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.

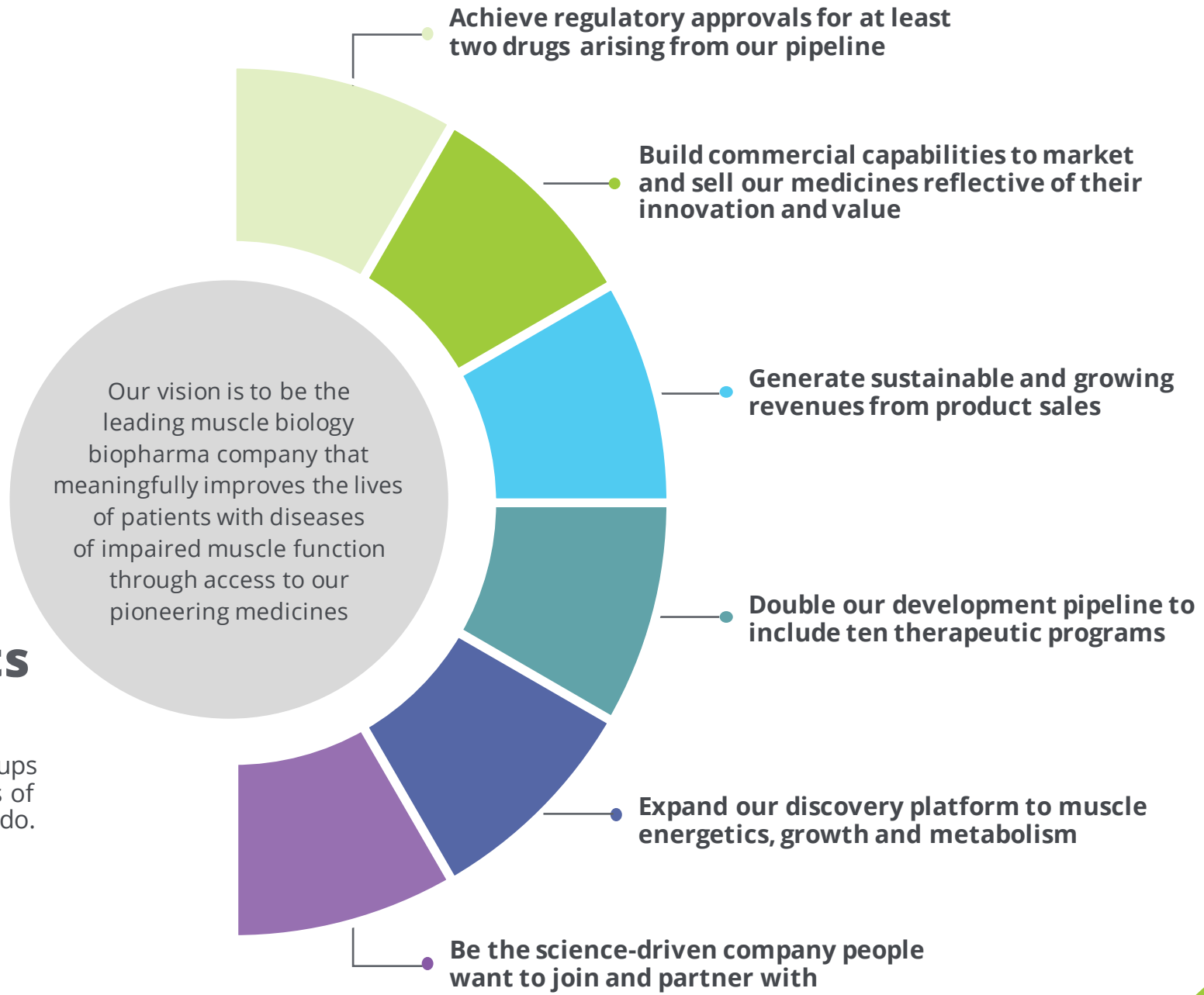
Forward-Looking Statements

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").

VISION 2025

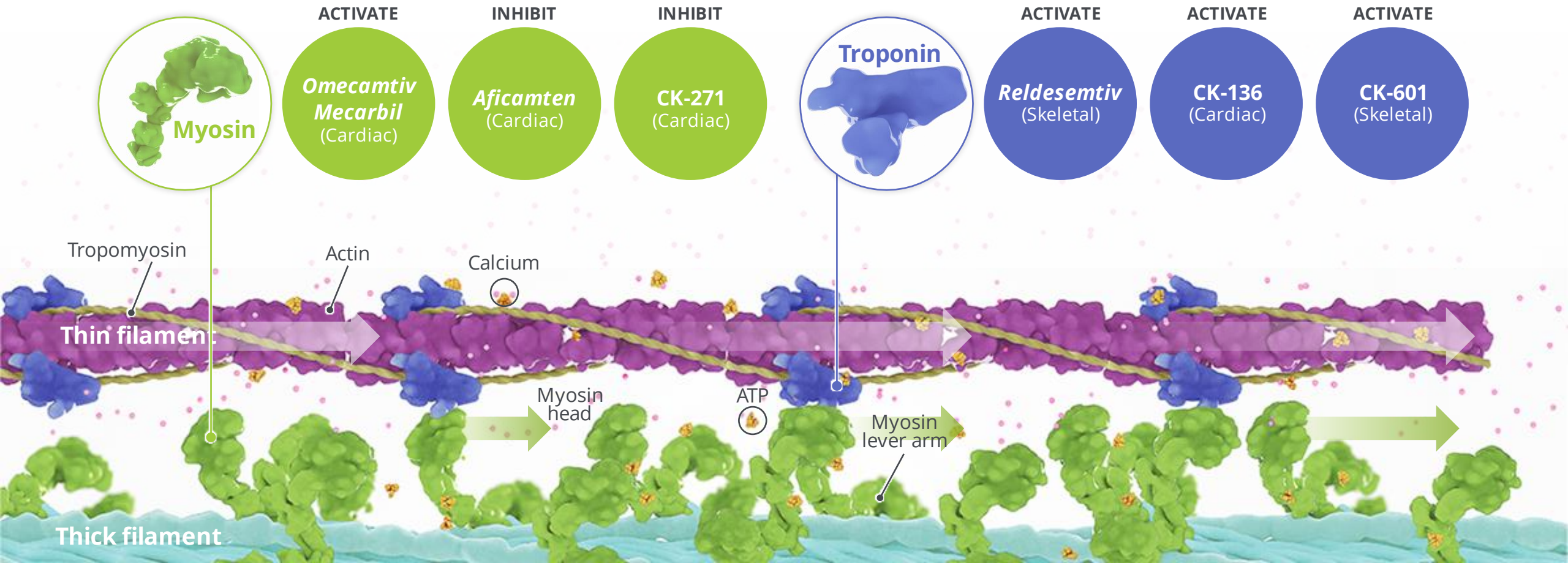
Leading with Science, **Delivering for Patients**

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.

