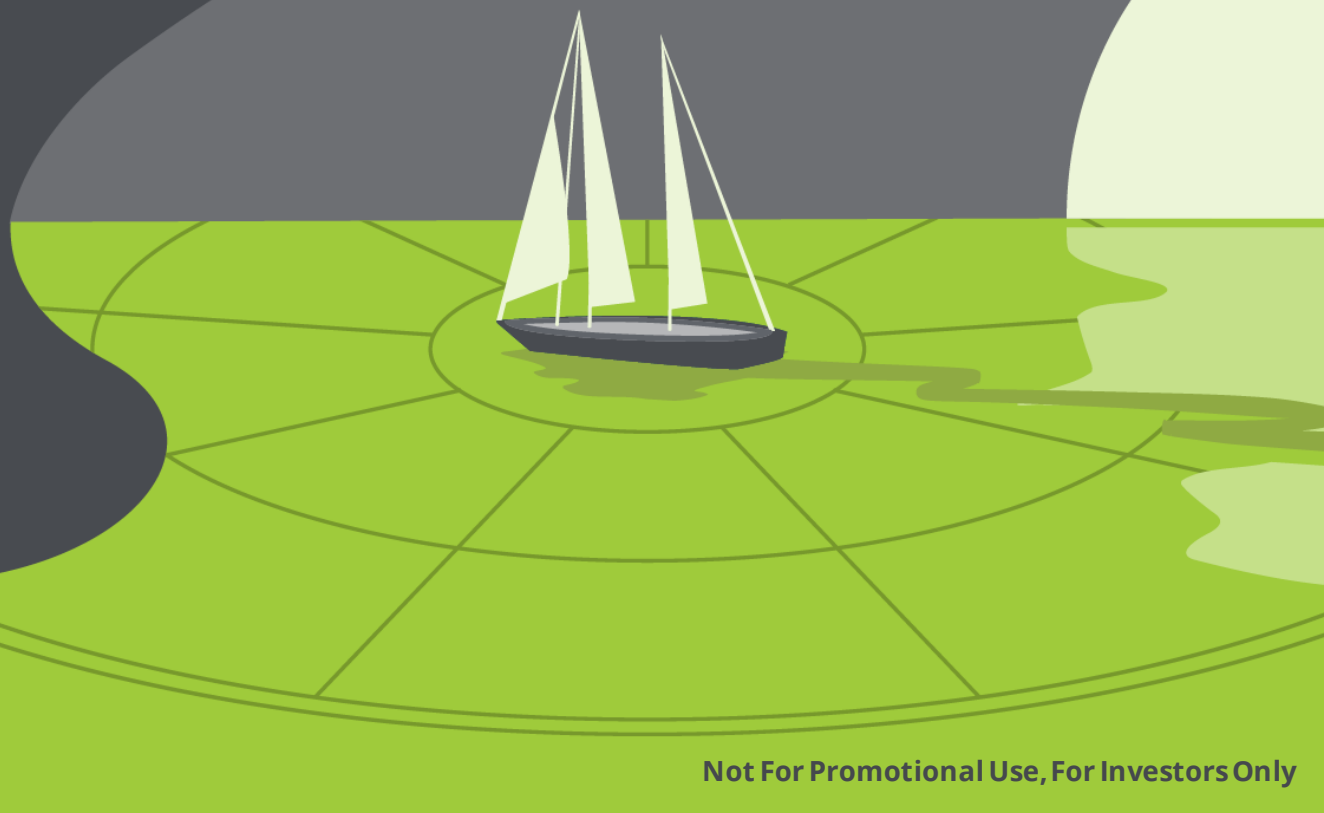
Cytokinetics

CHARTING THE COMMERCIAL COURSE

Analyst & Investor Day 2021

Program to begin at 8:30 AM ET



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 of a new drug application (NDA) to the FDA for *omecamtiv mecarbil* in 2021; the timing of commencement of COURAGE-ALS, a phase 3 clinical trial of *reldesemtiv* or the timing of commencement of a phase 3 clinical trial of *aficamten*; the timing of any potential commercial launch of our product candidates, if approved; commercial opportunities for our product candidates; Cytokinetics' cash runway, cash balances and estimated cash expenditures; interactions with the FDA; 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")

Company Speakers

Robert Blum
President & CEO

Fady Malik, M.D., Ph.D.
EVP, Research & Development

Andrew Callos
EVP, Chief Commercial Officer

Stuart Kupfer, M.D.
SVP, Chief Medical Officer

Ching Jaw
Chief Financial Officer

Jennifer Laux
VP, Cardiovascular Marketing

Diann Potestio
VP, Global Value, Access & Distribution

Steve Heitner, M.D.
Senior Medical Director, Clinical Research, Cardiovascular

Joanna Siegall
Senior Manager, Corporate Communications & Investor Relations

Expert Panel

Alanna Morris, MD MSc, FHFSA, FACC, FAHA
Associate Professor of Medicine, Division of Cardiology; Director of Heart Failure Research, Emory University Clinical Cardiovascular Research Institute

Tariq Ahmad, MD, MPH
Associate Professor of Medicine; Medical Director of Advanced Heart Failure, Cardiovascular Medicine, Yale School of Medicine

Charting the Commercial Course: Today's Agenda

Topic	Presenter
Intro	Joanna Siegall
Welcome	Robert Blum
Heart Failure Landscape	Fady Malik, MD, PhD
***Omecamtiv Mecarbil*: GALACTIC-HF**	Stuart Kupfer, MD
Expert Panel Discussion	Tariq Ahmad, MD, Alanna Morris, MD
***Omecamtiv Mecarbil*: Filling an Unmet Patient Need**	Andrew Callos
US Go-to-Market Strategy	Andrew Callos, Jennifer Laux, Diann Potestio
Q&A	
Break (approx. 10:15 AM)	
HCM Landscape	Andrew Callos
***Aficamten*: Potential Next-in-Class Therapy**	Steve Heitner, MD
Franchise Strategy	Andrew Callos
Financial Foundation & Corporate Development	Ching Jaw
Q&A	
Closing Remarks	Robert Blum

Engaging in Today's Meeting

In Person Attendees:

- **Masks**: Masks are not required for those who are fully vaccinated. However, we encourage mask wearing whenever you are not eating or drinking.
- **Refreshments**: Please help yourself to coffee and breakfast. We will have boxed lunches available for all attendees at the end of our program.
- **Questions**: To ask a question please raise your hand and we will bring a microphone to you.

Online Attendees:

- **Resources**: Use the tabs to the left to view speaker bios, the event agenda and supplementary resources.
- **Questions**: To ask a question type your question into the tab called "Ask a Question". Questions will be relayed to our team in the room during the event.
- **Technical Issues**: Visit the "Help Desk" tab for support related to any technical issues.

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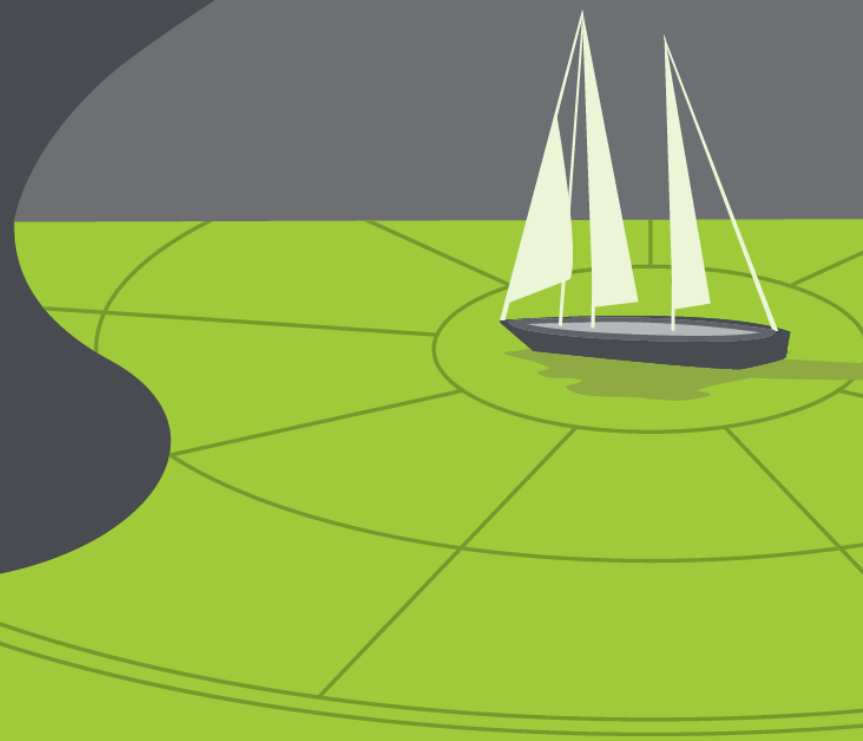
Introduction

Robert Blum, President & CEO



Sarcomere Directed Therapies

OUR MISSION

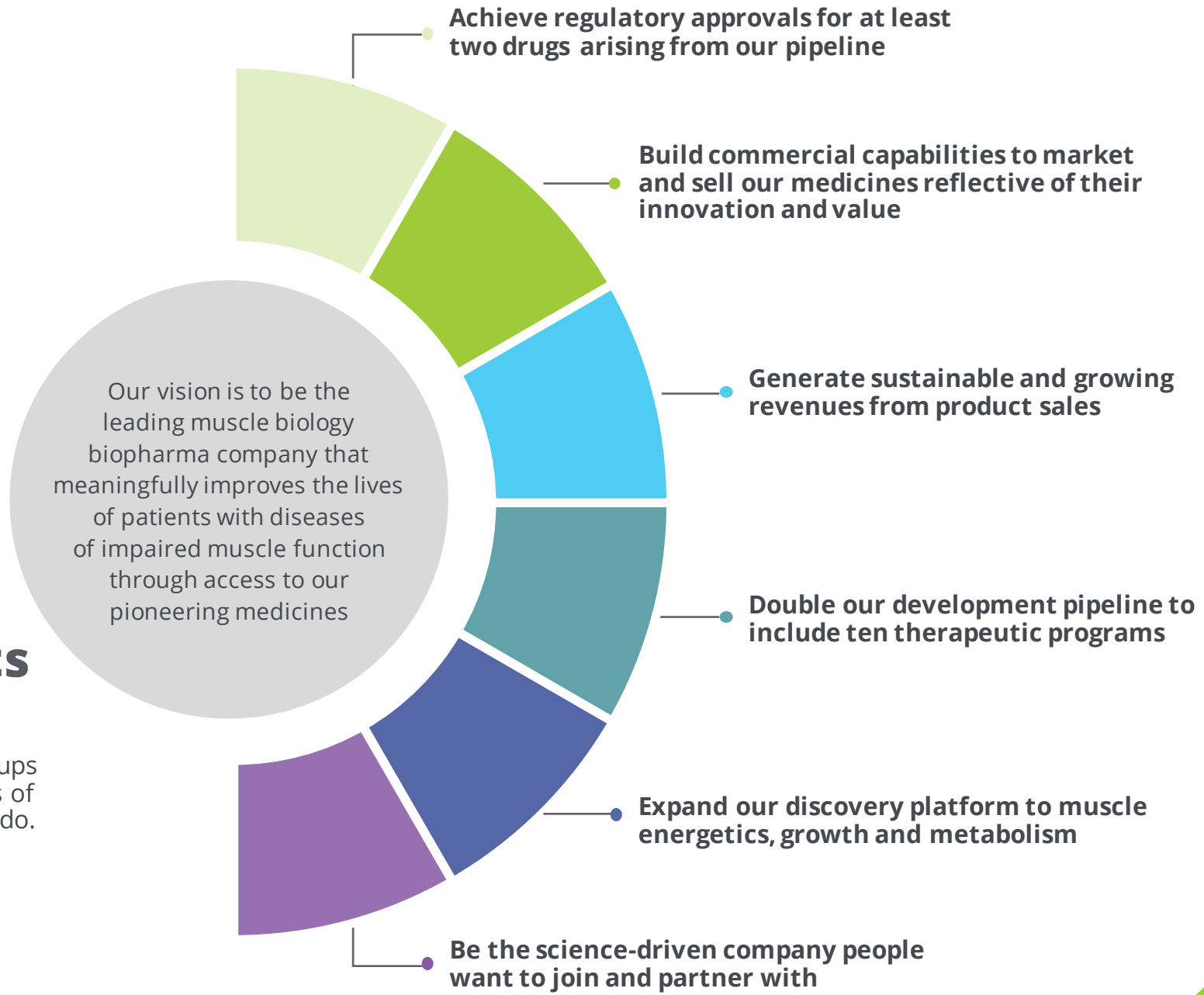
To bring forward new medicines to improve the healthspan of people with devastating cardiovascular and neuromuscular diseases of impaired muscle function.

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

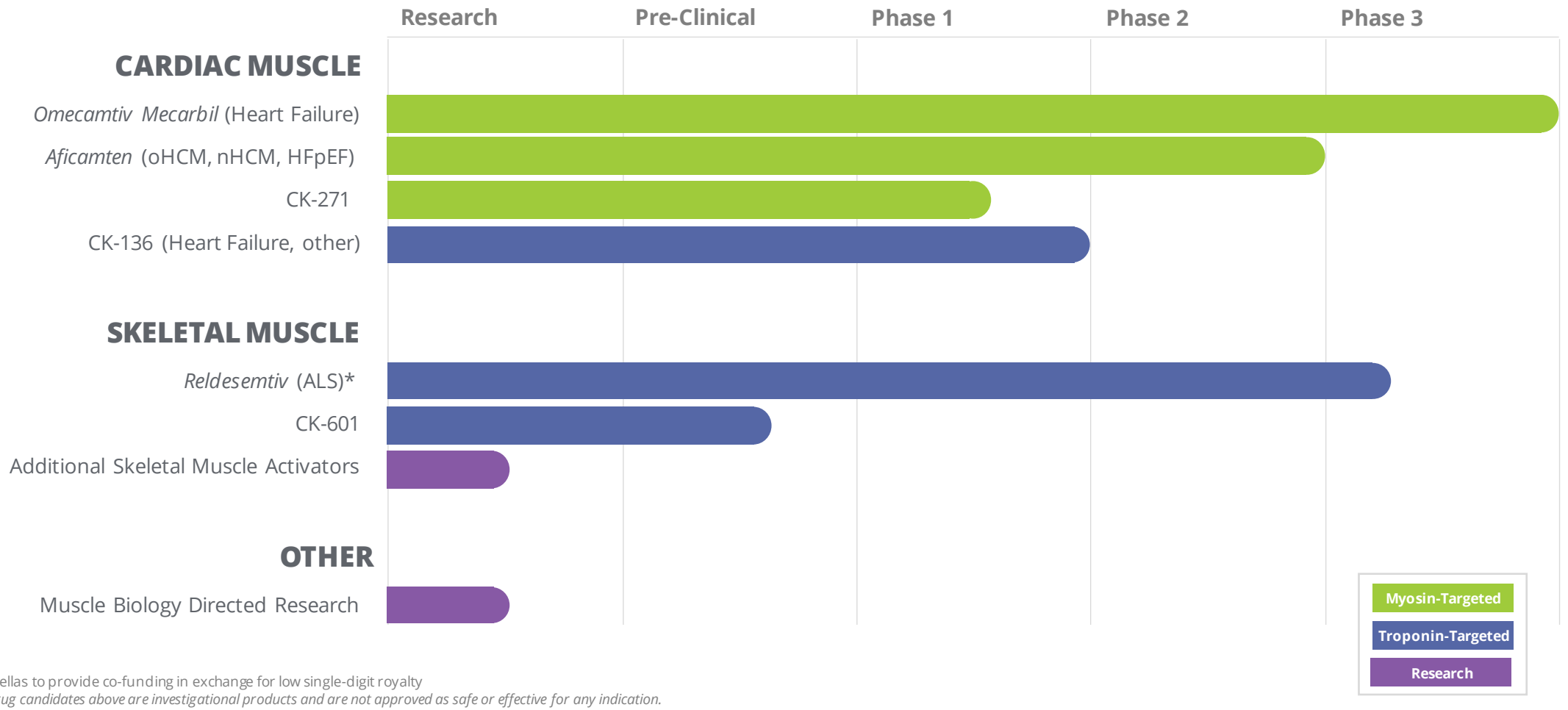
- Scientific innovation driven by modulating cardiac myosin
- First-in-class myosin activator
- Next-in-class myosin inhibitor
- Expansion beyond contractility to muscle energetics, metabolism

