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

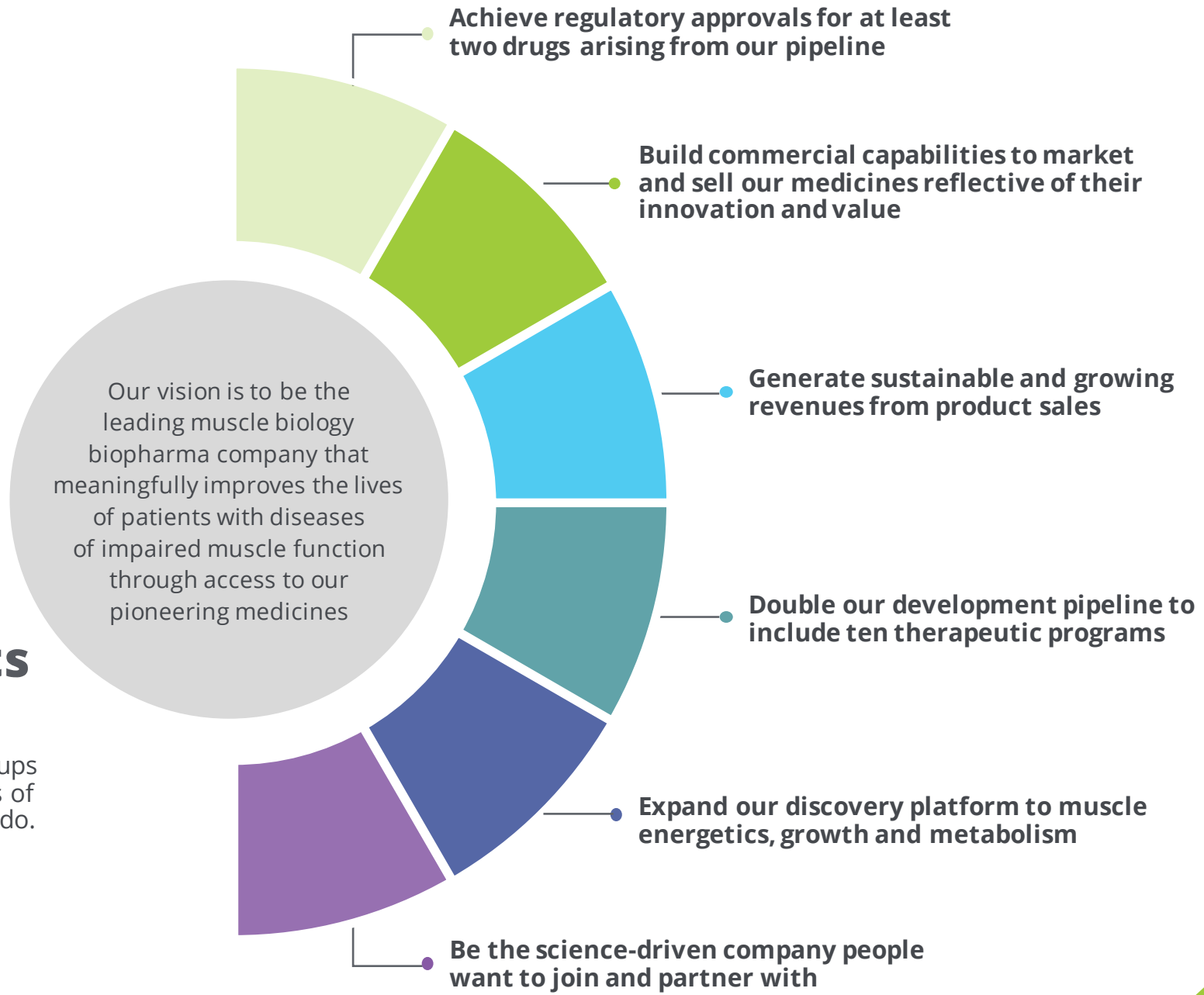
To bring forward new medicines to improve the healthspan of people with devastating cardiovascular and neuromuscular diseases of impaired muscle function.

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

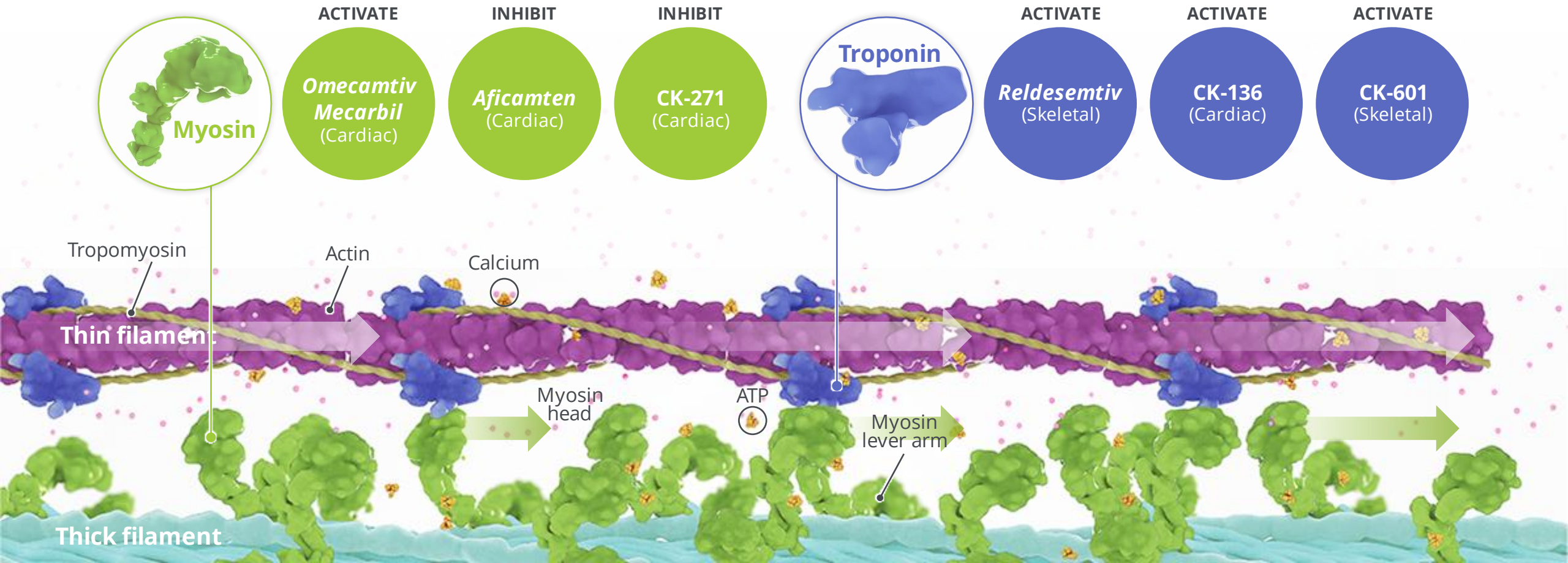
- Customer-centric approach to portfolio management
- Overlap between HFrEF and HCM accounts
- Commercial build in HFrEF supports future HCM business
- Lifecycle management extends and expands franchise

- Positive Phase 3 results from GALACTIC-HF
- Positive Phase 2 results from REDWOOD-HCM; start-up activities underway for Phase 3 clinical trial
- Clinical trial results from METEORIC-HF expected in early 2022

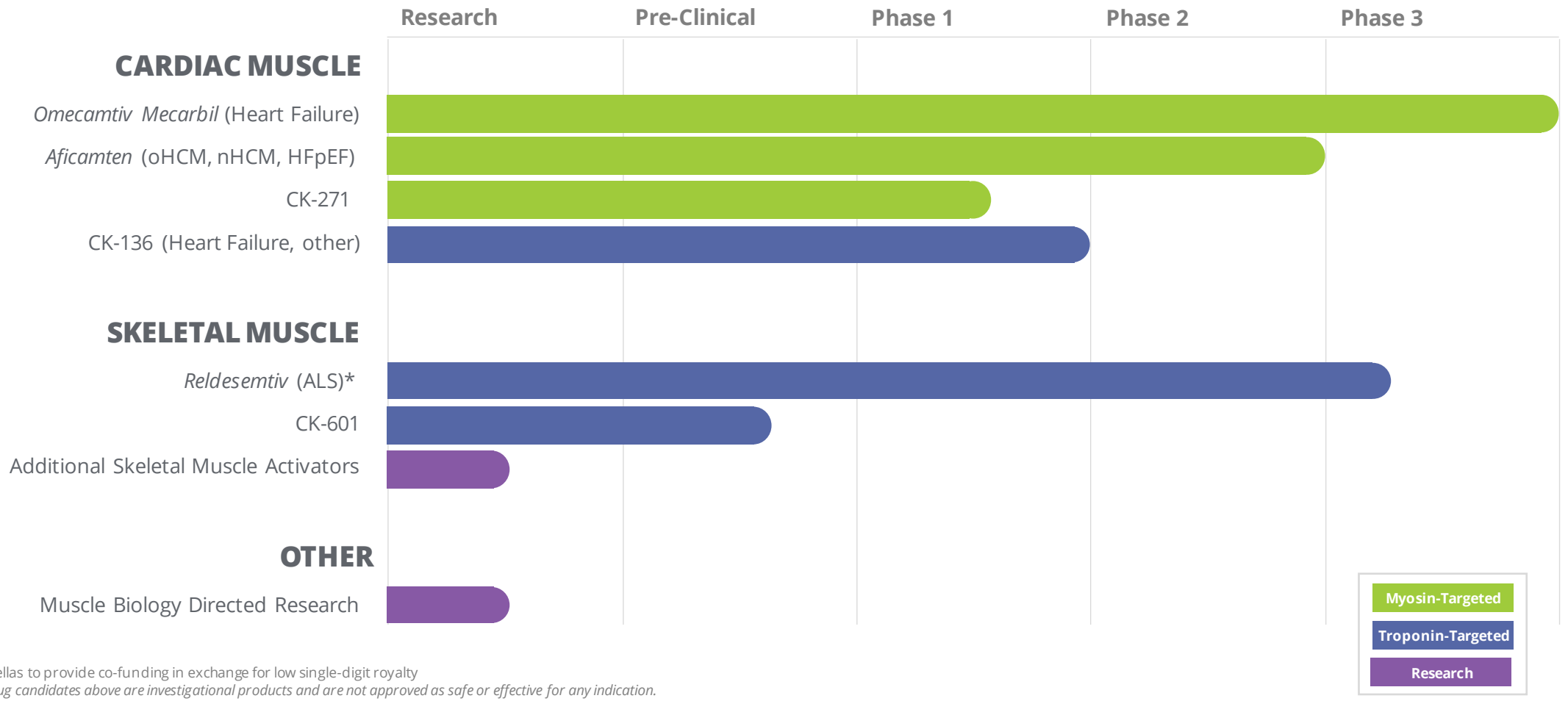
- Regular input, collaboration and guidance
- Elevate patient voice
- Improve function, performance and healthspan