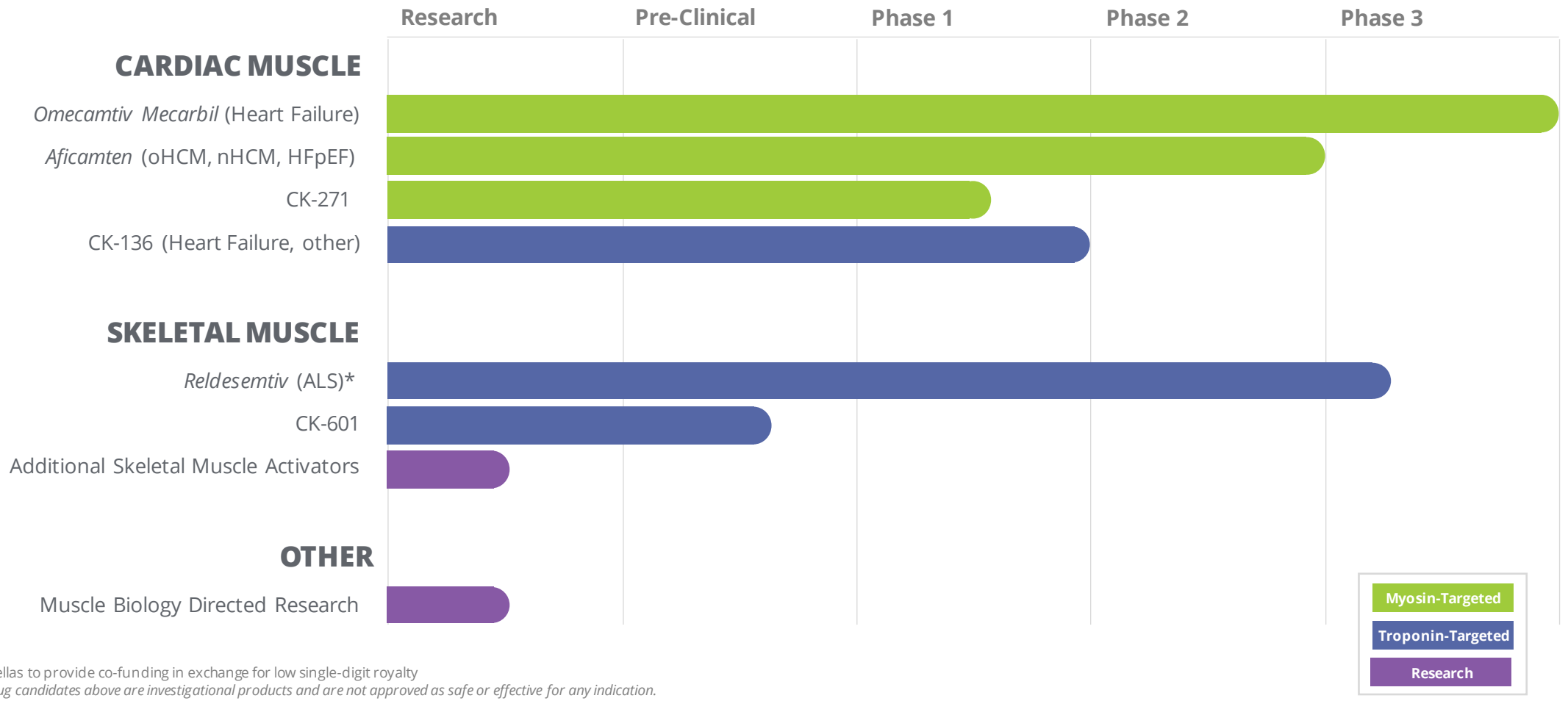


Sarcomere Directed Drug Development

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

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

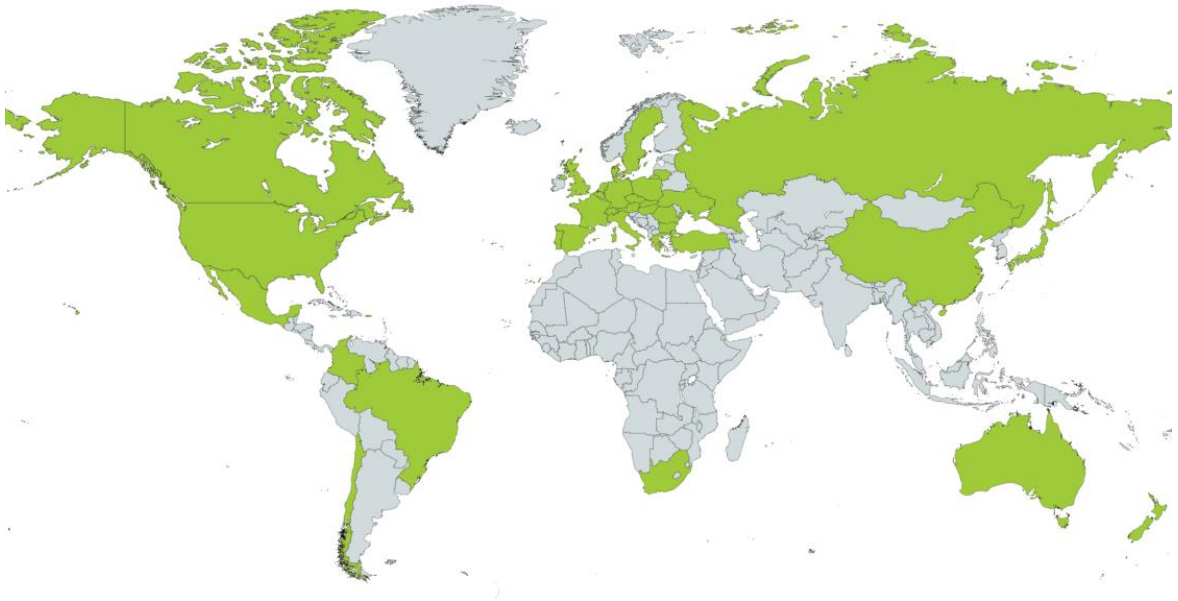
1. Benjamin EJ, et al. *Circulation*. 2018;137:e67-e492;
2. Gaziano et al, AMA Cardiol. 2016;1(6):666-672. doi:10.1001/jamacardio.2016.1747
3. Urbich, M., Globe, G., Pantiri, K. et al. A Systematic Review of Medical Costs Associated with Heart Failure in the USA (2014–2020). PharmacoEconomics 38, 1219–1236 (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

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



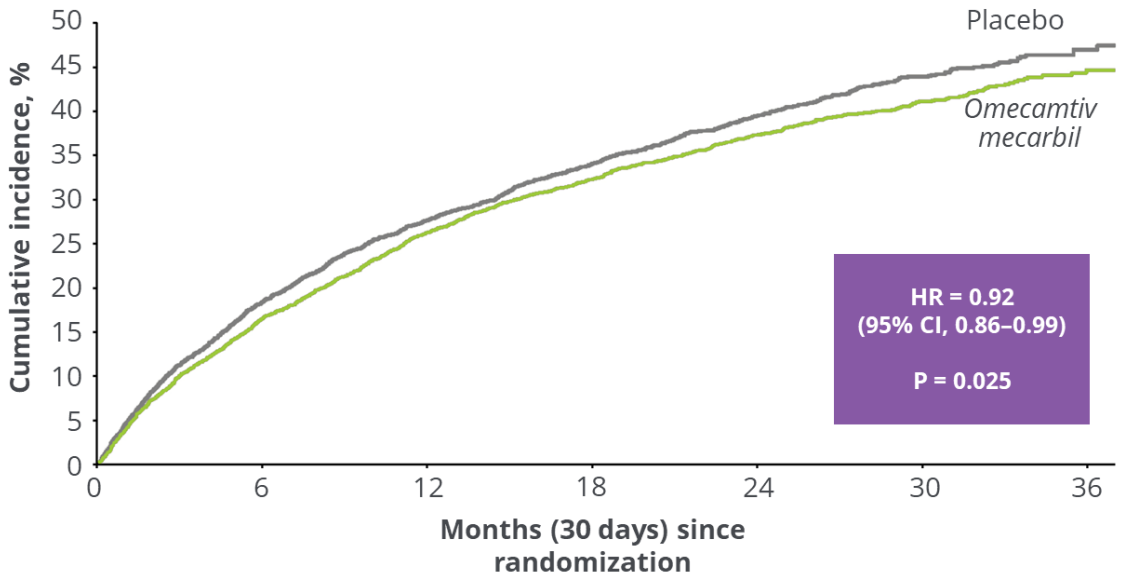
*An HF event defined as the presentation of the subject for an urgent, unscheduled clinic/office/ED visit, or hospital admission, with a primary diagnosis of HF, where the patient exhibits new or worsening symptoms of HF on presentation, has objective evidence of new or worsening HF, and receives initiation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

Positive Primary Composite Endpoint

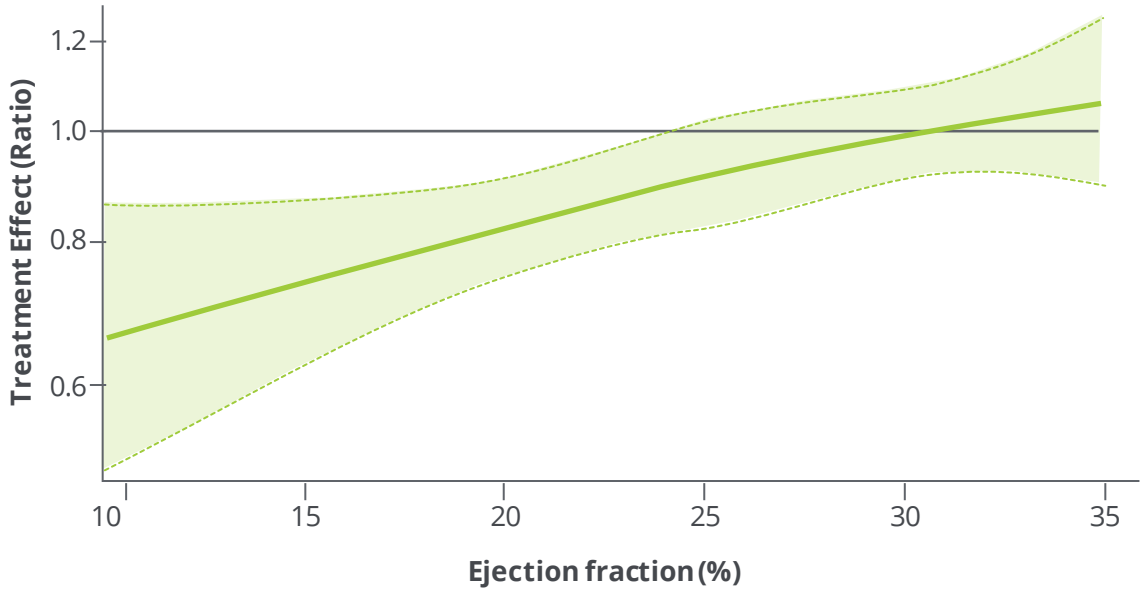
Treatment effect increased in more advanced patients

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]