- 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; NDA submission expected in 2H 2021
- Reported positive Phase 2 results from REDWOOD-HCM; Phase 3 clinical trial expected by year-end
- Clinical trial results from METEORIC-HF expected in early 2022

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

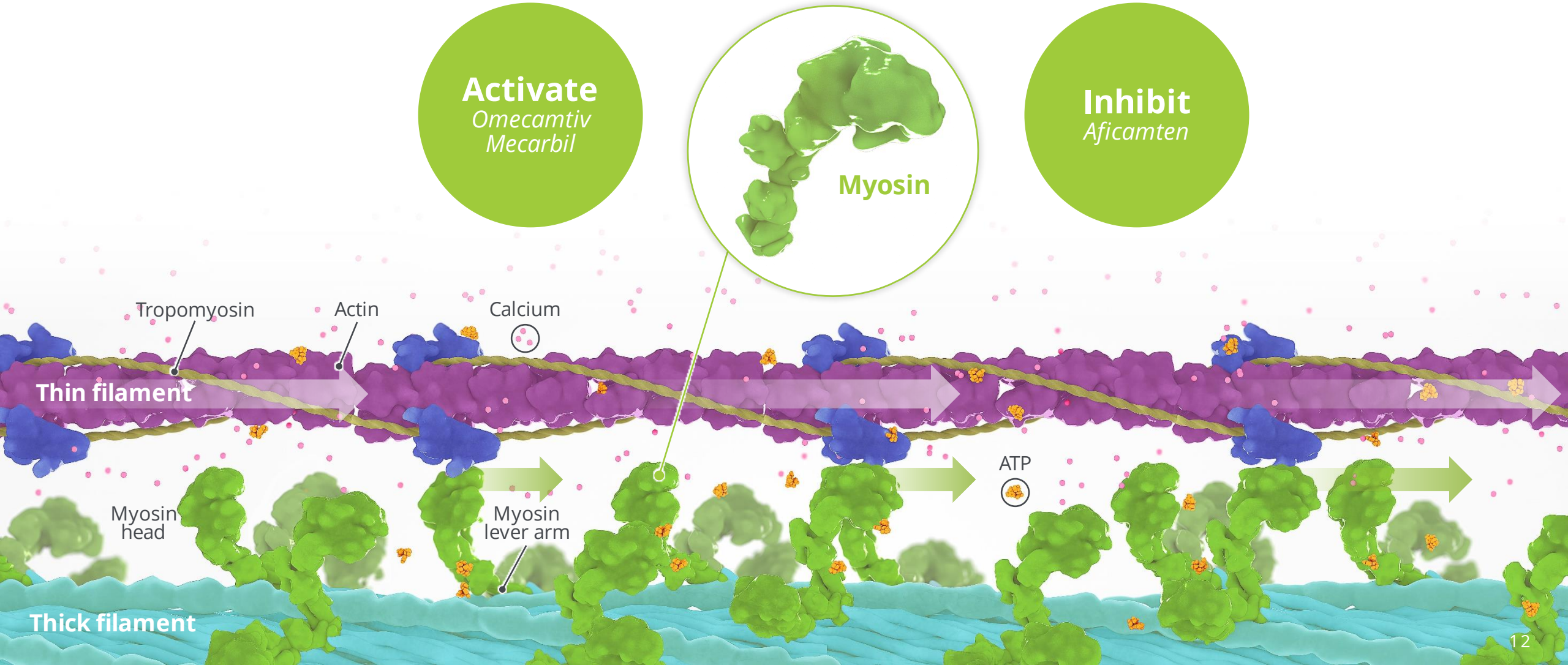
Pipeline of Novel Muscle-Directed Drug Candidates



* 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.

One Molecular Target Supports Emerging CV Franchise



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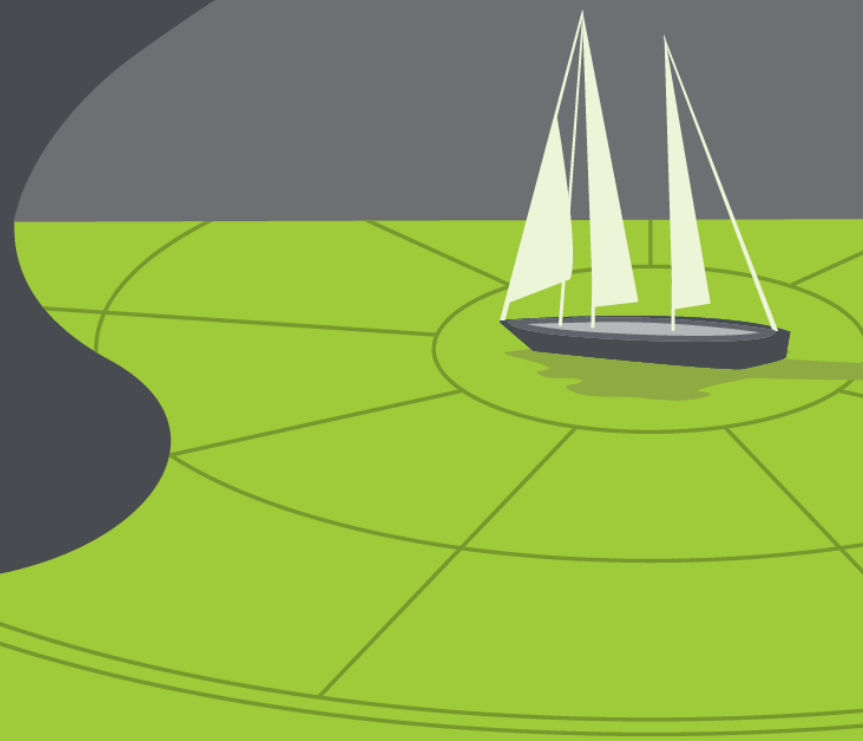
HF Treatment Landscape

Fady Malik, M.D., Ph.D.

EVP, Research & Development

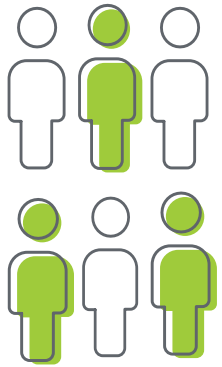


Heart Failure Is a Public Health Emergency

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

46%

Increase in Americans living with HF through 2030 owing to aging population and decline in mortality[1]



50%

HF patients who will die within 5 years[1]

127%

Cost increase of HF through 2030
(increasing from $43.6[2] billion to $69.7 billion)3

HF: heart failure

1. Benjamin EJ, et al. *Circulation*. 2018;137:e67-e492;
1. Urbich, M., Globe, G., Pantiri, K. et al. A Systematic Review of Medical Costs Associated with Heart Failure in the USA (2014–2020). PharmacoEconomics 38, 1219–1236 (2020). https://doi.org/10.1007/s40273-020-00952-0
2. Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail. 2013;6(3):606–19. https://doi.org/10.1161/HHF.0b013e318291329a.

Hospitalization & Rehospitalization Rates Are Burdensome

Despite treatment advances, nearly 50% of patients are readmitted to the hospital within 5 years[3,b]

~900,000

Annual HF hospitalizations in the US[1]

24%

Patients readmitted to hospital within 30 days[2,a]

49%

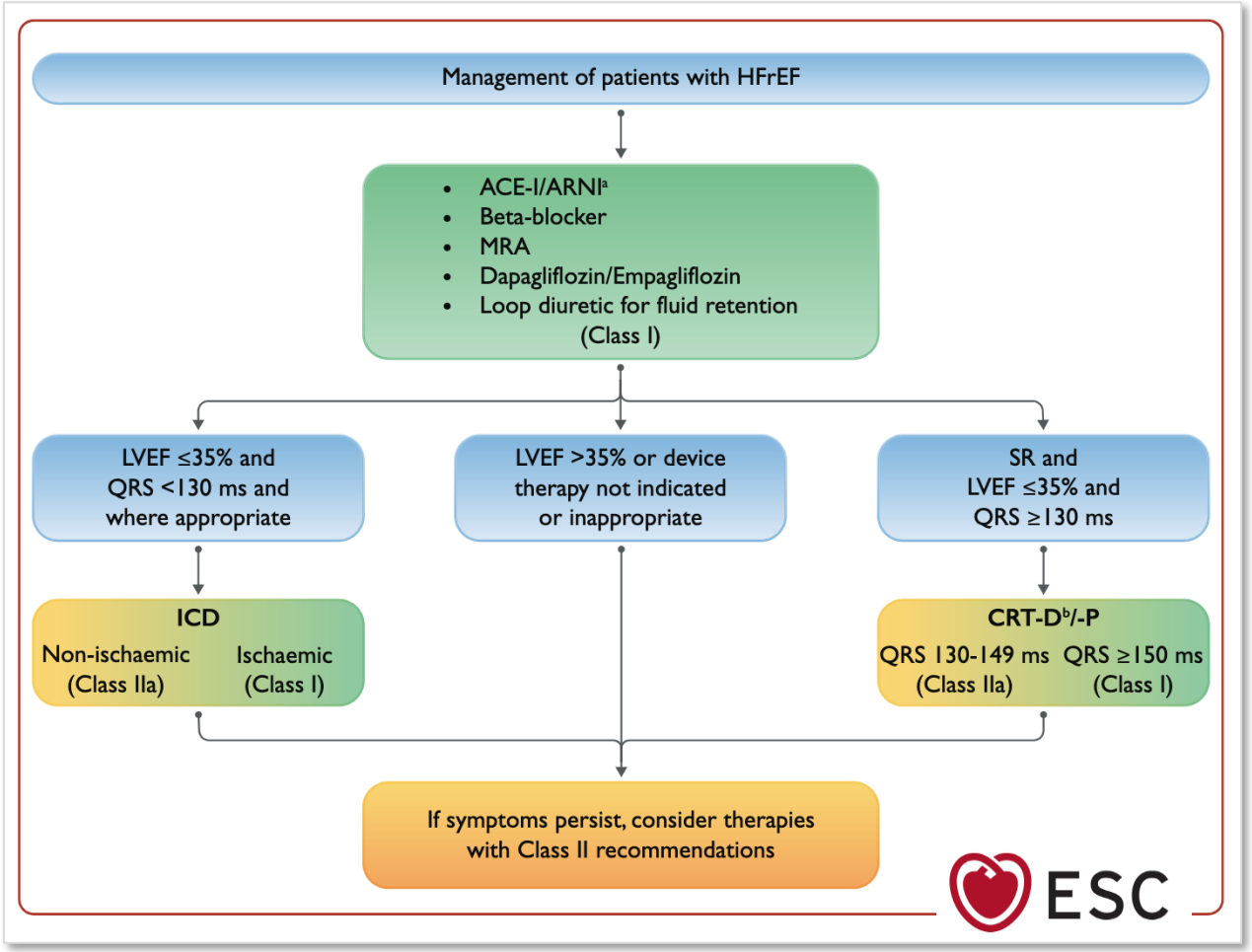
Patients readmitted to hospital within 5 years[3,b]

HF, heart failure; HFbEF, heart failure with borderline ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.

1. Benjamin EJ, et al. *Circulation*. 2019;139:e56-e528;
2. 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).
3. 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

Foundational GDMT – Problem Solved?

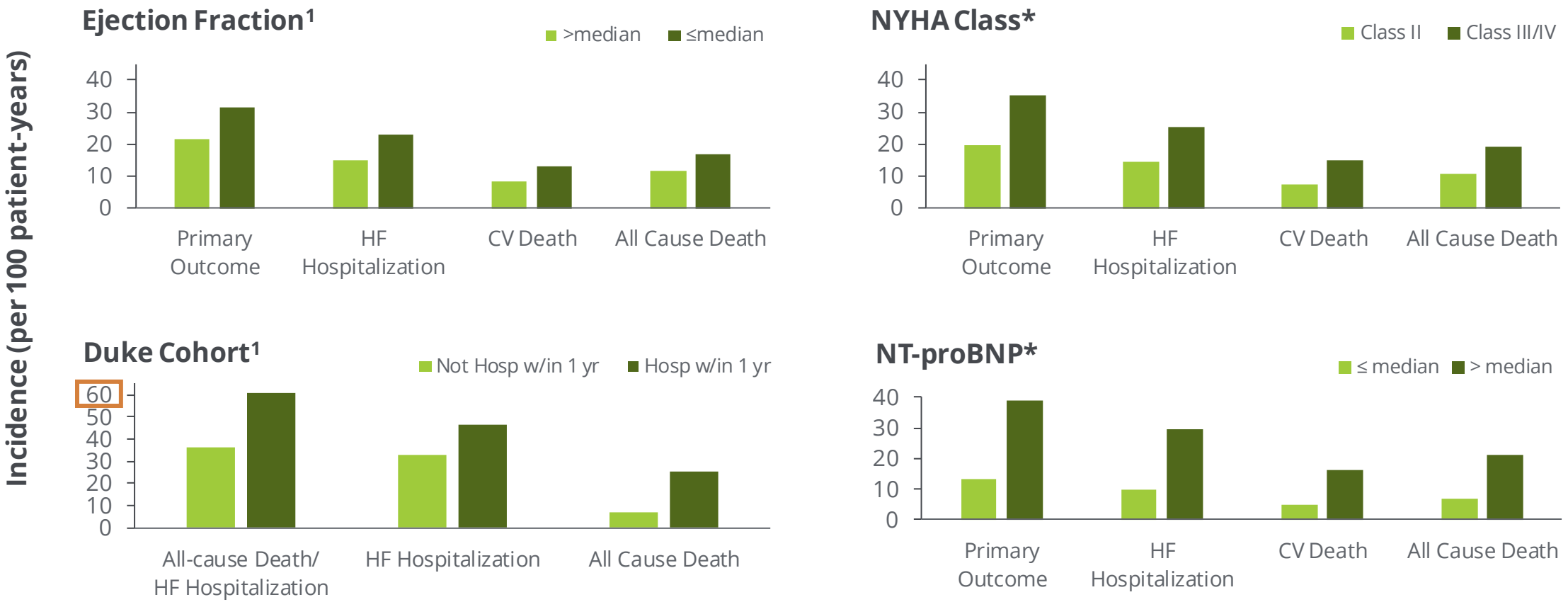
2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure



GDMT: Guideline directed medical therapy
Source: *Eur Heart J.* 2021 Sep 21;42(36):3599-3726.