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

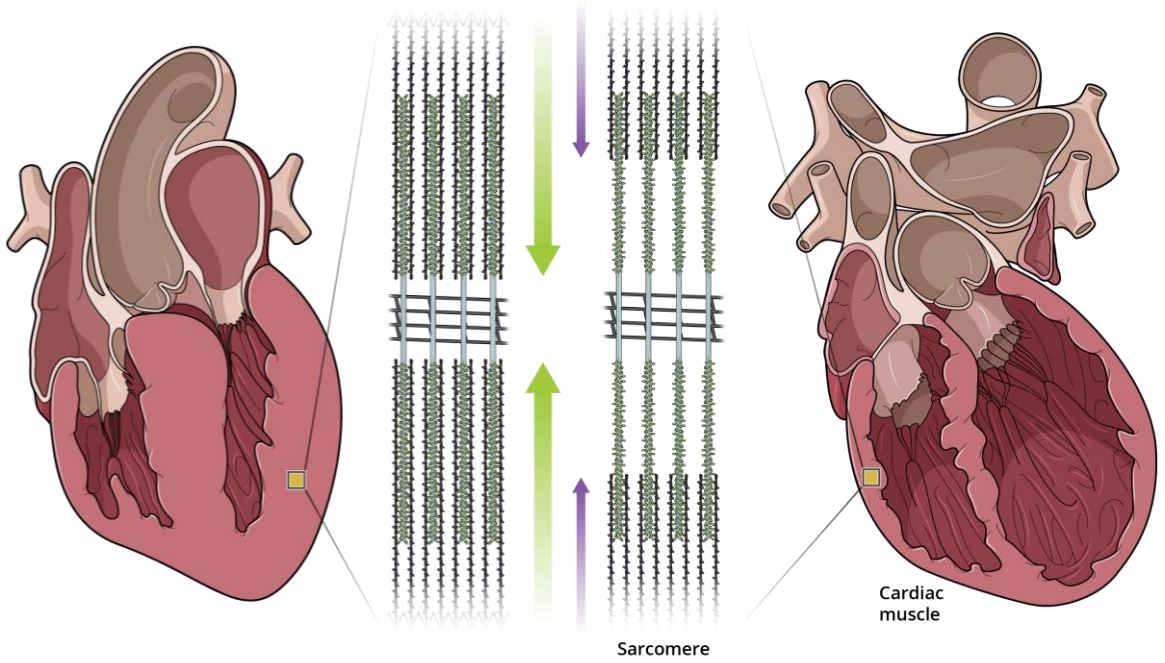
Aficamten

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**

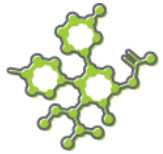
Drugs that do not affect renal function

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**

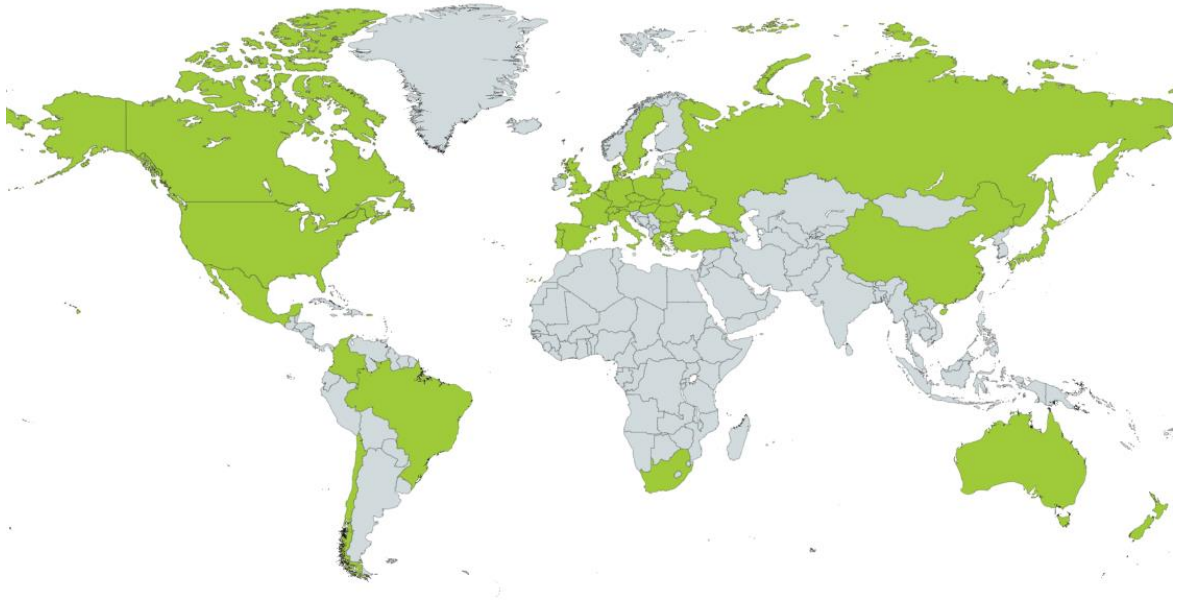
Patient QoL decreases as they lose the ability to perform daily tasks

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

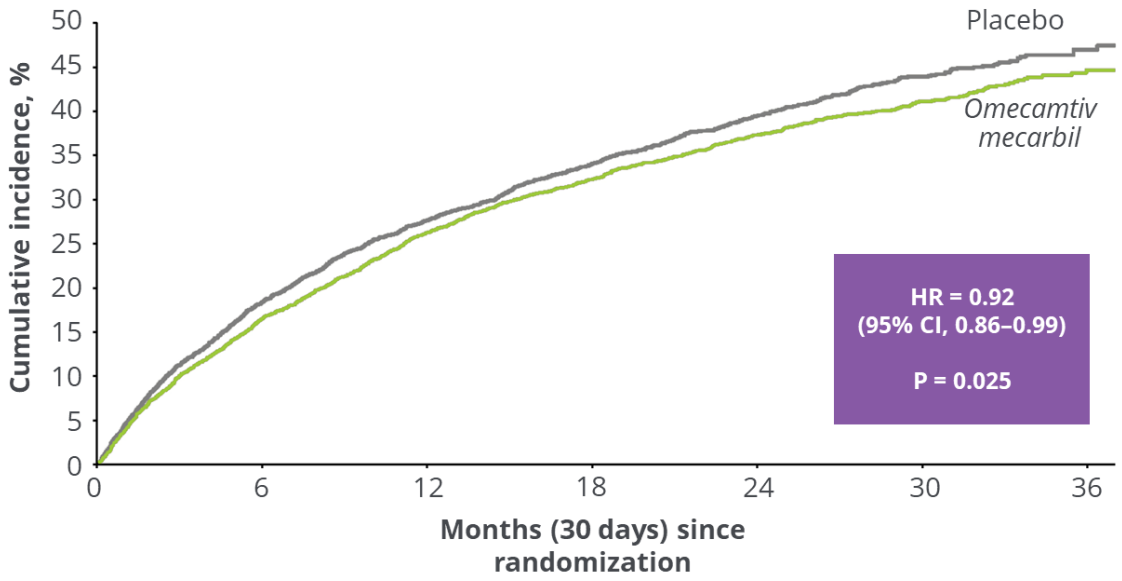
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; BB, beta blocker; CRT, cardiac resynchronization therapy; eGFR, estimated glomerular filtration rate; fib, fibrillation; hsTnI, high-sensitivity troponin I; ICD, implantable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

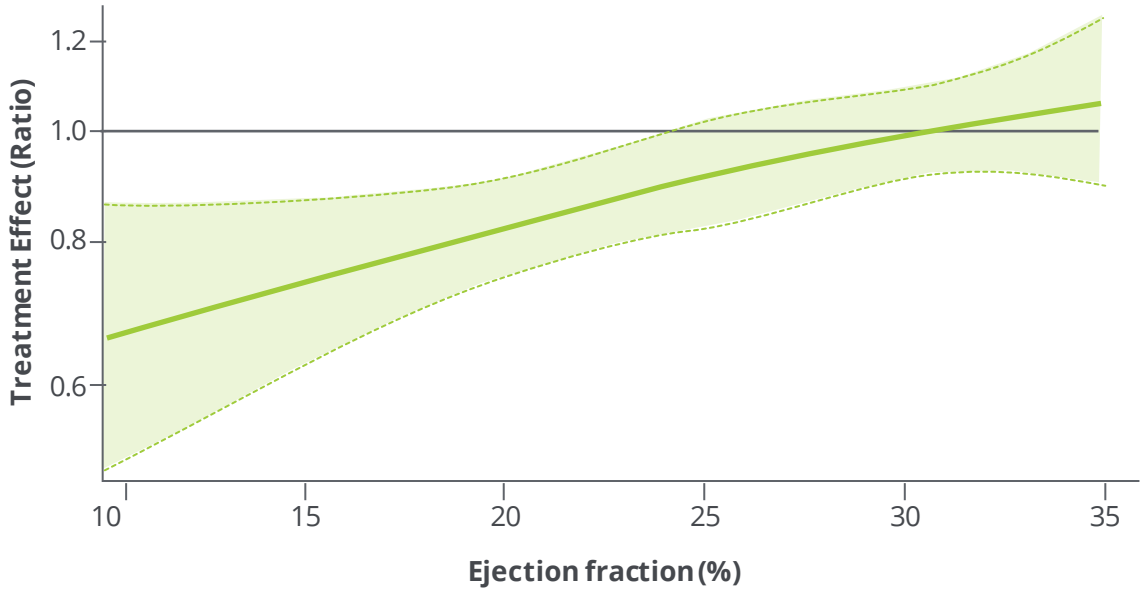
Treatment effect increased in more advanced patients

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

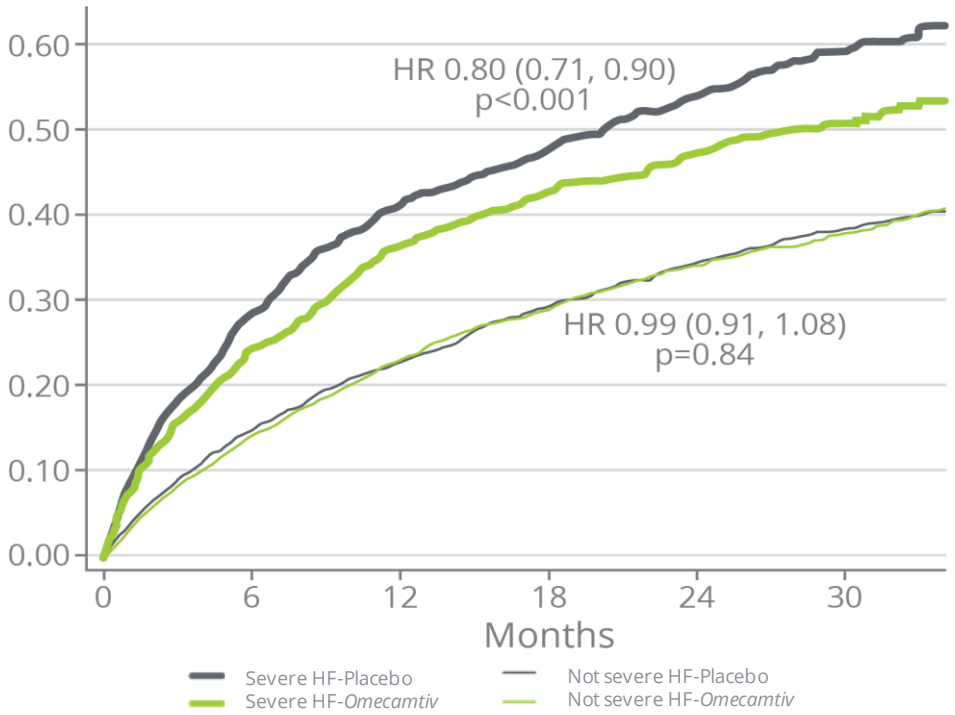
1. Teerlink JR et al., Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure; N Eng J Med 2020, 384:105-116.
2. Teerlink JR., Diaz R., Felker GM., et al. Effect of Ejection Fraction on Clinical Outcomes in Patients treated with Omecamtiv Mecarbil in GALACTIC-HF. JACC. 2021

