Cytokinetics

empowering

muscle

empowering

lives

Sarcomere directed therapies

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 express or implied 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 and/or timing of regulatory approval for our new drug application for *omecamtiv mecarbil* or any future new drug application for any of our other drug candidates; the timing of a second interim analysis of COURAGE-ALS, the timing of commencement of a second phase 3 clinical trial of *aficamten* as a monotherapy in patients with obstructive HCM, the timing of commencement of a phase 3 clinical trial of *aficamten* in nonobstructive HCM, our ability to fully enroll or to announce the results of any of our clinical trials by any particular date; Cytokinetics' cash expenditures or runway; the results of any of our interactions with the FDA or any other regulatory authority regarding *omecamtiv mecarbil* or any of our other drug candidates; the properties, potential benefits and commercial potential of *aficamten*, *omecamtiv mecarbil*, *reldesemtiv* and Cytokinetics' other drug candidates. Such statements are based on management's current expectations; but actual results may differ materially due to various risks and uncertainties, including, but not limited to, potential difficulties or delays in the development, testing, regulatory approvals for trial commencement, progression or product sale or manufacturing, or production of Cytokinetics' drug candidates that could slow or prevent clinical development or product approval, including risks that current and past results of clinical trials or preclinical studies may not be indicative of future clinical trial results, patient enrollment for or conduct of clinical trials may be difficult or delayed, Cytokinetics' drug candidates may have adverse side effects or inadequate therapeutic efficacy, the FDA or foreign regulatory agencies may delay or limit Cytokinetics' ability to conduct clinical trials, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Cytokinetics may incur unanticipated research, development and other costs or be unable to obtain financing necessary to conduct development of its products; standards of care may change, rendering Cytokinetics' drug candidates obsolete; and competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target. These forward-looking statements speak only as of the date they are made, and Cytokinetics undertakes no obligation to subsequently update any such statement, except as required by law. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission (the "SEC").

Our Mission

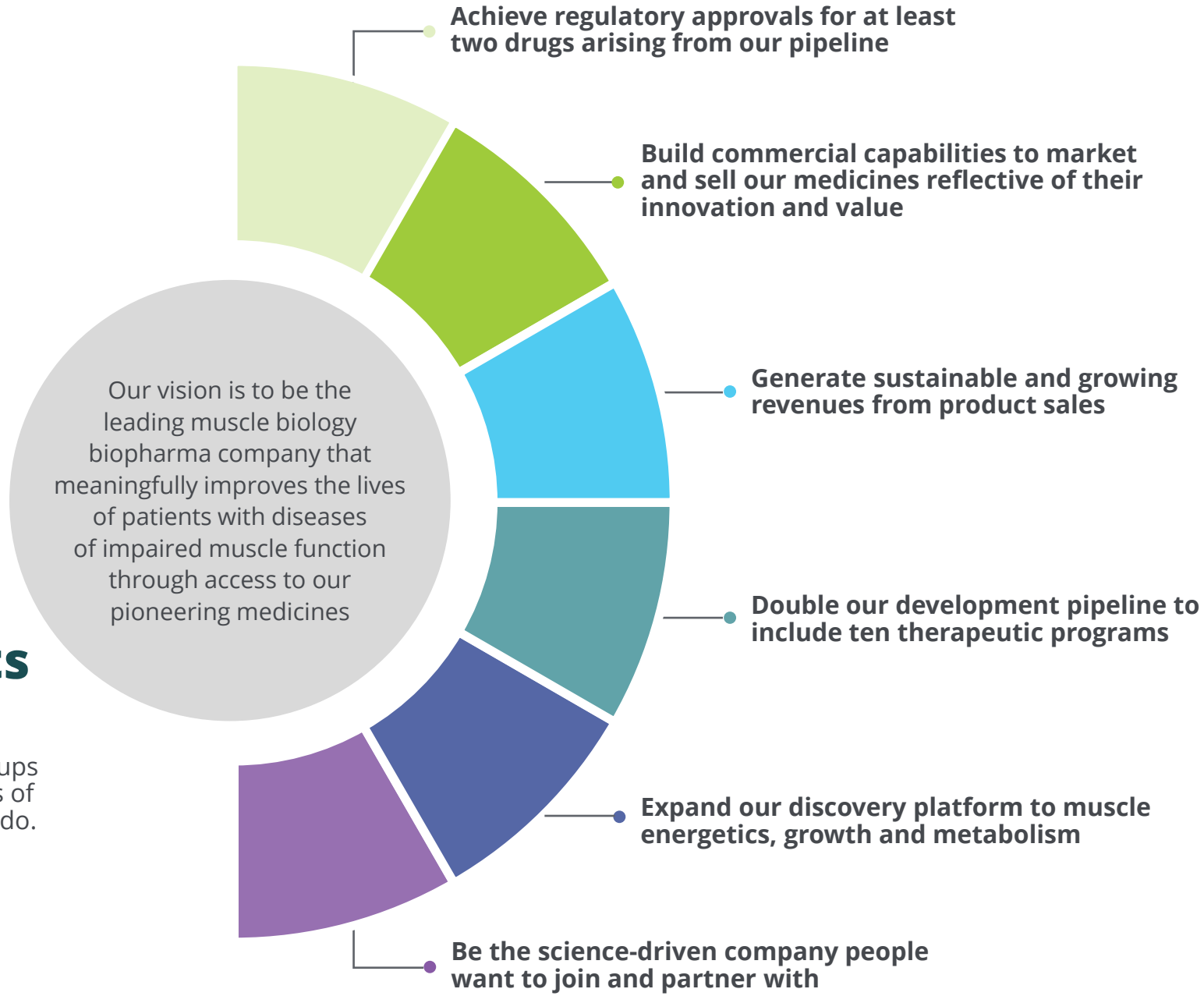
To bring forward new medicines to improve the healthspan of people with devastating cardiovascular and neuromuscular diseases of impaired muscle function.

Cytokinetics

VISION 2025

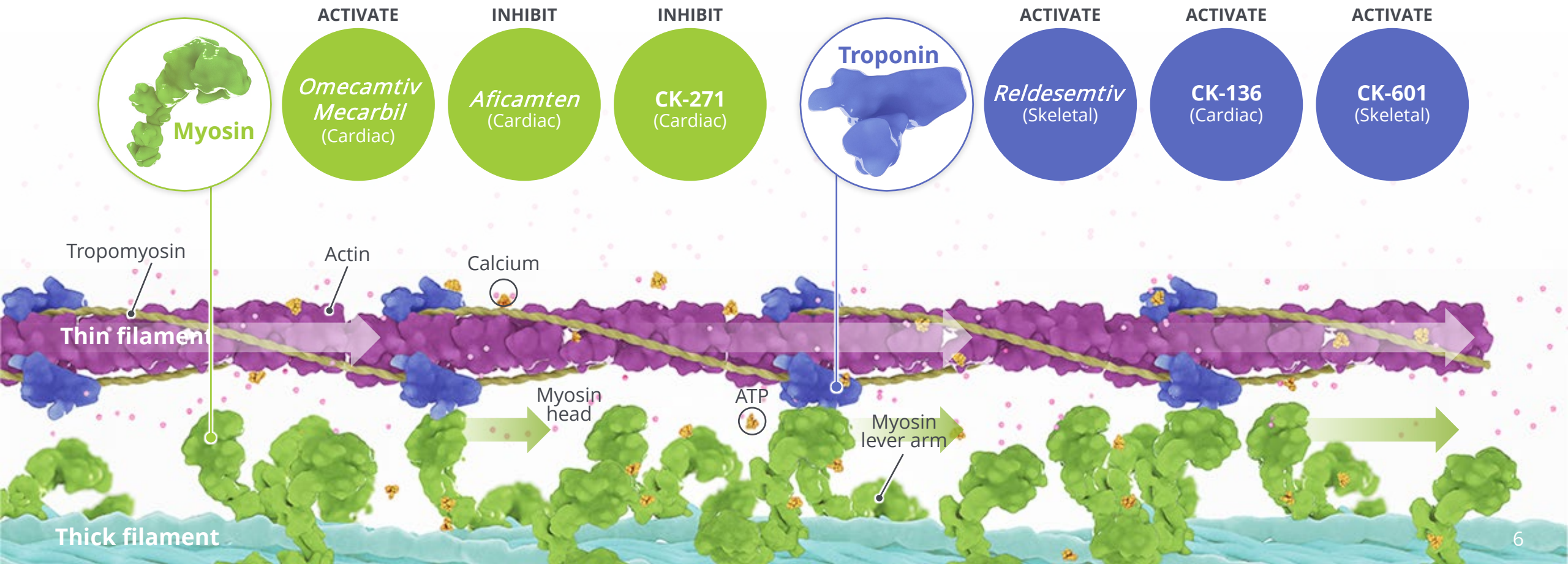
Leading with Science, **Delivering for Patients**

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.

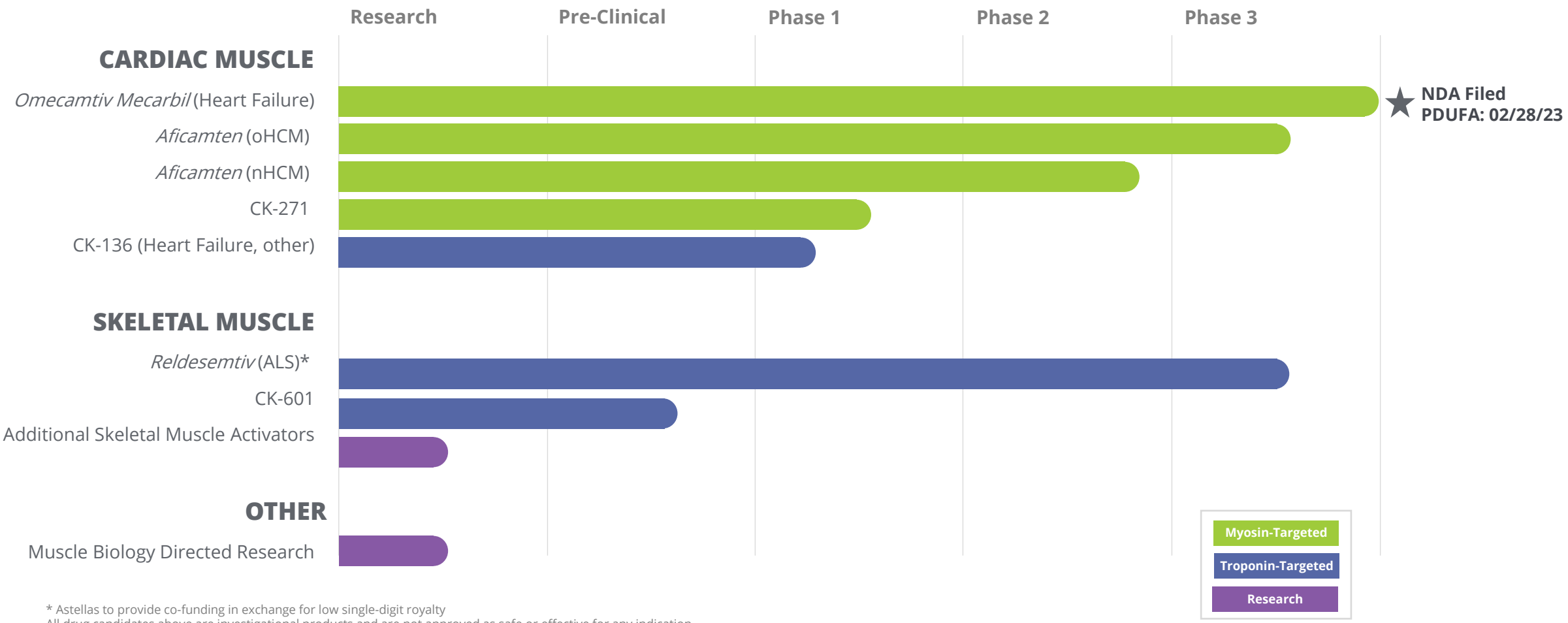


Sarcomere Directed Drug Development

The sarcomere is a molecular structure found in skeletal and cardiac muscle that enables 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.

