000 Hospitals & HF Clinics

<10,000 Cardiologists

~15% Additional Targets

Coverage of vast majority of HCM

Go-to-Market Synergies for *Omecamtiv Mecarbil* & *Aficamten*

Sales Team	**Given target overlap, leveraging same sales team**
Commercial Support Functions	**Utilize resources across brands (e.g., access, analytics, …)**
Medical Affairs	**MSLs qualified to cover both HFrEF and HCM**
Corporate Support Functions	**Avoid costs of duplication (IT, Finance, HR, …)**

→ **Synergy PV of ~ $500M**

Sarcomere Directed Drug Development

SKELETAL MUSCLE

Reldesemtiv

Cytokinetics

Reldesemtiv

Cytokinetics

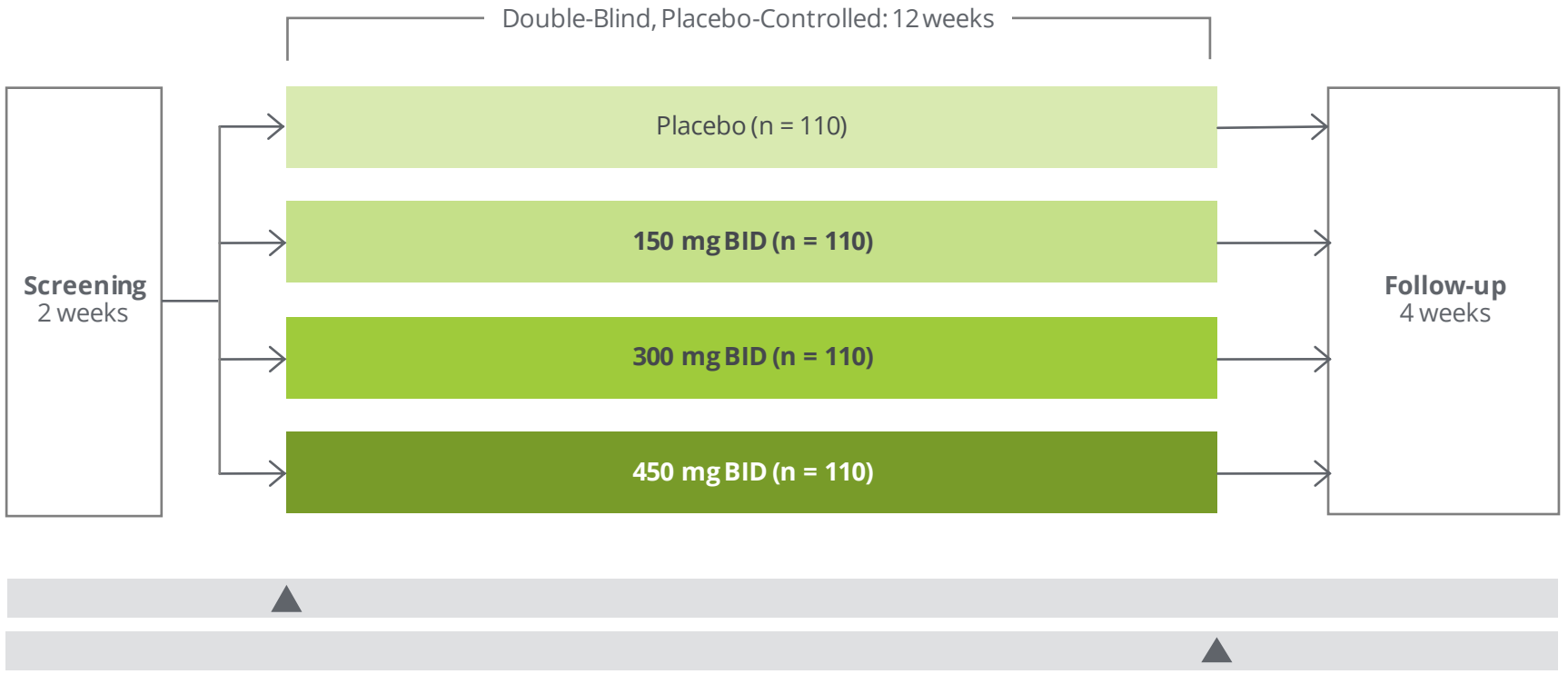
Reldesemtiv is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.