Greater Treatment Effect in Worsening HF

GALACTIC-HF

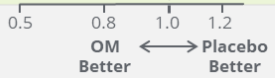
Primary Outcome in Severe HF: HR = 0.80 (0.71, 0.90)

(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%



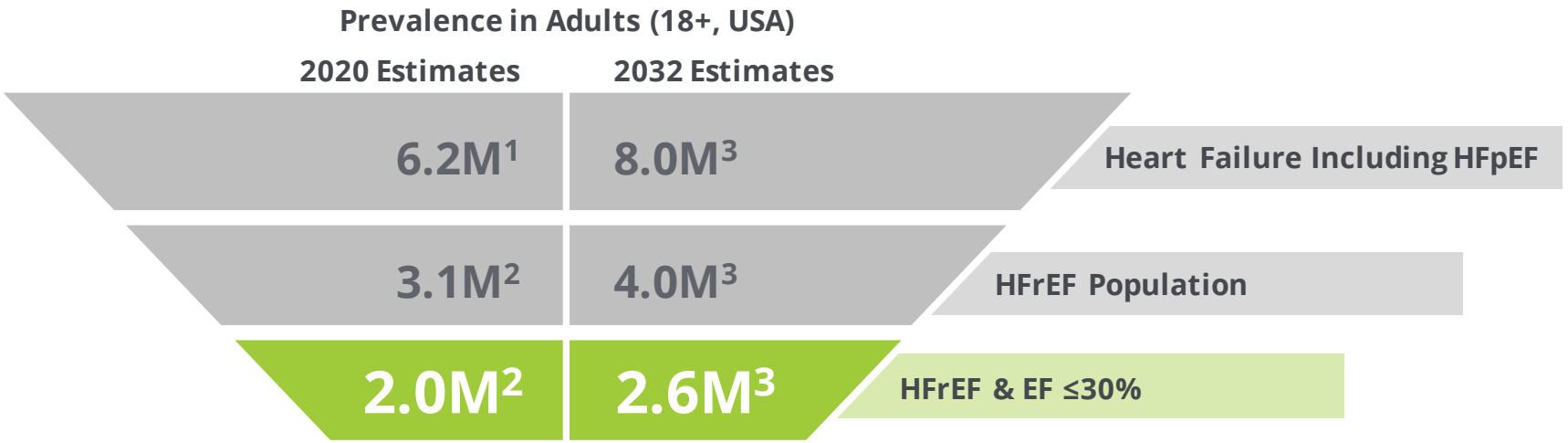
1. Felker GM, Omecamtiv Mecarbil in Patients with Severe Heart Failure: An Analysis from GALACTIC-HF, ESC Heart Failure 2021, June 2021
2. Felker GM, et al. Assessment of Omecamtiv Mecarbil for the Treatment of Patients With Severe Heart Failure. JAMA Cardiology, October 2021.

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**

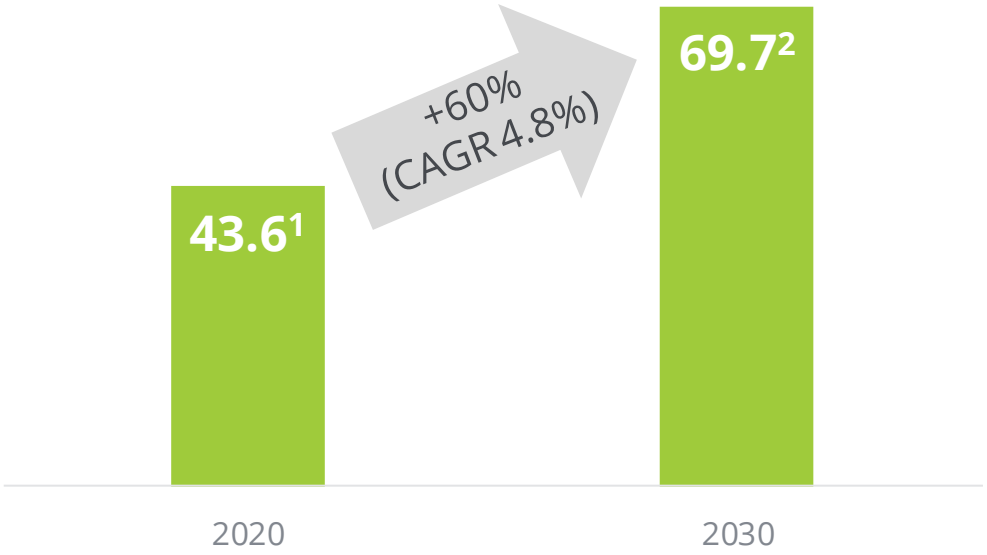
* HF Event: Urgent, unscheduled outpatient visit or hospitalization ** Due to renal impairment, low BP and/or hyperkalemia

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 With Lion's Share Due to Hospitalizations

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]

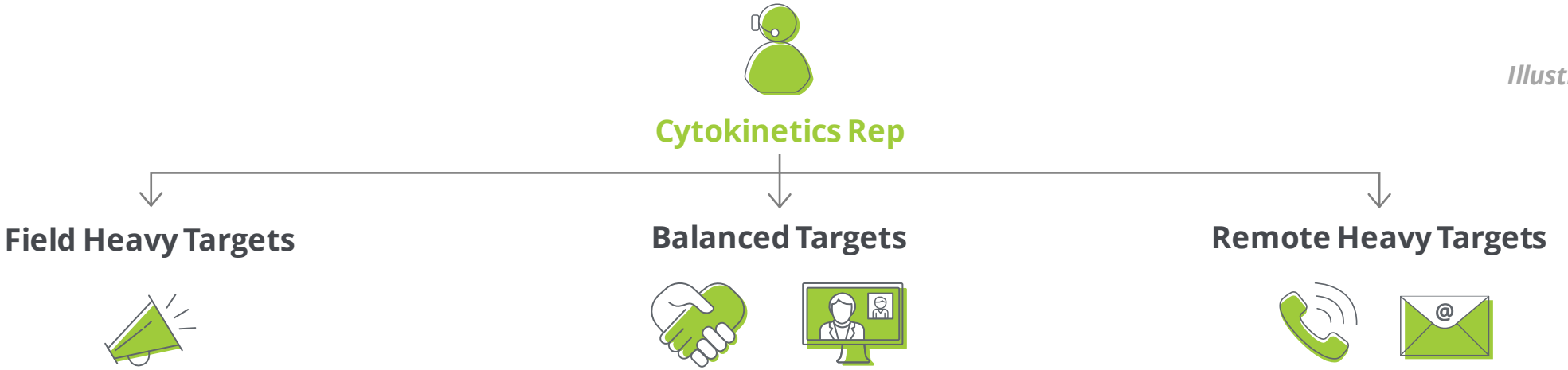
Of total lifetime HF cost burden, **~80% due to hospital stays**[5]

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

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.0b013e3182913 29a.
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

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

Illustration



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

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

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

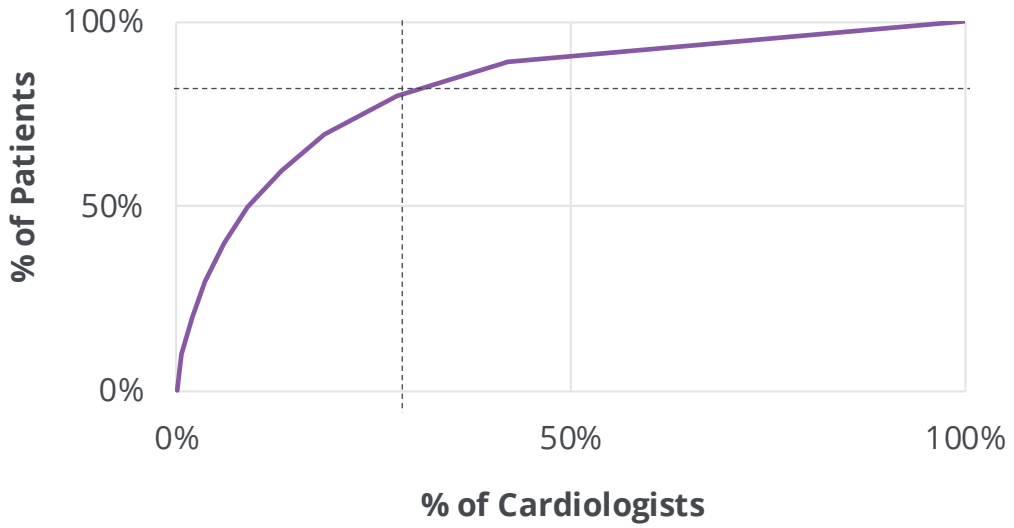
Using **HEOR** and clinical results to demonstrate the economic impact and value

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

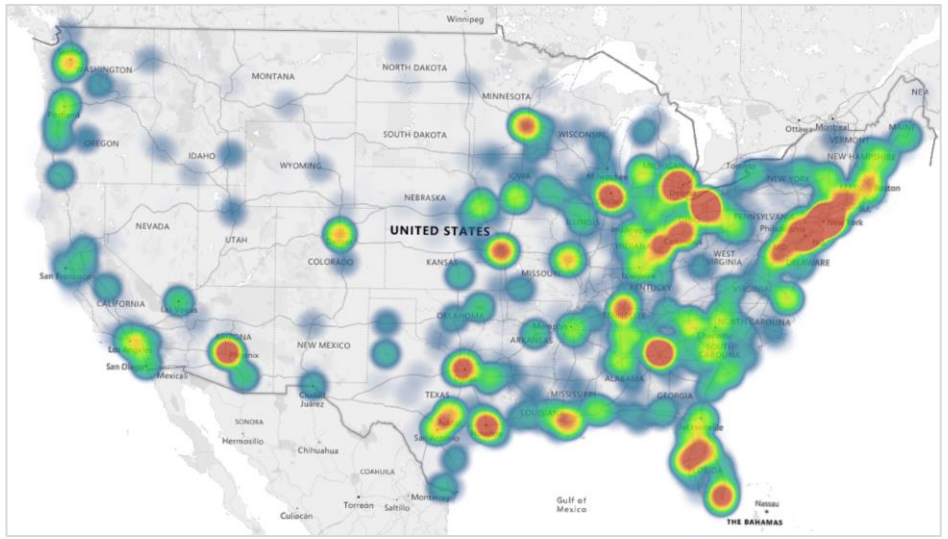
1. Based on Solomon S, Influence of Ejection Fraction on Cardiovascular Outcomes in a Broad Spectrum of Heart Failure Patients, Circulation 2005
2. Felker GM. *ESC Heart Fail* 2021 Oral Presentation. Data based on post hoc analyses.