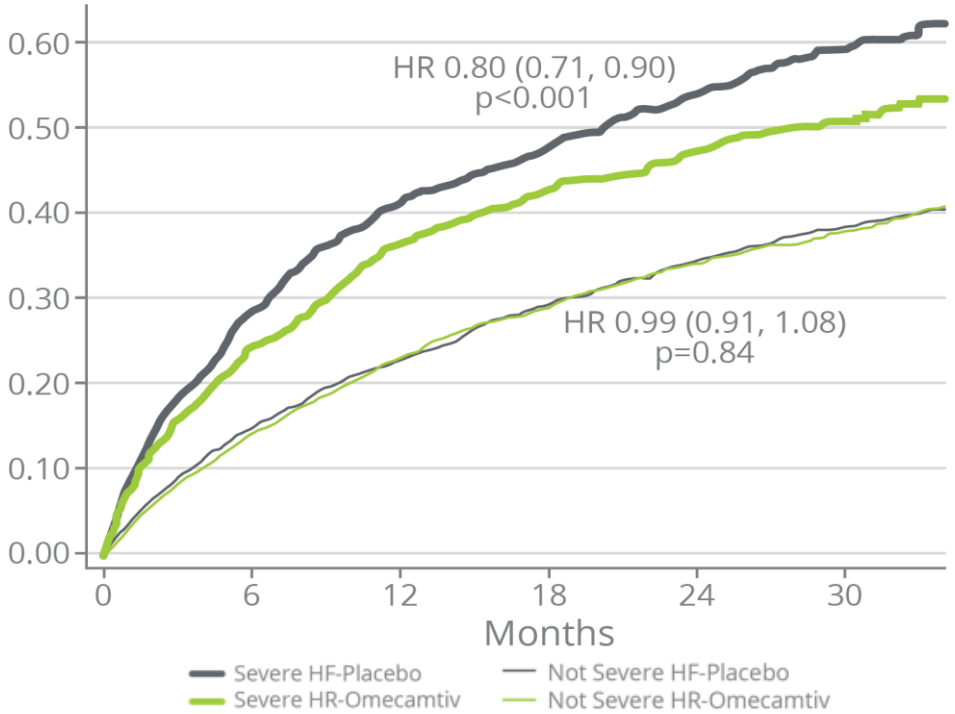
AEs and treatment discontinuation balanced between treatment arms

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

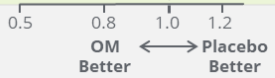
GALACTIC-HF

Primary Outcome in Severe HF: HR = 0.80 (0.71, 0.90)
(Severe HF defined as NYHA III-IV, EF ≤ 30%, HF hospitalization <6 mos)[1,2]



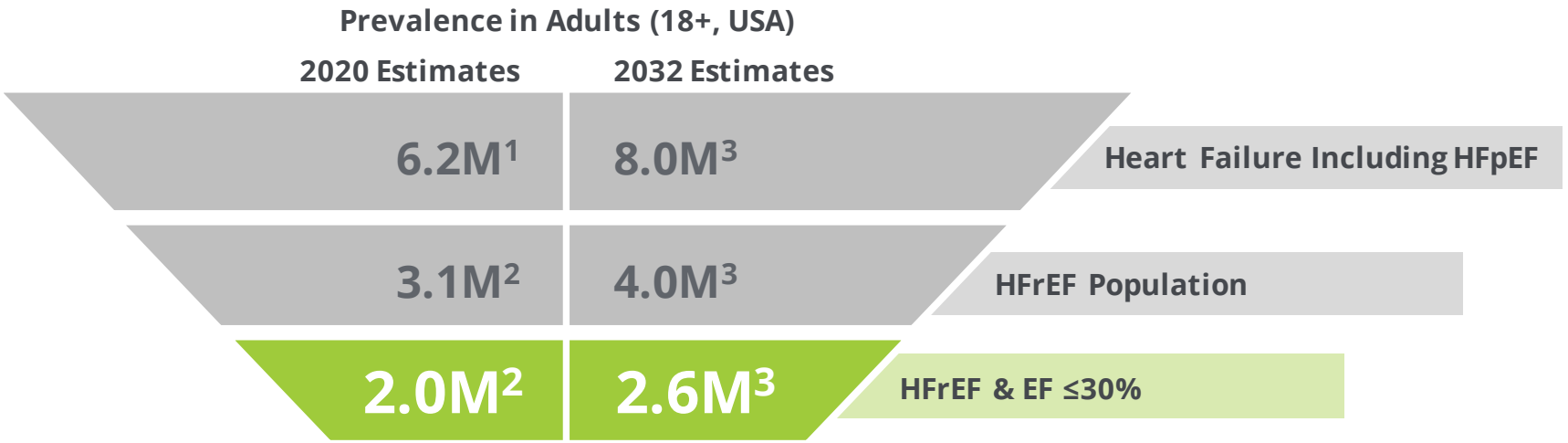
Primary Outcome in Patients with LVEF ≤28%: HR 0.84; 95% CI 0.77, 0.92

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.

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

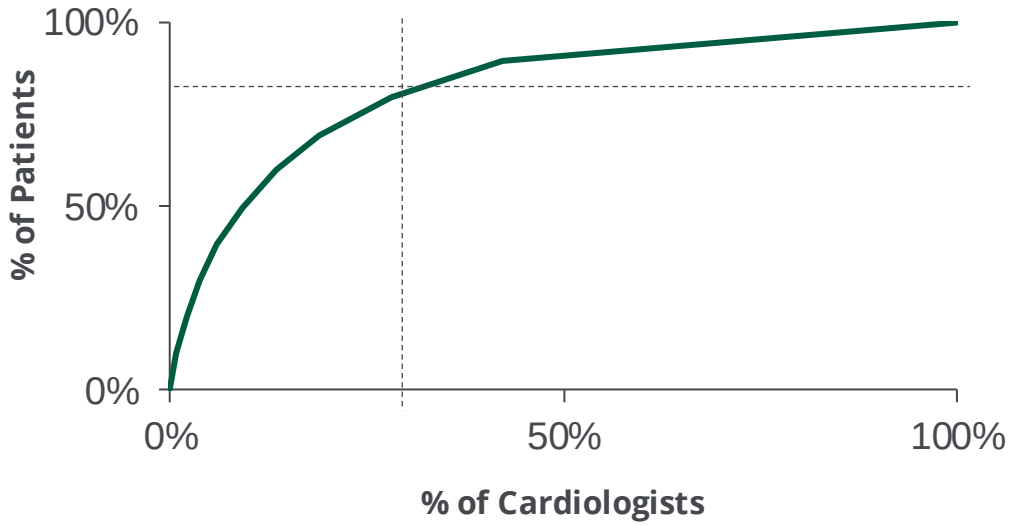
Co-morbidities and/or tolerability**

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

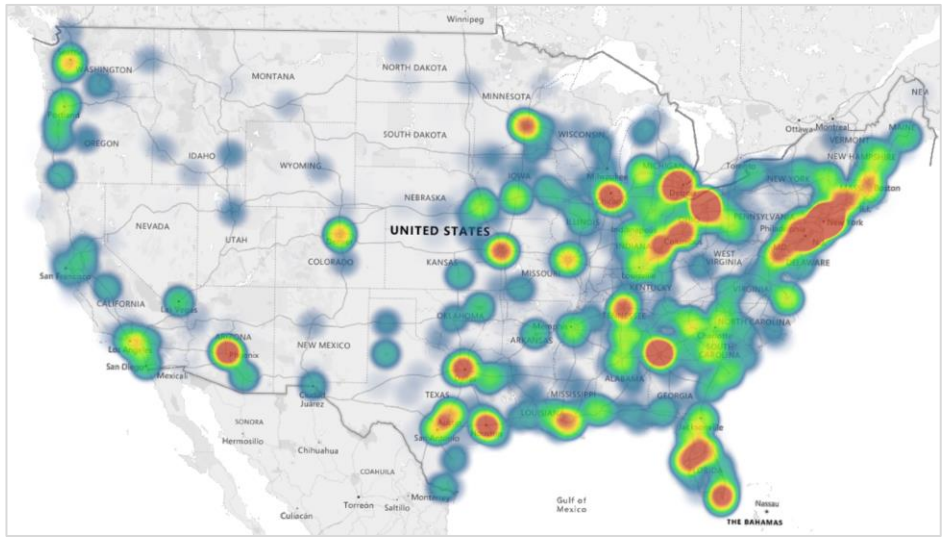
1. National Center for Health Statistics. National Health and Nutrition Examination Survey (NHANES) as accessed 4/1/2019 at website. https://www.cdc.gov/nchs/nhanes/. – data from 2013-2016 as quotes in Benjamin 2019 Circulation. 2019;139:e56–e528. DOI: 10.1161/
2. EF based on distribution as presented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

Small Subset of Cardiologists Manage Majority of Patients

HFrEF Patient Concentration in Cardiologists



Distribution of High-Volume Cardiologists



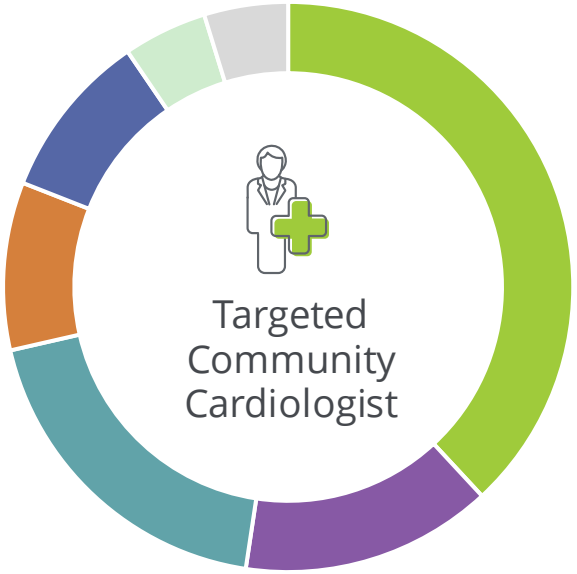
Allows for more targeted field team approach, focusing on <10,000 HCPs