Phase 2 Clinical Trial in ALS

FORTITUDE ALS

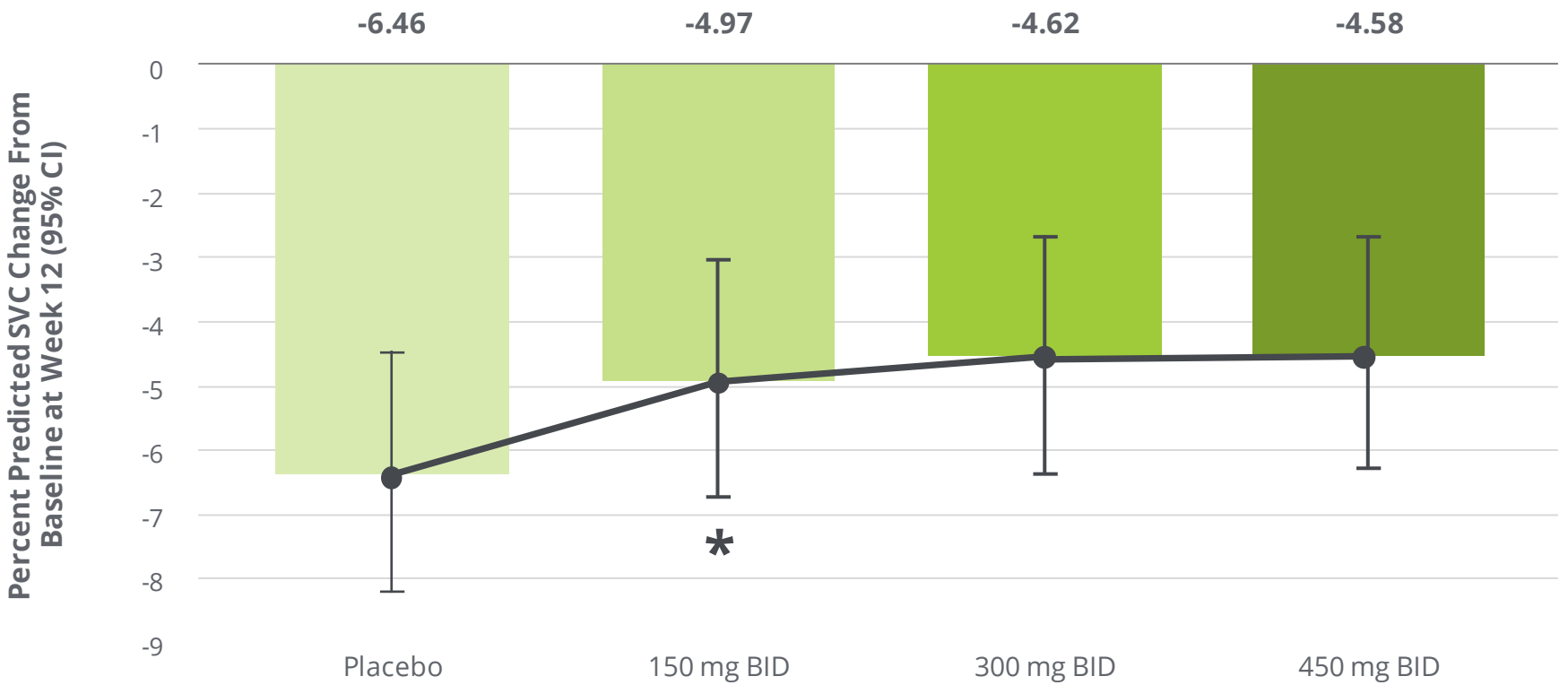
Results presented at American Academy of Neurology 2019 Annual Meeting