Small Subset of Cardiologists Manage Majority of Patients

HFrEF Patient Concentration in Cardiologists



Distribution of High-Volume Cardiologists



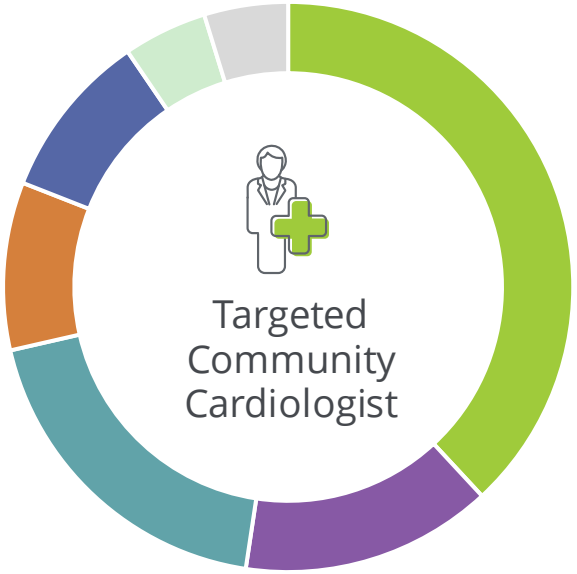
Allows for more targeted field team approach, focusing on <10,000 HCPs

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

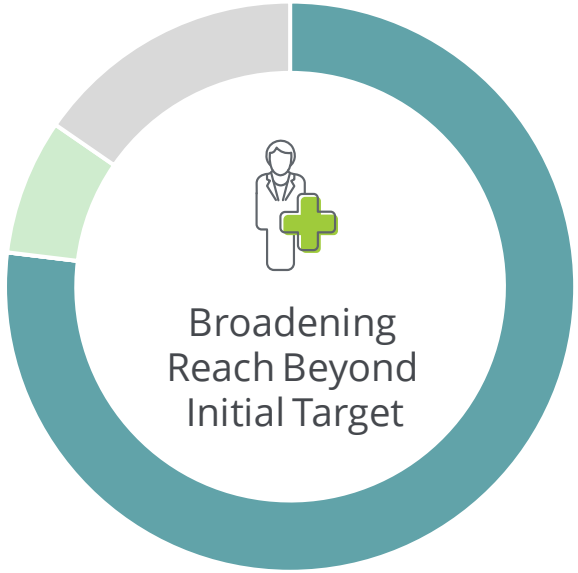
Customizing engagement by different types of customers

~~ illustrative ~~



Digital allows broader reach

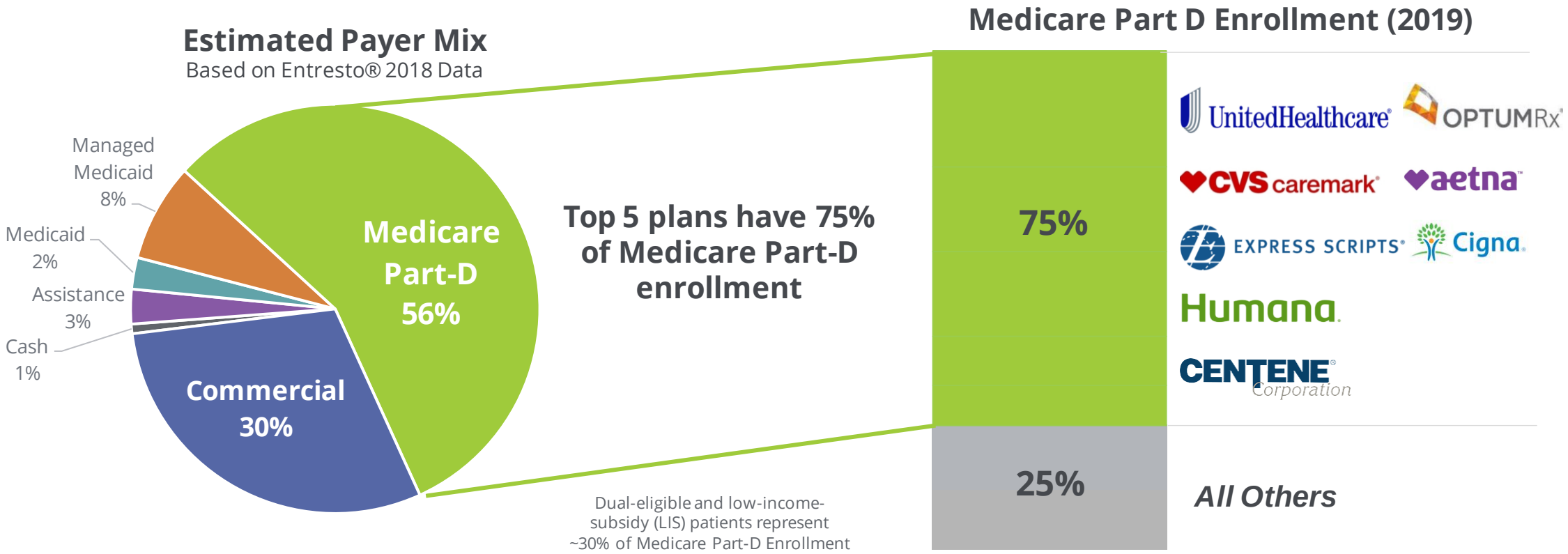
~~ illustrative ~~



Field & Account Reps | Inside Sales | Digital Engagement | Reimbursement Specialists | MSLs | Patient Services | Online communities

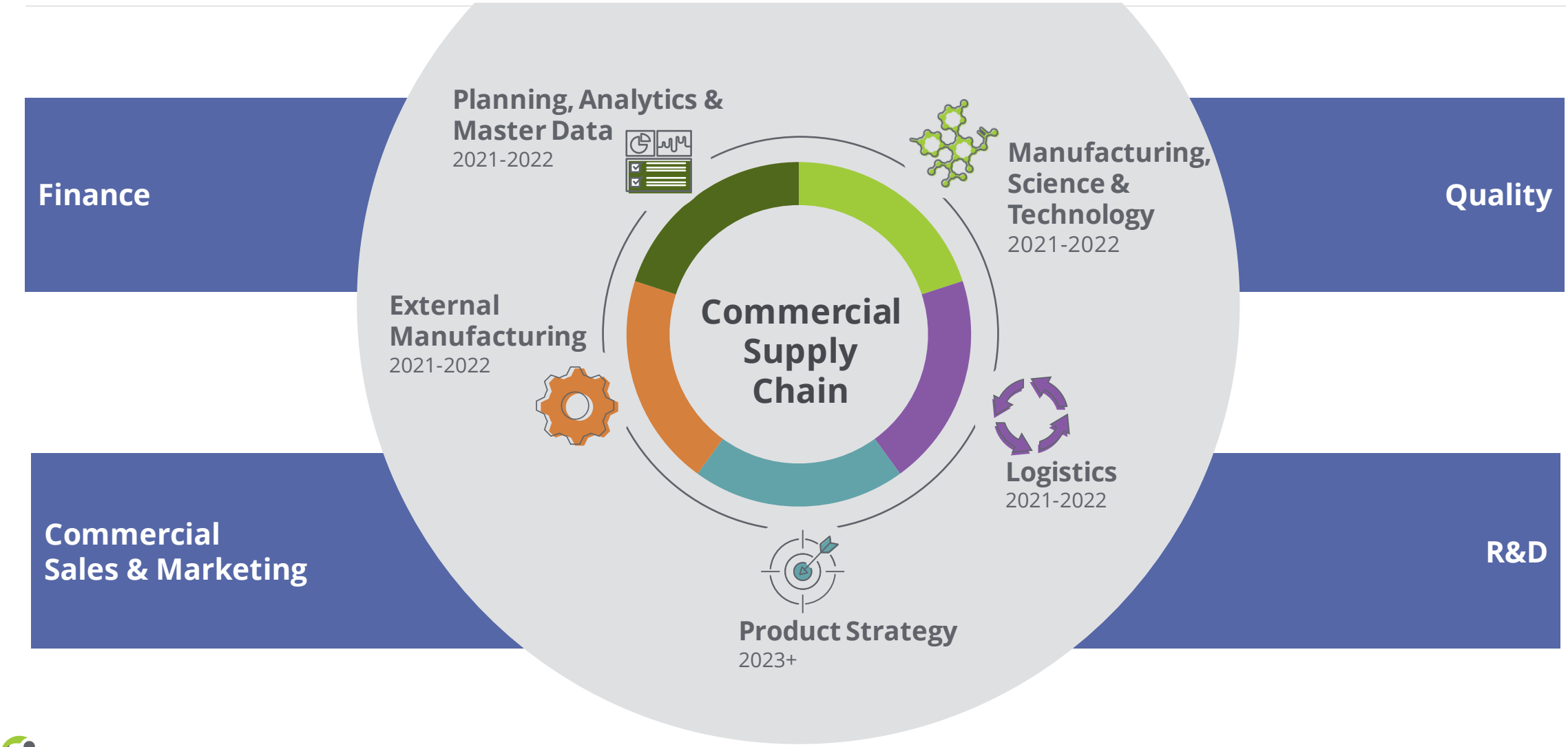
Medicare Is Major Payer with Select Key Players

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

Commercial Supply Chain Operating Model



Second Phase 3 Clinical Trial Underway

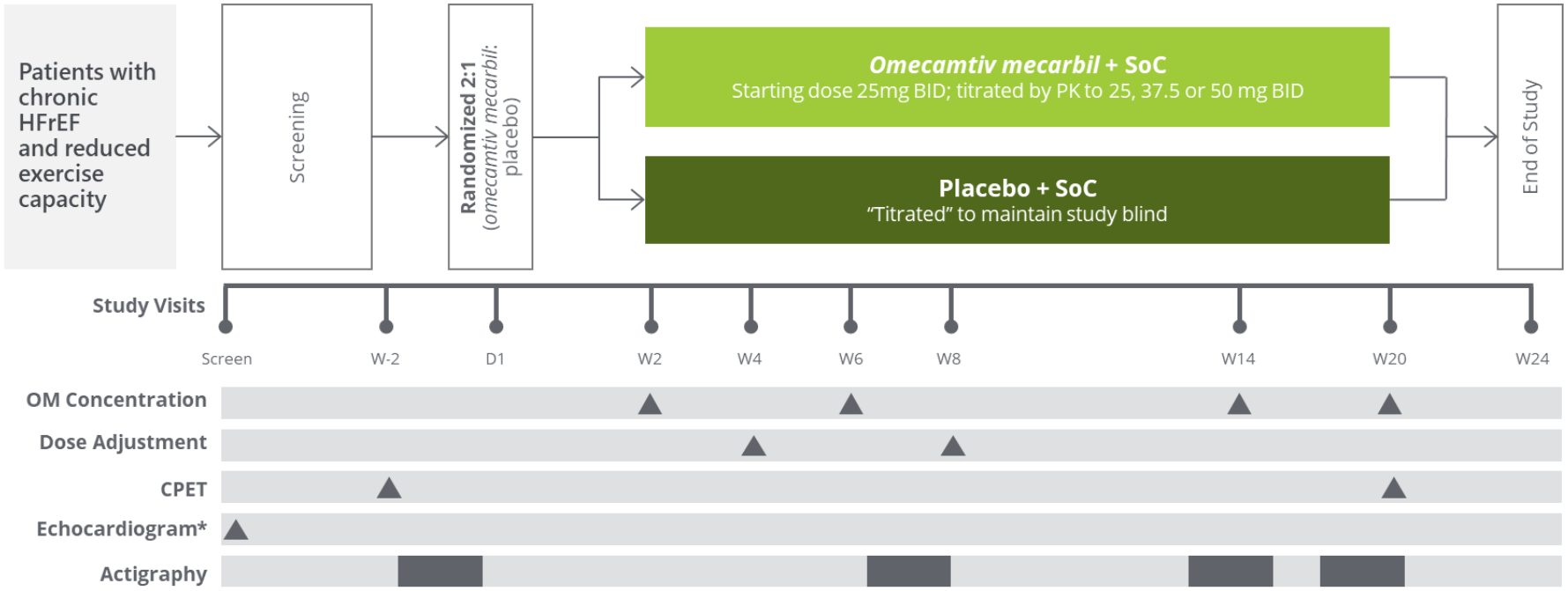
Investigating effect of *omecamtiv mecarbil* on exercise tolerance

METEORIC-HF

Results expected in early 2022

Primary endpoint:
Exercise tolerance -
Change in pVO_2 by CPET from baseline to Week 20