Key Priorities in 2023

Continue execution of SEQUOIA-HCM and advance **broad development program** and go-to-market strategy for *aficamten*

Engage with FDA ahead of February 28 **PDUFA date** for *omecamtiv mecarbil*

Continue execution of **COURAGE-ALS** and OLE

Advance **early-stage pipeline** of contractility drug candidates

Expand research beyond contractility to muscle energetics, growth and metabolism

Sarcomere Directed Drug Development

Cardiac Muscle

Cardiovascular Franchise Strategy
Aficamten
Omecamtiv Mecarbil

Cytokinetics

Omecamtiv mecarbil and 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.

Cardiovascular Franchise Strategy

Cytokinetics

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

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

→ **Significant Cost Savings**

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

~15-30% Additional Targets

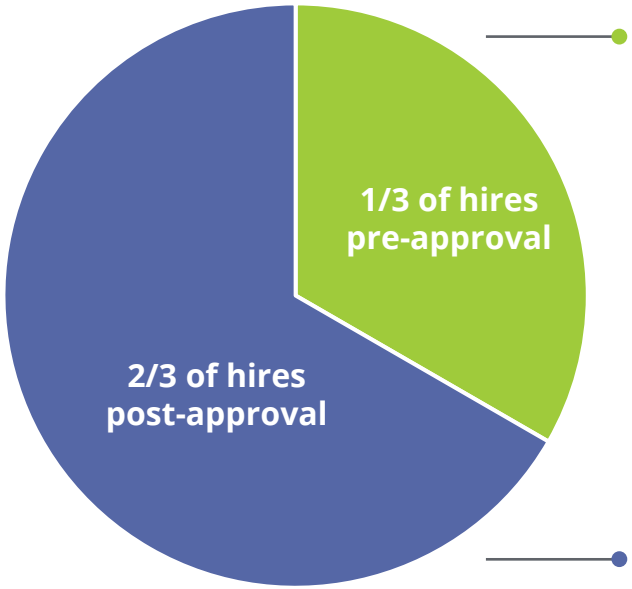
= Coverage of vast majority of HCM

Gated Build of Commercial Infrastructure

Engagement ongoing with FDA post Advisory Committee meeting

Cardiovascular franchise commercial team comprised of 75, with 10 dedicated to *omecamtiv mecarbil*

2/3 of hiring to occur after potential 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

Aficamten

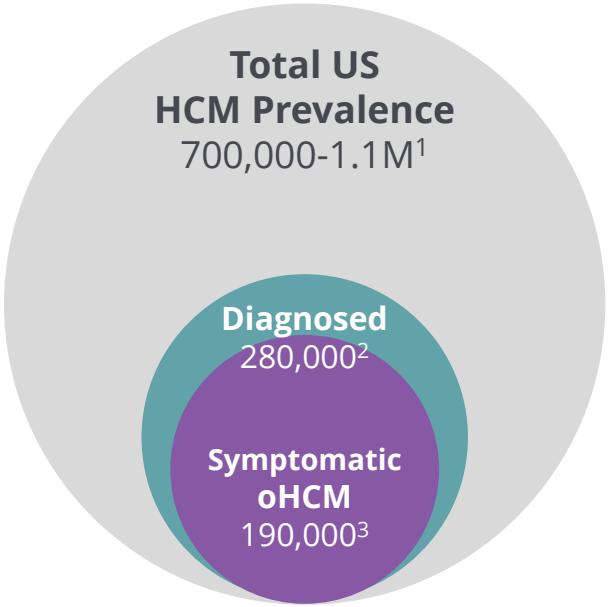
Cytokinetics

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.

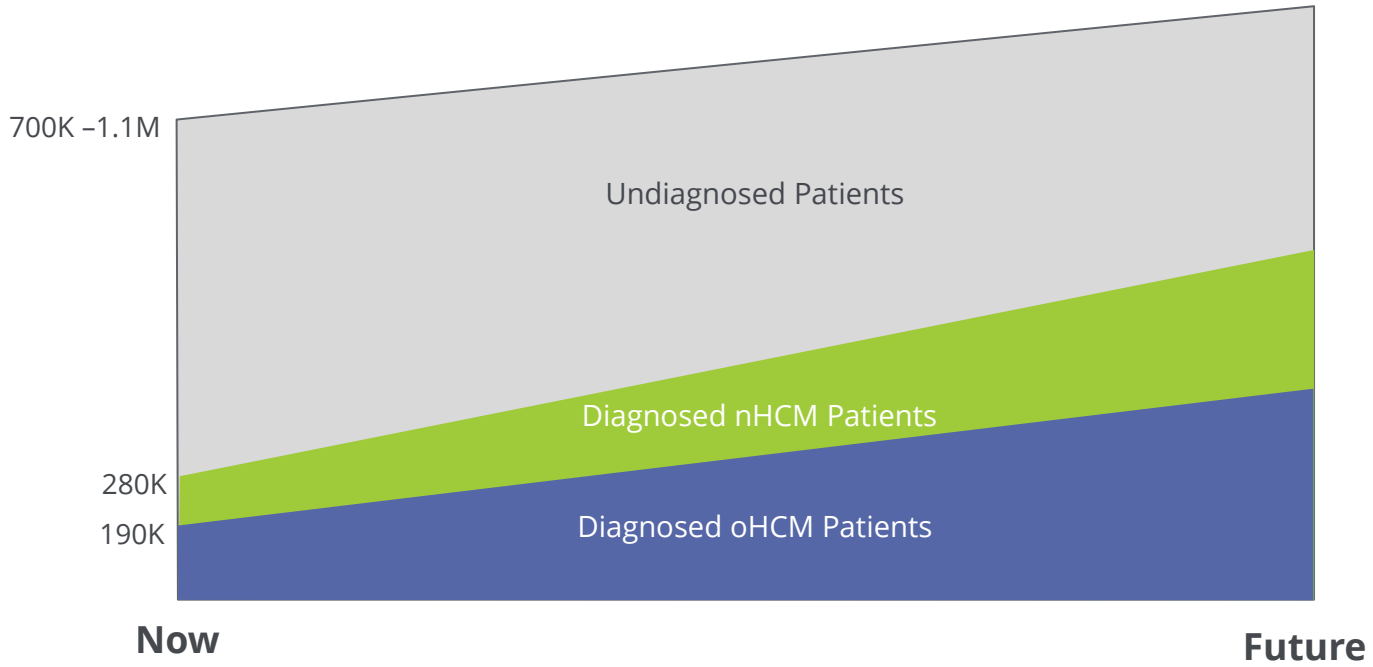
In US, Large HCM Population With Many Undiagnosed

280K Diagnosed HCM Patients; Estimated 400-800K Undiagnosed

Current US HCM Prevalence



Growing HCM Prevalence



nHCM: non-obstructive HCM; oHCM: obstructive HCM

1. CVrg: Heart Failure 2020-2029, p 44; Maron et al. 2013 DOI: 10.1016/S0140-6736(12)60397-3; Maron et al 2018 10.1056/NEJMra1710575
2. Symphony Health 2016-2021 Patient Claims Data DoF;
3. Maron MS, Hellawell JL, Lucove JC, Farzaneh-Far R, Olivotto I. Occurrence of Clinically Diagnosed Hypertrophic Cardiomyopathy in the United States. Am J Cardiol. 2016; 15;117(10):1651-1654.

Aficamten: Aspirational Target Profile

Potential next-in-class cardiac myosin inhibitor

Rapid Onset

Symptom relief as early as within 2 weeks initiation and dose adjustment possible biweekly if indicated

Precise Dosing

Echo guided dose titration allows both dose increases and decreases at the patient visit

Simplicity of Use

No off-target effects and use in combination with β-blockers, CCB, Disopyramide, and/or Ranolazine

Rapid Reversibility

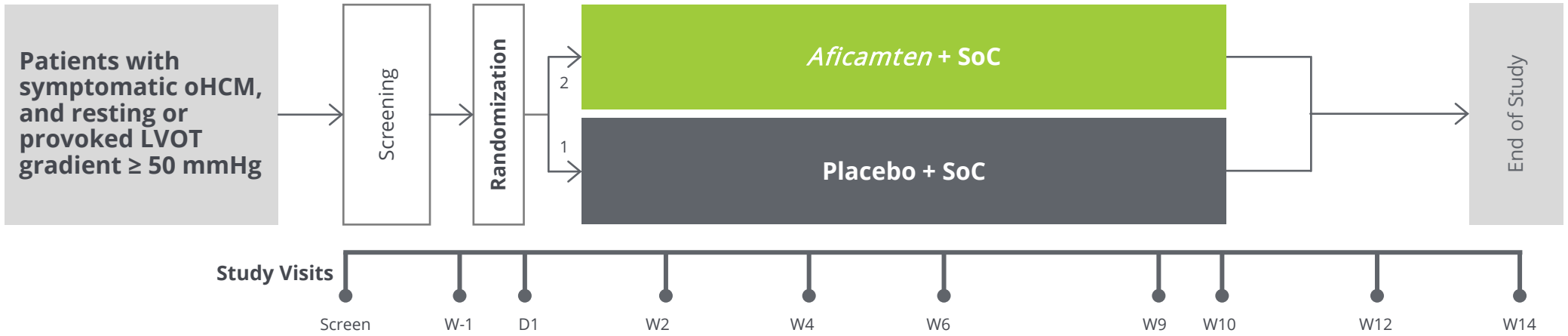
Washout of pharmacodynamic effect within 2 weeks

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.