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

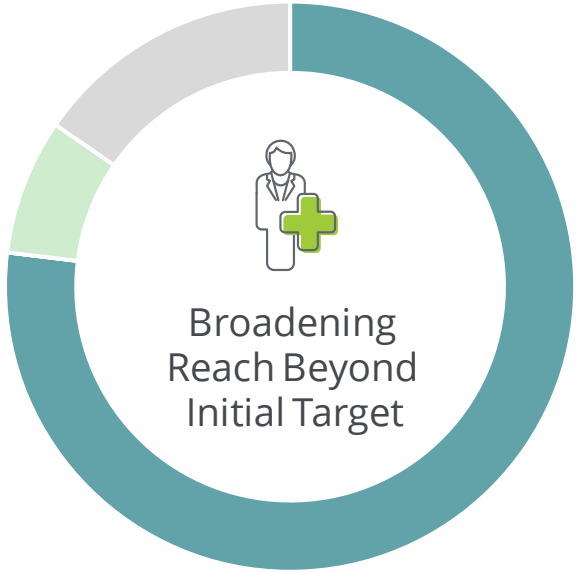
Customizing engagement by different types of customers

~~ illustrative ~~



Digital allows broader reach

~~ illustrative ~~




Field &
Account Reps


Inside
Sales


Digital
Engagement


Reimbursement
Specialists

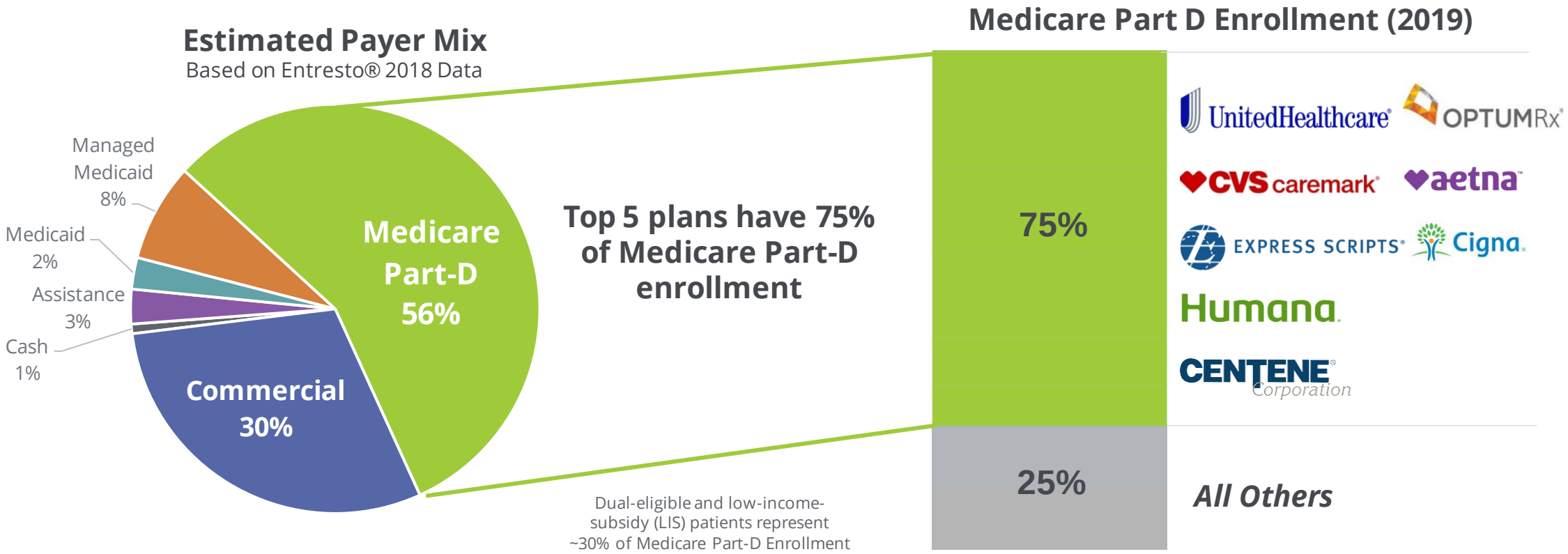

MSLs


Patient
Services


Online
communities

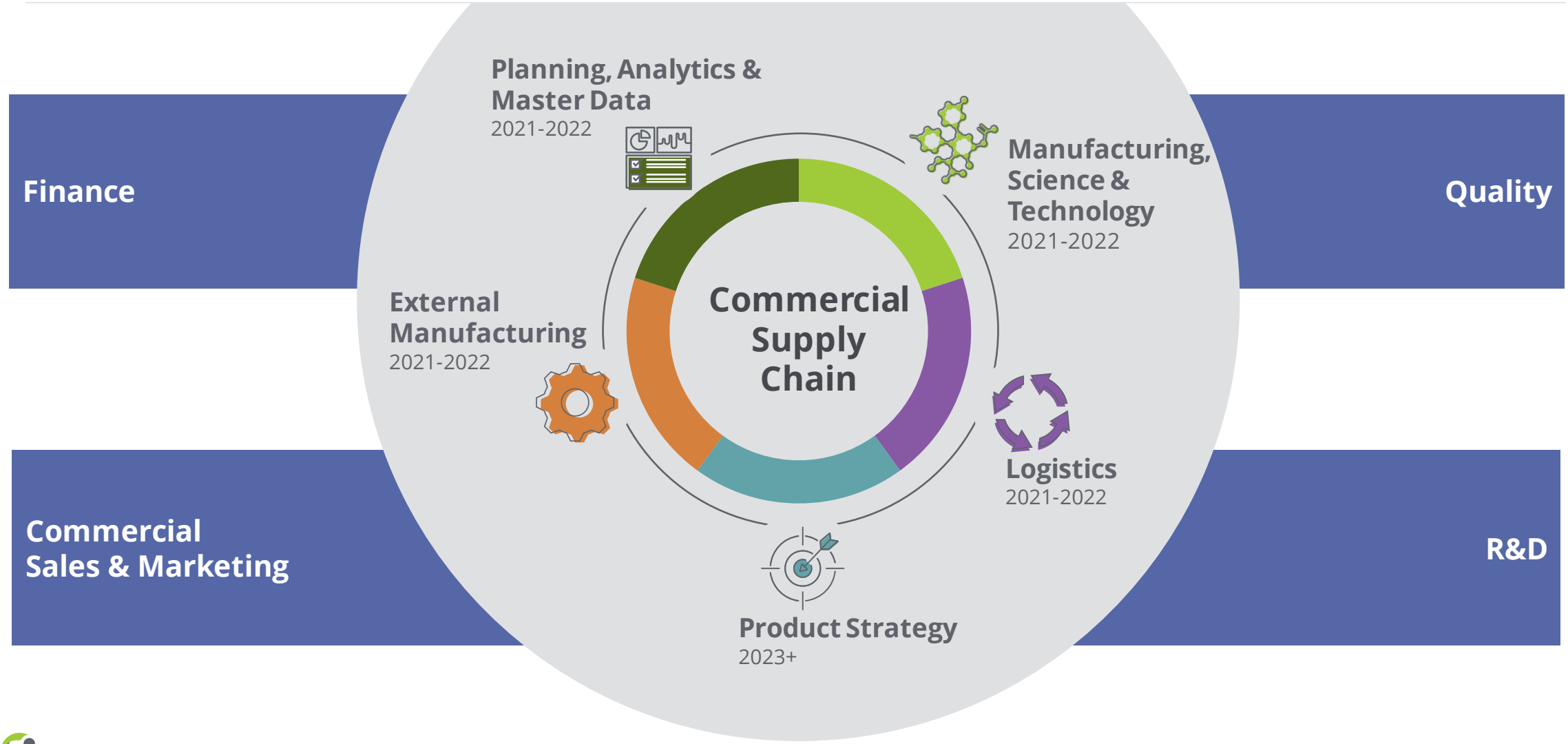
Medicare Is Major Payer with Select Key Players