Enrolling patients with **LVEF ≤35 percent, NYHA heart failure class II or III, and reduced exercise capacity**



CPET: cardiopulmonary exercise testing
*Screening echocardiogram is not required if an appropriate LVEF assessment has been performed within one year
VO2 = Oxygen Uptake; CPET = Cardio-Pulmonary Exercise Testing; VE = Ventilatory Efficiency

Aficamten

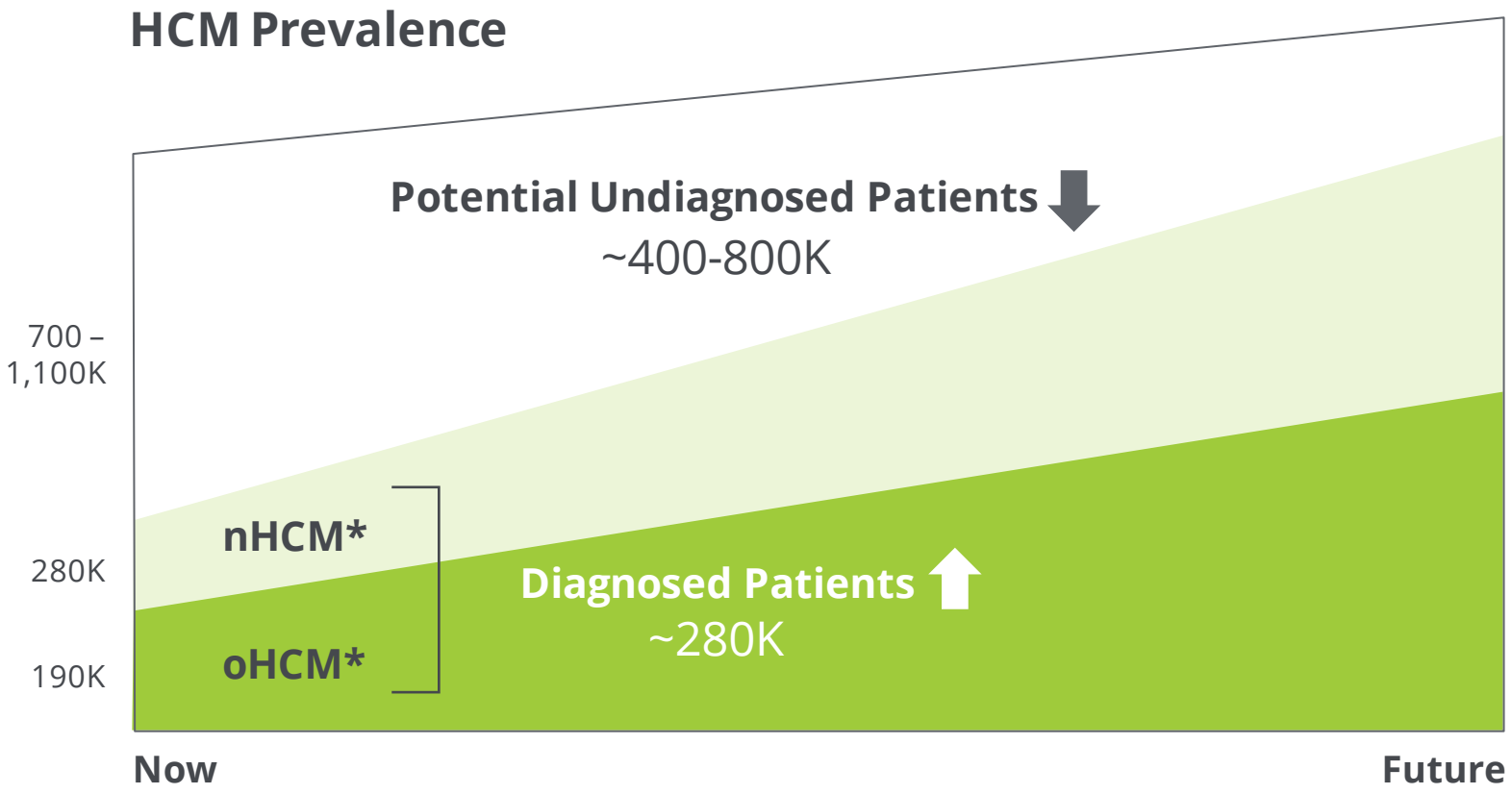
Cytokinetics

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

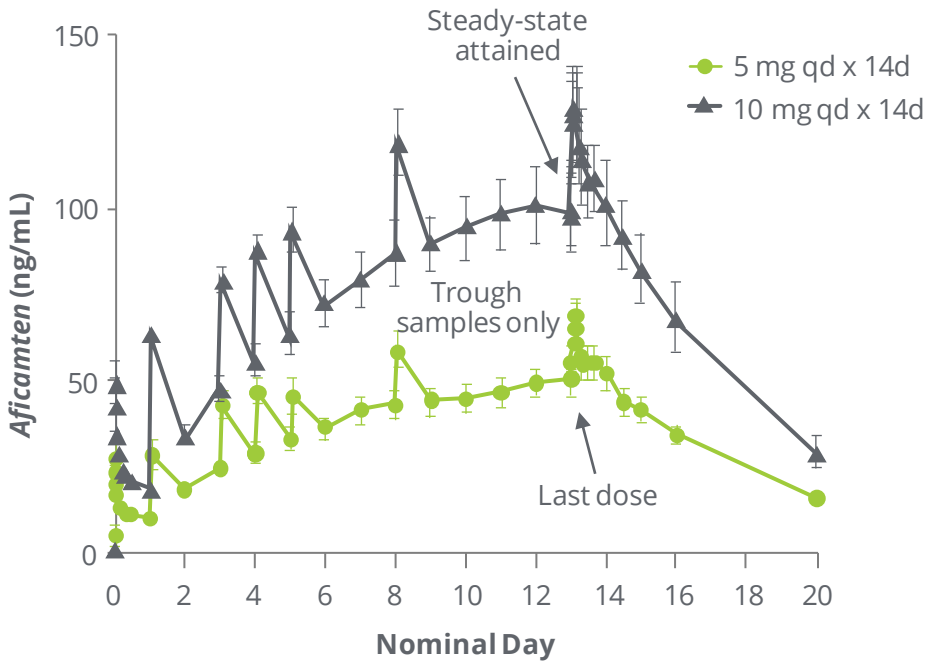
Product not FDA approved, aspirational profile dependent on phase 3 data

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

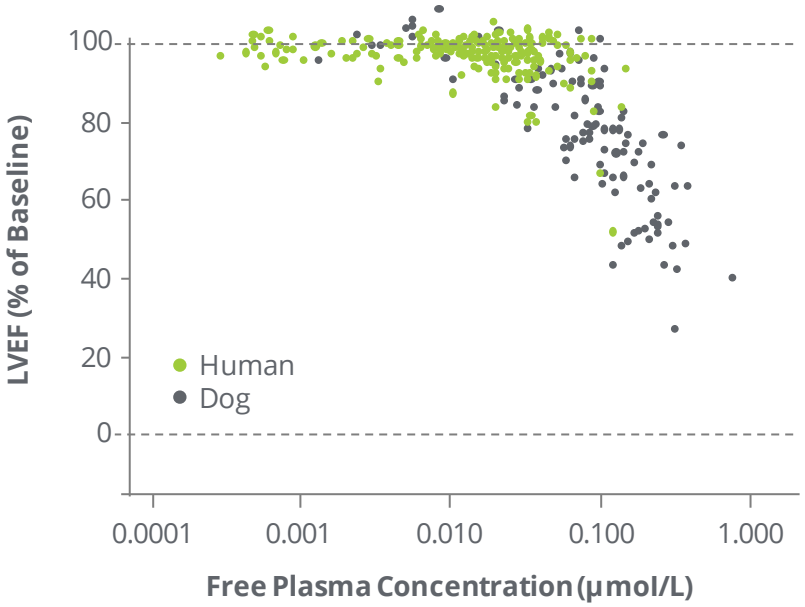
Preclinical data translated to healthy participants

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)

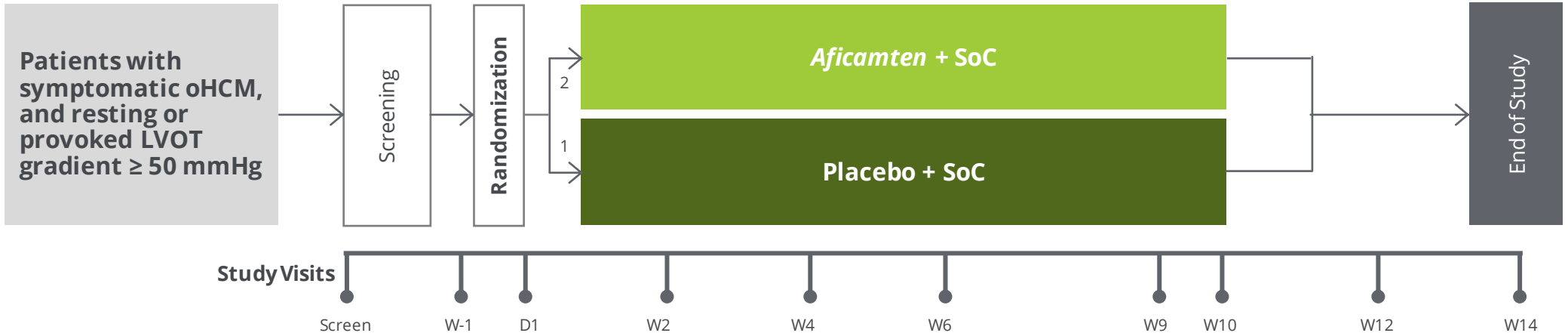


Graphs show LVEF as a function of exposure; data points represent observed values in dogs and humans.