REDWOOD-HCM: Cohorts 1 & 2

Patients with symptomatic oHCM on background therapy excluding *disopyramide*

Two sequential dose-finding cohorts

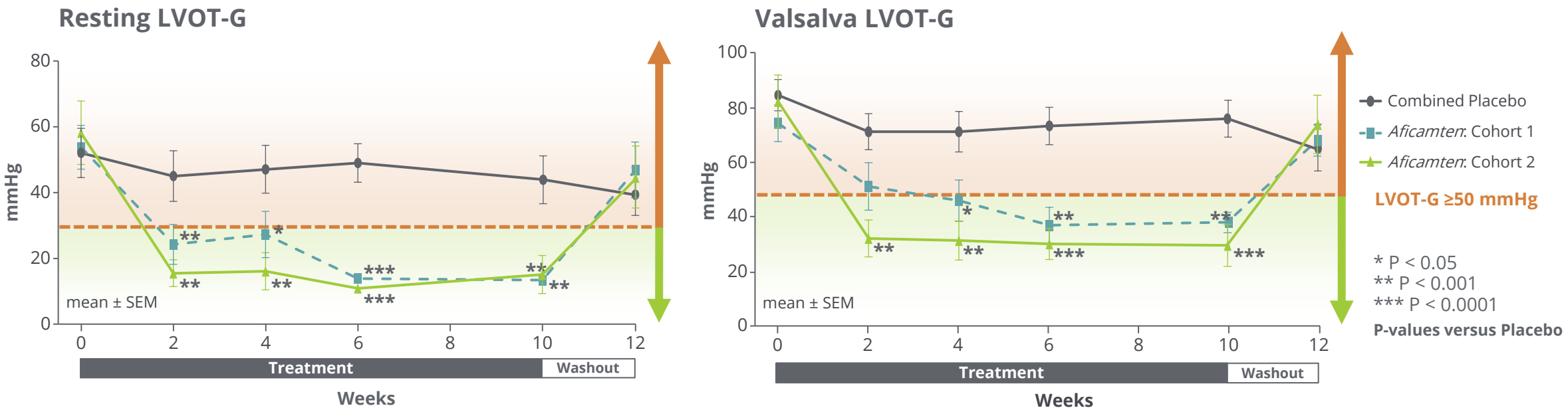


	Dose 1	Dose 2	Dose 3
Cohort 1	5 mg	10 mg	15 mg
Cohort 2	10 mg	20 mg	30 mg

REDWOOD-HCM: Efficacy

Cohorts 1 & 2

Results published in *JACC* in January 2023

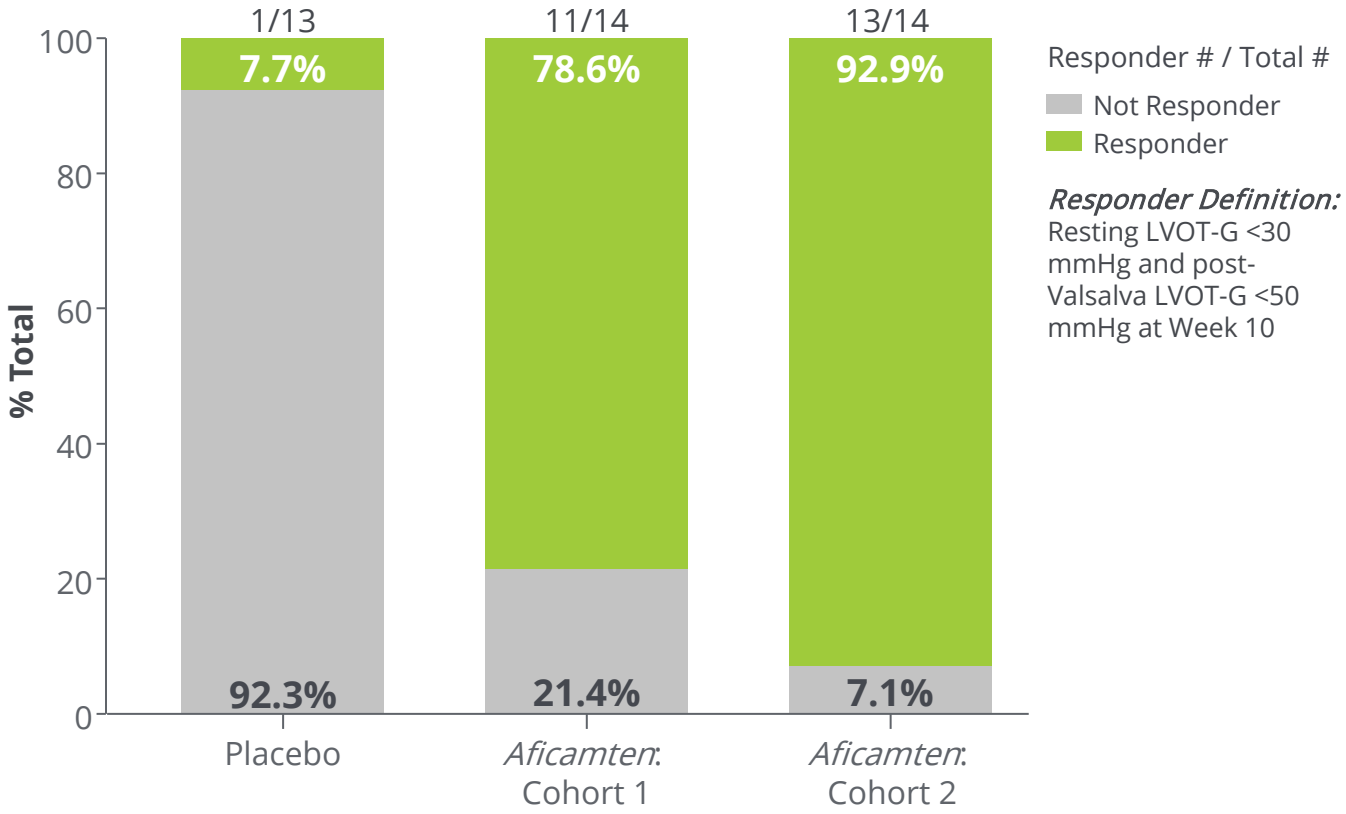


Dose finding study
Cohort 1 (n=21), Cohort 2 (n=20)

Maron M, et. al. Phase 2 Study of *Aficamten* in Patients With Obstructive Hypertrophic Cardiomyopathy. JACC. January 2023.

Response Rates on Treatment with *Aficamten*

Cohorts 1 & 2



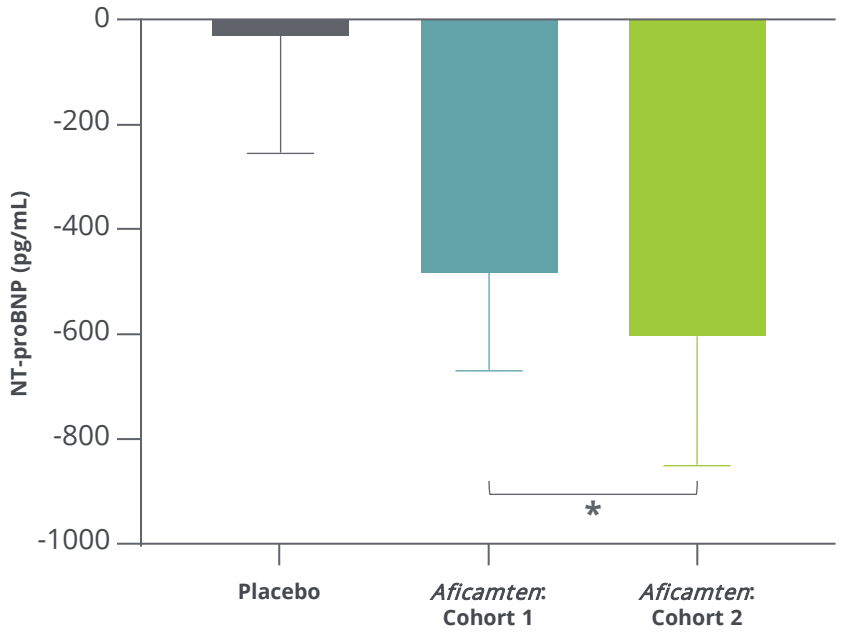
- Consistent, **clinically meaningful reductions in LVOT gradients** within two weeks
- **No treatment interruptions** or discontinuations
- No treatment-related SAEs
- **Reversibility of drug effect** demonstrated
- Statistically significant reductions in NT-proBNP
- Improvement in NYHA class

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"
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.

Change from Baseline in NT-proBNP & NYHA Class

Cohorts 1 & 2

Change from Baseline NT-proBNP to Week 10

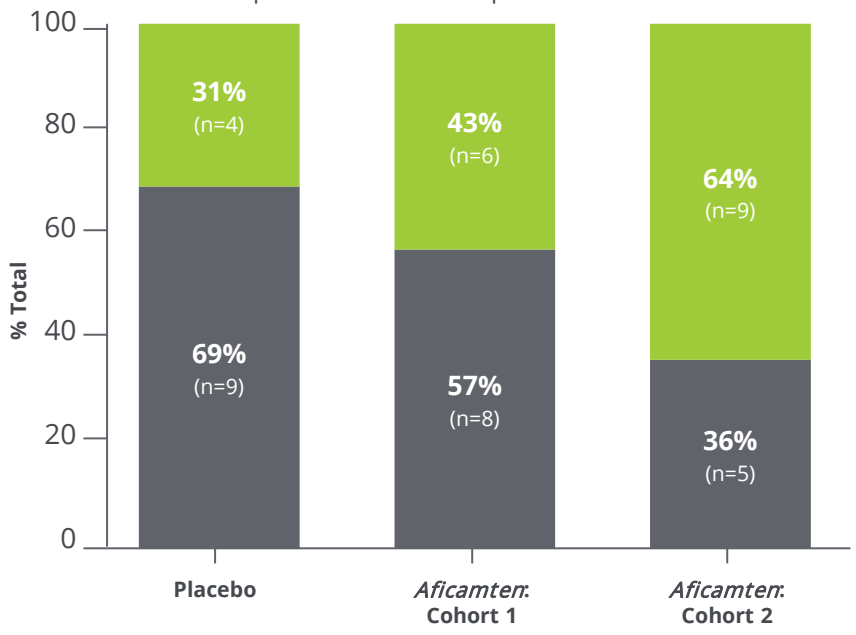


*** p = 0.003 for Pooled Cohort 1 & 2 vs. Placebo**

- 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

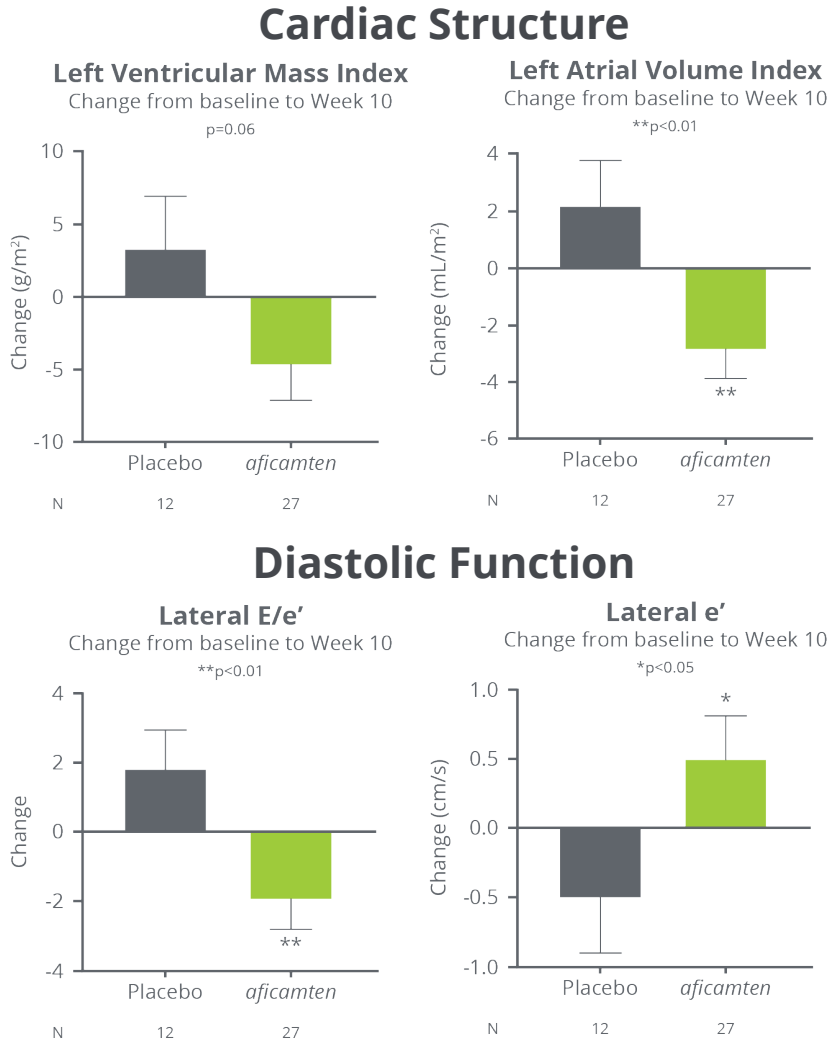
Maron M, Abraham T, Masri A, et al. "REDWOOD-HCM: A Randomized, Double-blind, Placebo-controlled, Dose-finding Trial of the Cardiac Myosin Inhibitor, *Aficamten*, In Obstructive Hypertrophic Cardiomyopathy"

Improved Cardiac Structure and Diastolic Function

Cohorts 1 & 2: Early signs of improvement in cardiac structure and myocardial relaxation

Treatment with *aficamten* for 10 weeks resulted in:

- **Significant reduction in left atrial volume index**
- Trend towards a **reduction in LV mass index**
- **Improved diastolic function**
  - reduction in lateral E/e' ($p<0.01$)
  - increase in lateral e' ($p<0.05$))



REDWOOD-HCM: Cohort 4

Patients with symptomatic nHCM on background therapy

Patient enrollment completed in Q4 2022; results expected 1H 2023

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

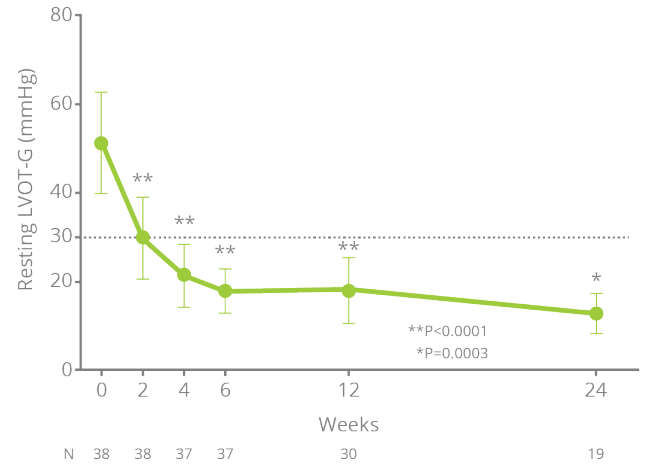
hs-cTnI: high- sensitivity cardiac troponin
*Telephone visits
**Patient can only be down-titrated at Week 6