Not Yet – Event Rates in HFrEF Remain Startling High

Event Rates in Placebo Group of GALACTIC-HF on Excellent GDMT

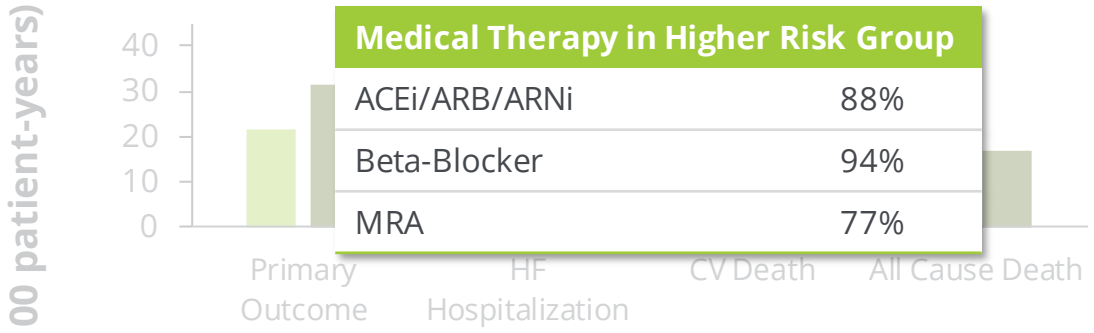


1. Teerlink J et al, JACC 2021
2. Carnicelli AP et al, J Am Heart Assoc, 2021
*Cytokinetics, Data on File

Not Yet – Event Rates in HFrEF Remain Startling High

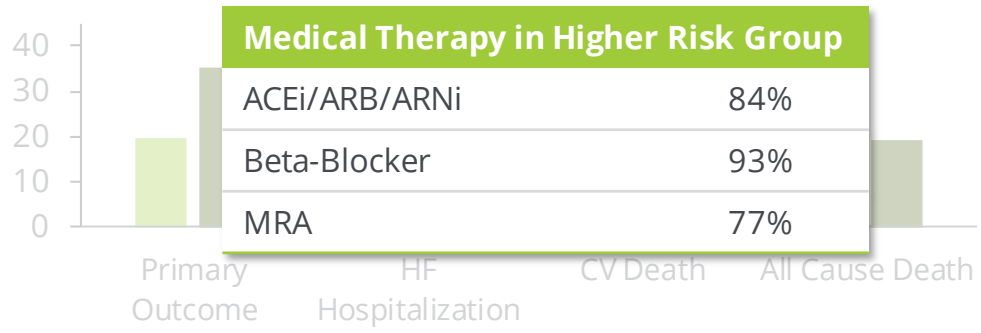
Event Rates in Placebo Group of GALACTIC-HF on Excellent GDMT

Ejection Fraction[1]



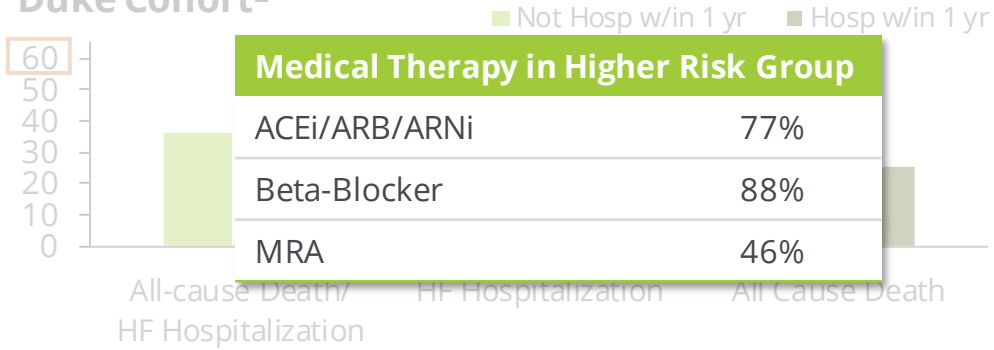
Medical Therapy in Higher Risk Group	
ACEi/ARB/ARNi	88%
Beta-Blocker	94%
MRA	77%

NYHA Class*



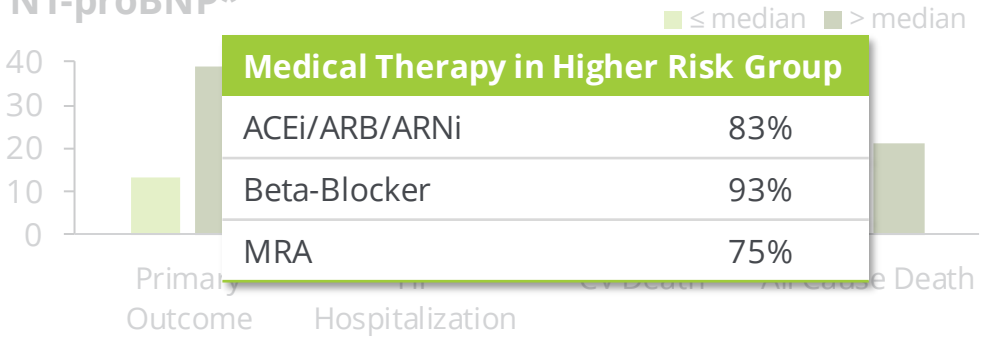
Medical Therapy in Higher Risk Group	
ACEi/ARB/ARNi	84%
Beta-Blocker	93%
MRA	77%

Duke Cohort[2]



Medical Therapy in Higher Risk Group	
ACEi/ARB/ARNi	77%
Beta-Blocker	88%
MRA	46%

NT-proBNP*

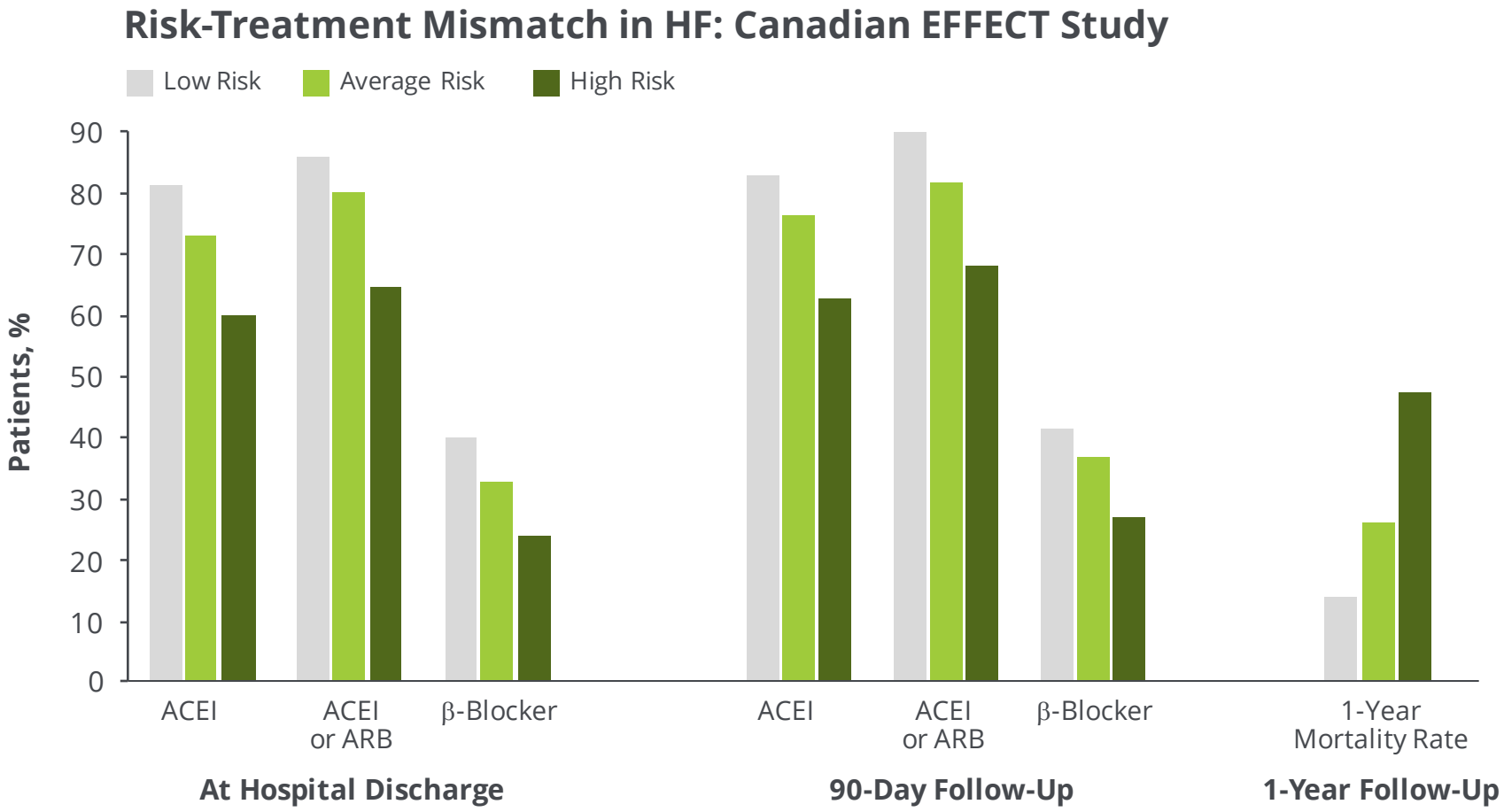


Medical Therapy in Higher Risk Group	
ACEi/ARB/ARNi	83%
Beta-Blocker	93%
MRA	75%

1. Teerlink J et al, JACC 2021
2. Carnicelli AP et al, J Am Heart Assoc, 2021
*Cytokinetics, Data on File

Higher Risk Patients Tolerate Less GDMT

The sickest patients are the most difficult to treat with GDMT



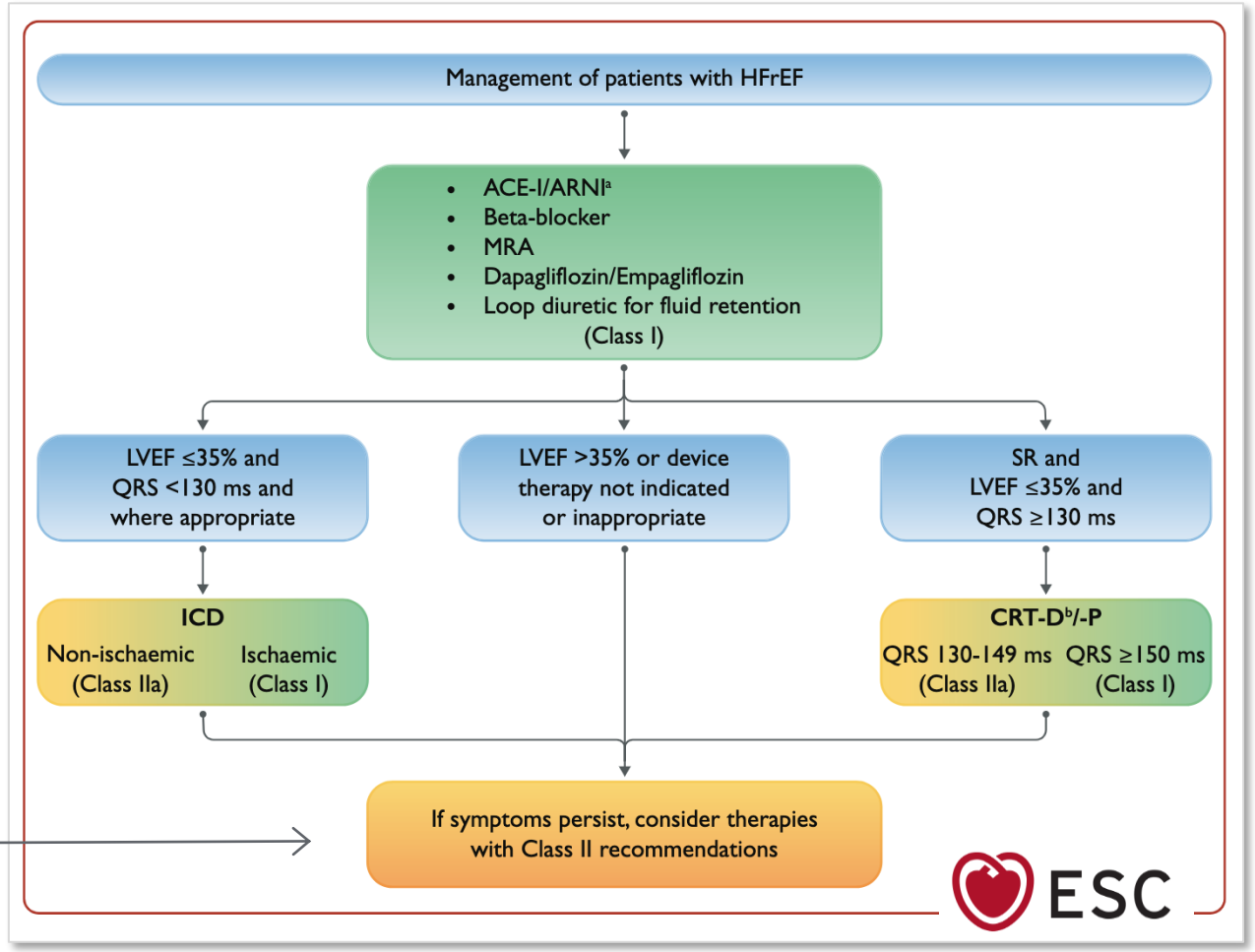
GDMT limitations

- Renal Dysfunction
- Azotemia
- Hypotension
- Hyperkalemia
- Angioedema
- Bradycardia
- Fatigue

Lee D. *JAMA*. 2005;294:1240-1247

After Foundational GDMT – What Next?

Patients with worsening HF need alternatives



GDMT: Guideline directed medical therapy
Eur Heart J. 2021 Sep 21;42(36):3599-3726.

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**

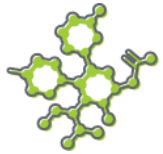
Drugs that do not affect renal function

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

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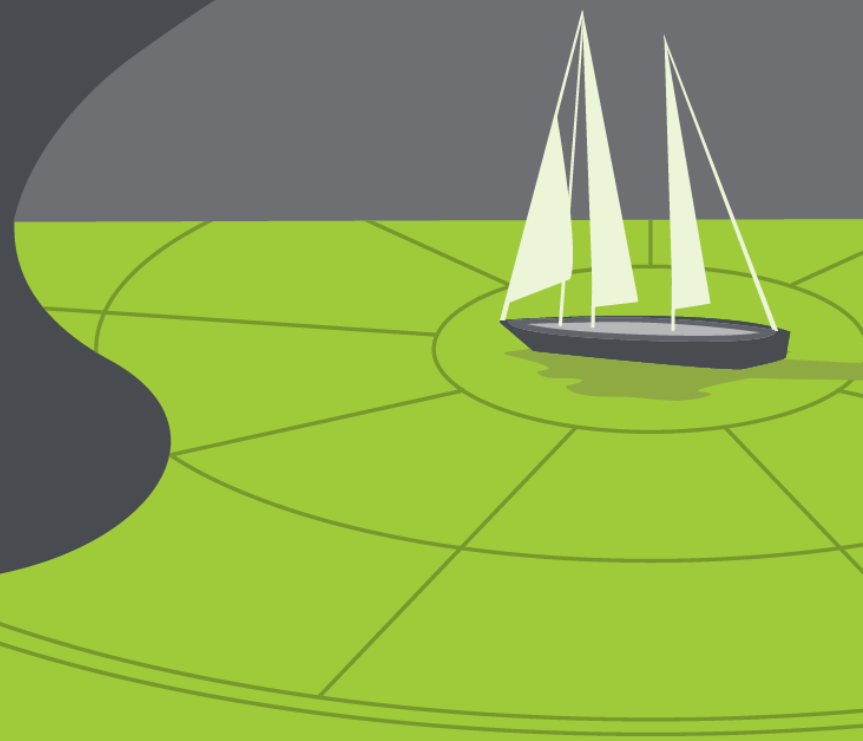
Omecamtiv Mecarbil:

GALACTIC-HF

Stuart Kupfer, M.D., SVP, Chief Medical Officer



Pivotal Phase 3 Trial Design

GALACTIC-HF

Landmark clinical trial results published in NEJM

Overview
Enrolled 8,256 patients at ~1,000 sites in 35 countries
Primary Endpoint
Composite of time to cardiovascular (CV) death or first HF event*, whichever occurs first
Secondary Endpoints
• Time to CV death • Change in Kansas City Cardiomyopathy Questionnaire Total Symptoms Score (KCCQ TSS) from baseline to Week 24 • Time to first HF hospitalization • Time to all-cause death

Key Design Points

- Dose optimization based on trough concentration of *omecamtiv mecarbil* at 2 weeks and 6 weeks
- High risk patients enrolled from inpatient and outpatient settings
- Designed to provide 90% statistical power to assess risk of CV death

*An HF event defined as the presentation of the subject for an urgent, unscheduled clinic/office/ED visit, or hospital admission, with a primary diagnosis of HF, where the patient exhibits new or worsening symptoms of HF on presentation, has objective evidence of new or worsening HF, and receives initiation or intensification of treatment specifically for HF (Hicks et al, 2015). Changes to oral diuretic therapy do not qualify as initiation or intensification of treatment.