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

Phase 2 Clinical Trial Design

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



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

Patient Enrollment and Dosing

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

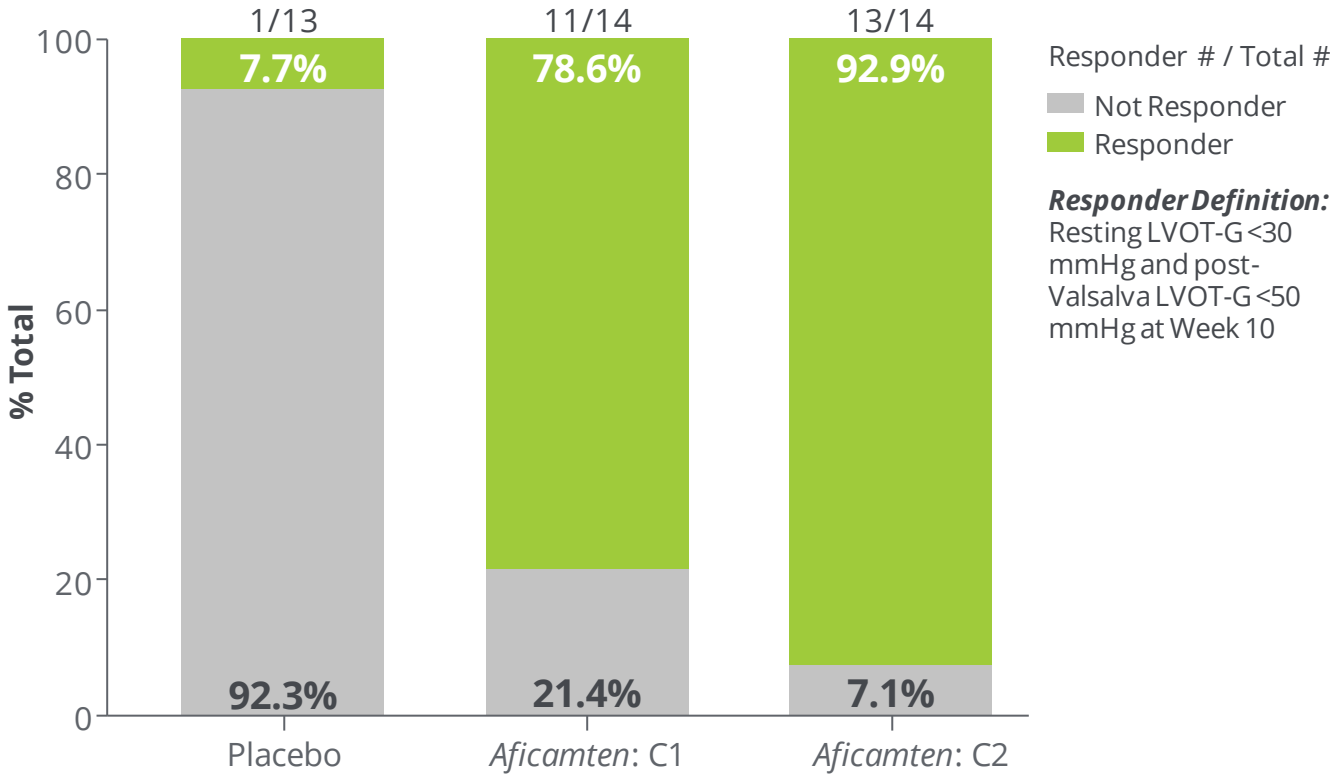
Baseline Characteristics

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*



- 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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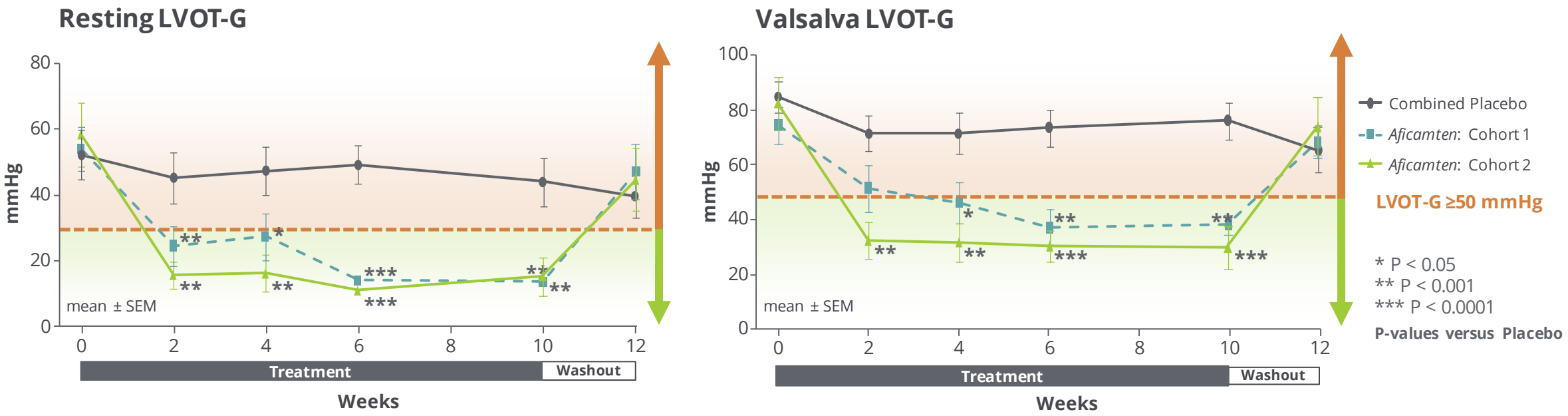
REDWOOD-HCM: Efficacy

Reductions in LVOT gradients

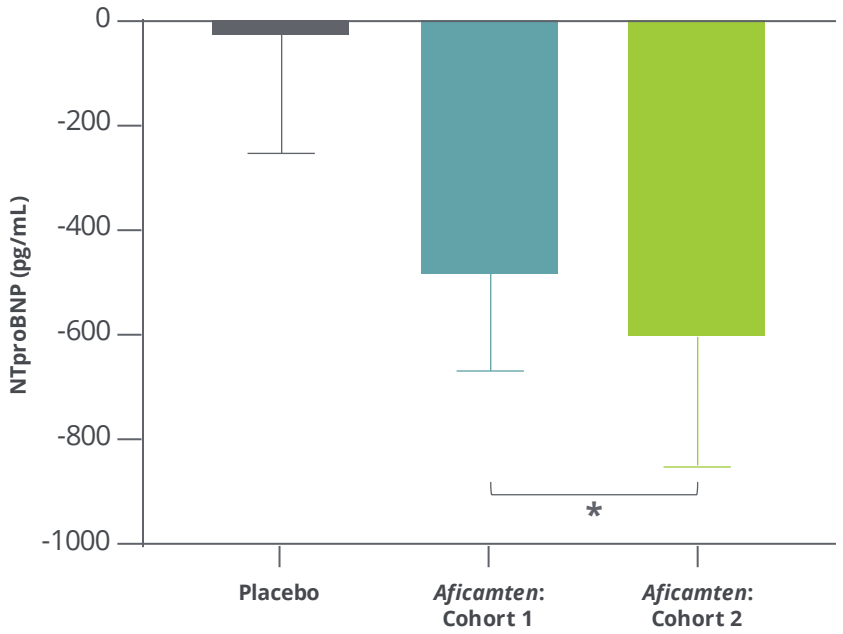


Dose finding study
Cohort 1 (n=21), Cohort 2 (n=20)