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

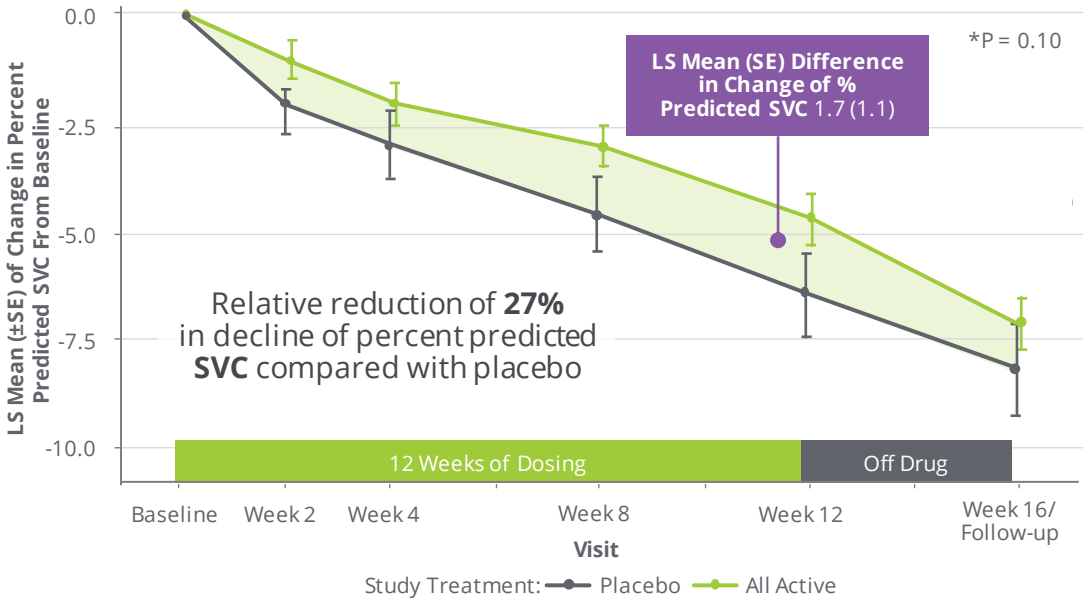
*Based on Mixed Model for Repeated Measures (MMRM) with the contrasts of (-5, -1, 3, 3) for placebo, *reldesemtiv* 150 mg, 300 mg and 450 mg BID, respectively