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

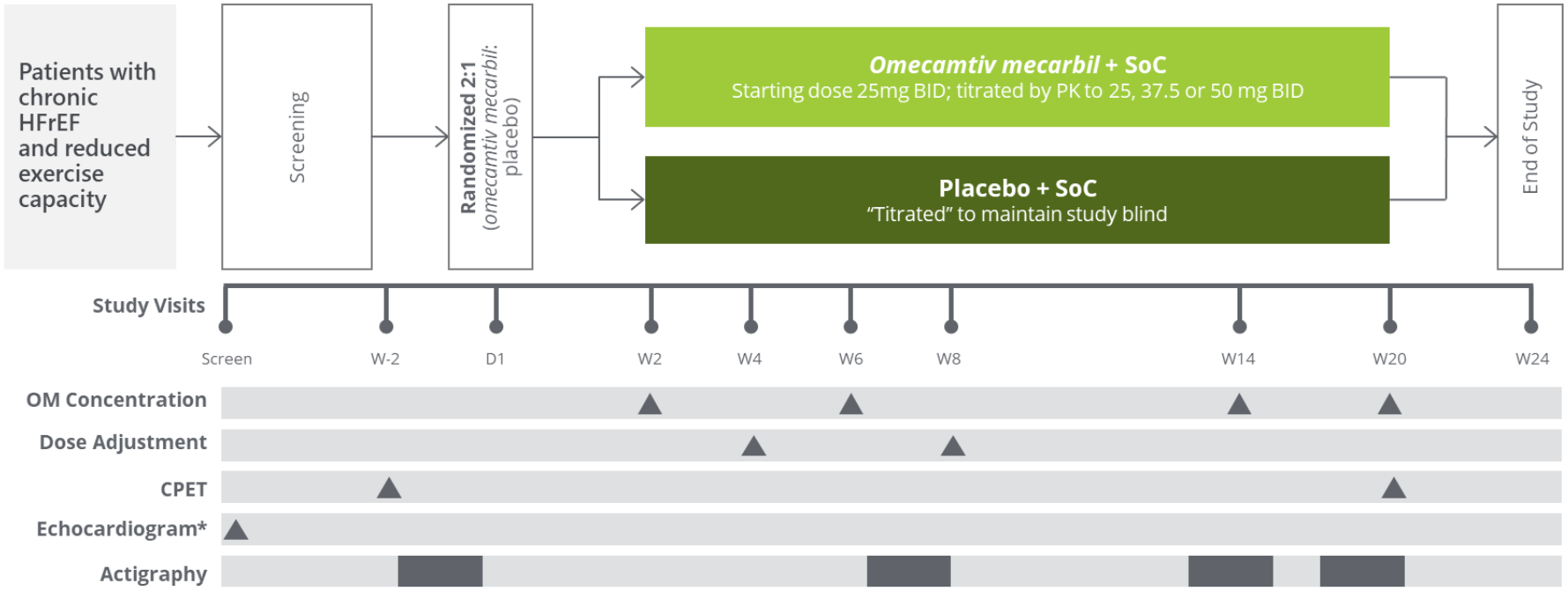
Investigating effect of *omecamtiv mecarbil* on exercise tolerance

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 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

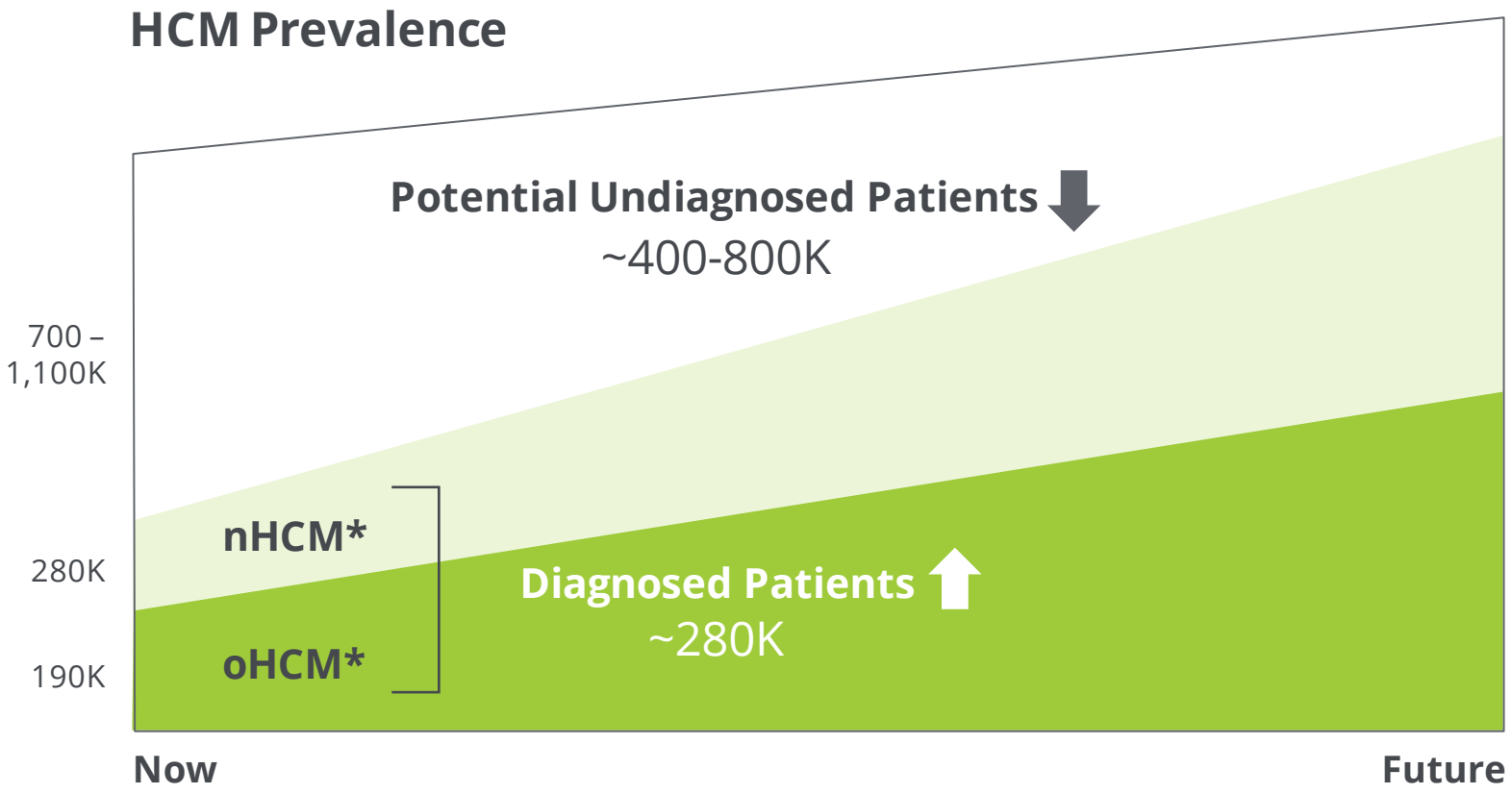
Aficamten is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.

Cytokinetics

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

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

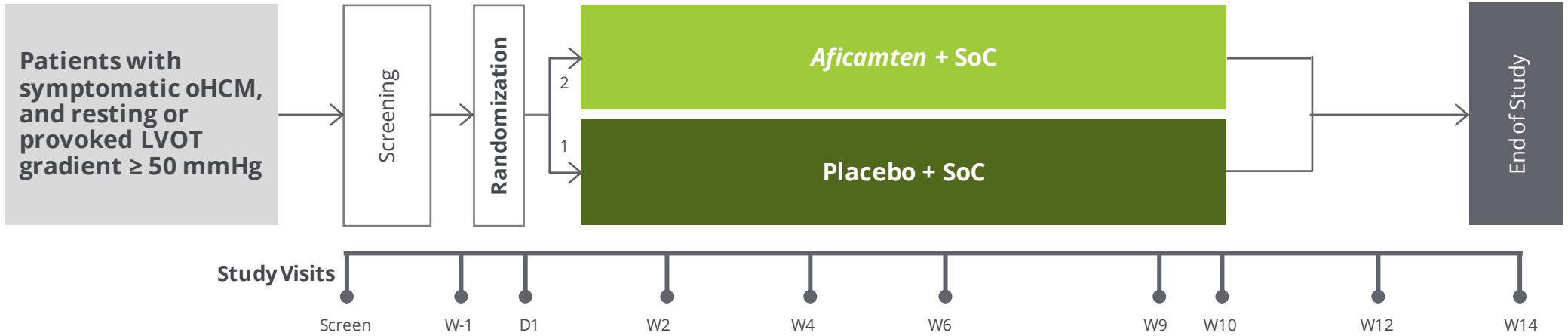
No monitoring of plasma concentrations

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.