FOREST-HCM: Open Label Extension

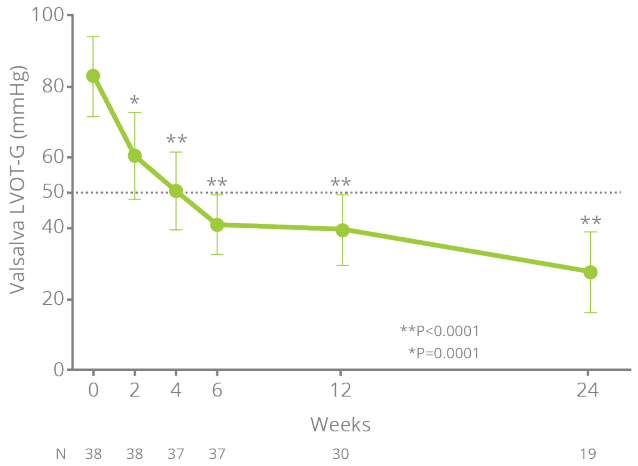
Initial data through 24 weeks shows improvement in LVOT-G, NYHA class, KCCQ

Treatment was well-tolerated: one temporary discontinuation, one temporary down-titration (neither related to treatment)

Resting LVOT Gradient

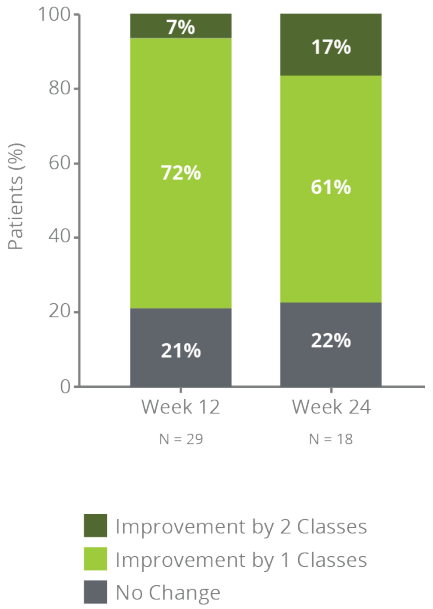


Valsalva LVOT Gradient

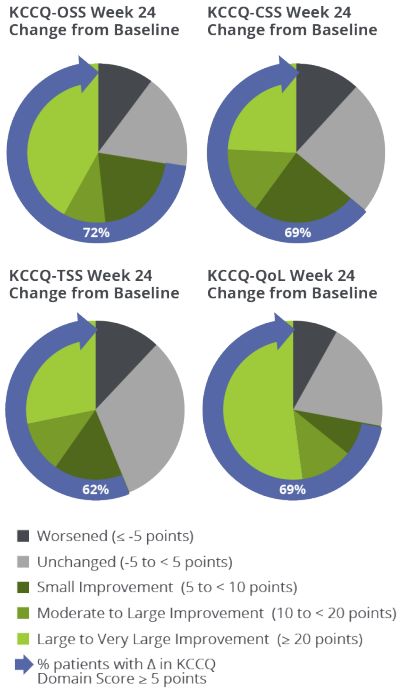


Data presented as mean ±95% Confidence Interval

Improvement in NYHA Class



Change from Baseline in KCCQ Scores



FOREST-HCM was previously known as REDWOOD-HCM OLE
FOREST-HCM is enrolling patients who complete REDWOOD-HCM and SEQUOIA-HCM

Safety Data

REDWOOD HCM

- **REDWOOD-HCM → 2 SAEs reported in 41 *aficamten*-treated patients from Cohorts 1,2 and 3 (10-weeks of treatment)**
  - None were related to *aficamten* treatment per investigator assessment.
- **No imbalance in adverse events between *aficamten* and placebo treated arms**
- **No treatment interruptions or discontinuations.**
- **No patients met the "stopping criteria" of LVEF < 40%**
- **Transient decrease in LVEF < 50% occurred in 2 of 41 *aficamten*-treated patients**

FOREST HCM

- **FOREST-HCM → 3 SAEs reported out of 42 patients with up-to 6-months of treatment**
  - None were related to *aficamten* treatment per investigator assessment.
- **No treatment interruptions or discontinuations.**
- **No patients met the "stopping criteria" of LVEF < 40%**
- **Transient decrease in LVEF < 50% occurred in 1 of 42 *aficamten*-treated patients**

SEQUOIA-HCM: Phase 3 Trial

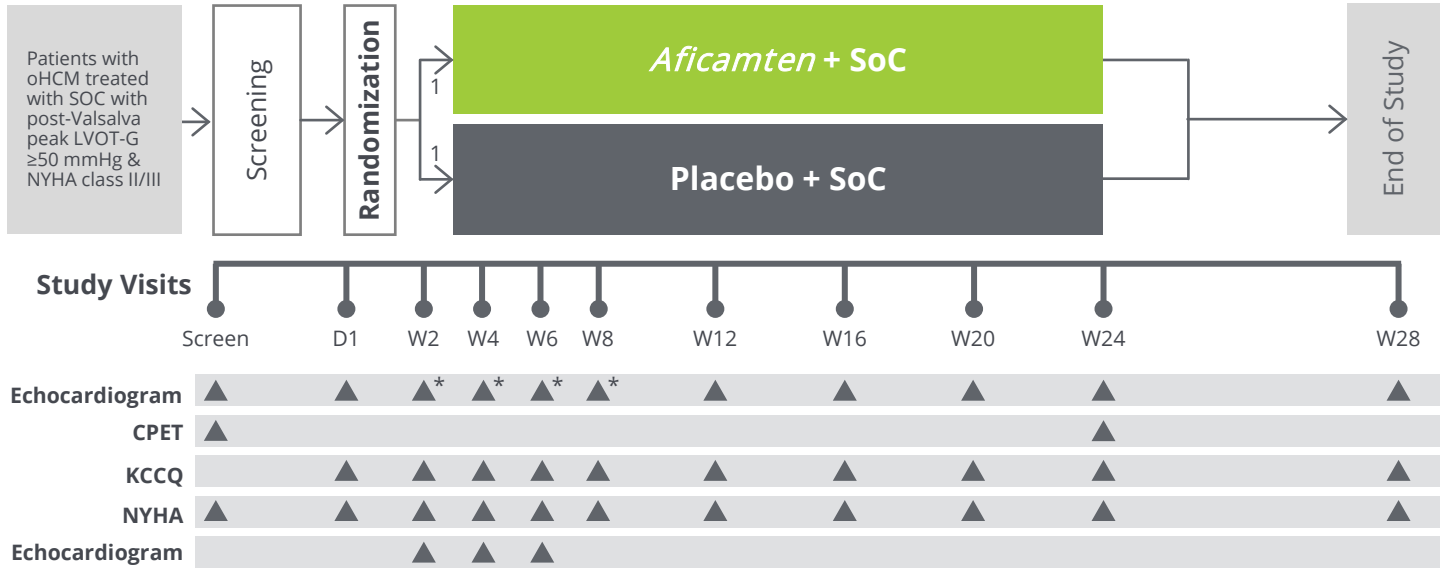
Plan to enroll at >100 sites in US, Europe and Asia**

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



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

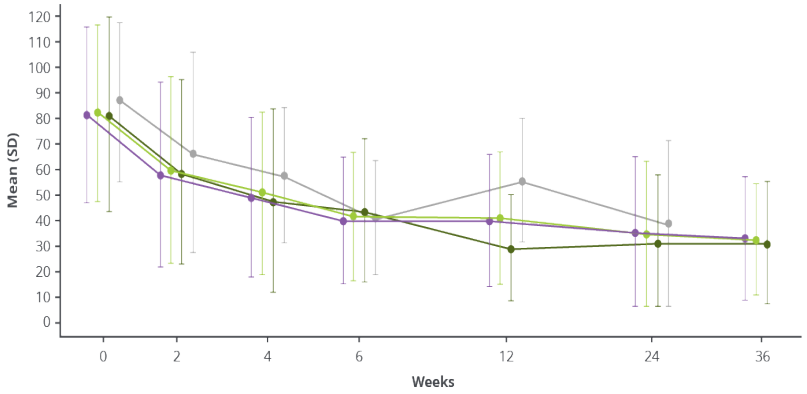
SOC: standard of care
* Focused echocardiogram
** Plan to enroll in US, Italy, France, Germany, Czech Republic, Denmark, Hungary, Netherlands, Poland, Portugal, Spain, UK, Israel & China

Monotherapy Trial, Supported by FOREST-HCM

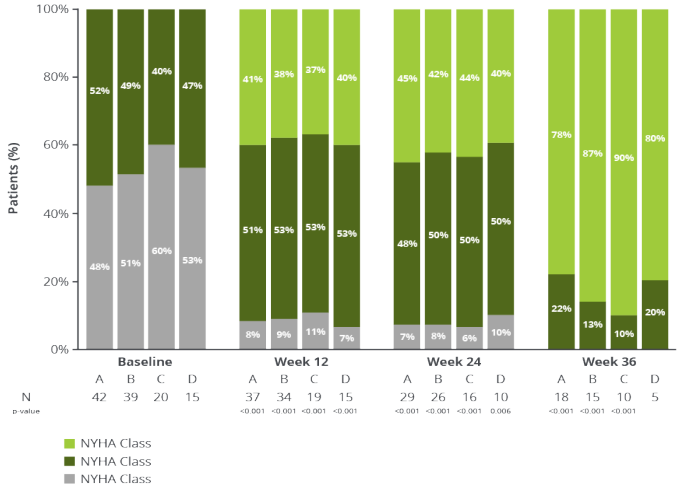
Initial FOREST-HCM data on reduction/withdrawal of background medications supports monotherapy trial