Phase 2 Clinical Trial

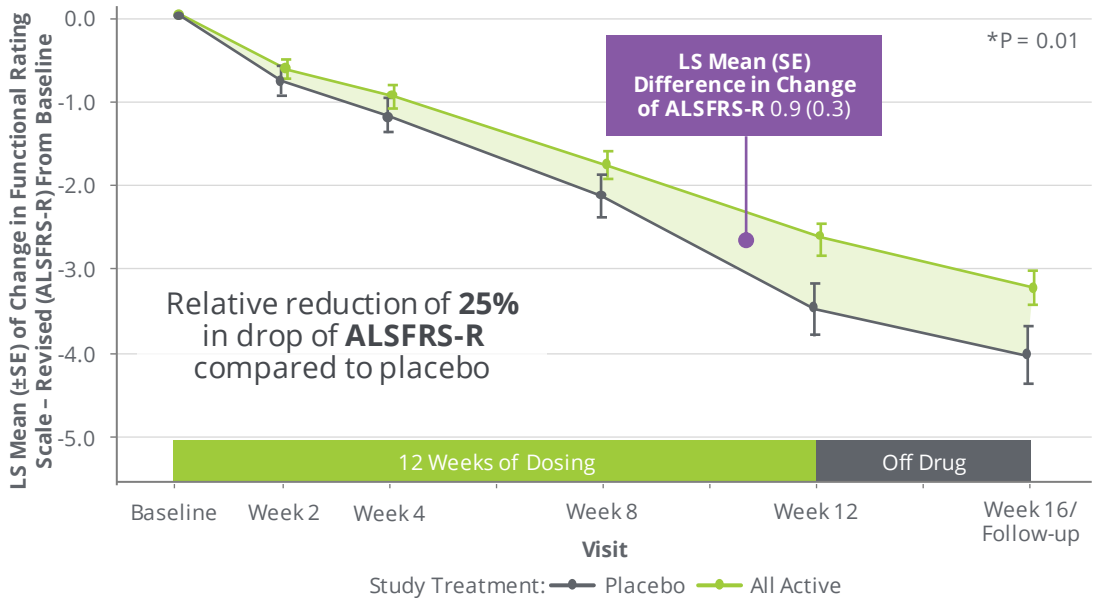
FORTITUDE ALS

Primary analysis not statistically significant; patients on all doses of *reldesemtiv* declined less than patients on placebo*

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

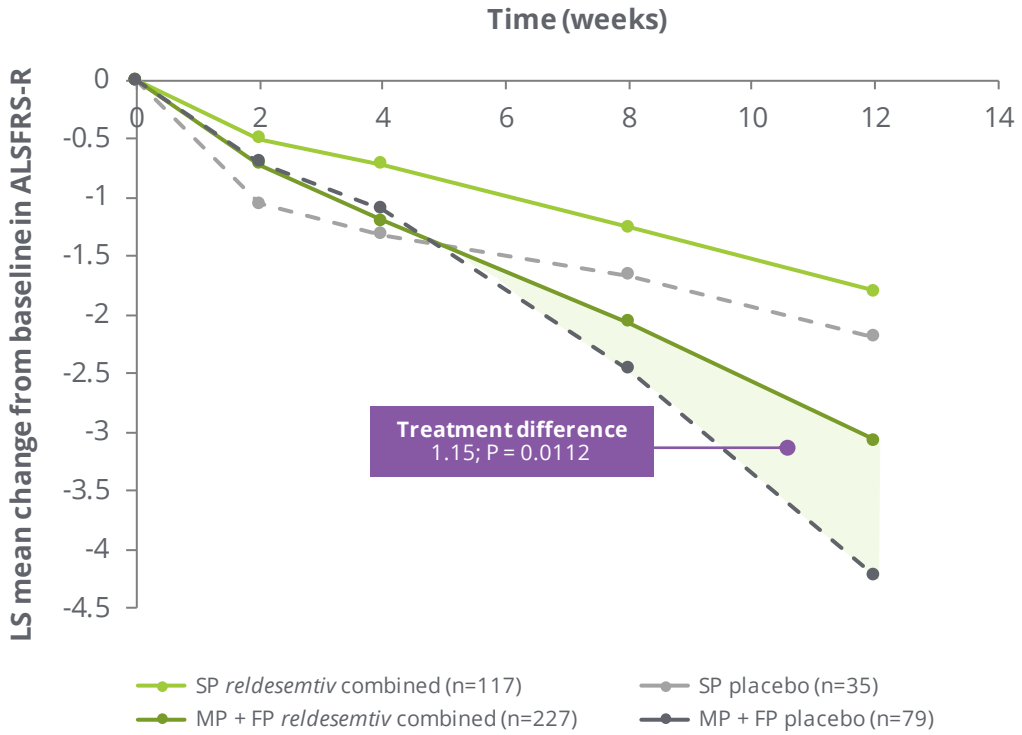
	No. of Patients (pbo/ *reldesemtiv*)	LSM Difference (95% CI)	Estimate	*P* value
Percent predicted SVC at baseline				
<80	43/109		1.588	0.0089
≥80	57/196		0.264	0.5296
ALSFRS-R total score at baseline				
<Median (38.0)	48/129		1.107	0.0585
≥Median (38.0)	52/176		0.685	0.0987
ALSAQ-5 total score at baseline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