Baseline Demographics

Worsening HF population with high level of GDMT

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

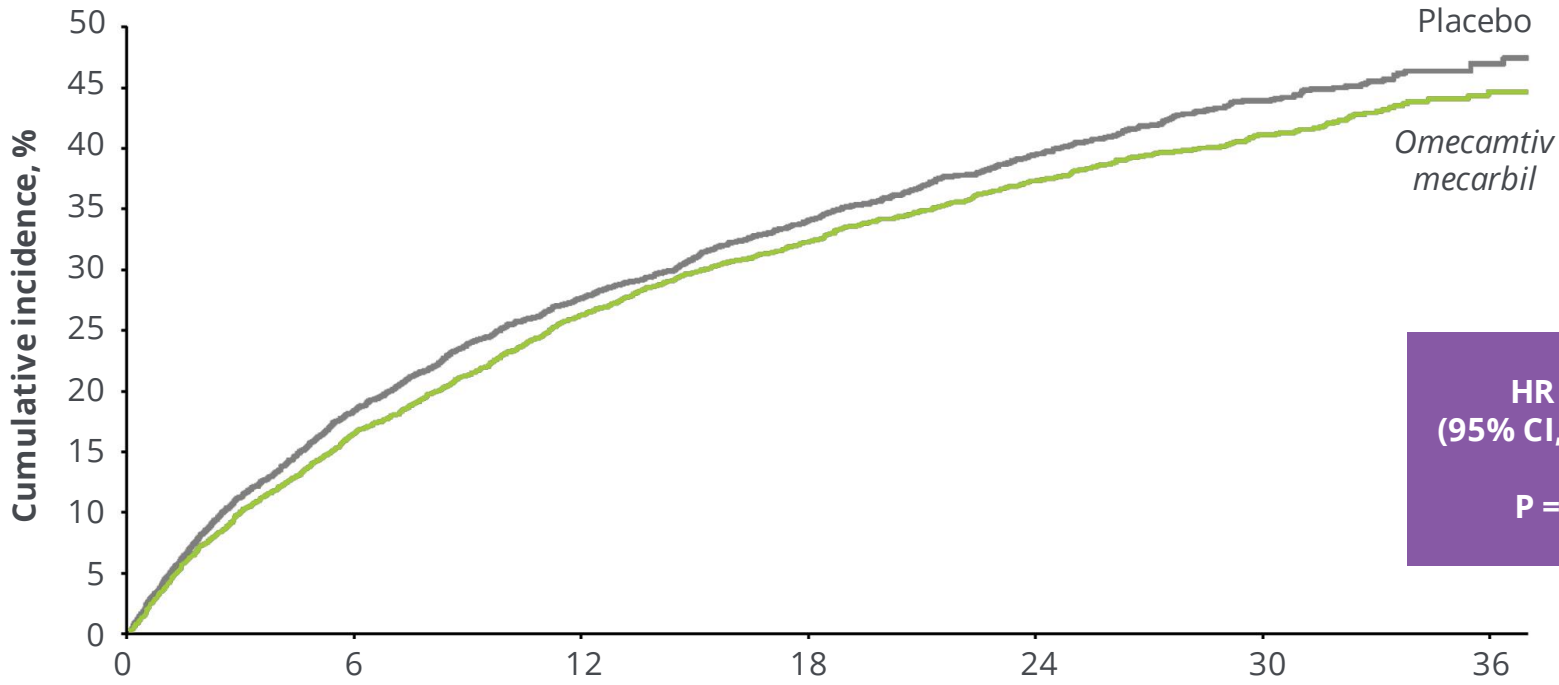
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; BB, beta blocker; CRT, cardiac resynchronization therapy; eGFR, estimated glomerular filtration rate; fib, fibrillation; hsTnI, high-sensitivity troponin I; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; Q, quartile; SBP, systolic blood pressure; SGLT2i, sodium-glucose co-transporter 2 inhibitor.

Teerlink JR et al., Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure; N Eng J Med 2020, 384:105-116.

Positive Primary Composite Endpoint

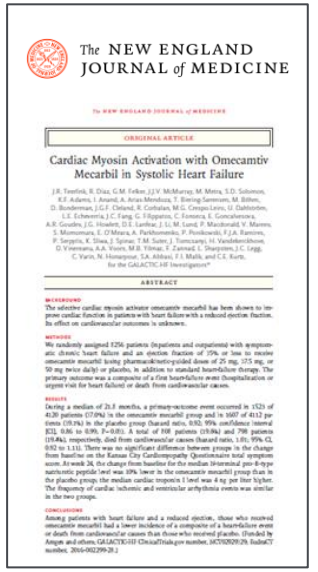
Time to first HF event or CV death – 8% relative risk reduction

GALACTIC-HF



HR = 0.92
(95% CI, 0.86–0.99)

P = 0.025


The NEW ENGLAND JOURNAL of MEDICINE

Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure

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

Teerlink JR et al., Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure; N Eng J Med 2020, 384:105-116.

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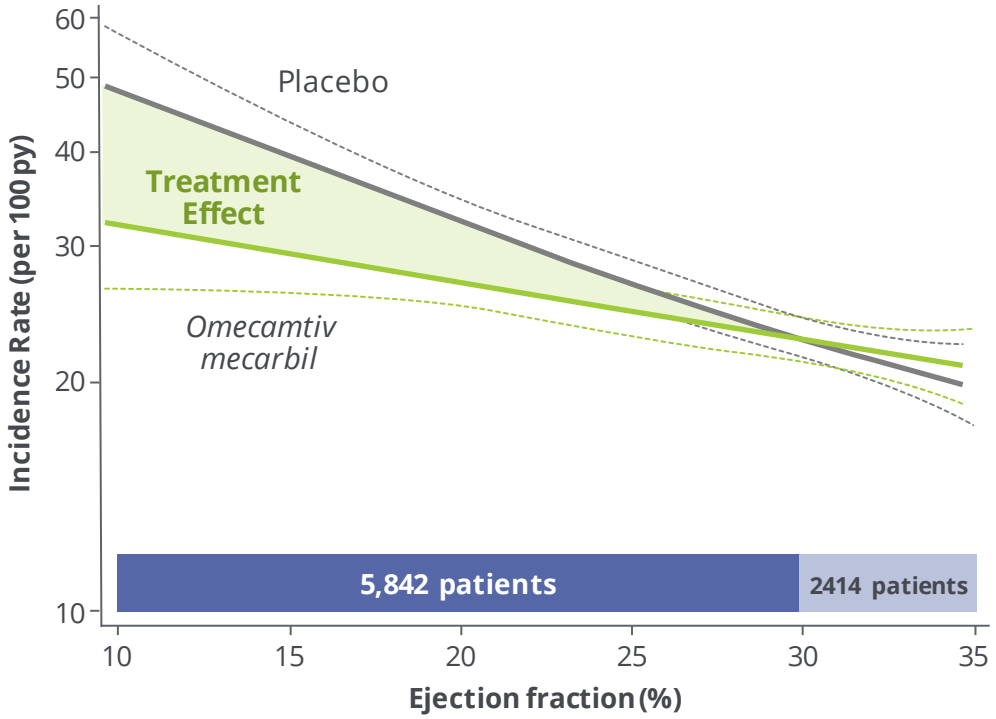
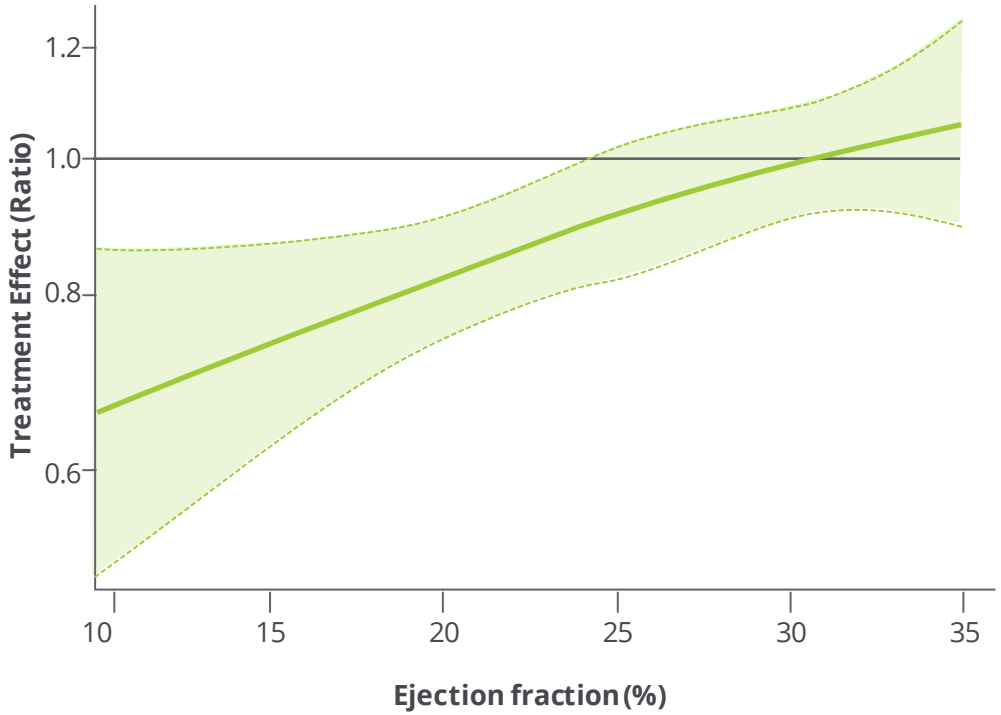
Treatment Effect Increased Progressively As Baseline LVEF Decreased

GALACTIC-HF

Incidence of Primary Composite Endpoint



Relative Treatment Effect on Primary Endpoint




JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Effect of Ejection Fraction on Clinical Outcomes in Patients treated with Omecamtiv Mecarbil in GALACTIC-HF

ARR = Absolute Risk Reduction
RRR = Relative Risk Reduction
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 with Higher NT-proBNP

GALACTIC-HF

Heart Failure & World Congress on Acute Heart Failure 2021

Primary Composite Outcome: Time to first HF event or CV death

McMurray JM, Efficacy of omecamtiv mecarbil in HFrEF according to NT-proBNP level: Insights from the GALACTIC-HF trial, ESC Heart Failure 2021, June 2021

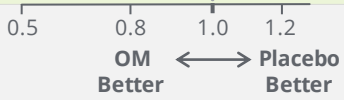
Cytokinetics

Greater Treatment Effect in Higher-Risk, Worsening HF

GALACTIC-HF

Results of the primary outcome in pre-specified subgroups showed greater treatment effect in patients with markers of worsening heart failure, including patients with LVEF ≤28%: (n=4,456) 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%



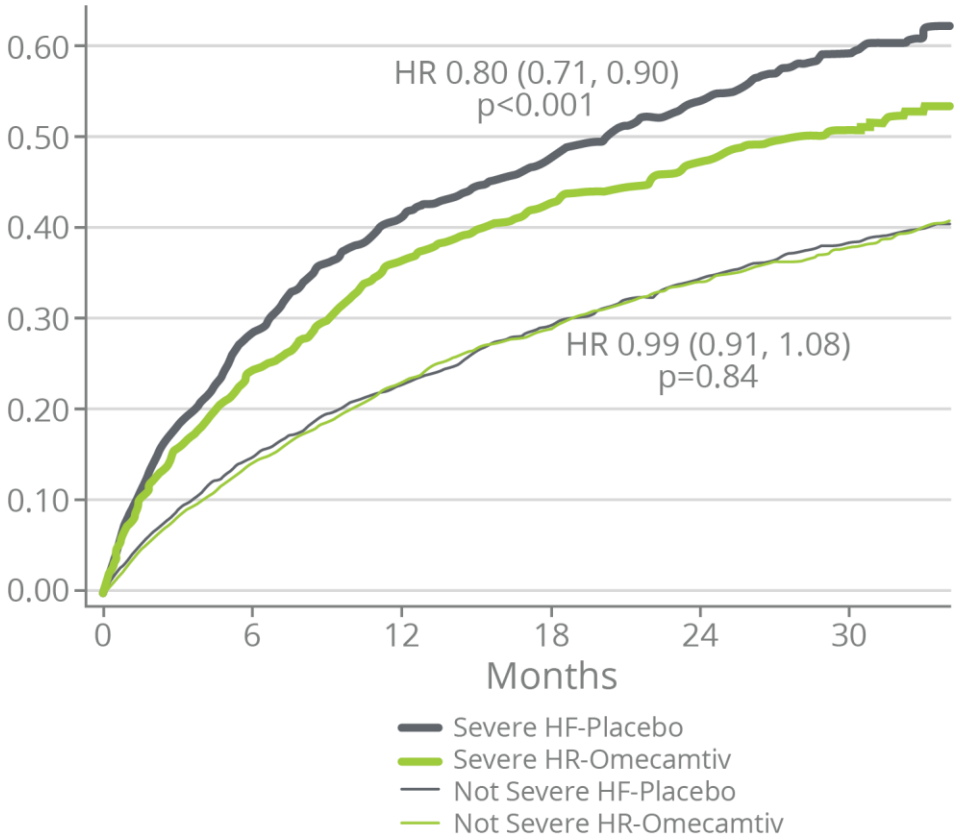
Teerlink JR et al., Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure; N Eng J Med 2020, 384:105-116.