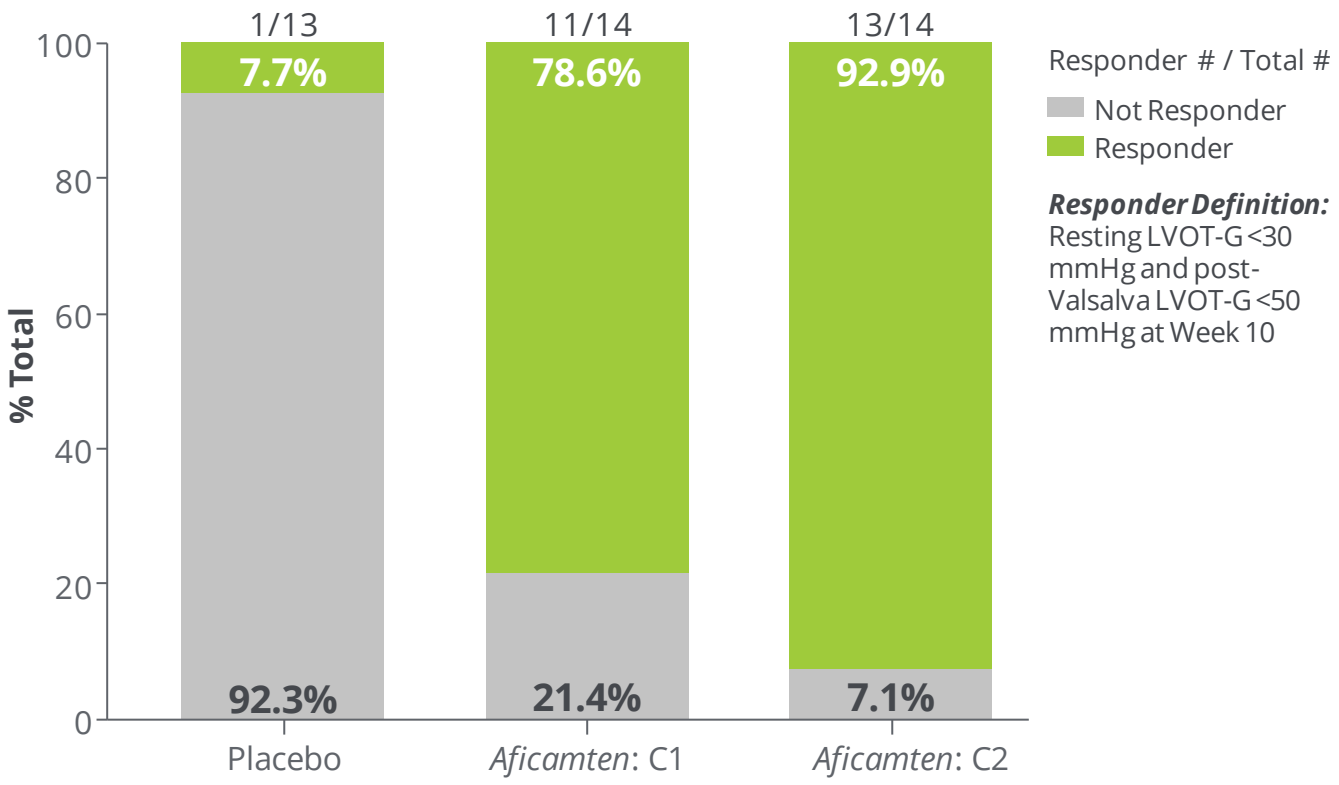
Phase 2 Clinical Trial Design

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

Response Rates on Treatment with *Aficamten*

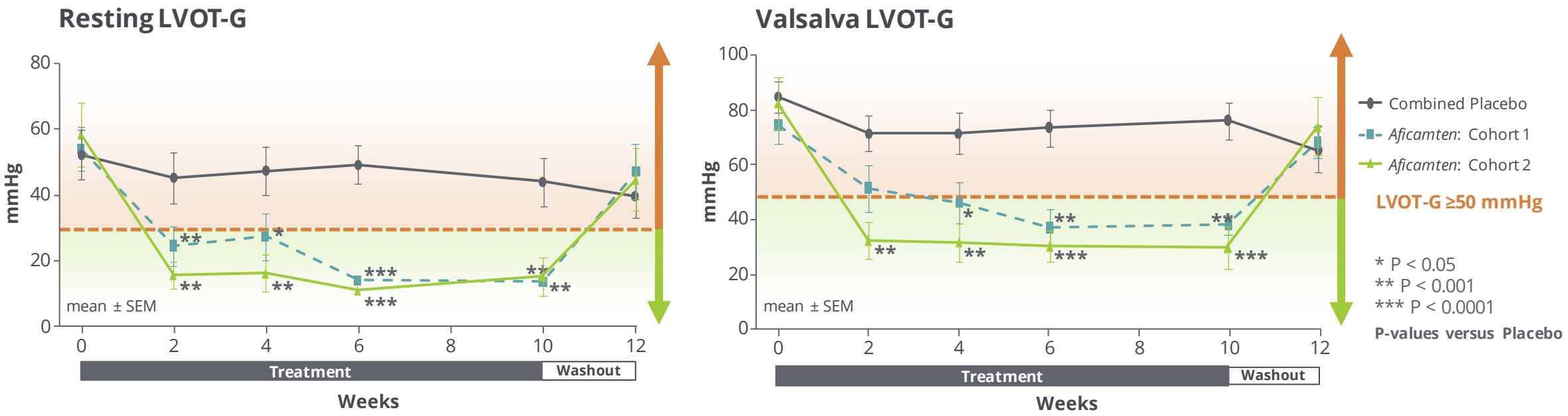


- Consistent, **clinically meaningful reductions in LVOT gradients** within two weeks
- **No treatment interruptions** or discontinuations
- No treatment-related SAEs
- **Reversibility of drug effect** demonstrated
- Statistically significant reductions in NT-proBNP
- Improvement in NYHA class

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"
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: Efficacy

Reductions in LVOT gradients

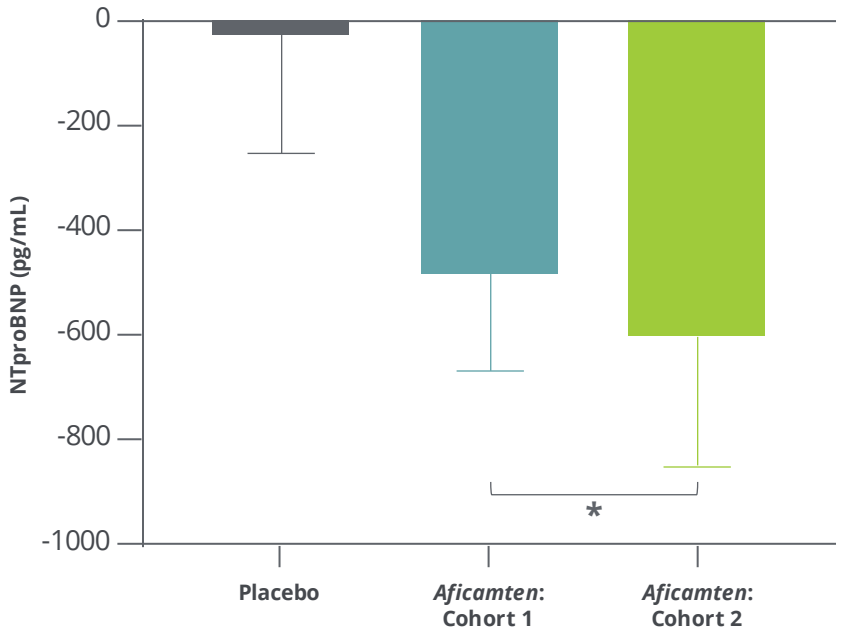


Dose finding study
Cohort 1 (n=21), Cohort 2 (n=20)