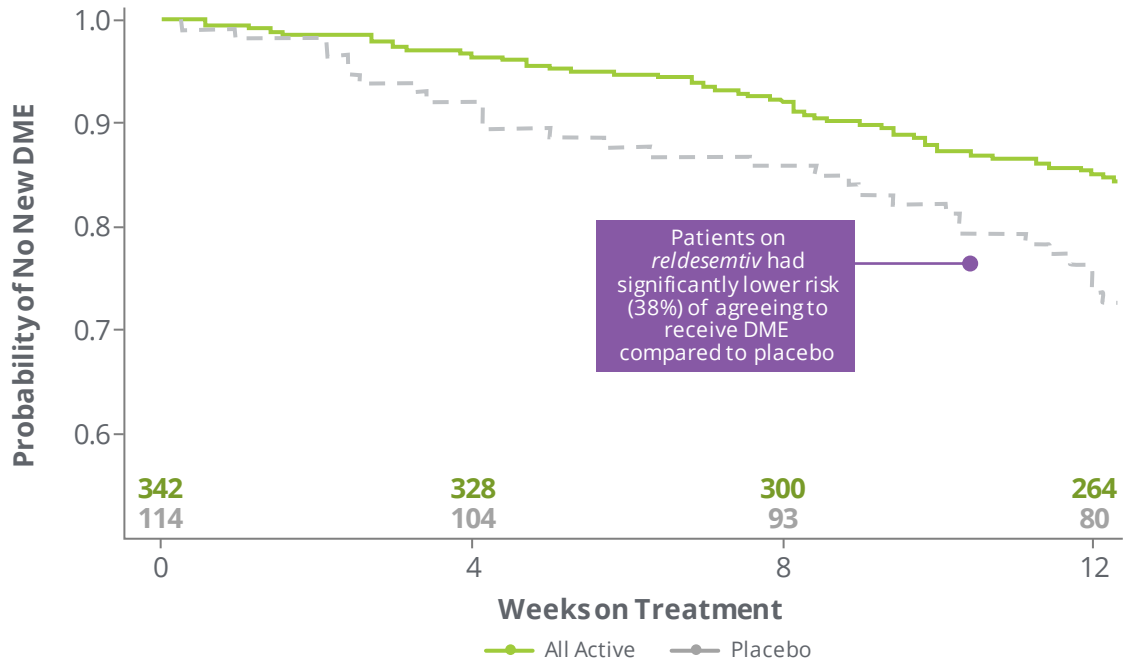
Change From Baseline in ALSFRS-R by Progressor Tertiles