Greater Treatment Effect in More Severe HF

Severe HF defined as NYHA III-IV, EF ≤ 30%, HF hospitalization in last 6 months

GALACTIC-HF

Heart Failure & World Congress on Acute Heart Failure 2021



Treatment effect for primary endpoint in severe HF
HR = 0.80 (0.71, 0.90)

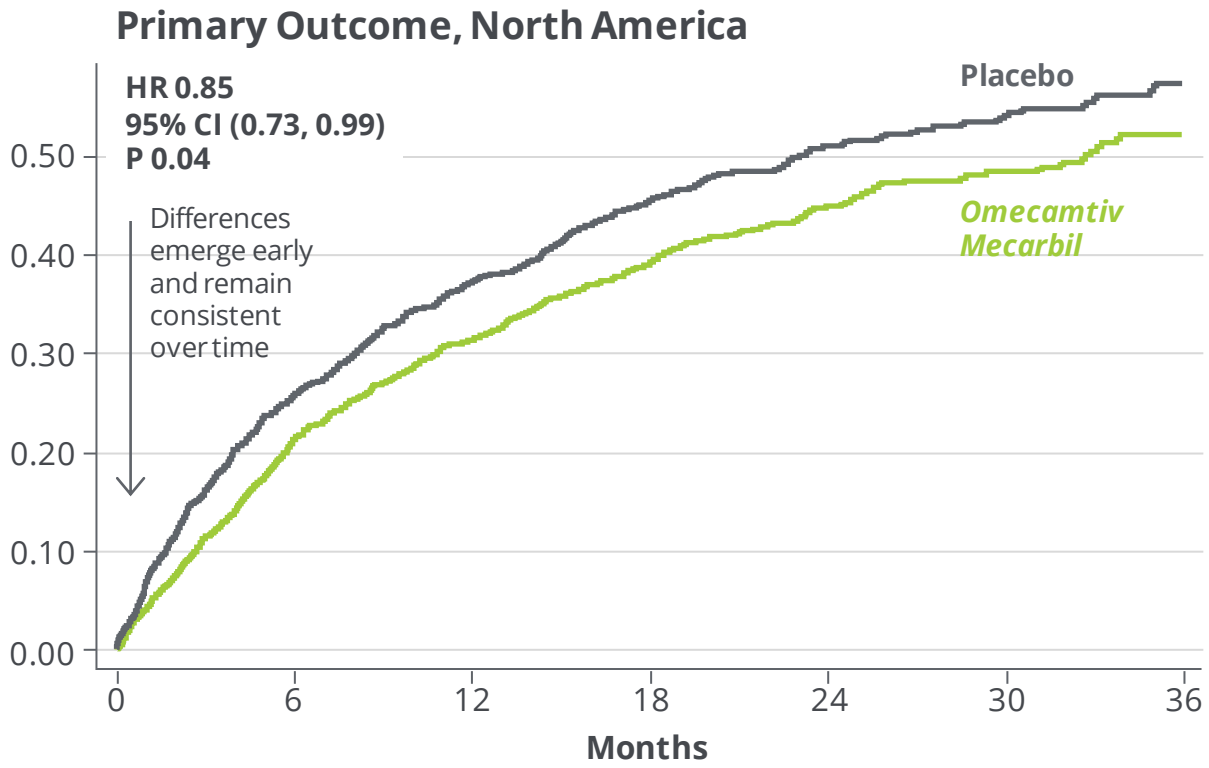
Absolute risk reduction 8.3 events/100 pt-years
NNT = 12

Felker GM, Omecamtiv Mecarbil in Patients with Severe Heart Failure: An Analysis from GALACTIC-HF, ESC Heart Failure 2021, June 2021

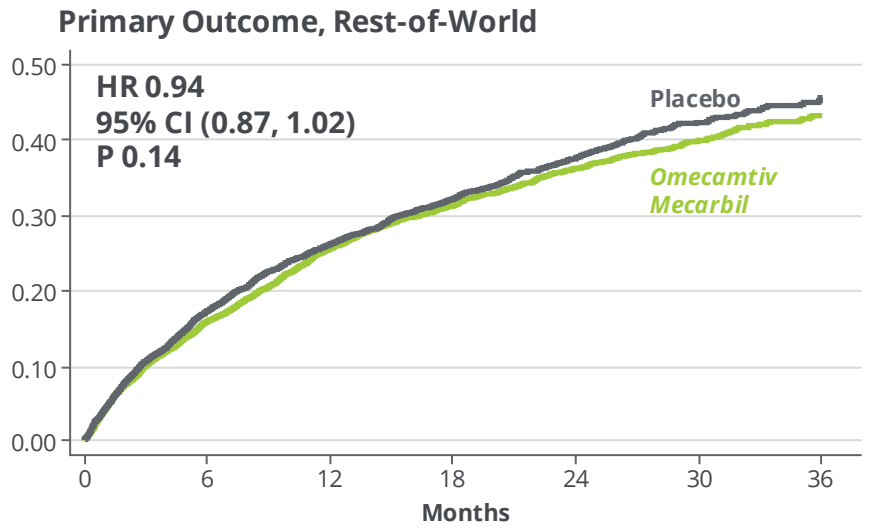
Clinically Meaningful Treatment Effect in North America

Significant Risk Reduction of the Primary Composite Outcome

GALACTIC-HF



Primary Composite Outcome: Time to first HF event or CV death



Teerlink JR et al., Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure; N Eng J Med 2020, 384:105-116.

Safety and Tolerability Profile Comparable to Placebo

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)

Teerlink JR et al., Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure; N Eng J Med 2020, 384:105-116.

Greater Effects in HF Patients with Highest Need

GALACTIC-HF

- Significant risk reduction of the primary composite endpoint in patients with worsening HF receiving excellent GDMT
- Greater treatment benefit in higher risk patients
  - Lower baseline LVEF
  - Higher baseline NT-proBNP
  - Higher baseline NYHA Class
- Good safety and tolerability with no adverse effects on blood pressure, heart rate, renal function, or electrolytes

Teerlink JR et al., Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure; N Eng J Med 2020, 384:105-116
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.

Selected Comments from Key Opinion Leaders

GALACTIC-HF

Overall

"This is the **holy grail** for inotropes"

"The first inotropic agent that doesn't increase arrhythmias or mortality"

"OM's greatest potential is in **severe, sicker patients**"

"*Omecamtiv mecarbil* can **serve a large, unmet need**"

MOA

"**Unique mechanism** that is a viable target"

"Molecule is innovative and **gets to the root cause of HF**"

Safety

"**Safety is very good** – it opens it up to a **wide range of patients**"

"Potential utility in patients unable to tolerate or titrate GDMT"

"Lack of effect on BP is a huge plus"

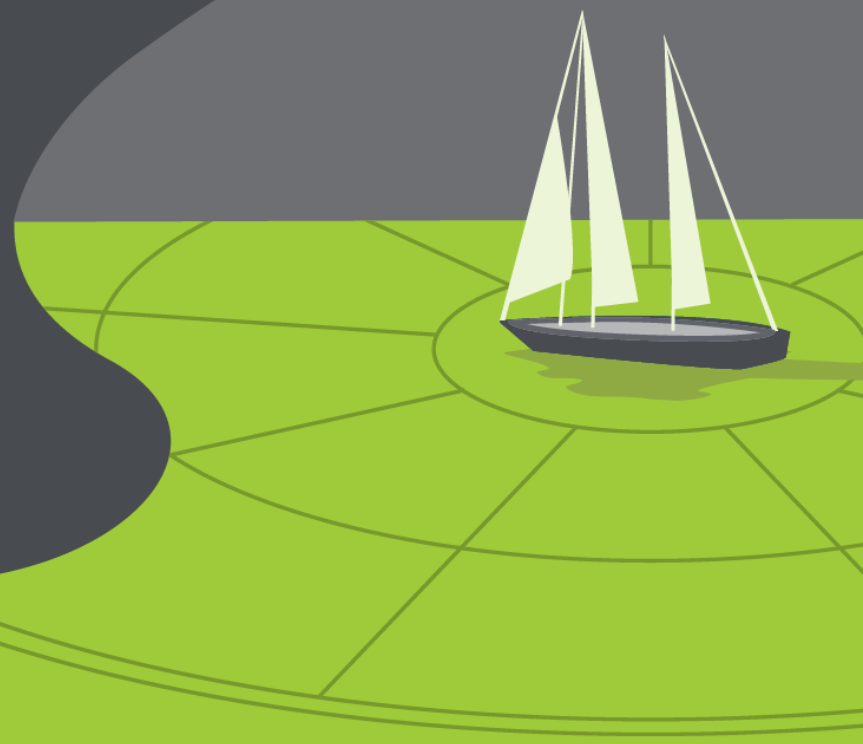
CHARTING THE COMMERCIAL COURSE

Analyst & Investor Day 2021

Cytokinetics

Expert Panel

Moderated by Fady Malik, M.D., Ph.D., EVP, Research & Development



Expert Panel

Alanna Morris, MD MSc, FHFSA, FACC, FAHA
Associate Professor of Medicine, Division of Cardiology; Director of Heart Failure Research, Emory University Clinical Cardiovascular Research Institute

Tariq Ahmad, MD, MPH
Associate Professor of Medicine; Medical Director of Advanced Heart Failure, Cardiovascular Medicine, Yale School of Medicine

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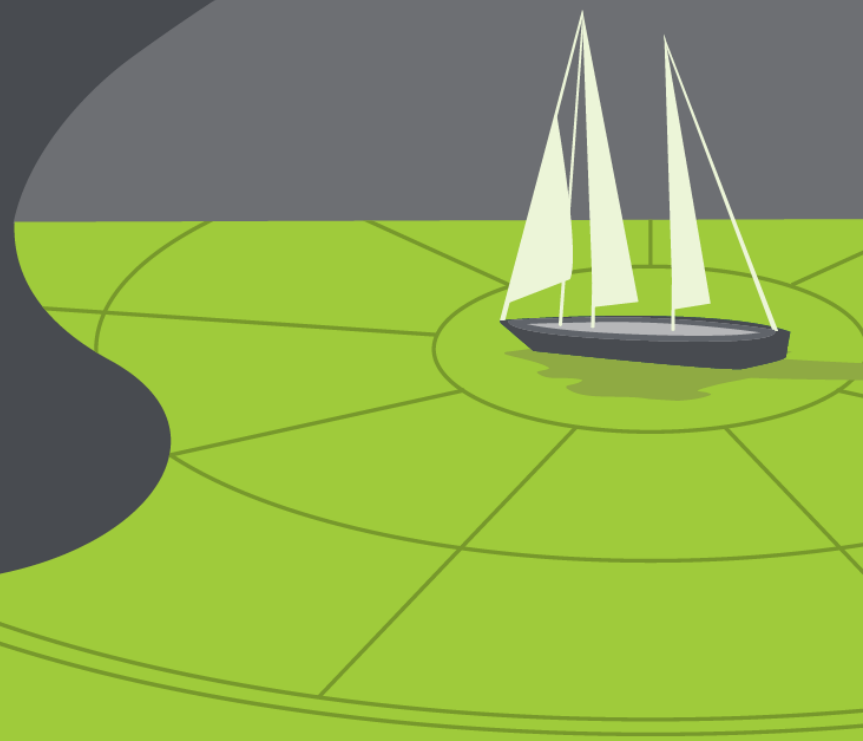
Analyst & Investor Day 2021

Cytokinetics

Omecamtiv Mecarbil:

Filling an Unmet Patient Need

Andrew Callos, EVP, Chief Commercial Officer



Omecamtiv Mecarbil: Value Proposition

KEY MARKET DYNAMICS		OM VALUE PROPOSITION
Large unmet need	→	**OM delivers clinical value to *worsening* HF patients**
Limitations of current regimens	→	**OM is an add-on therapy for worsening HF patients**
High cost burden to society	→	**OM reduces hospitalizations and their associated costs[1]**

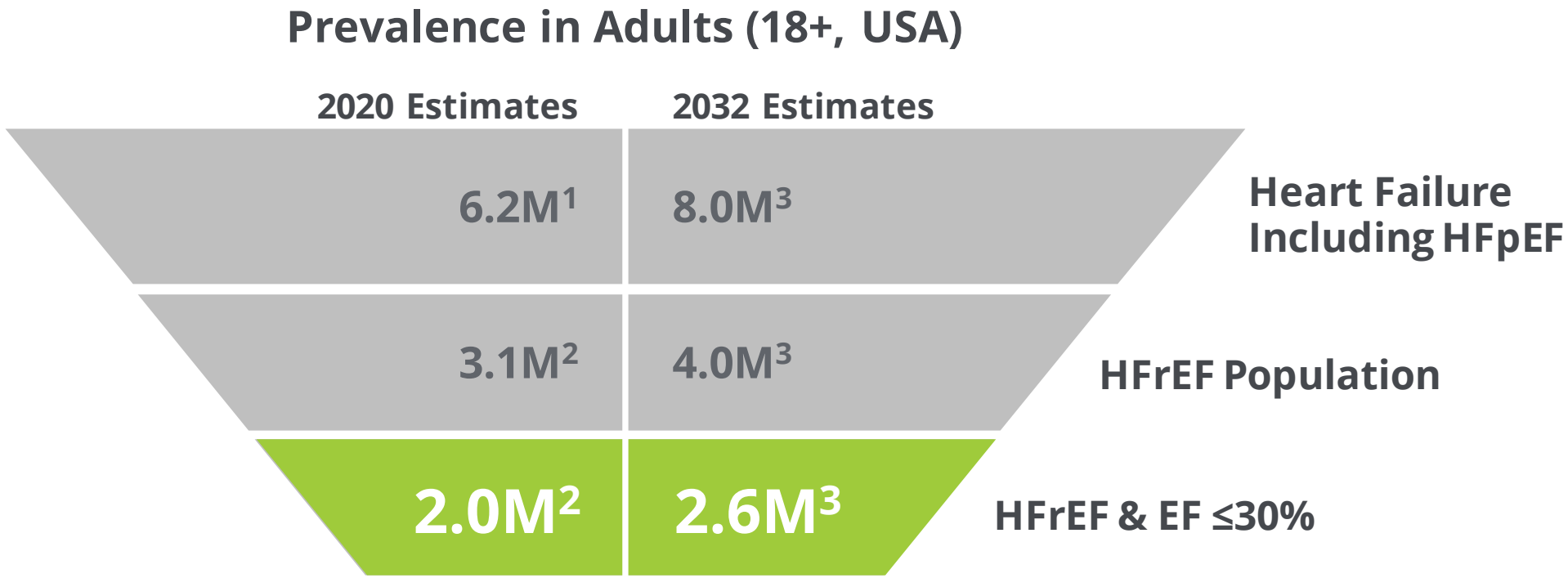
1. Felker GM. *ESC Heart Fail* 2021 Oral Presentation. Data based on post hoc analyses.
Investigational product. Not approved as safe or effective for any indication.