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

Change from Baseline NT-proBNP to Week 10

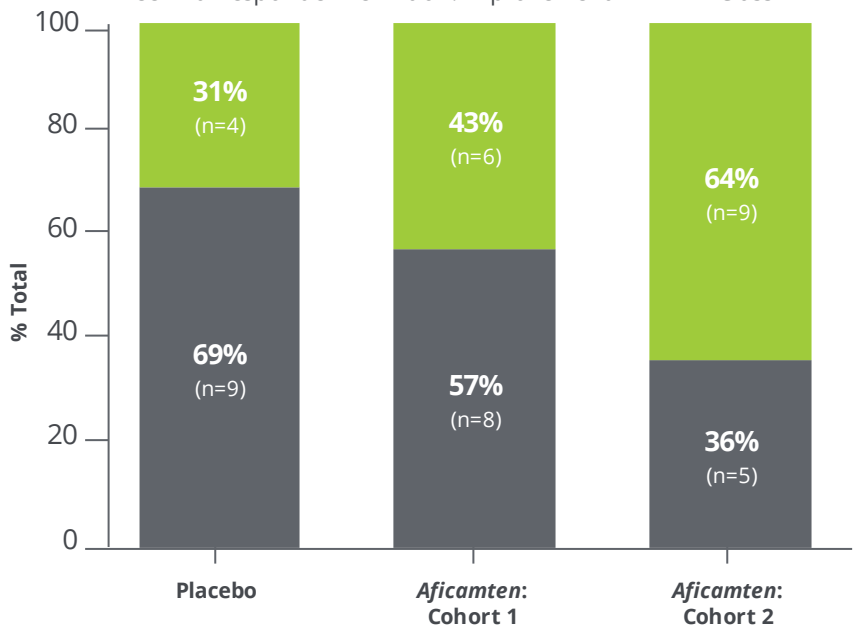


*** p = 0.003 for Pooled Cohort 1 & 2 vs. Placebo**

- 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

Enrolling patients on background therapy of *disopyramide*

REDWOOD HCM

Results expected in Q1 2022

	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

Cytokinetics

REDWOOD-HCM: Open Label Extension

REDWOOD HCM OLE

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

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

OLE: Escalating doses based on echo-guided dose titration

SEQUOIA-HCM: Phase 3 Trial

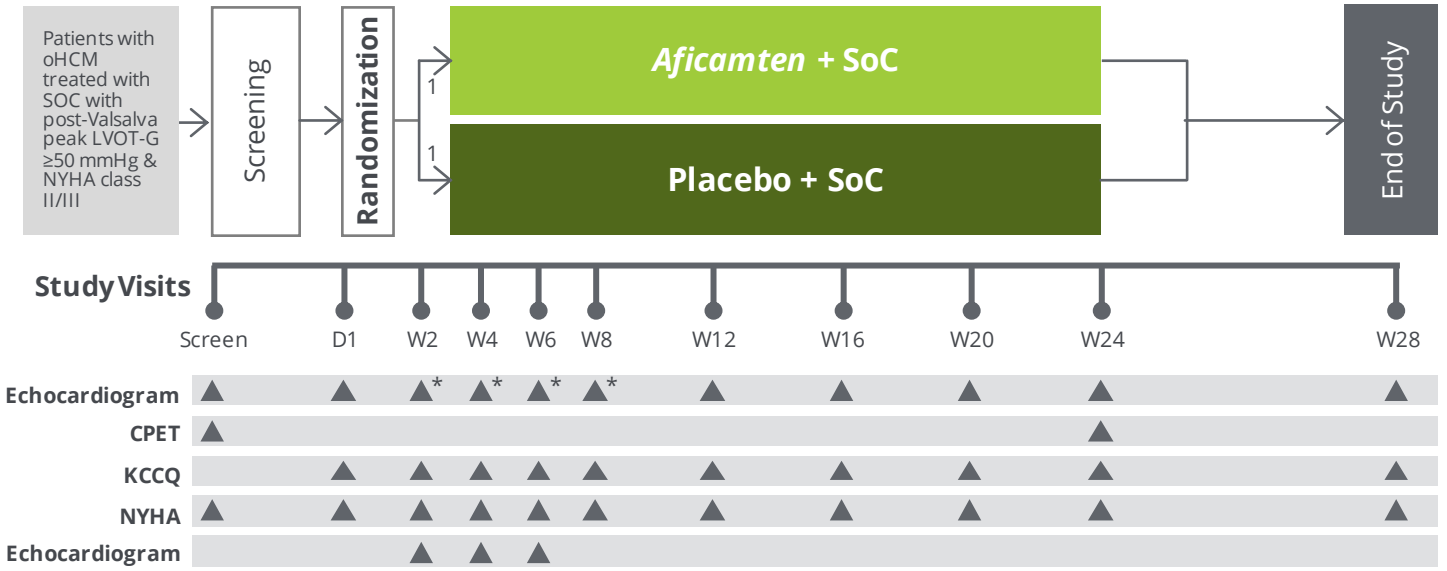
Start-up activities underway

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

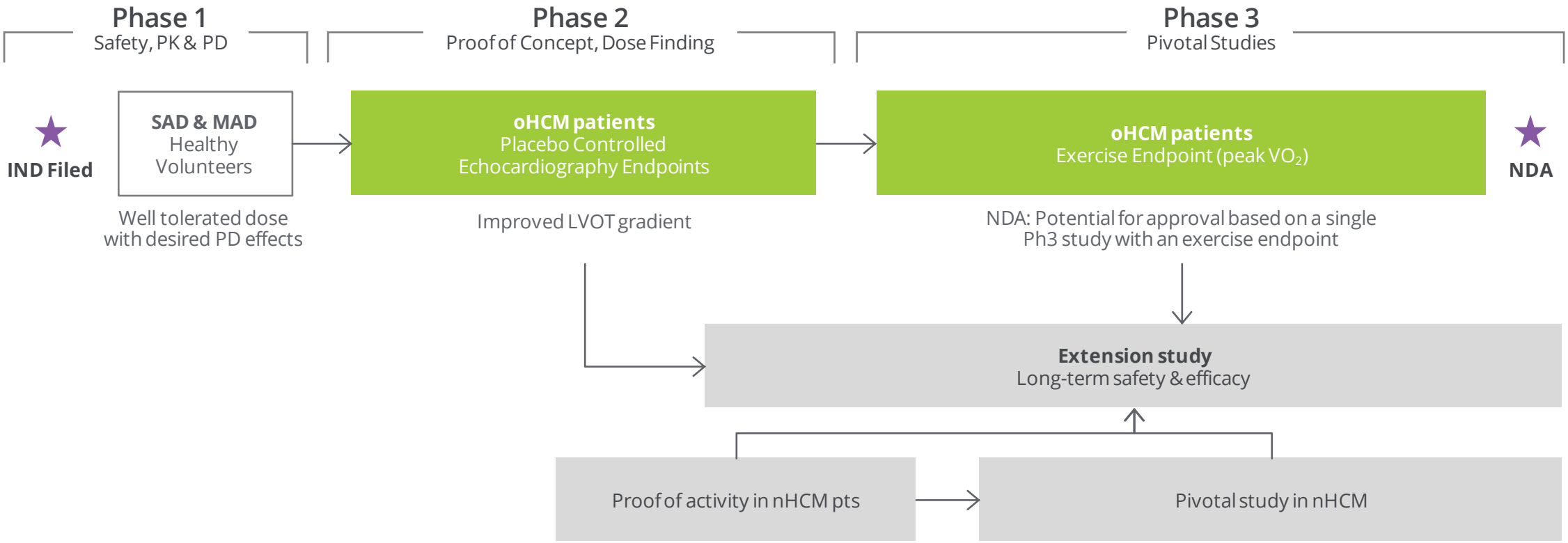


Dose Options (Dose optimization completed by Week 8)			
5 mg QD	10 mg QD	15 mg QD	20 mg QD

* Focused echocardiogram
SOC: standard of care

Aficamten: Clinical Development Plan for HCM

Start-up activities underway for SEQUOIA-HCM: Phase 3 clinical trial in oHCM



Novel Approach May Address Multiple Unmet Patient Needs

No FDA-approved therapies

Obstructive HCM

oHCM

Aficamten
(Cardiac myosin Inhibitor)

nHCM

Non-Obstructive HCM

HFpEF

Heart Failure with Preserved Ejection Fraction

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

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.

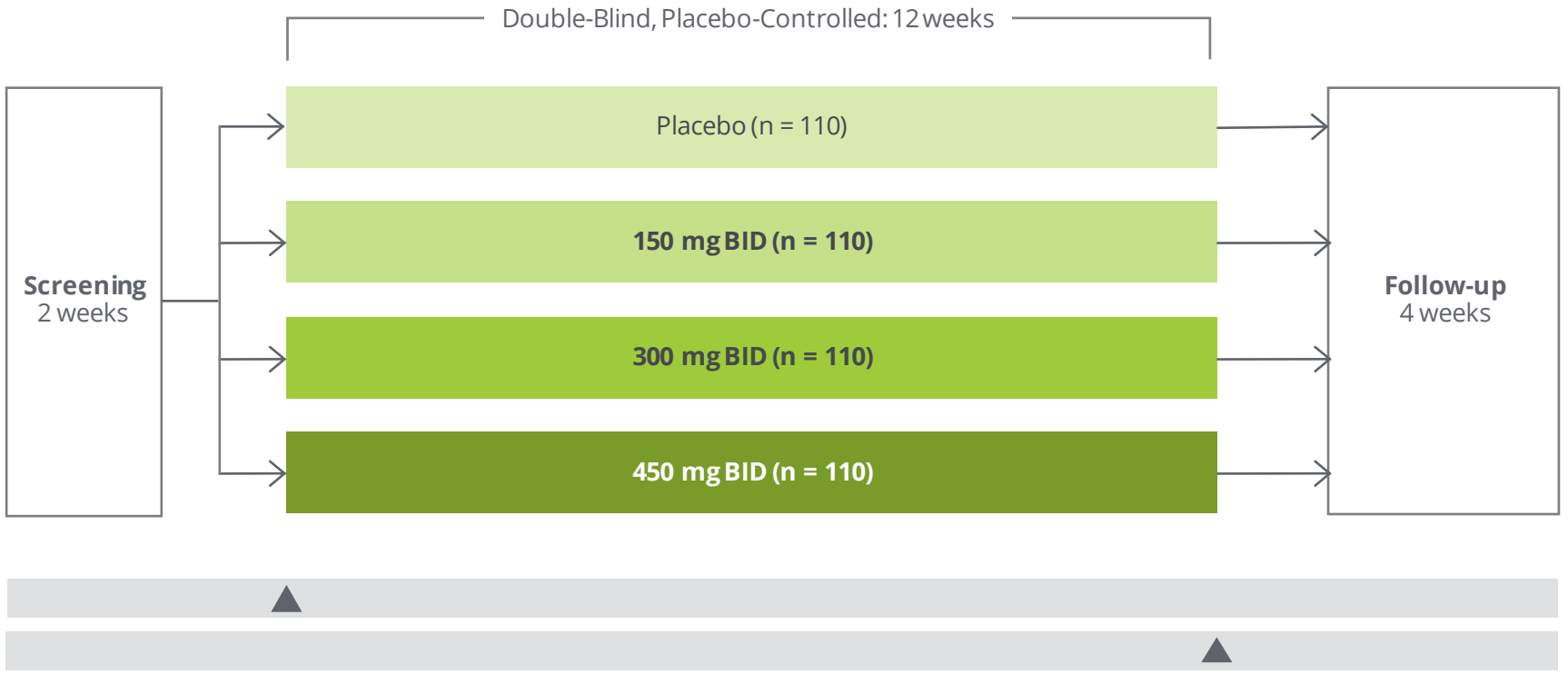
Cytokinetics

Phase 2 Clinical Trial in ALS

FORTITUDE ALS

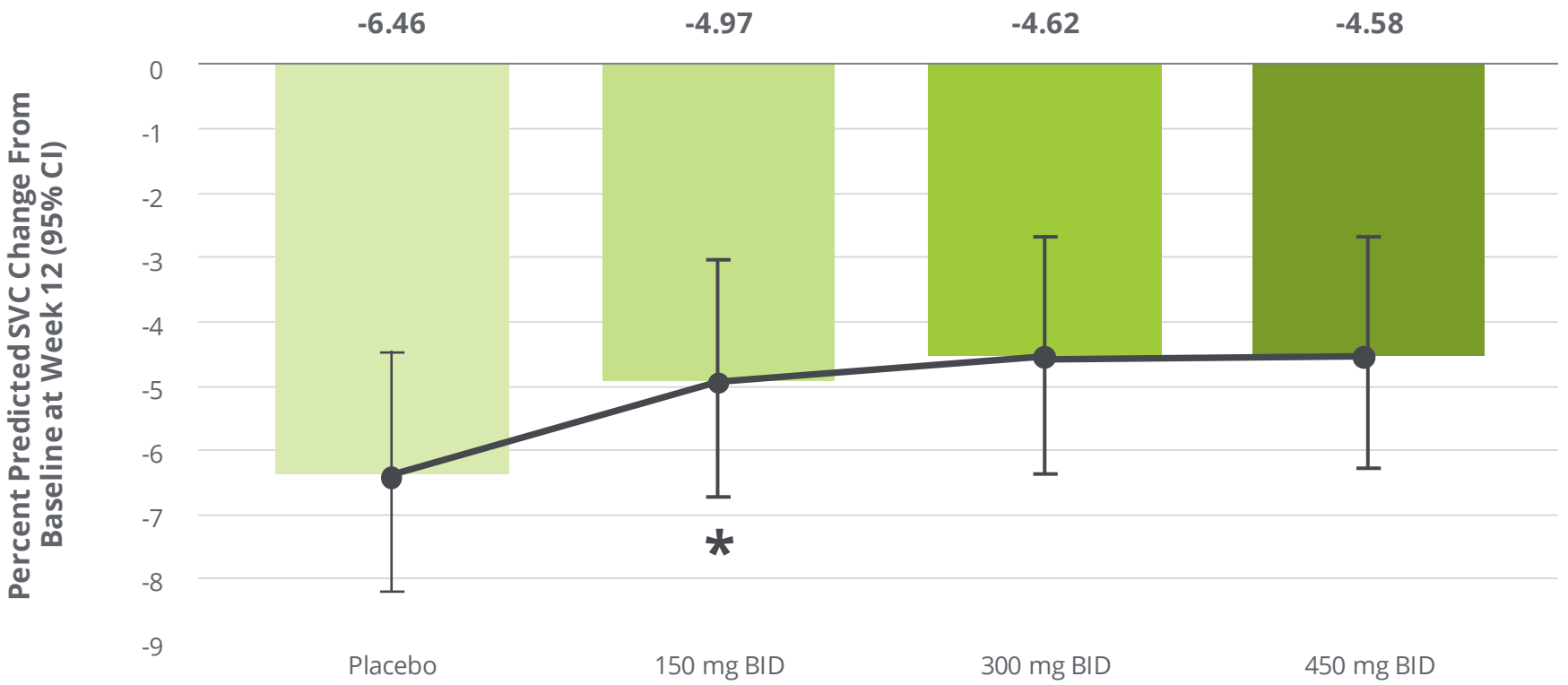
Results presented at American Academy of Neurology 2019 Annual Meeting

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

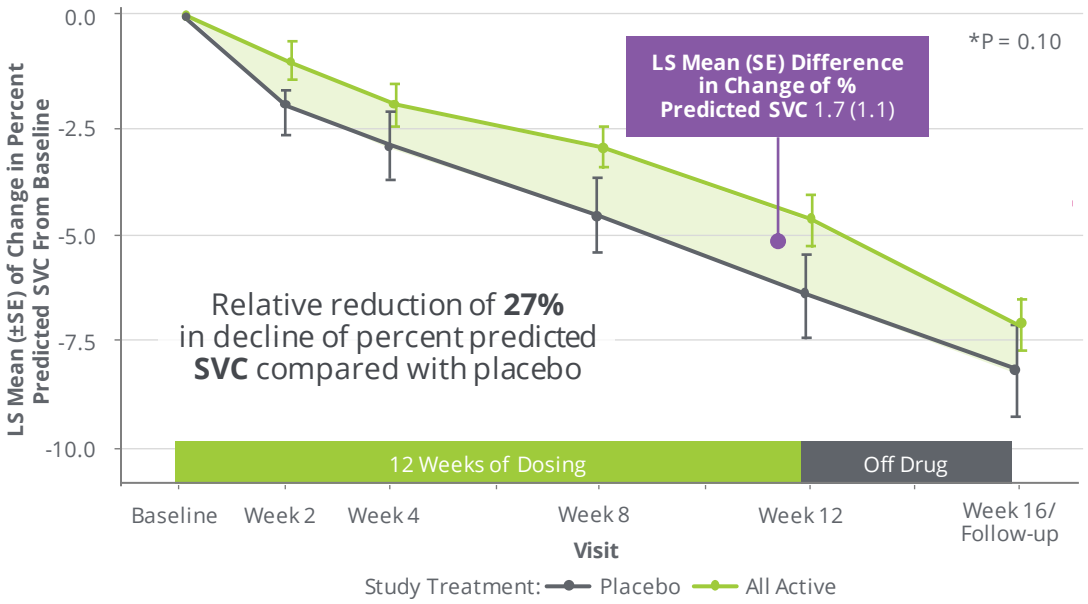
*Based on Mixed Model for Repeated Measures (MMRM) with the contrasts of (-5, -1, 3, 3) for placebo, *reldesemtiv* 150 mg, 300 mg and 450 mg BID, respectively