SP: slow progressor; MP: middle progressor; FP: fast progressor

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

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

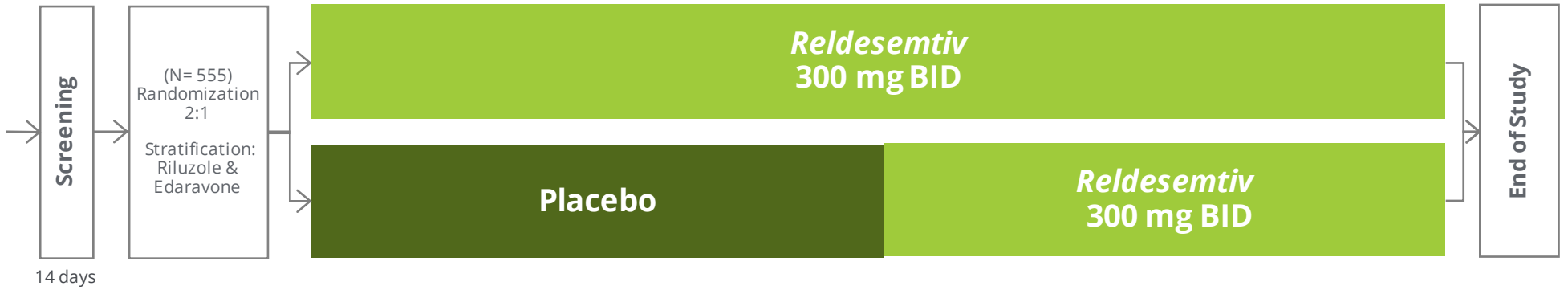


Phase 3 Clinical Trial Design

COURAGE ALS

Plan to enroll 555 patients; interim analysis for futility in 2H 2022

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



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

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

Sarcomere Directed Therapies

CORPORATE PROFILE

Cytokinetics

Robust Pipeline, Solid Financial Position

Pipeline

1 Potential commercial launch in 2022

2 Programs in Phase 3 trials

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
- NDA filed; PDUFA 11/30/22

CK-136

- Phase 1

HCM

Aficamten

- Phase 3 trial SEQUOIA-HCM, enrolling patients with oHCM
- Cohort 4 of Phase 2 trial REDWOOD-HCM enrolling patients with nHCM

ALS

Reldesemtiv

- Phase 3 trial, COURAGE-ALS ongoing

Ongoing R&D

Additional research in muscle biology, energetics & metabolism

Foundations

300

Full time employees

$624M

At Q4 2021

Does not include $150 million in proceeds received from transactions executed in late 2021 and early 2022

>2 years

Cash runway

Timelines and milestones reflect Cytokinetics' current expectations and beliefs

Monetizing Our Pipeline to Bolster Balance Sheet

Symmetry of deals for *omecamtiv mecarbil* and *aficamten* affords synergies for development and potential launches and supports franchise strategies

Transactions with Royalty Pharma	Sold 4.5% royalty on worldwide net sales of ***omecamtiv mecarbil**** **2017**	→ Sold 3.5-4.5% royalty on worldwide net sales of ***aficamten**** **2022**
Partnerships with Ji Xing	Granted exclusive rights to develop and commercialize ***aficamten*** in Greater China **2020**	→ Granted exclusive rights to develop and commercialize ***omecamtiv mecarbil*** in Greater China **2021**

* 4.5% on worldwide net sales of *omecamtiv mecarbil* (and potentially other compounds with same mechanism of action), subject to potential increase of up to an additional 1% under certain circumstances
** 4.5% for annual worldwide net sales of *aficamten* up to $1 billion and 3.5% for annual worldwide net sales of *aficamten* in excess of $1 billion, subject to reduction in certain circumstances

Balance Sheet & Financial Guidance

2021 Condensed Balance Sheet
As of 12/31/2021

in millions

	Total
Cash and investments	$623.7*
Accounts receivable	$51.8
PPE	$73.3
Leased assets	$73.1
Other assets	$19.4
Total Assets	**$841.3**
Debt	$134.0
Liability related to sale of future royalties	$179.1
Deferred Revenue	$87.0
Lease liability	$127.1
Other liabilities	$70.2
Total Liabilities	**$597.4**
Working capital	$463.8
Accumulated deficit	($1,207.6)
Stockholders' equity	$243.9
Wtd Avg Basic Shares Outstanding	**84.1**

2022 Financial Guidance

in millions

	Total
Cash Revenue	$20 – 25
Cash Operating Expenses	$380 – 400
Net	**~ $365 - 385**

**Does not include $150 million in proceeds received from transactions executed in late 2021 and early 2022*

Expected Milestones in 2022

Launch *omecamtiv mecarbil* in the U.S. pending FDA approval in Q4 2022

Continue enrollment in **SEQUOIA-HCM** through 2022

Begin second Phase 3 **trial of *aficamten* in oHCM** in 2H 2022

Expect to share data from **REDWOOD-HCM OLE** in 2022

Continue enrollment in **Cohort 4 of REDWOOD-HCM** in 2022

Expect **first interim analysis from COURAGE-ALS** in 2H 2022

Cytokinetics

THANK YOU

Sarcomere Directed Therapies

Nefertari, *diagnosed with heart failure*

Jillian, *diagnosed with HCM*

Chuck, *diagnosed with ALS*

Actual patients who consented to use of their name, image, and condition.