Key US HFrEF Market Dynamics

Large unmet need	• **Large HFrEF patient population**, ~ 50% of total HF (~3M patients) [1] • HFrEF with **worsening** symptoms (≤ 30% EF), about 2/3rd of HFrEF (~2M patients) [2]
Limitations of current treatments	• **Few patients receive guideline-recommended target doses** of current treatments [3] • Additional treatment options are needed in **patients with EF ≤ 30%**
High cost burden to society	• **Driven by hospitalizations,** HF is the **biggest cost driver in Medicare**: 4% of costs [5] • **Rate of hospitalization increases as EF declines** [4]

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 and 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. Greene et. al.: Medical Therapy for Heart Failure With Reduced Ejection Fraction The CHAMP-HF Registry. JACC, VOL. 72, NO. 4, 2018
4. Angaran P, Association of Left Ventricular Ejection Fraction with Mortality and Hospitalizations, Journal of the American Society of Echocardiography, July 2020.
5. Fitch K , The Cost Burden for WHF in the Medicare FFS Population, Milliman, 2015

Large and Growing Heart Failure Patient Population



1. National Center for Health Statistics. National Health and Nutrition Examination Survey (NHANES) as accessed ‹ /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)

HFrEF Treatment Approaches and Guidelines Are Evolving

Trend in treatment approaches to prescribe *initial multi-drug* regimens *earlier*…

ARNi "preferred" RAASi [1]

"aldosterone antagonist should be considered" [1]

"SGLT2 should be considered" [1]

RAASi: ARNi *(preferred)* or ACEi or ARB + **beta-blocker** + **Loop diuretic (as needed)** + MRA + SGLT2 inhibitor

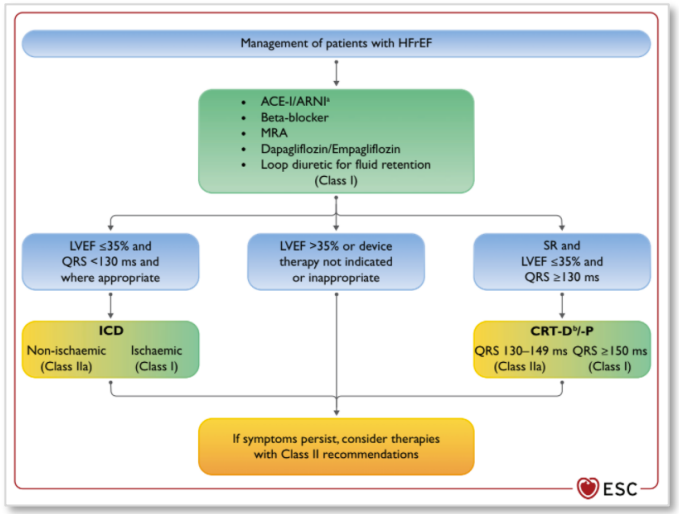
Plus ivabradine and / or hydralazine + nitrate and / or thiazide diuretic

"If resting HR is ≥70 bpm in sinus rhythm" [1]

"For persistently symptomatic Black patients" [1]

Current ACC / AHA Step 1 guidelines

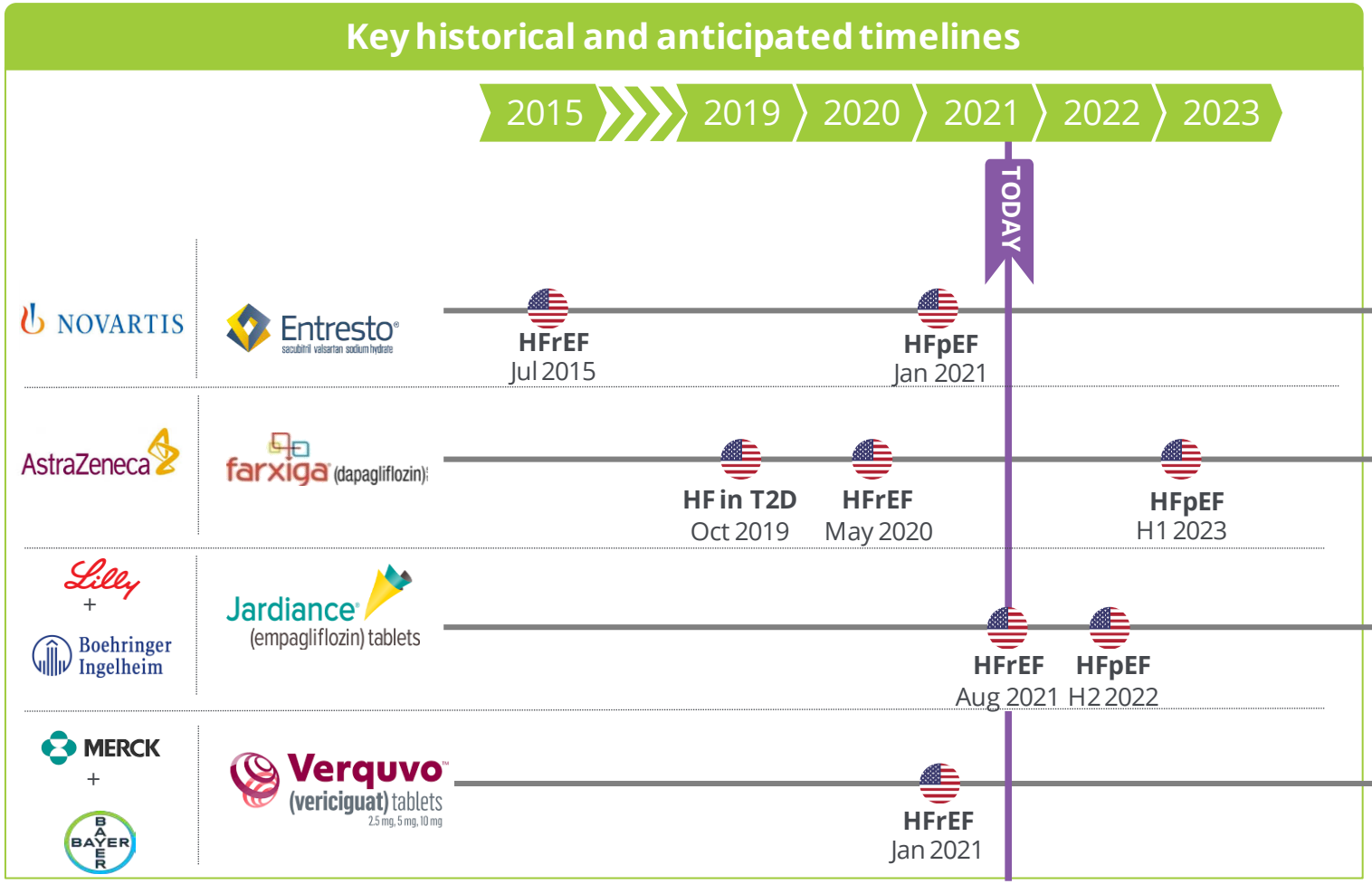
… Also reflected in updated 2021 ESC guidelines[2]



ACEi angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi: angiotensin receptor-neprilysin inhibitor; MRA: mineralocorticoid receptor antagonist; SGLT2: sodium-glucose co-transporter-2

1. Maddox TM, et al *J Am Coll Cardiol 2021; 77(6): 772-810* (https://www.acc.org/Latest-in-Cardiology/ten-points-to-remember/2021/01/2021/21/56/2021-Update-Expert-Consensus-for-HFrEF.)
2. European Heart Journal (2021) 42, 3599 - 3726

Recent Entrants Have Expanded Treatment Options



Company press releases or investor events

Co-Morbidities & Tolerability Can Lead to Under-Treatment

Conditions of concern
Due to Co-Morbidity and/or Tolerability

Implications for patients
Confirmed in registries and primary research

	Low BP	Renal Insufficiency	Elevated Serum Potassium	% Patients Receiving Target Dose
ACEi/ARB	X	X	X	17%
ARNI	X	X	X	14%
Beta Blocker	X			28%
MRAs	X	X	X	77%

> *"Obviously [goal is to] help increase their longevity, reduce their morbidity and mortality with [being] able to tolerate the side effects of the medications." - KOL*

Patients not reaching recommended doses, linked to higher mortality

Greene et. al.: Medical Therapy for Heart Failure With Reduced Ejection Fraction The CHAMP-HF Registry . JACC, VOL. 72, NO. 4, 2018 ; HCP interviews

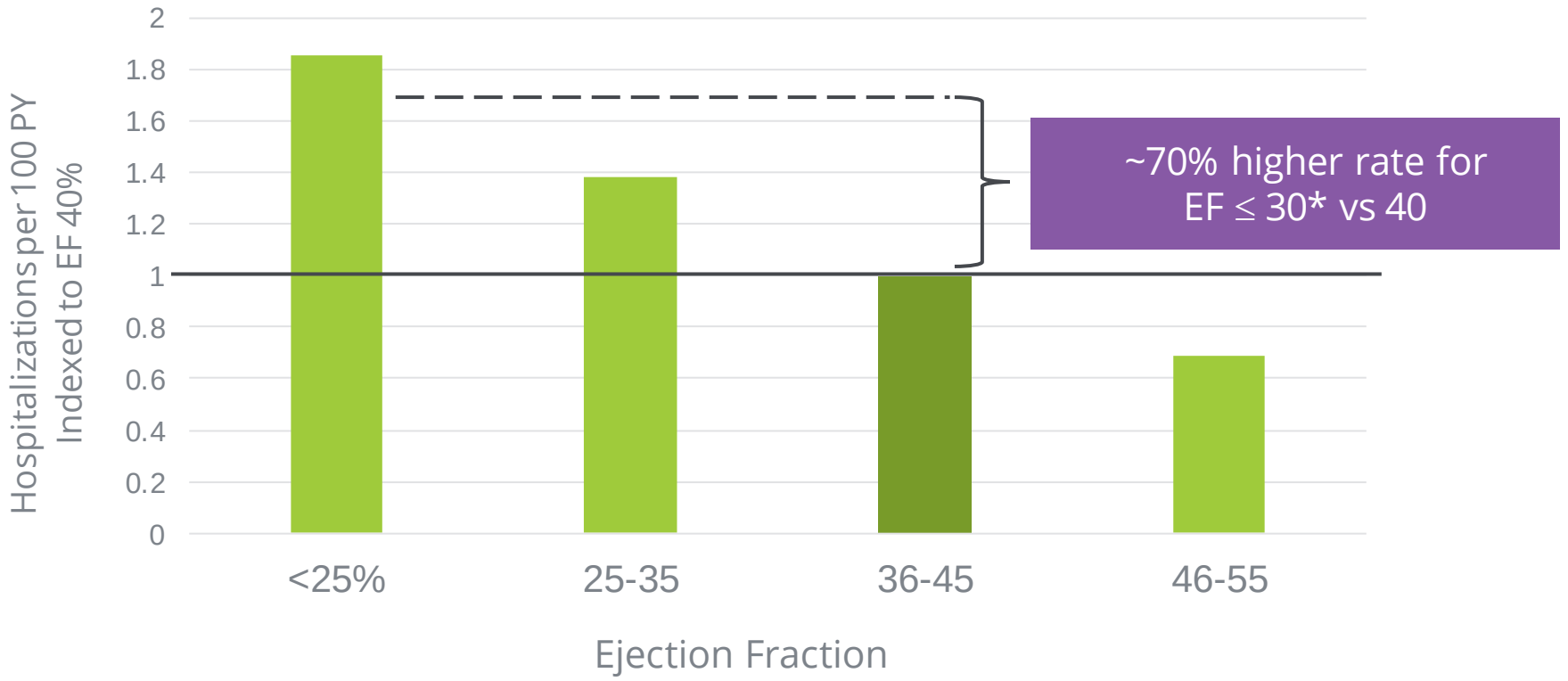
HF Patients Often Cycle Through Frequent Hospitalizations

Majority have 3 or more heart failure hospitalizations over their lifetime[9]

Almost 2 in 3 patients re-hospitalized within 12 months

1, Adams et al. *Am Heart J* 2006; 149:209-16
2. Chen et al. *JAMA* 2011;306:1669-78
3. Dickstein et al. *Eur Heart J* 2008;29:2388-442
4. Korda,, et al. *BMC Health Serv Res*. 2017;21;17(1):220.
5. Krumholz et al. *Arch Intern Med* 1997;15799 – 105
6. Krumholz et al. *Circ Cardiovasc Qual Outcomes* 2009;2(5):407-13
7. Loehr et al. *Am J Cardiol* 2008;101:1016-22
8. Whellan et al. *Circulation* 2010 Jan;3(1):33-40
9. Dunlay et al J Am Coll Cardiol. 2009 Oct 27; 54(18): 1695–1702.

Lower EF Associated With Increased Risk of Hospitalization

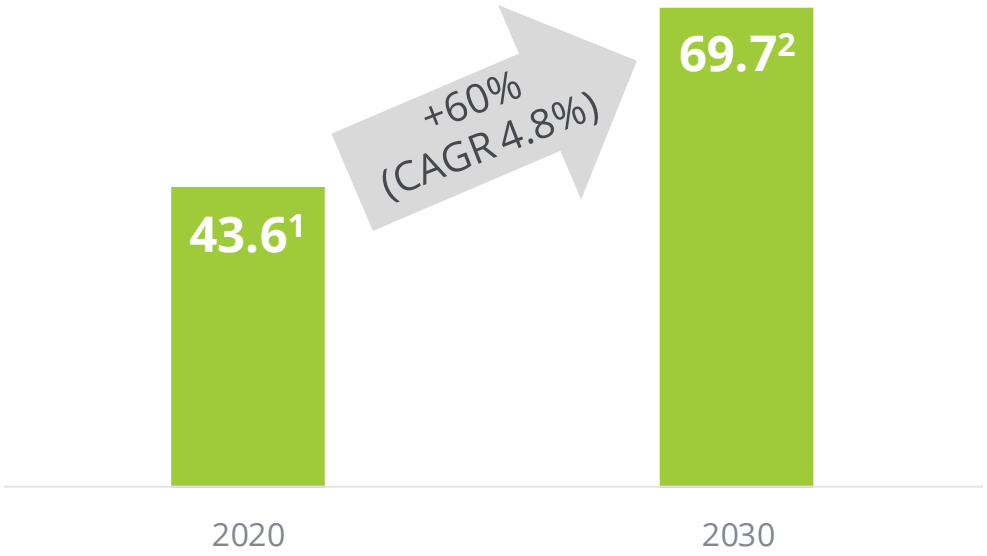


Adapted from Angaran P, Association of Left Ventricular Ejection Fraction with Mortality and Hospitalizations, Journal of the American Society of Echocardiography, July 2020.
Based on 27,323 patients evaluated over 4+ years follow-up;
* EF estimated for ≤30

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]

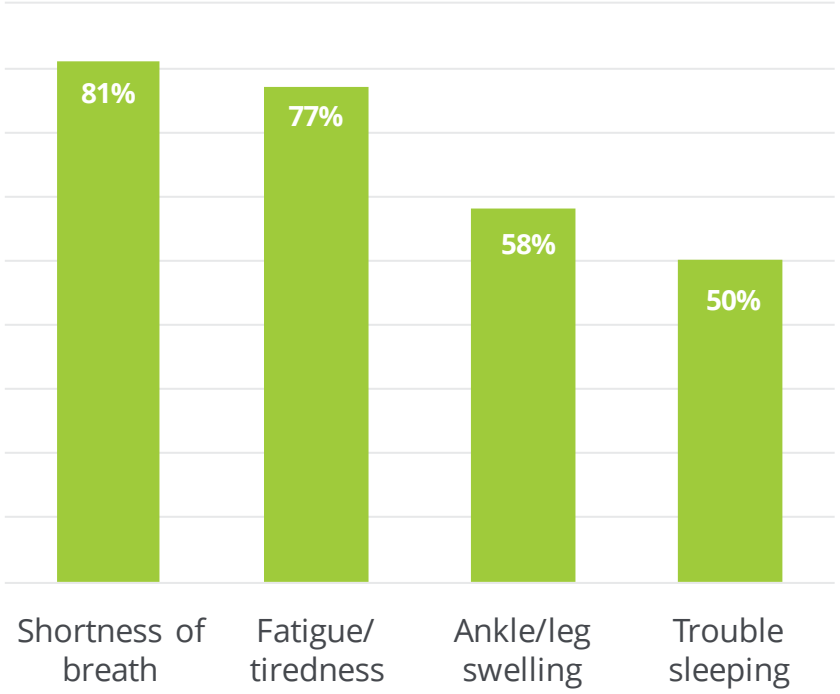
Of total lifetime HF cost burden, **~80% due to hospital stays**[5]

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

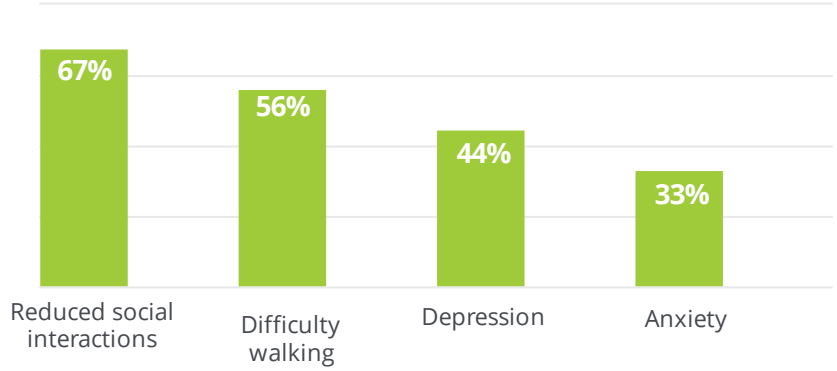
1. Urbich, M., Globe, G., Pantiri, K. et al. A Systematic Review of Medical Costs Associated with Heart Failure in the USA (2014–2020). PharmacoEconomics 38, 1219–1236 (2020). https://doi.org/10.1007/s40273-020-00952-0
2. Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, et al. Forecasting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