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

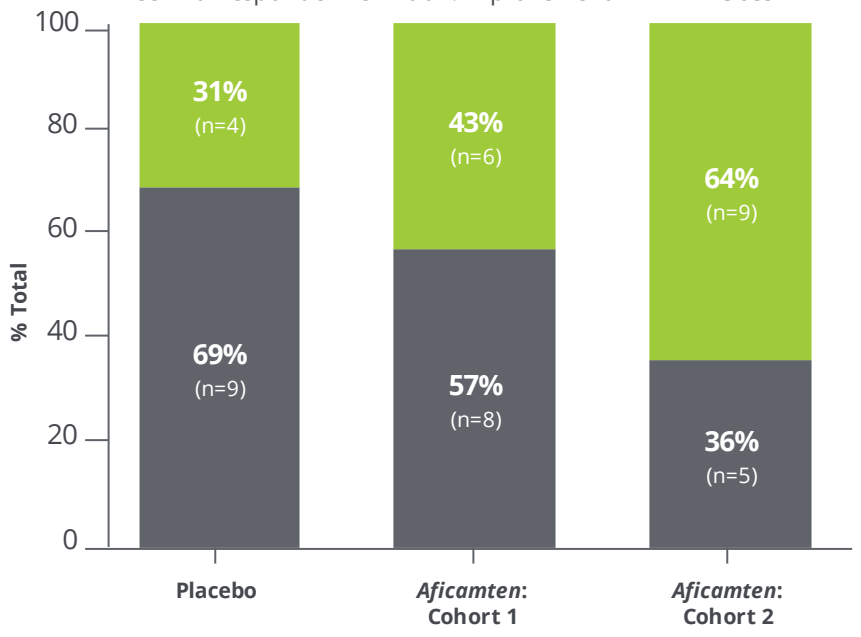


*** p = 0.003 for Pooled Cohort 1 & 2 vs. Placebo**

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*

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

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

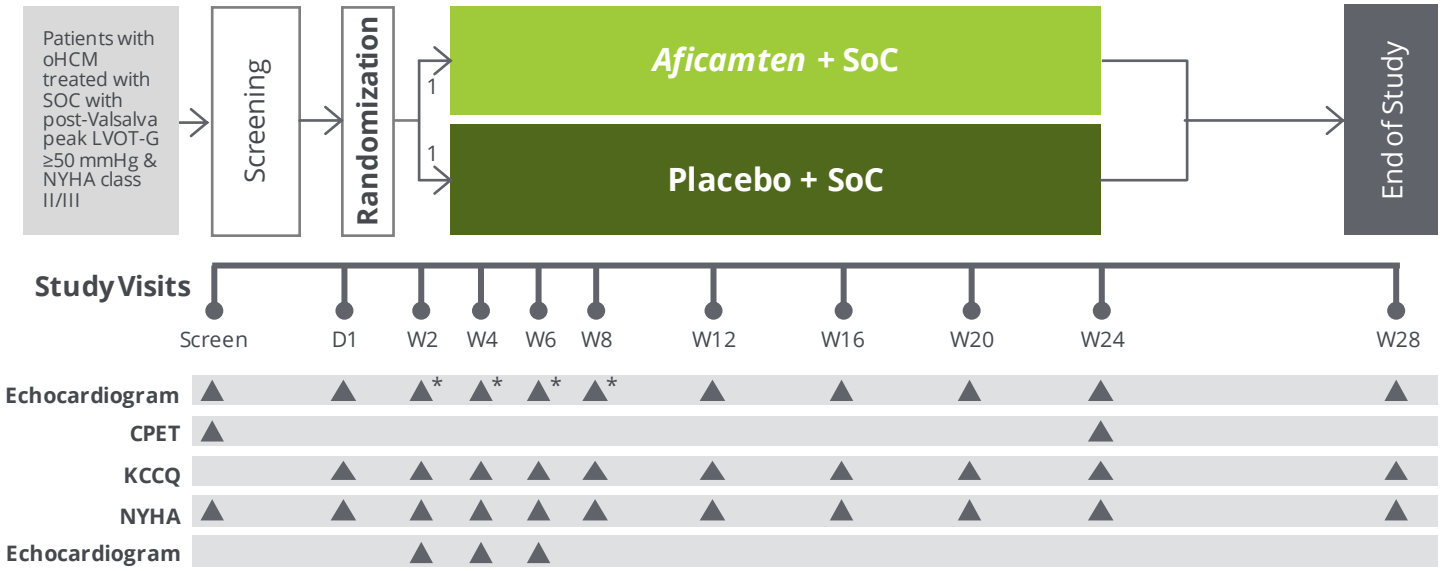
Start-up activities underway

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 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

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 potential U.S. launch of *omecamtiv mecarbil*, enable geographic expansion & partnerships, and potential 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

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.

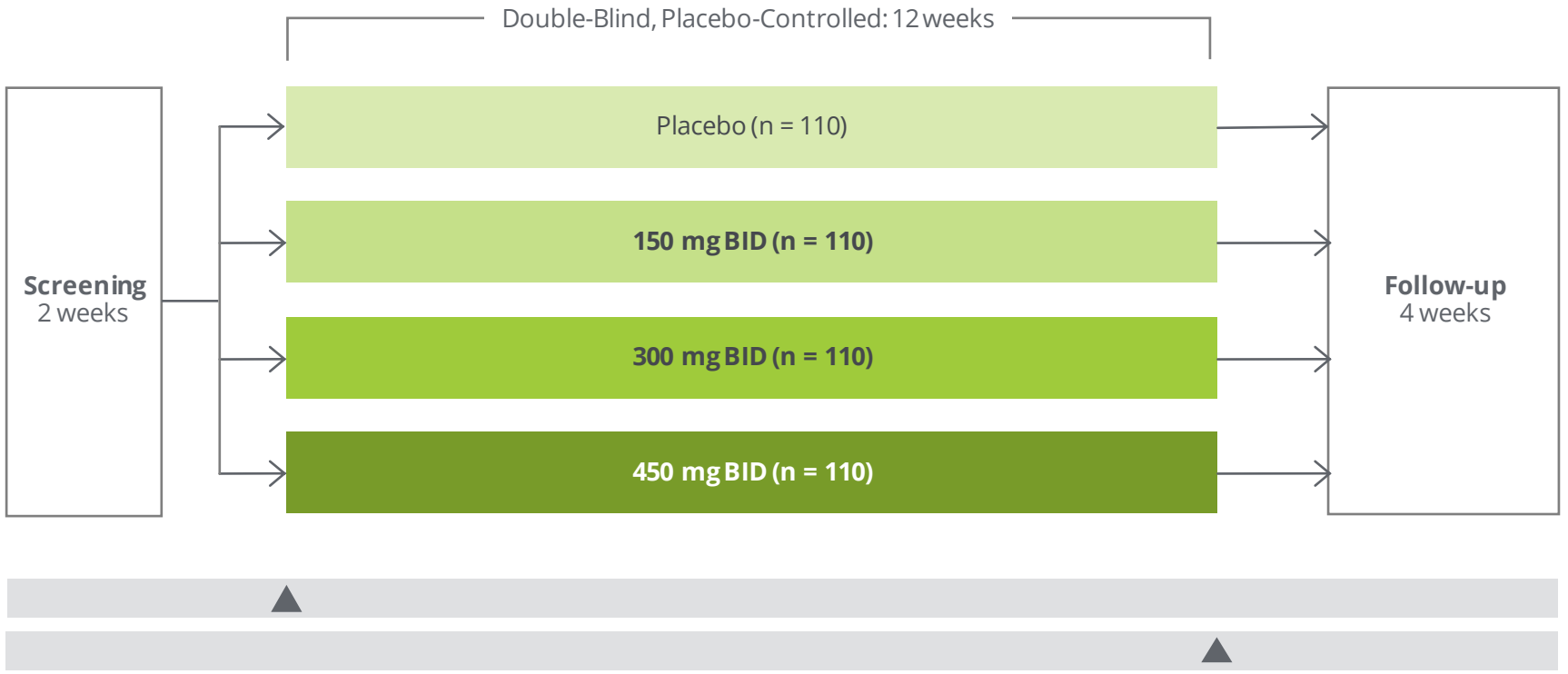
Cytokinetics

Phase 2 Clinical Trial in ALS

FORTITUDE ALS

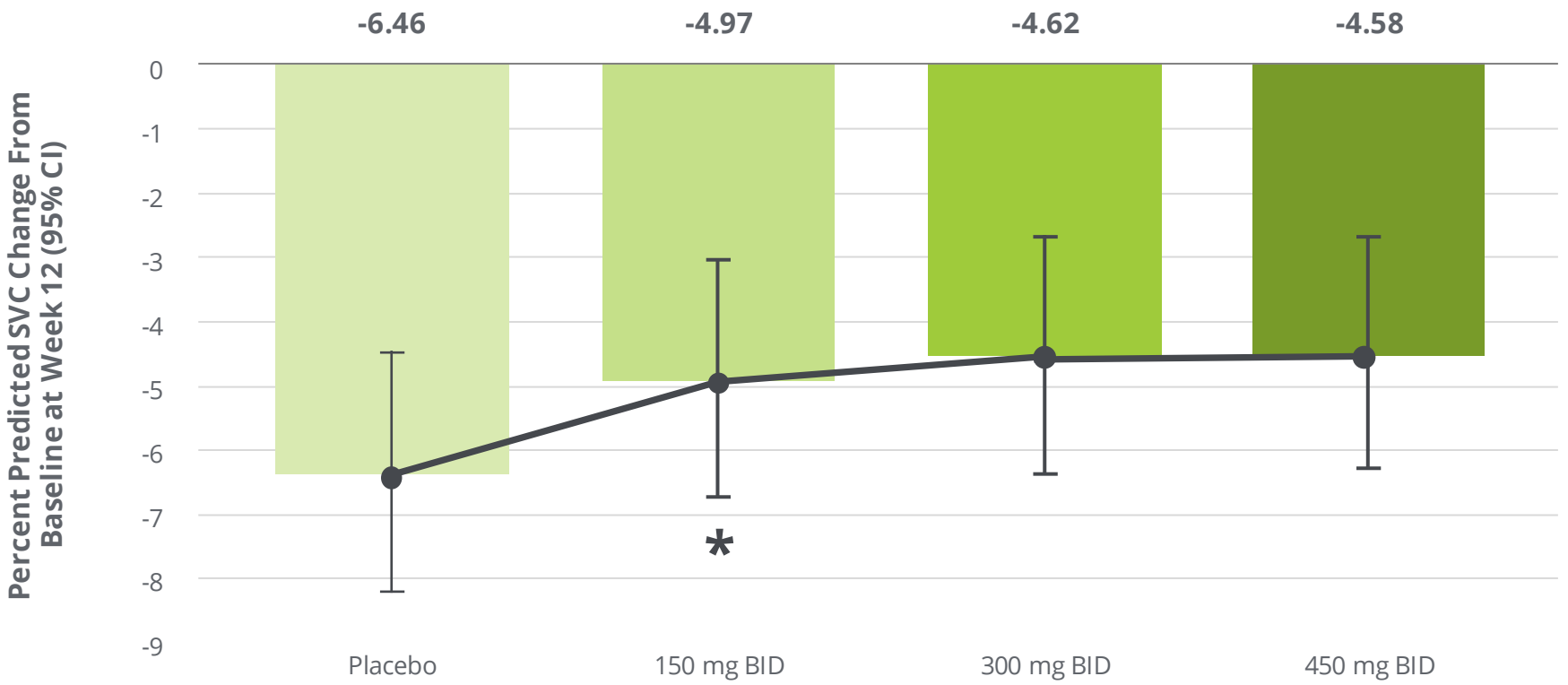
Results presented at American Academy of Neurology 2019 Annual Meeting