Reduction or Withdrawal of Standard of Care Therapies

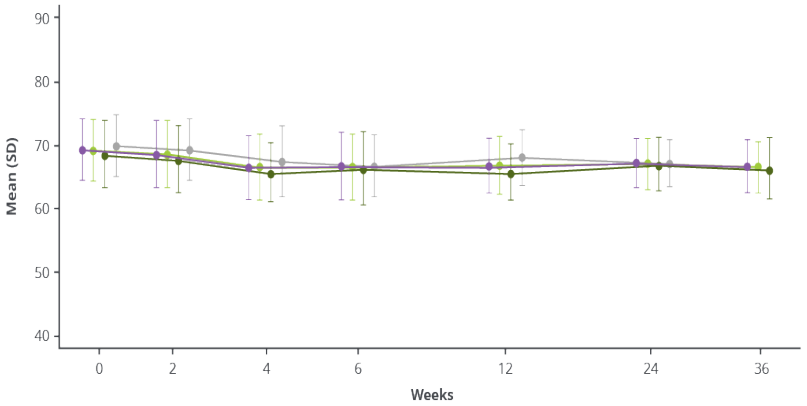
Valsalva LVOT-G



NYHA Class



LVEF

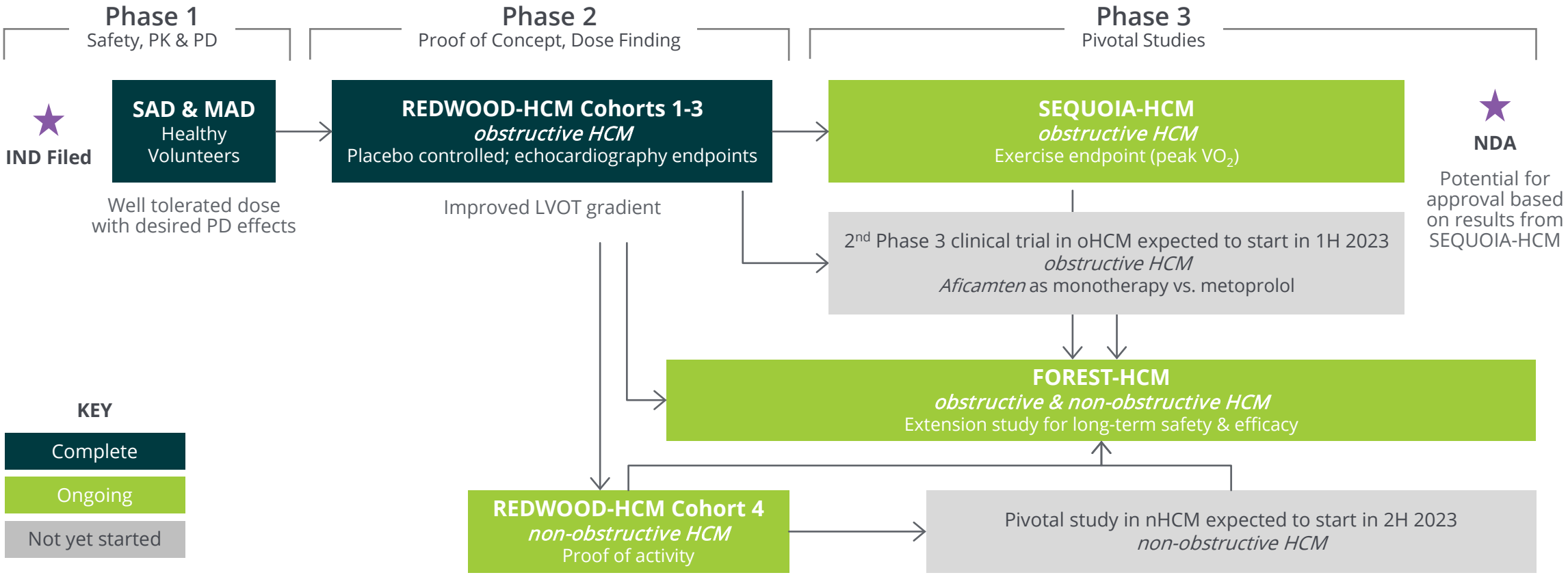


A: All patients
B: On background therapy (BT)
C: Patients with background therapy reduction/withdrawal (BTR/W) attempt
D: Patients on BT without BTR/W attempt

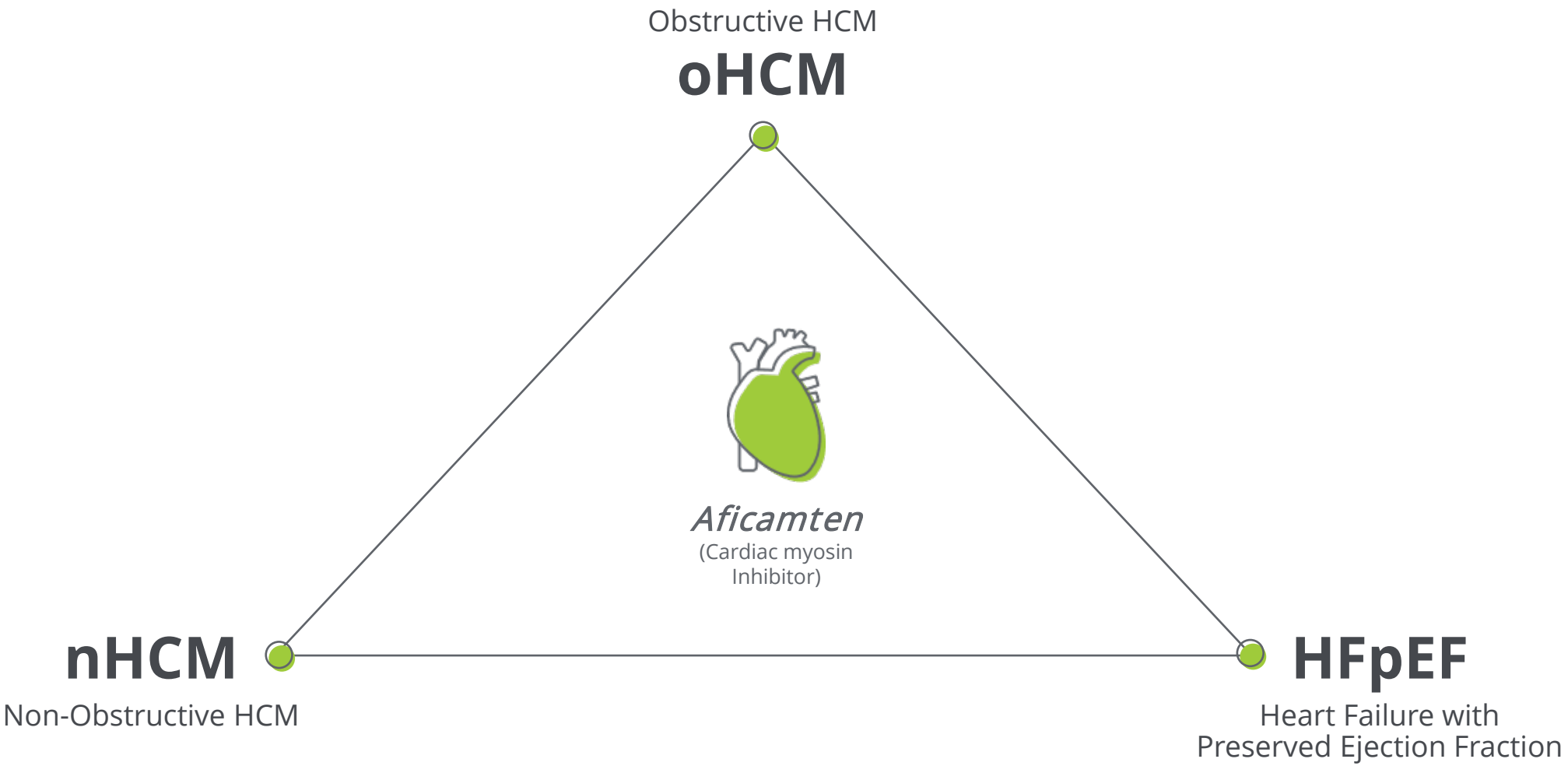
**** = p < 0.0001
*** = p < 0.001
** p = < 0.005
* = p < 0.05

Aficamten: Clinical Development Plan for HCM

Second Phase 3 trial in oHCM beginning in 1H 2023; pivotal Phase 3 trial in nHCM beginning 2H 2023



Novel Approach May Address Multiple Unmet Patient Needs



Aficamten: Targeting Patients with Unmet Need

Positive HCP Anticipation for *Aficamten*

Majority of KOLs see *aficamten* as an improvement to standard-of-care given the unique MOA; particularly interested in:

- Rapid and sustained LVOT-G reduction
- Rapid improvement in symptoms
- Reduction in septal wall thickness

Characteristics of the Ideal US HCM Patient for *Aficamten*

- Symptomatic, uncontrolled (non-responsive, refractory) to standard-of-care

  or

- Contra-indication for standard-of-care or other cardiac myosin inhibitors

  or

- Newly diagnosed patients

Cogent Primary Mkt Research, USA 2022 (n = 150)
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.

Aficamten: Brand Strategy

Aspirational Brand Goal: Establish *aficamten* as foundational therapy for HCM patients

COMPETE: In HCM Market

- Differentiate on product attributes of value to patients and physicians

EXPAND: Customer Base

- Leverage differentiated safety profile and limited drug-drug interactions
- Leverage CV franchise infrastructure, market understanding, and relationships

MAINTAIN: Patient on Therapy

- Ensure access through patient support services
- Provide patient support tools to manage dosing regimens and persistence

GROW: Undiagnosed

- Invest in disease education and genetic testing programs

Aficamten: Market Access Strategy

Get rapid and parity access

- Learn from first to market access experience
- Leverage existing access relationships
- Secure profitable access to support efficient, desired prescribing position
- Devise distribution network to complement product strategy

Clear pricing based on benefit

- Relative pricing position to be supported by market research
- Pricing strategy consistent with product strategy

Develop value proposition and value story

- Driven by clinical benefit and utility relative to alternatives
- Generate, disseminate and communicate health economics & outcomes research supporting value of differentiated treatment

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.

Omecamtiv Mecarbil: Current Status

Advisory Committee Conducted Dec. 13, 2022

8 to 3 vote that the benefits of *omecamtiv mecarbil* do not outweigh its risks for the treatment of HFrEF

Engaging with FDA

Ongoing engagements with FDA

Preparing for Launch

Continuing launch preparedness and commercial readiness activities

PDUFA Feb. 28, 2023

PDUFA target action date is February 28, 2023

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

HFrEF Patients Have Challenges Getting & Staying on Optimal Therapy

Challenges Getting on Therapy[1]

HFrEF patients have at least one comorbidity that prevents use of at least one guideline-directed therapy

- 48% of all HFrEF patients
- 66% of HFrEF patients with prior hospitalization

Comorbidities include: 34+% Chronic Kidney Disease, 21+% Hypotension, 13+% Hyperkalemia

Challenges Staying on Optimal Therapy[2]

Cycling through GDMT pillars[2]

- 50% of HFrEF patients have cycled through 3+ pillars since 2015
- Only 23% are on 3+ pillars in Q2/22

Reaching optimal/therapeutic dose[2]

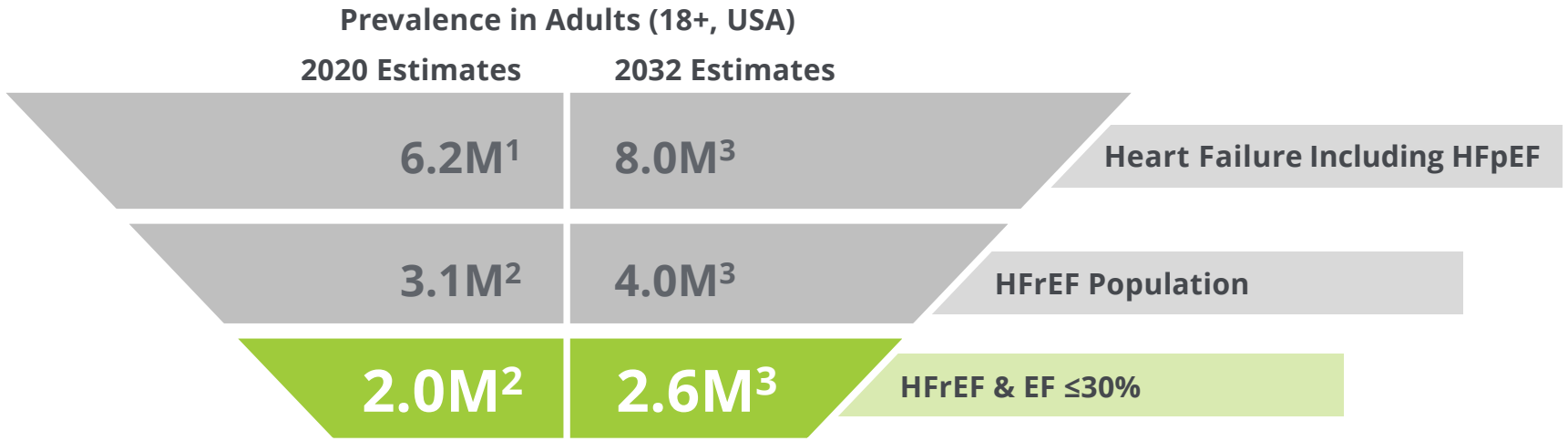
- Patients do not reach optimal doses, with many on low doses of GDMT therapies

Dropping off therapy[3]

- Many patients drop off therapy within a year
- For patients with co-morbidities, drop off rates are worse

1. SHA: Patient Claims Data; Co-morbidities of HFrEF patients diagnosed with ICD10 code I50.20/1/2/3 and treated by drugs that are part of GDMT in Q3 2022
2. SHA: Patient Claims Data - new patients initiating Oct 2020 to Sep 2021 with a 2-month titration look forward period through Nov 2021
3. SHA: Patient Claims Data 04/06/2022; Entresto cohort Jan 2018, Verquvo Cohorts first 8 months of launch 3/21-9/21; Patients dropping off within 12 months of treatment initiation

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)