Tremendous Burden on Patients and Caregivers

Most Frequently Reported Symptoms[1]



Impact on Patients



Impact on Caregivers

"This condition takes my life from me. I can't work anymore, walk my dog or go to dinner and movies with my daughters and husband." [2]

1 McHorney CA, et al. (2021) The impact of heart failure on patients and caregivers: A qualitative study. PLOS ONE 16(3): e0248240. https://doi.org/10.1371/journal.pone.0248240 https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0248240. N = 90 (64 Patients, 26 Caregivers)
2. Data on File (Market Research)

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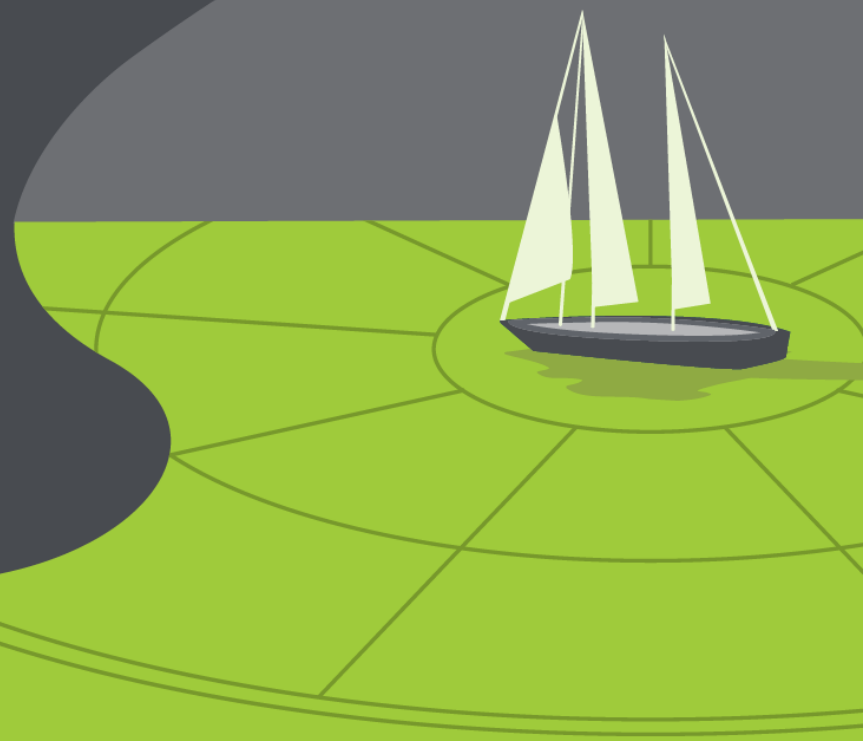
US Go-To-Market Strategy

Andrew Callos, EVP, Chief Commercial Officer
Jennifer Laux, VP, Cardiovascular Marketing
Diann Potestio, VP, Global Value, Access & Distribution



Omecamtiv Mecarbil: GTM is Critical Step for Our Vision 2025

Commercial Goals and Aspirations

Omecamtiv Mecarbil GTM Strategy

Strategy Driven by Key Choices

Market

- **Where to focus?**
  - Segmentation
  - Targeting
  - …
- **How to win?**
  - Positioning
  - Value
  - Access
  - Medical
  - …

Internal

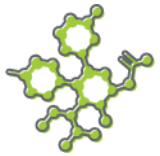
- **How to organize?**
  - Build vs Buy
  - Field Force
  - Digital
  - …
- **How to manage?**
  - Forecasts
  - Budget
  - Investments
  - …

GTM: Go-To-Market

GTM Is Based on Target Product Profile for *Omecamtiv Mecarbil*

Efficacy

Demonstrated in patients with symptomatic chronic heart failure with **EF ≤ 30%** (N=5,842), 12% (p<.002) RRR in composite of CV death or HF events vs. placebo (translates into 3.8% ARR, NNT=27)



Novel MOA

Omecamtiv mecarbil is the **first myotrope, a selective cardiac myosin activator,** that improves cardiac contractility without affecting cardiac myocyte calcium or myocardial oxygen consumption

Effects on BP and Renal

No difference in the change in systolic **blood pressure** vs placebo

No change in **potassium or creatinine levels** during GALACTIC-HF

GALACTIC-HF. GALACTIC-HF ClinicalTrials.gov number, NCT02929329

Our GTM Strategy: Gated Build of Core Capabilities

Strategic choices across each GTM block

Commercial organization + **Core capabilities to ensure success**

World class Organization	Gated Build	Insights	Education	Access	Support
Scalable organization, leveraging **best practices** and **innovative** solutions	Sequence, and **gate build-out** based on pre-defined milestones and metrics **to reduce risk**	Leverage **deep understanding** of patients, HCPs, and institutional settings	Engage and **educate cardiologists** in the field	Get **access** to our drug as soon as possible	Support **patients and caregivers**

Building a World Class Commercial Organization

Driven by a relentless focus on our North Star: the patient

Gated Build Based on Key Milestones to Enable De-Risking

*No regret** investments

Supply
Leadership
Data & Analytics
Access & HEOR
…

Sequenced investments

Campaign development
Sales leadership
Commercial operations
…

"All In" Post-Approval Investments

Sales force
Promotional spend
Patient support
…

* Given Cytokinetics pipeline, need to build these capabilities

Deep Understanding of the Patients, HCPs and Institutions

Insights | Education | Access | Support

Patient	**Worsening heart failure patient requiring more intensive treatment** due to decreasing LVEF (≤ 30%), recent heart failure event (≤ 12 months), often with co-morbidities / tolerability issues limiting GDMT treatment
HCP	**Concentrated** market with majority of patients seen by one third of cardiologists, clustered in large urban centers
Institutions	**HF Clinics** seeing worsening heart failure patients, and **select hospitals** where treatment changes are made during stay / recommended after discharge

High Unmet Need in Patients with Worsening Heart Failure

Insights | Education | Access | Support

Patient

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

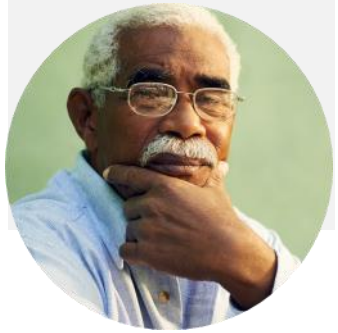
Cardiac Function		Recent Event		GDMT Limitations
	+		+ / -	
LVEF ≤ 30%		**HF Event* ≤ 12 months**		**Co-morbidities and/or tolerability****

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

Cytokinetics

Tremendous Burden of WHF on Patients and Caregivers

*"This condition **takes my life from me**"*



*"I've become such a **burden** to my wife and daughters"*

*"**I can't walk** anymore, or walk my dog"*

*"I **dread** having to be taken to the hospital again"*

*"**Despite all these meds**, I still can't tend to my garden"*

*"Caring for my loved one with HF is an **exhausting full-time job**"*

Patient and caregiver focused campaign: educate, activate, and support

Multiple Ways to Initiate *Omecamtiv Mecarbil*

Worsening Heart Failure

- **GDMT maxed out**
- **Symptoms deteriorating**
- **Further decrease in EF**
- **Tolerability issues**

Routine visit to cardiologist or Heart Failure clinic

Urgent, unscheduled outpatient visit

Hospitalization due to heart failure event

GDMT*

Add-on *omecamtiv mecarbil*

* Potentially limited by co-morbidities / tolerability

Deep Understanding of HCPs Managing WHF Patients

Insights | Education | Access | Support

HCP

Cardiologists

Affiliated with cardiology practice, HF clinic, or hospital

High Prescribers

About one third of cardiologists see majority of WHF patients

Geographic clusters

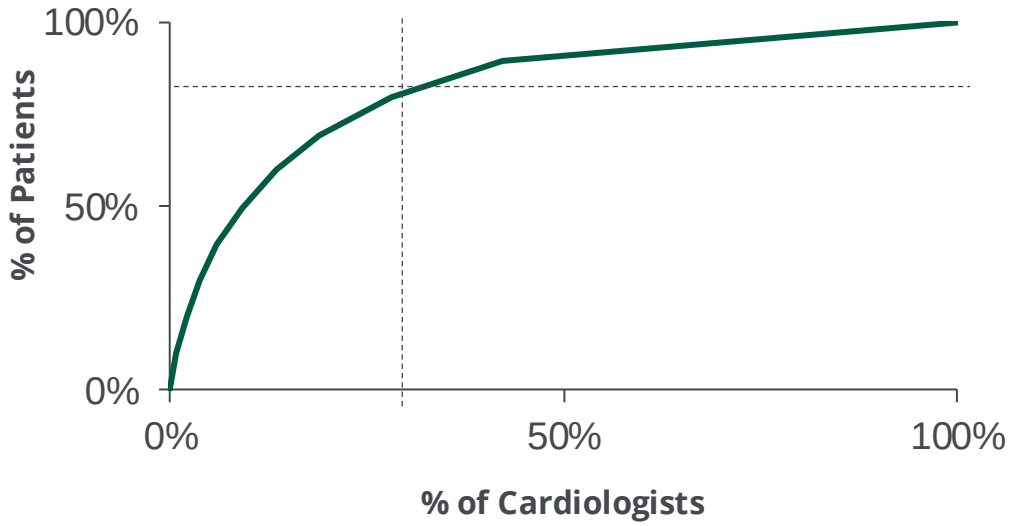
Mostly in urban centers

Going beyond GDMT

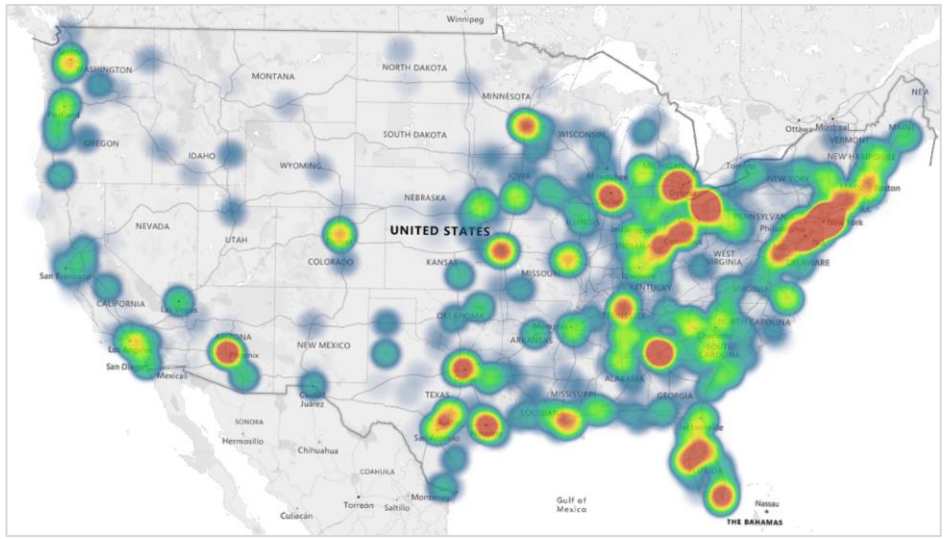
Early adopters, including heart failure / heart transplant specialists

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*

Positive HCP Reactions to Product Profile

High remaining unmet need in patients with worsening heart failure

*"I often **run out of** treatment options as my heart failure patients worsen"*

Positive Reactions From HCPs

Efficacy

*"We need drugs that can be used in worsening patients with low EF. Those with **worse disease benefit the most.**"*

Safety

*"It's a **game changer** when you don't have to worry as much about the kidney function, potassium or blood pressure in worsening patients."*

MoA

*"I like that it is a myosin activator. It is **novel and motivating**. It has a positive rational and emotional impact."*

Proprietary market research
Investigational products. Not approved as safe or effective for any indication

Deep Understanding of the Institutional Settings

Insights | Education | Access | Support

Institutions

HF Clinics

High WHF patient volume, early adopters, comprehensive care teams

Select Hospitals

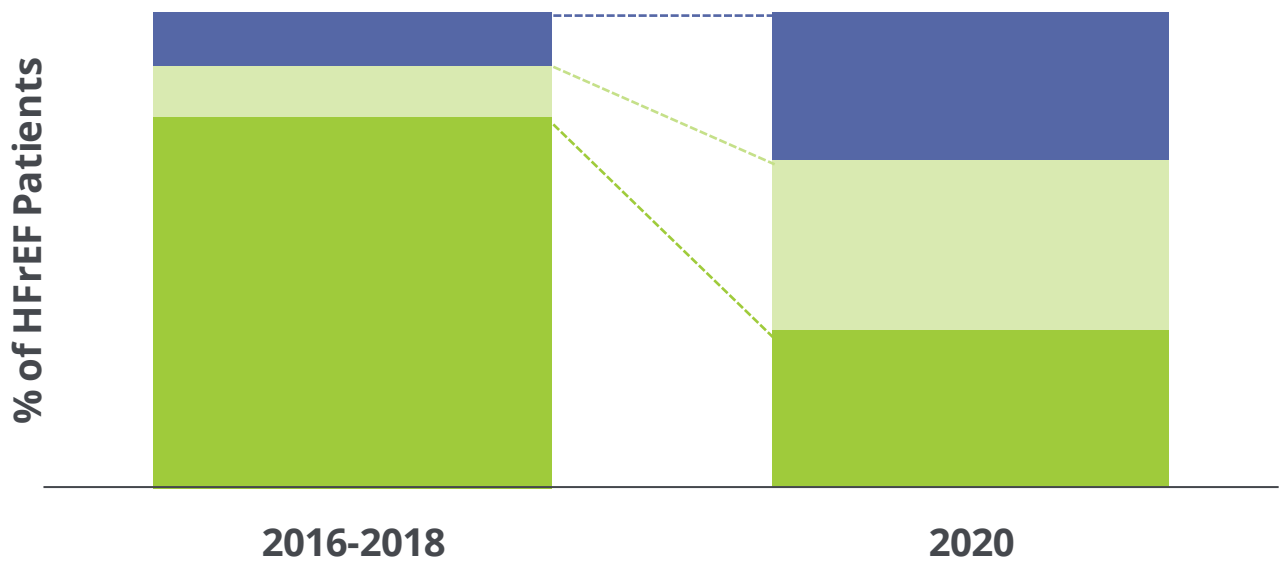
Managing WHF patients and making appropriate therapy adjustments

→ ***Subset*** **of institutions treat majority of heart failure patients[1]**

1. Symphony APLD (1/1/2019 – 12/31/2020);

Hospitals Increasingly Change Treatment Regimens

Treatment Changes During Hospital Stay Over Time



A drug in new class is added

A drug is replaced In same class

Titration of current treatment or no change

Treatment changes *increasingly* made in hospitals, once the patient is stabilized, including adding drugs from new classes