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

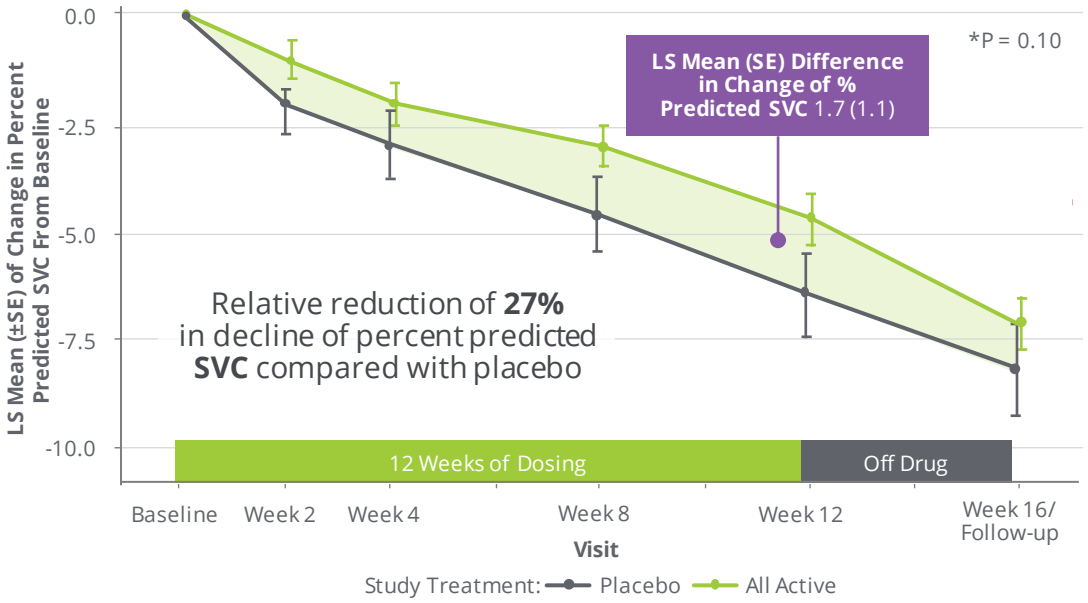
*Based on Mixed Model for Repeated Measures (MMRM) with the contrasts of (-5, -1, 3, 3) for placebo, *reldesemtiv* 150 mg, 300 mg and 450 mg BID, respectively

Change From Baseline: All Active vs Placebo*

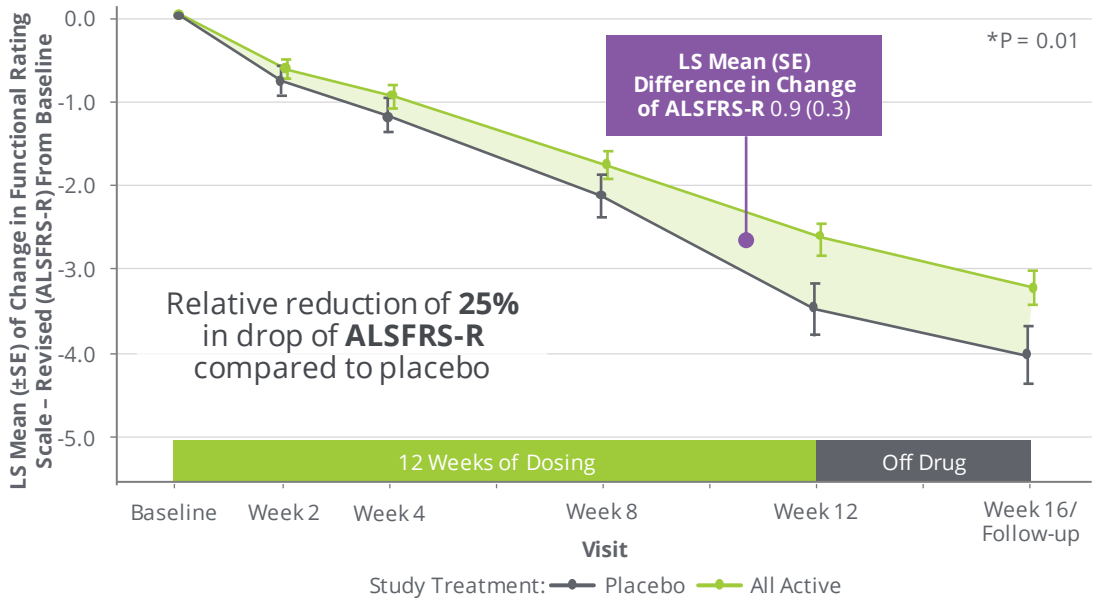
FORTITUDE ALS

Results support progression to potential Phase 3 clinical trial

SVC Change From Baseline
(All Active vs Placebo)



ALSFRS-R Change From Baseline
(All Active vs Placebo)



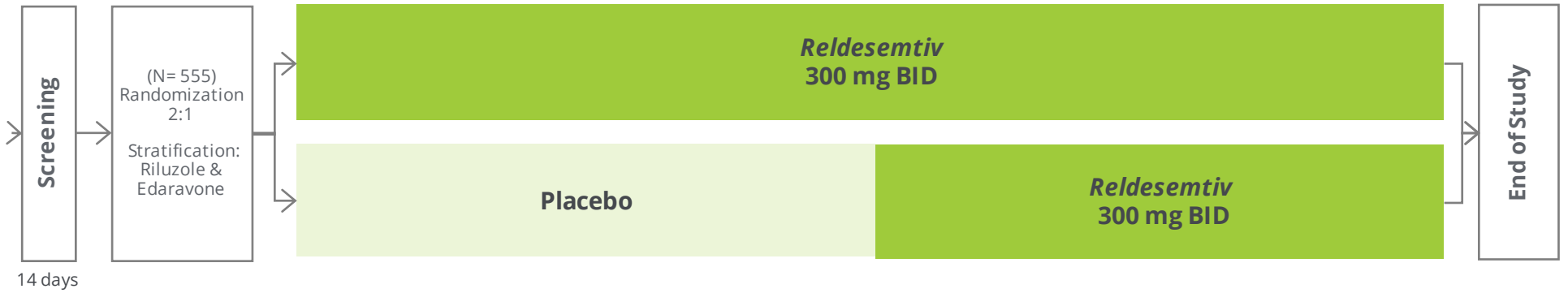
*post hoc analysis
FORTITUDE-ALS did not achieve statistical significance, but patients on all dose groups of *reldesemtiv* declined less than patients on placebo

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	↑	↑		↑		↑			↑				↑			↑	↑

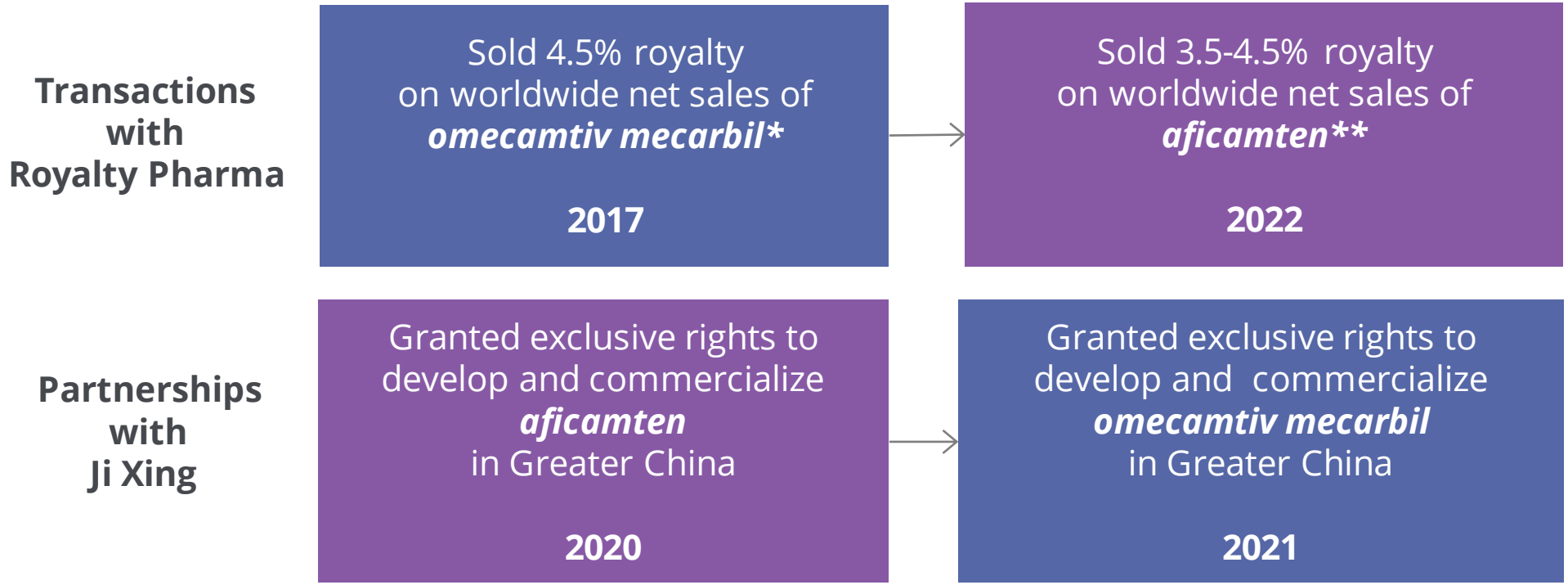
↑ In-Clinic ↑ Remote ↑ Both In-Clinic & Remote

Financial Outlook

Cytokinetics

Monetizing Our Pipeline to Bolster Balance Sheet

Symmetry of deals for *omecamtiv mecarbil* and *aficamten* affords symmetry for development and potential launches and supports franchise strategy



* 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 and 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

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.