Cytokinetics

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

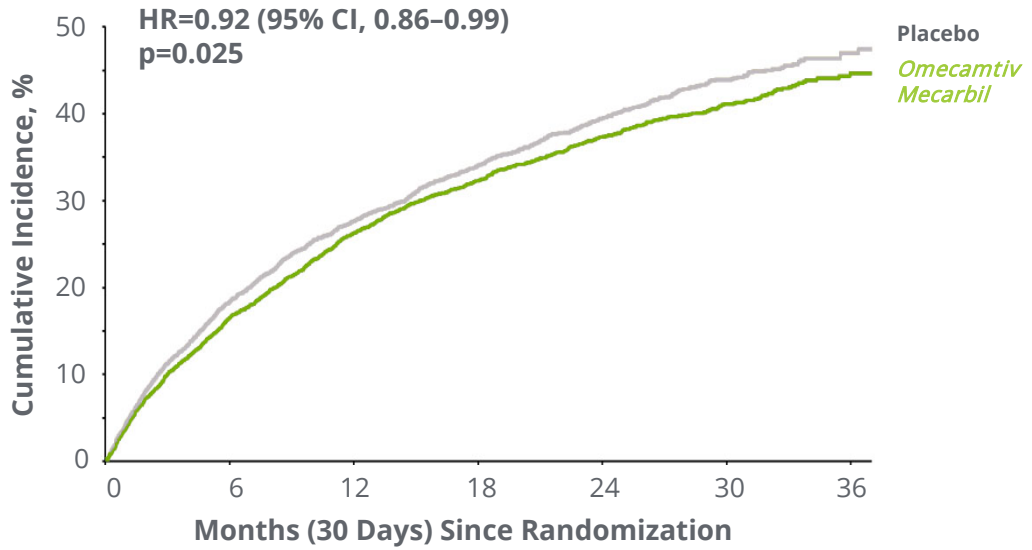
*An HF event defined as the presentation of the subject for an urgent, unscheduled clinic/office/ED visit, or hospital admission, with a primary diagnosis of HF, where the patient exhibits new or worsening symptoms of HF on presentation, has objective evidence of new or worsening HF, and receives initiation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

Primary Composite Endpoint

Time to First Heart Failure Event or Cardiovascular Death

GALACTIC-HF

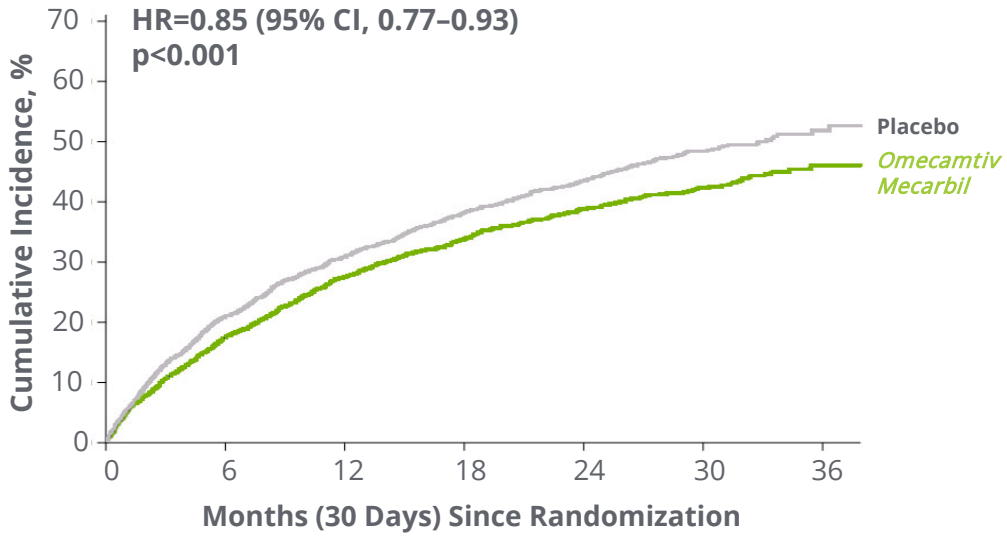
Primary Composite Endpoint (Overall Population)



Patients at risk, n

Placebo	4112	3310	2889	2102	1349	647	141
OM	4120	3391	2953	2158	1430	700	164

Primary Composite Endpoint (EF <30%)



Patients at risk, n

Placebo	2363	1838	1580	1103	701	315	69
OM	2341	1904	1646	1173	756	333	82

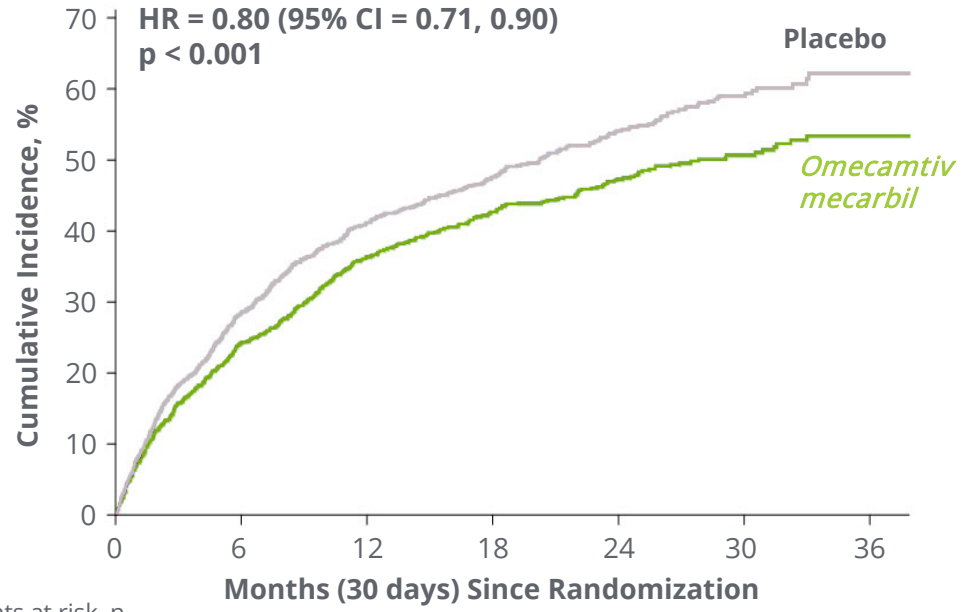
CI, confidence interval; HR, hazard ratio

Greater Treatment Effect in Worsening HF

GALACTIC-HF

Primary Outcome in Severe HF

(Severe HF: LVEF ≤30%, NYHA III/IV, HF hosp ≤ 6 mos)[1,2]



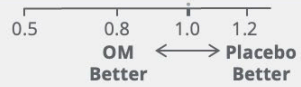
Patients at risk, n

Placebo	1152	808	650	464	290	119	13
OM	1106	814	671	480	320	137	31

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%**
+ 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%

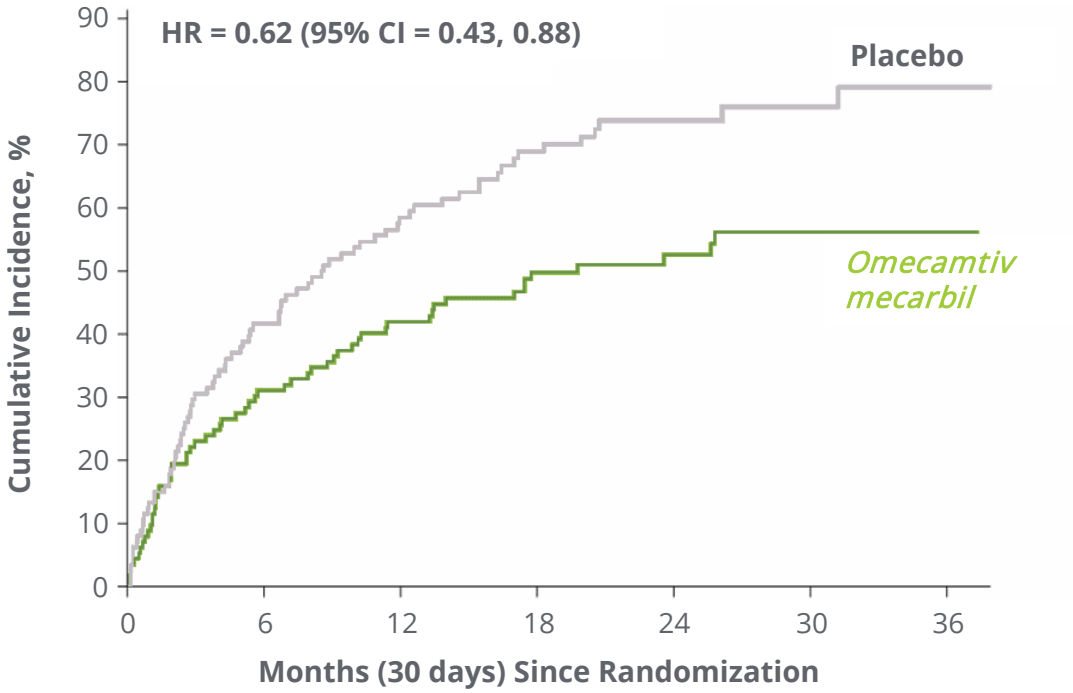


1. Felker GM, *Omecamtiv Mecarbil* in Patients with Severe Heart Failure: An Analysis from GALACTIC-HF, ESC Heart Failure 2021, June 2021
2. Felker GM, et al. Assessment of *Omecamtiv Mecarbil* for the Treatment of Patients With Severe Heart Failure. JAMA Cardiology, October 2021.

Greater Treatment Effect in Worsening HF with GDMT Intolerance

GALACTIC-HF

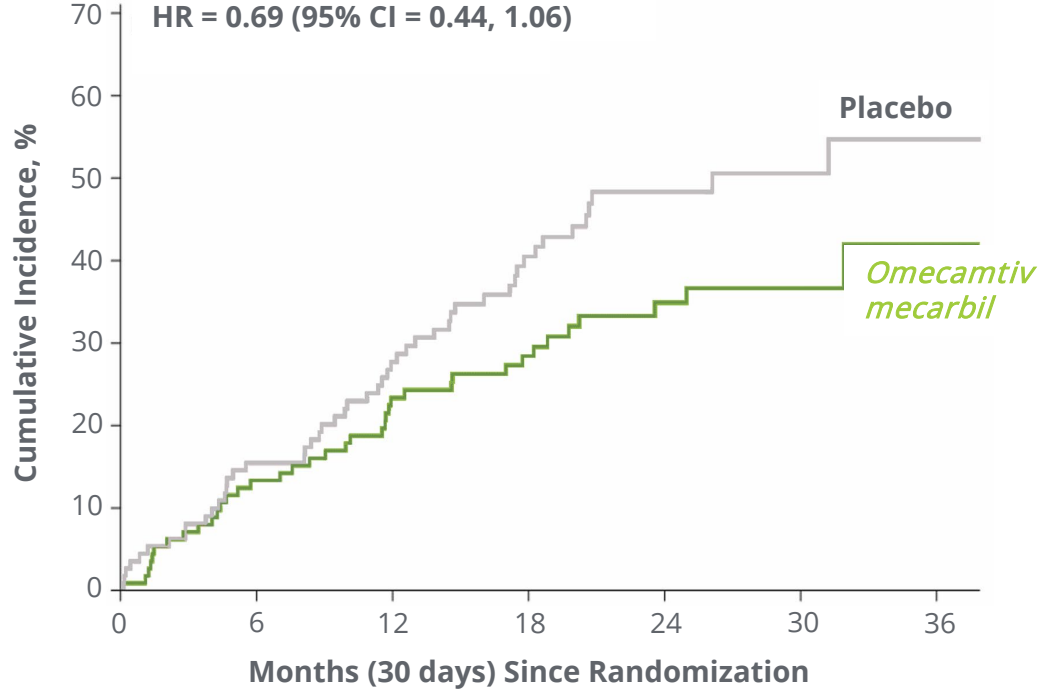
Primary Outcome In Patients with LVEF ≤28% Intolerant of ACE/ARB/ARNI