Phase 2 Clinical Trial

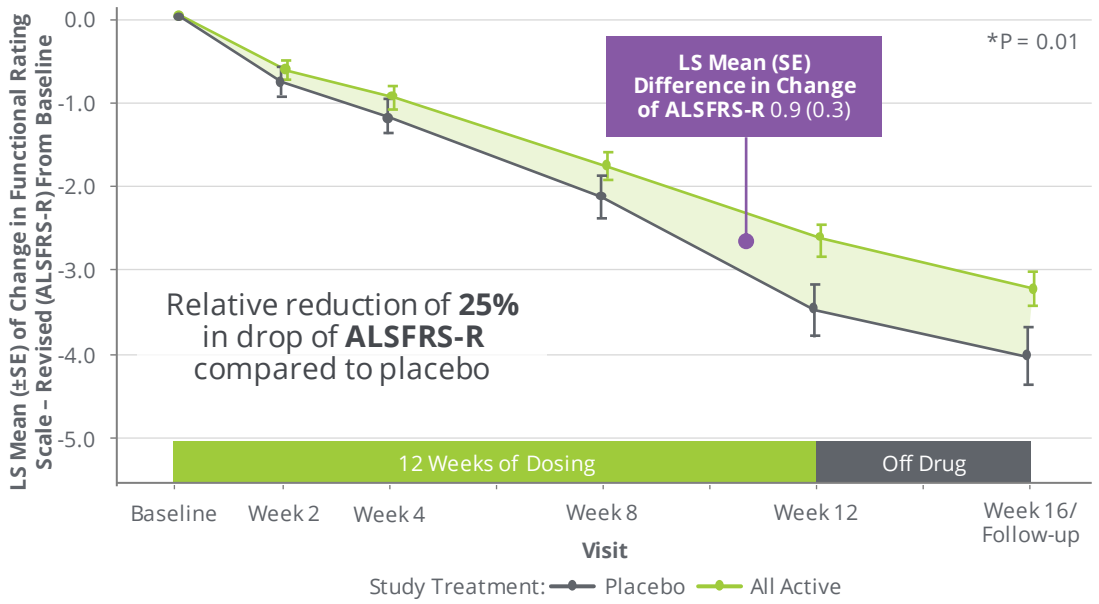
FORTITUDE ALS

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

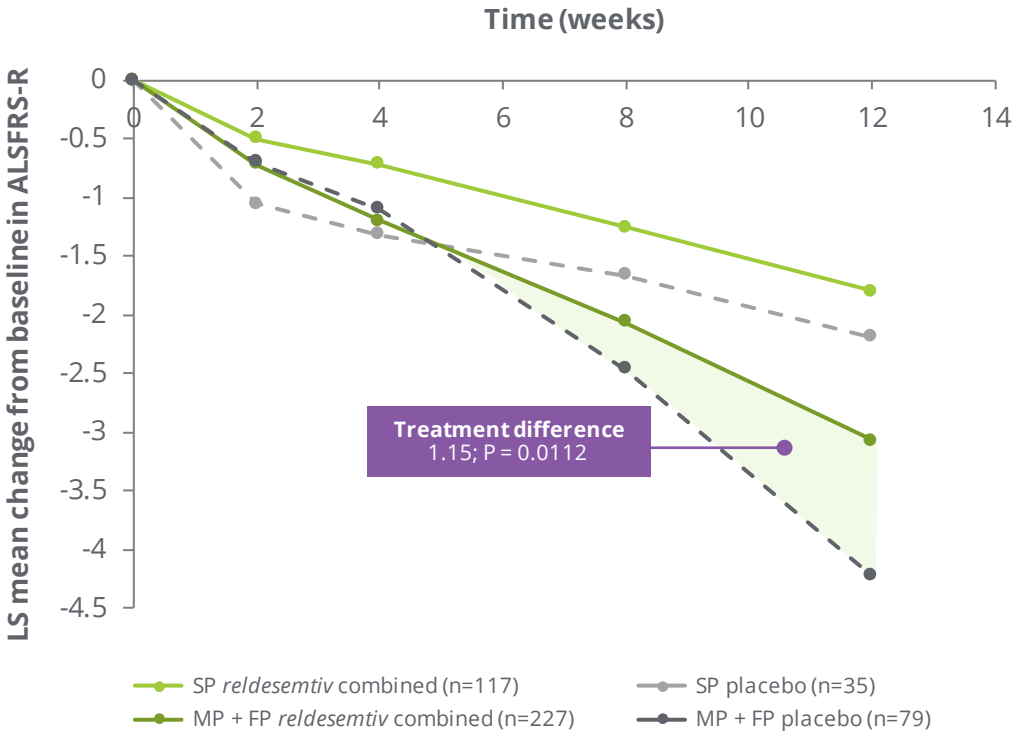
	No. of Patients (pbo/ *reldesemtiv*)	LSM Difference (95% CI)	Estimate	*P* value
Percent predicted SVC at baseline				
<80	43/109		1.588	0.0089
≥80	57/196		0.264	0.5296
ALSFRS-R total score at baseline				
<Median (38.0)	48/129		1.107	0.0585
≥Median (38.0)	52/176		0.685	0.0987
ALSAQ-5 total score at baseline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

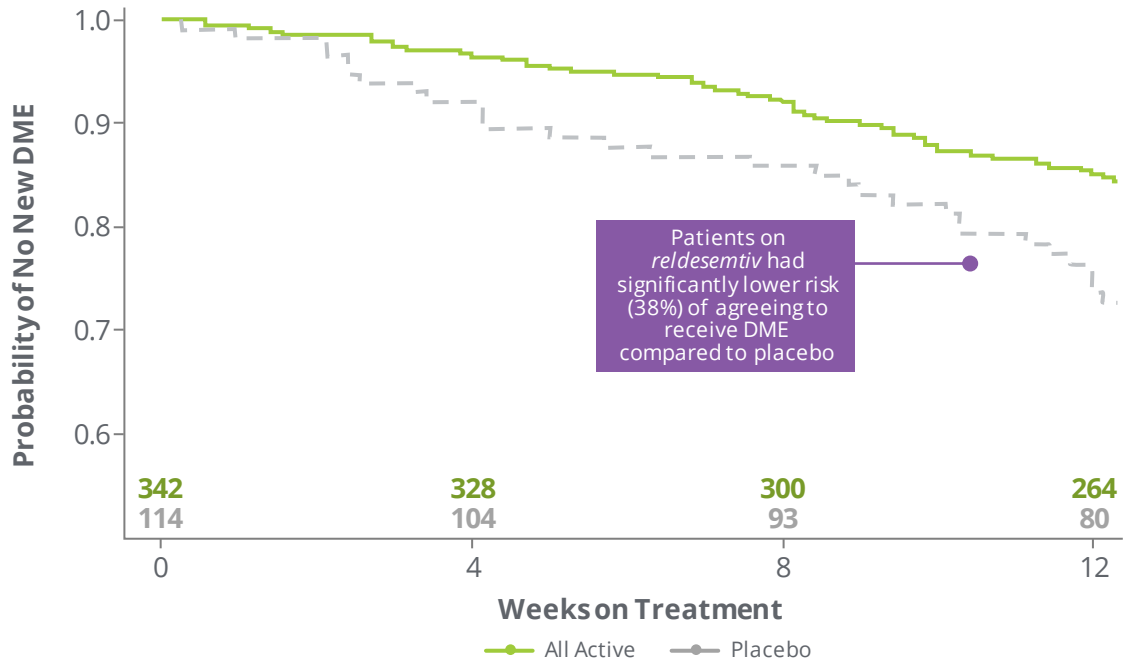
Change From Baseline in ALSFRS-R by Progressor Tertiles



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

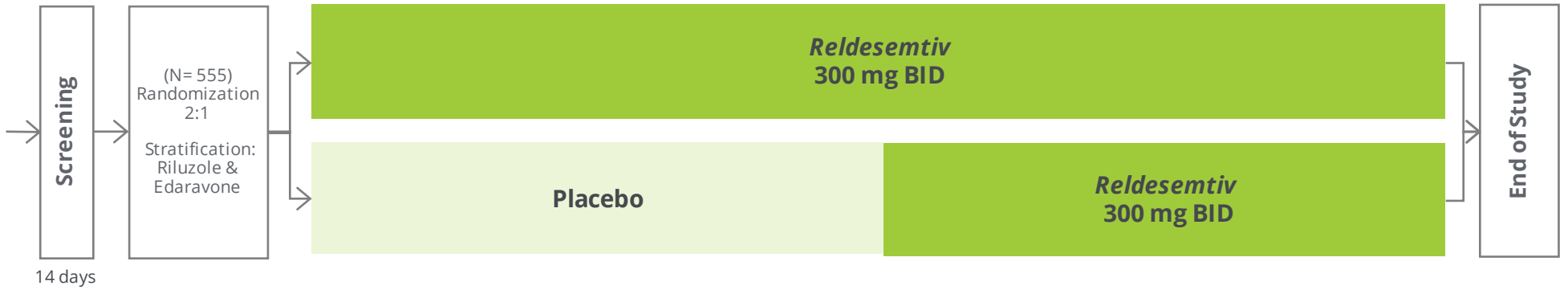


Phase 3 Clinical Trial Design

COURAGE ALS

Plan to enroll 555 patients; interim analysis for futility expected in 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

Cytokinetics

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
- Phase 3 exercise capacity trial results in early 2022

CK-136

- Phase 1

HCM

Aficamten

- Start-up activities underway for Phase 3 trial, SEQUOIA-HCM

ALS

Reldesemtiv

- COURAGE-ALS, Phase 3 trial ongoing

Ongoing R&D

Additional research in muscle biology, energetics & metabolism

Foundations

257

Full time employees

$669M

At Q3 2021

+ **$70M** upfront & near-term capital from Ji Xing & RTW

+ **$150M** at closing and near-term capital from Royalty Pharma

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

More Than 2 Years Cash Runway*

Recent deals support plans for commercial launch & expansion of late-stage pipeline

$669M

At Q3 2021

+ **$70M** upfront & near-term capital from Ji Xing & RTW

+ **$150M** at closing & near-term capital from Royalty Pharma

+ **$330M** in potential milestone payments + royalties from Ji Xing

+ **$300M** in potential additional funding from Royalty Pharma

Guidance to be updated with Q4 earnings

*Based on 2021 expenditures

Balance Sheet & Financial Guidance

2021 Condensed Balance Sheet
As of 9/30/2021

in millions

	Total
Cash and investments	$668.9
Leased assets	$80.7
Other assets	$77.9
Total Assets	**$827.5**
Debt	$134.0
Liability related to sale of future royalties	$174.8
Deferred Revenue	$87.0
Lease liability	$125.4
Other liabilities	$57.3
Total Liabilities	**$578.5**
Working capital	$414.1
Accumulated deficit	($1,177.1)
Stockholders' equity	$249.0
Wtd Avg Basic Shares Outstanding	**80.3**

2021 Financial Guidance

in millions

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

Expected Milestones in 2022

Financial guidance and elaboration on milestones during Q4 2021 earnings call in February

Results from **METEORIC-HF** expected in early 2022

Expect results from **Cohort 3 of REDWOOD-HCM** in Q1 2022

Update on plans for expansion of **development program for *aficamten*** in Q1 2022

Start-up activities underway for **SEQUOIA-HCM**, Phase 3 trial of *aficamten*

Interim analysis for futility for **COURAGE-ALS** in 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.