Patients at risk, n

Placebo	113	63	43	28	15	9	3
OM	113	76	64	46	30	9	3

CV Death In Patients with LVEF ≤28% Treated with ACE/ARB/ARNI



Placebo	113	91	75	51	30	15	5
OM	113	96	83	62	40	15	5

Laboratory and Safety Events

GALACTIC-HF

Variable	Relative Risk or Difference (95% CI)
Laboratory value change from baseline to Week 24	
Systolic blood pressure – mmHg, mean (SD)	-0.1 (-0.9, 0.6)
Heart rate, bpm, mean (SD)	-1.6 (-2.2, -1.0)
Cardiac Troponin I, ng/L, median (Q1, Q3)	0.004 (0.003, 0.005)
NT-proBNP, pg/mL, median (Q1, Q3)	0.90 (0.86, 0.94)
Adverse events (AEs)	
Any serious AE, n (%)	0.97 (0.94, 1.01)
Drug discontinuation due to AE, n (%)	0.97 (0.85, 1.11)
Adverse events of interest	
Ventricular tachyarrhythmias	0.95 (0.82, 1.11)
Torsade de pointes/QT prolongation	0.90 (0.74, 1.10)
SAE of ventricular arrhythmia requiring treatment	0.93 (0.73, 1.20)
Adjudicated major cardiac ischemic events, n (%)	1.06 (0.87, 1.29)
Adjudicated Strokes	0.68 (0.51, 0.91)

Sarcomere Directed Drug Development

Skeletal Muscle

Reldesemtiv

Cytokinetics

Reldesemtiv

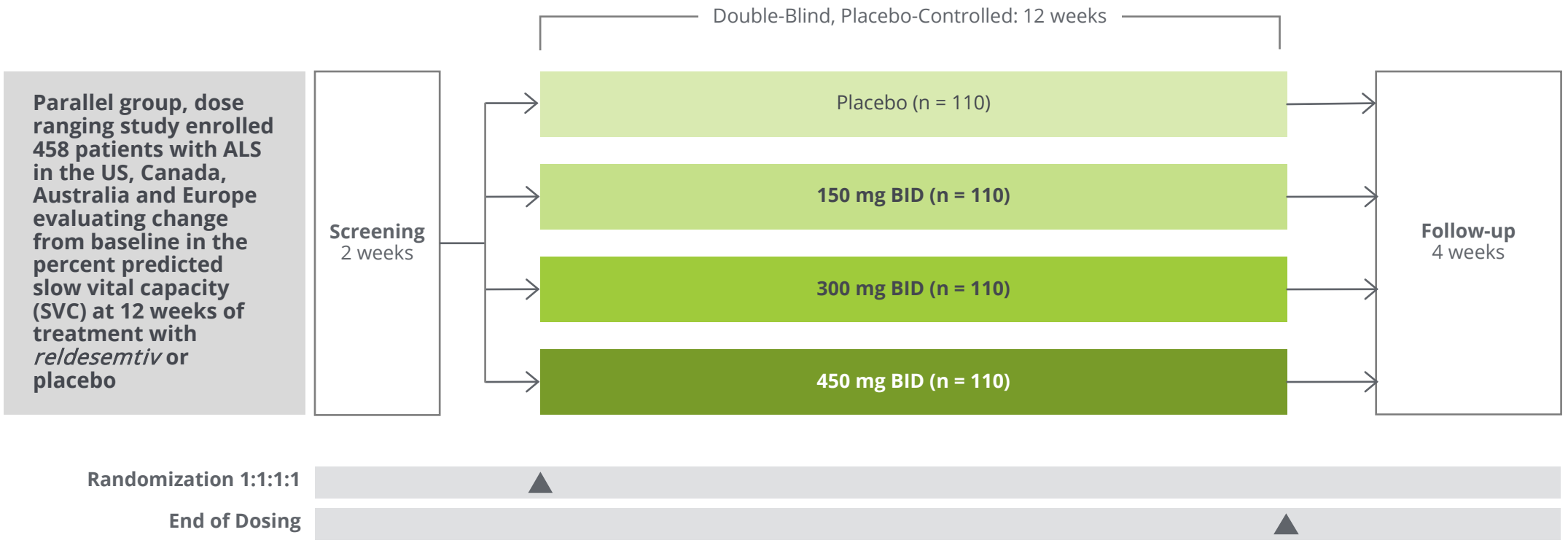
Cytokinetics

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

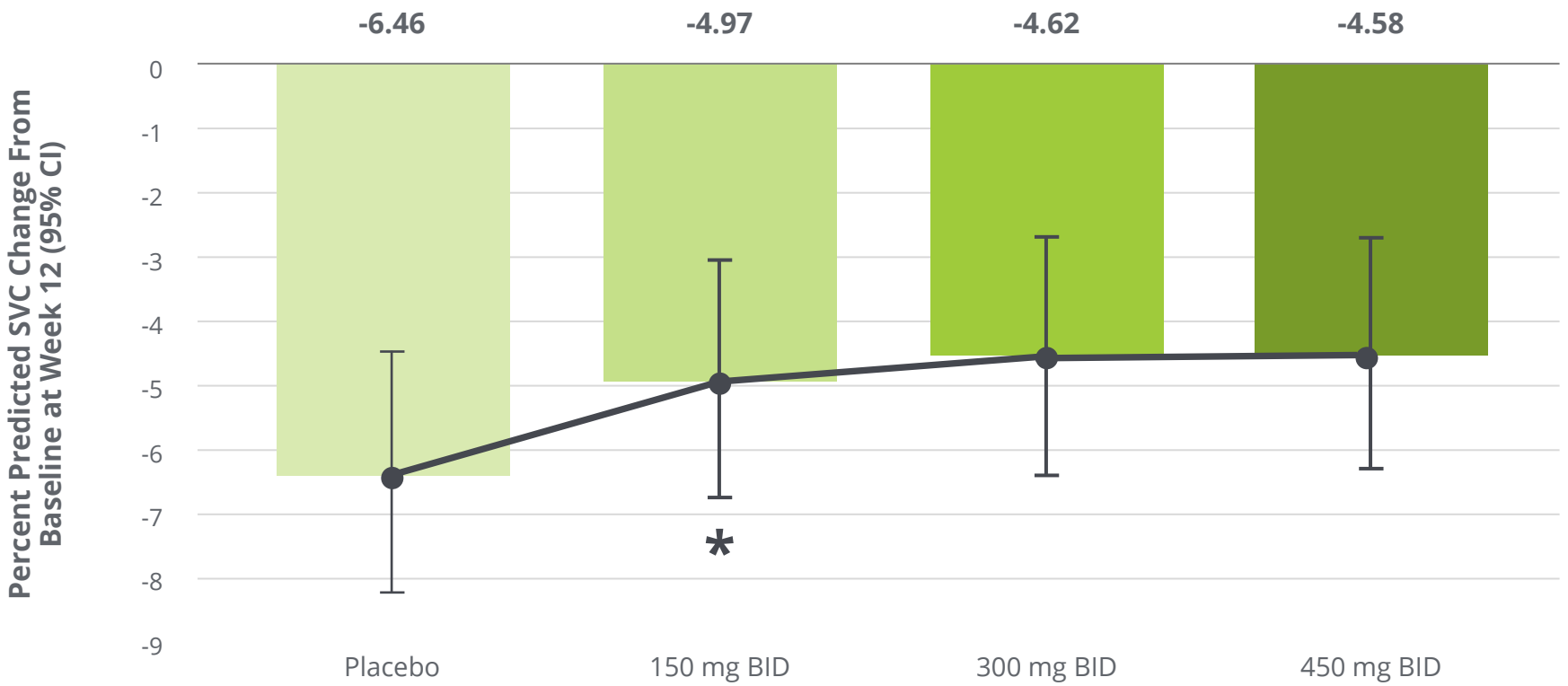
FORTITUDE ALS

Results presented at American Academy of Neurology 2019 Annual Meeting



Primary Endpoint: SVC

Change from baseline in percent predicted SVC at week 12



Primary Analysis*

P = 0.11 for weighted dose-response relationship

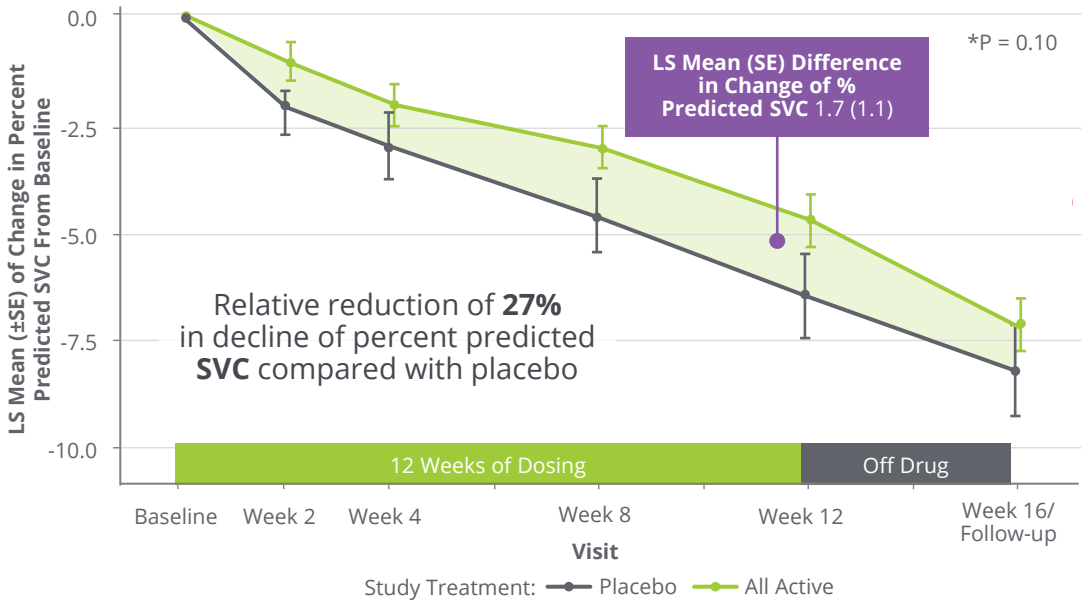
*Based on Mixed Model for Repeated Measures (MMRM) with the contrasts of (-5, -1, 3, 3) for placebo, *reldesemtiv* 150 mg, 300 mg and 450 mg BID, respectively

Phase 2 Clinical Trial

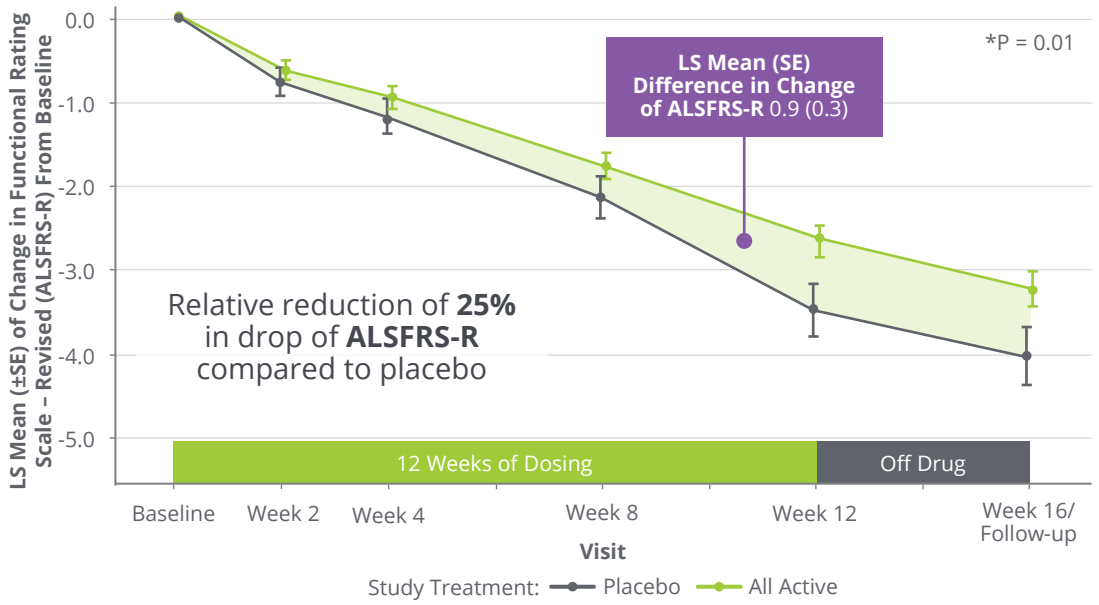
FORTITUDE ALS

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)



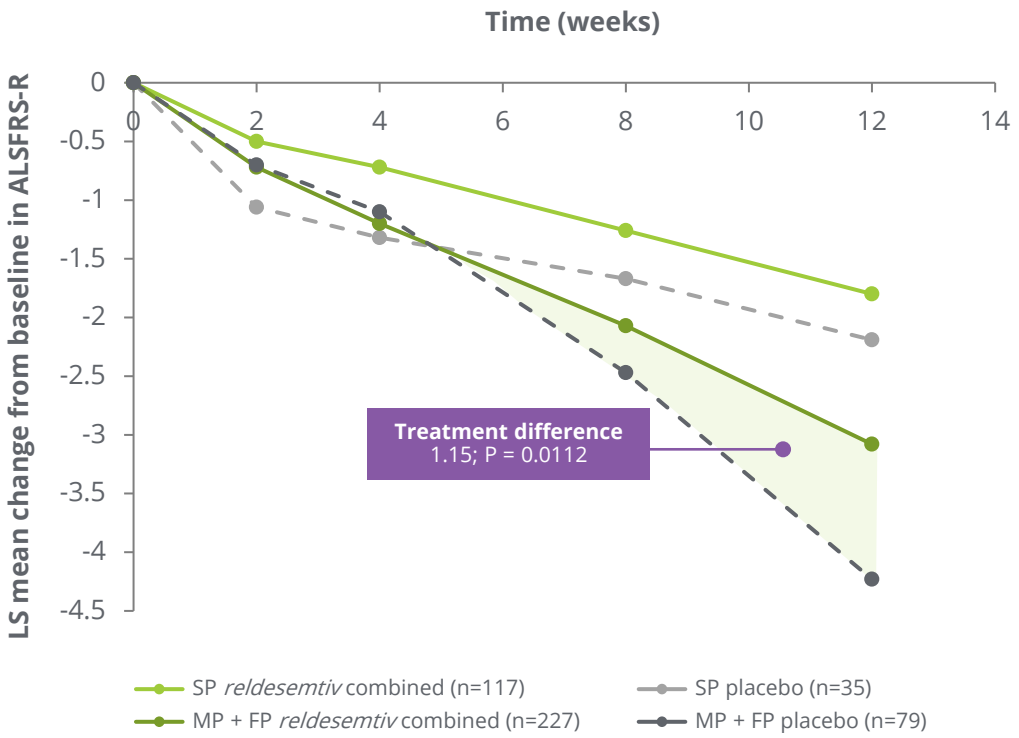
*post hoc analysis
FORTITUDE-ALS did not achieve statistical significance, but patients on all dose groups of *reldesemtiv* declined less than patients on placebo

Cytokinetics

Post-Hoc Analyses Inform Phase 3 Design

FORTITUDE ALS

Change From Baseline in ALSFRS-R by Progressor Tertiles



Majority of Patients Who Meet 24/44 Criteria Have Short or Intermediate Predicted Survival

24/44 criteria: symptoms for ≤24 months; baseline ALSFRS-R total score ≤44

All patients in COURAGE-ALS must meet the 24/44 criteria

Risk Group (Predicted Survival) n (%)	Met 24/44 Criteria (n=272)	Did not meet 24/44 criteria (n=184)	P value
G1 (very short)	38 (14.0)	0 (0)	<0.0001
G2 (short)	81 (29.8)	8 (4.3)	<0.0001
G3 (intermediate)	80 (29.4)	26 (14.1)	0.0002
G4 (long)	61 (22.4)	68 (37.0)	0.0007
G5 (very long)	12 (4.4)	82 (44.6)	<0.0001

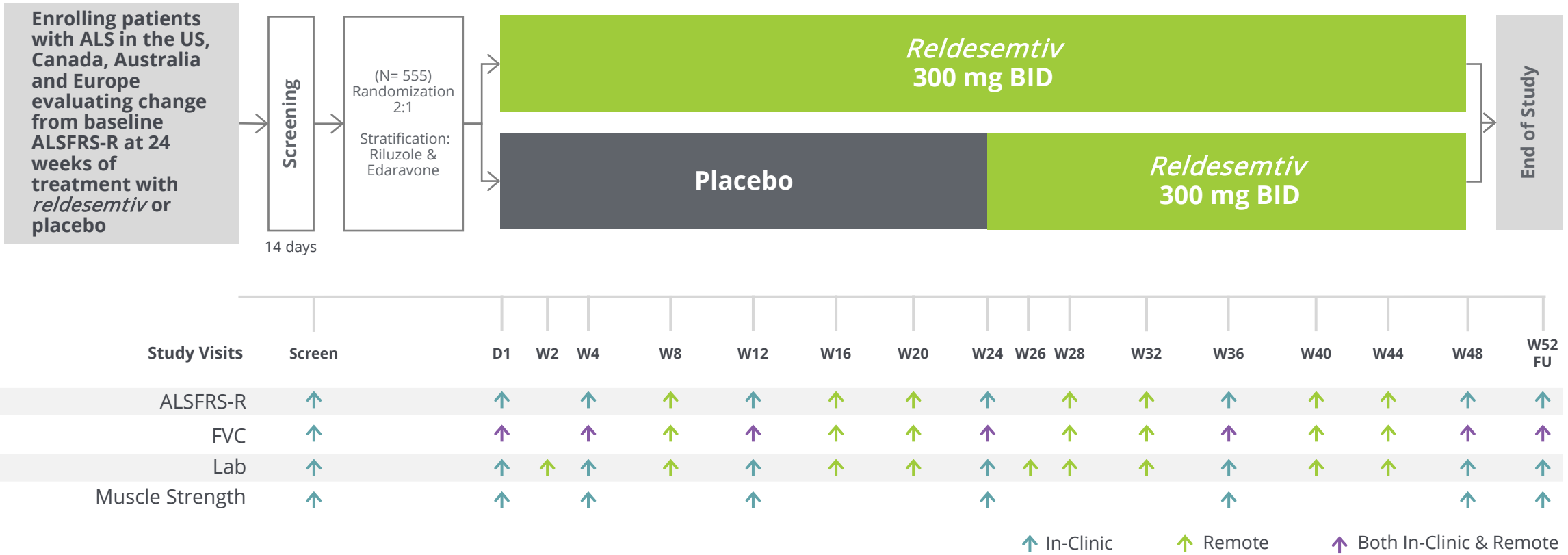
FP, fast progressing; MP, medium progressing; SP, slow progressing
*post hoc analysis
FORTITUDE-ALS did not achieve statistical significance, but patients on all dose groups of *reldesemtiv* declined less than patients on placebo

Phase 3 Clinical Trial Design

>300 patients enrolled

COURAGE ALS

Second interim analysis expected in 1H 2023 (futility & potential fixed increase in enrollment)



Sarcomere Directed Therapies

Corporate Profile

Cytokinetics

Robust Pipeline, Solid Financial Position

Pipeline

1 Potential commercial launch in 2023

2 Programs in Phase 3 trials

3 Potential FDA approvals by 2025

5 Clinical stage programs

10 Development programs by 2025

Programs

HCM

Aficamten

- 2 Phase 3 trials in HCM
- 1 planned Phase 3 trial in nHCM
- Ongoing OLE

Heart Failure

Omecamtiv mecarbil

- Positive trial results from GALACTIC-HF
- PDUFA 02/28/23

CK-136

- Started Phase 1 study in Q4 2022

ALS

Reldesemtiv

- Phase 3 trial, COURAGE-ALS ongoing

Ongoing R&D

Additional research in muscle biology, energetics & metabolism

Foundations

~400
Full time employees

>$800M
At EOY 2022

>2 years
Cash runway
based on 2022 Financial Guidance

Timelines and milestones reflect Cytokinetics' current expectations and beliefs
>$800M and >2 years cash runway based on estimates for Q4

Balance Sheet (Q3 2022) & Estimated 2023 R&D Spending

2023 guidance to be provided on Q4 2022 earnings call

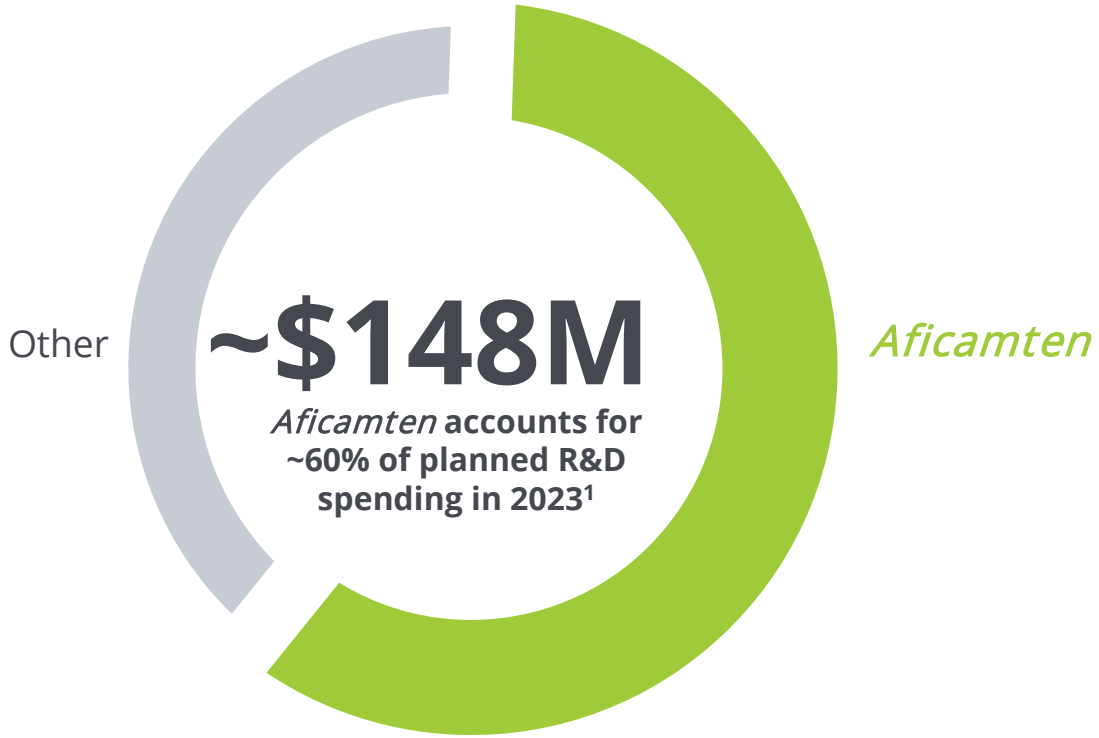
2022 Condensed Balance Sheet
As of 9/30/2022

in millions

	Total
Cash and investments	$896.2
Accounts receivable	$2.3
PPE	$80.3
Leased assets	$75.1
Other assets	$22.1
Total Assets	**$1,076.0**
Debt	$545.0
Liability related to sale of future royalties	$291.3
Deferred Revenue	$0
Lease liability	$130.5
Other liabilities	$125.2
Total Liabilities	**$1,092.0**
Working capital	$807.8
Accumulated deficit	($1,448.6)
Stockholders' deficit	($16.0)
Wtd Avg Basic Shares Outstanding	**88.2**

1. Cytokinetics internal planning data. Outside services spend for clinical trials, CMC and toxicology studies
* Spend is for outside services

2023 Estimated R&D Spend*



Expected 2023 Milestones

Aficamten		*Omecamtiv Mecarbil*	*Reldesemtiv*	**Early Pipeline**
Begin **second Phase 3 trial of** *aficamten* in oHCM in 1H 2023	**Complete conduct in Cohort 4** of REDWOOD-HCM; results expected 1H 2023	Continue to engage with FDA in advance of **Feb 28, 2023 PDUFA** for *omecamtiv mecarbil*	Expect **second interim analysis** from COURAGE-ALS in 1H 2023	Expect results from **Phase 1 study of CK-136** in 2H 2023
Continue **enrollment in SEQUOIA-HCM** through 1H 2023; results expected 2H 2023	Begin **Phase 3 trial of** *aficamten* **in nHCM** in 2H 2023	**Launch** *omecamtiv mecarbil* in the U.S. subject to FDA approval in Q1 2023	Complete **enrollment in COURAGE-ALS** in 1H 2023	File **new IND** in 1H 2023

Cytokinetics

Thank You

Sarcomere directed therapies