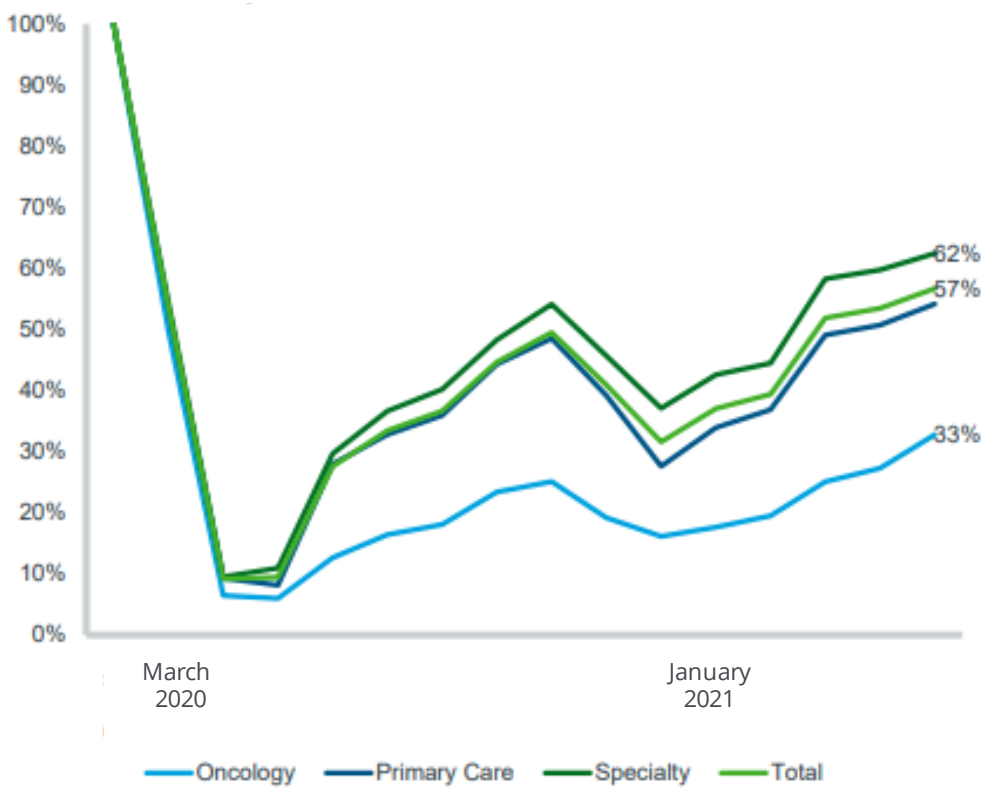
IQVIA 206-2018, IQVIA 2020

Educating and Engaging HCPs

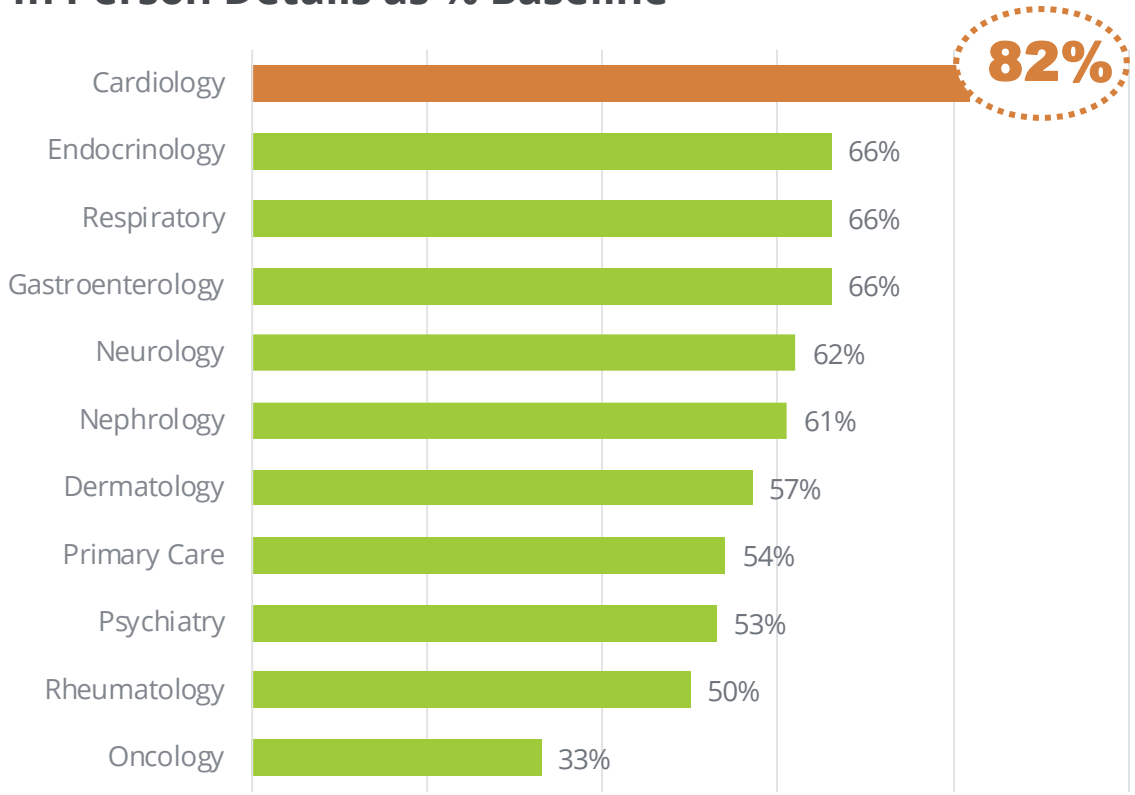
- Despite COVID impact, in-person details continue to rise
- Personalized engagement approach via targeted sales force interactions and digital channels

Despite COVID, In-Person Details Continue to Rise

Biopharma In-Person Details vs. Baseline



In Person Details as % Baseline

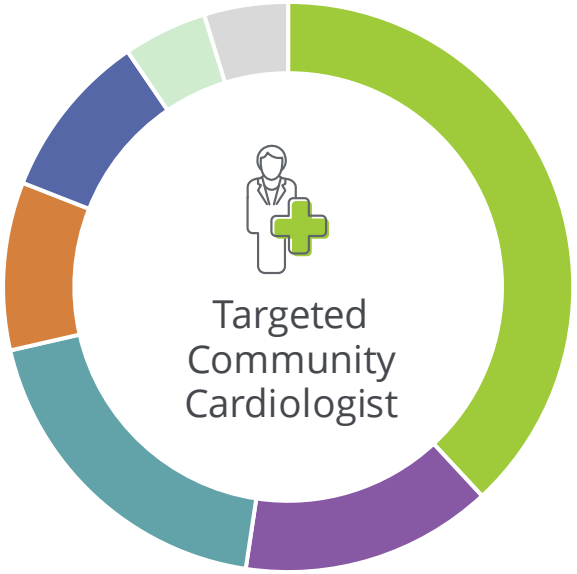


IQVIA – Covid-19 Market Impact
Baseline is the monthly average of Jan and Feb 2020 consisting of stable detail, patient visit and treatment volumes; Brandimpact HCP Network = ~3,600 unique HCPs incl. Oncology, Specialty and Primary Care. Specialty includes (not limited to) Allergy, Cardiology, Dermatology, Gastroenterology, Endocrinology, Neurology, Nephrology, Pulmonology, Psychiatry, Rheumatology and Urology
In-person details continued to increase in all three groups in May. Only oncology in-person remains below 50% of baseline

Engagement Approach Allows Customizing and Broadening

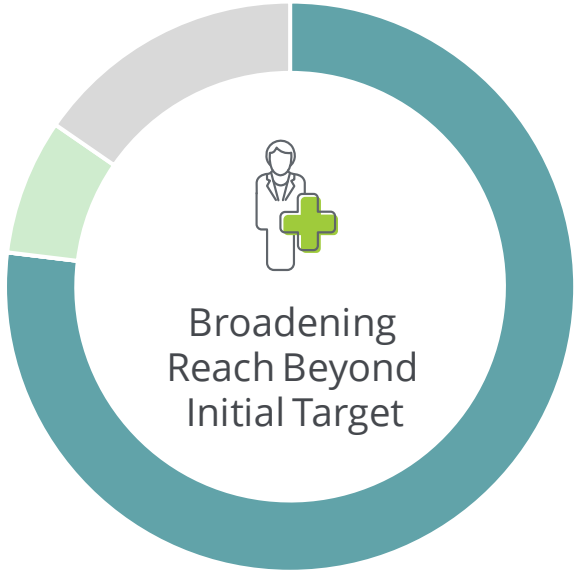
Customizing engagement by different types of customers

~~ illustrative ~~

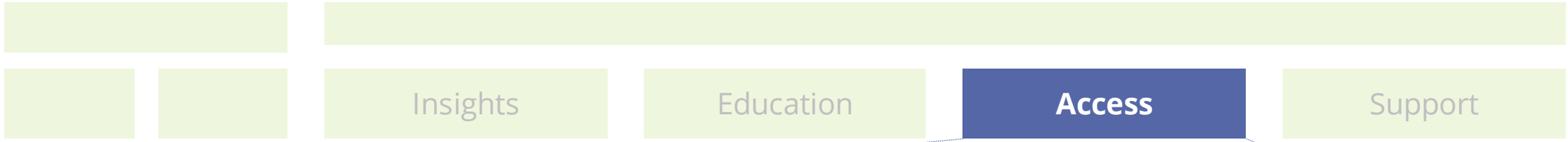


Digital allows broader reach

~~ illustrative ~~



Getting Access



- *Omecamtiv mecarbil* may create significant value by reducing hospitalizations (and associated costs)[1]
- Given importance of Medicare Part D, we aim to minimize time to coverage given annual bid process
- To accelerate access, we are investing in highly experienced staff with existing relationships

1. Felker GM. *ESC Heart Fail* 2021 Oral Presentation. Data based on post hoc analyses.

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

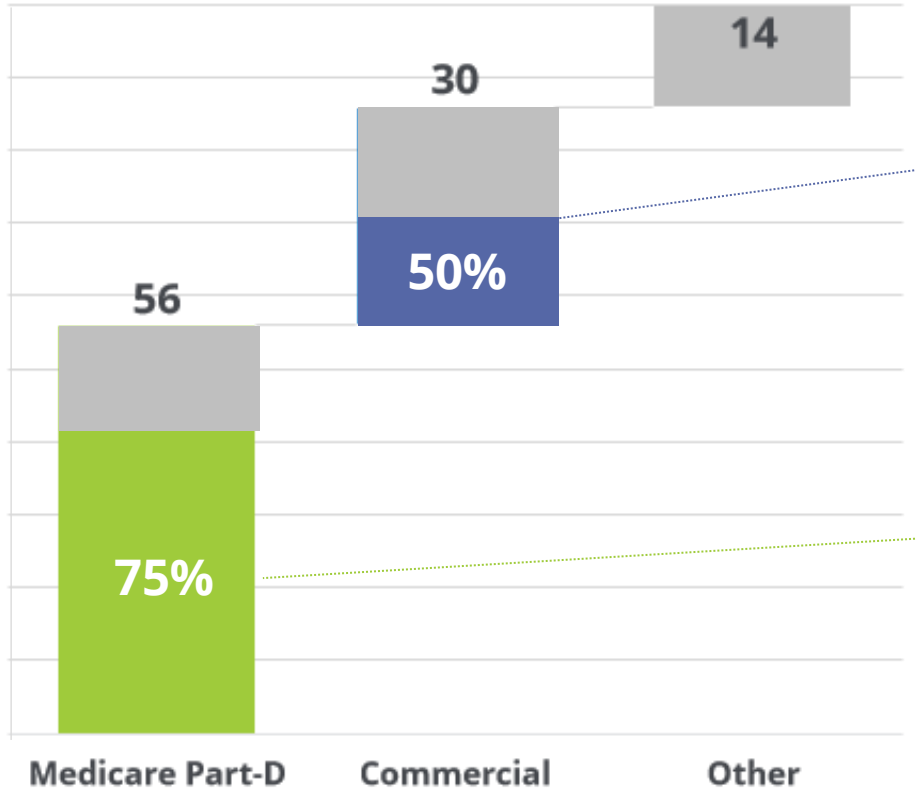
Using **HEOR** and clinical results to demonstrate the economic impact and value

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.

Medicare, By Far The Largest Payer, Will Be a Key Focus

Estimated Payer Mix Based On Other HF Brands



UnitedHealthcare® Anthem®
aetna™ (CVS) Cigna® (ESI)
KAISER PERMANENTE®

UnitedHealthcare® OPTUMRx®
CVS caremark® aetna™
EXPRESS SCRIPTS® Cigna®
Humana® CENTENE® Corporation

National Trends in Heart Failure Hospitalizations and Readmissions From 2010 to 2017
Agarwal, Fonarow, 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

To Accelerate Access, Hiring Highly Experienced Staff

Cytokinetics Account Director Customer Relationship Experience

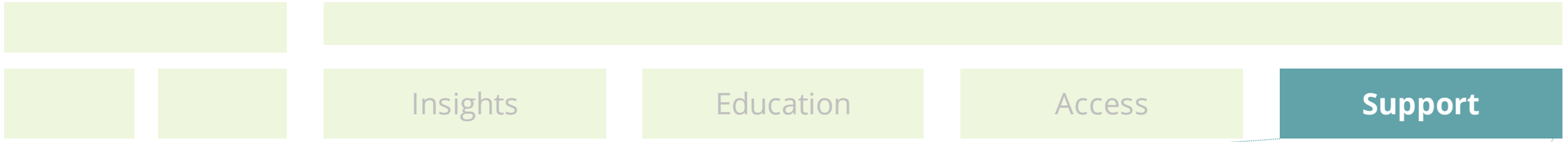
Individually, **15-25 years** of experience

Collectively ~**200 years** of Payer / PBM Relationship Experience

≥250 years of Bio-Pharma Industry Experience

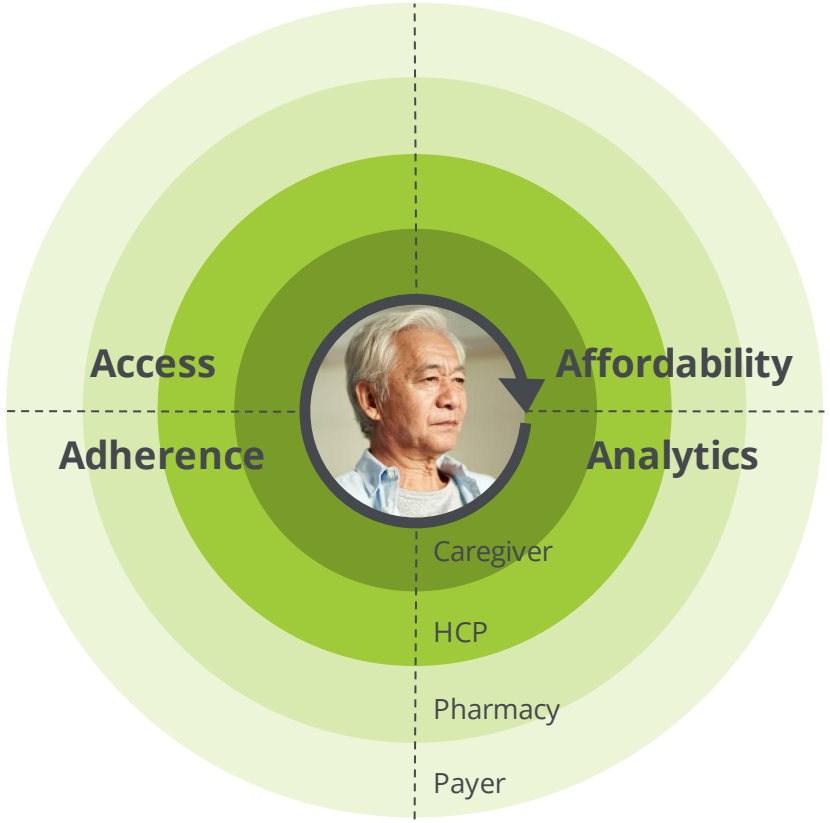
Anthem Blue Cross
CVS Health
Cigna
EXPRESS SCRIPTS
OPTUM
UnitedHealthcare
KAISER PERMANENTE
Humana
MedImpact Healthcare Systems

Supporting Patients and Caregivers



- Providing patient and caregiver education about disease and (post-approval) about product
- Evaluating innovative models for patient services, including a patient hub and digital approaches

We Put The *Patient* At The Center of Our GTM Strategy

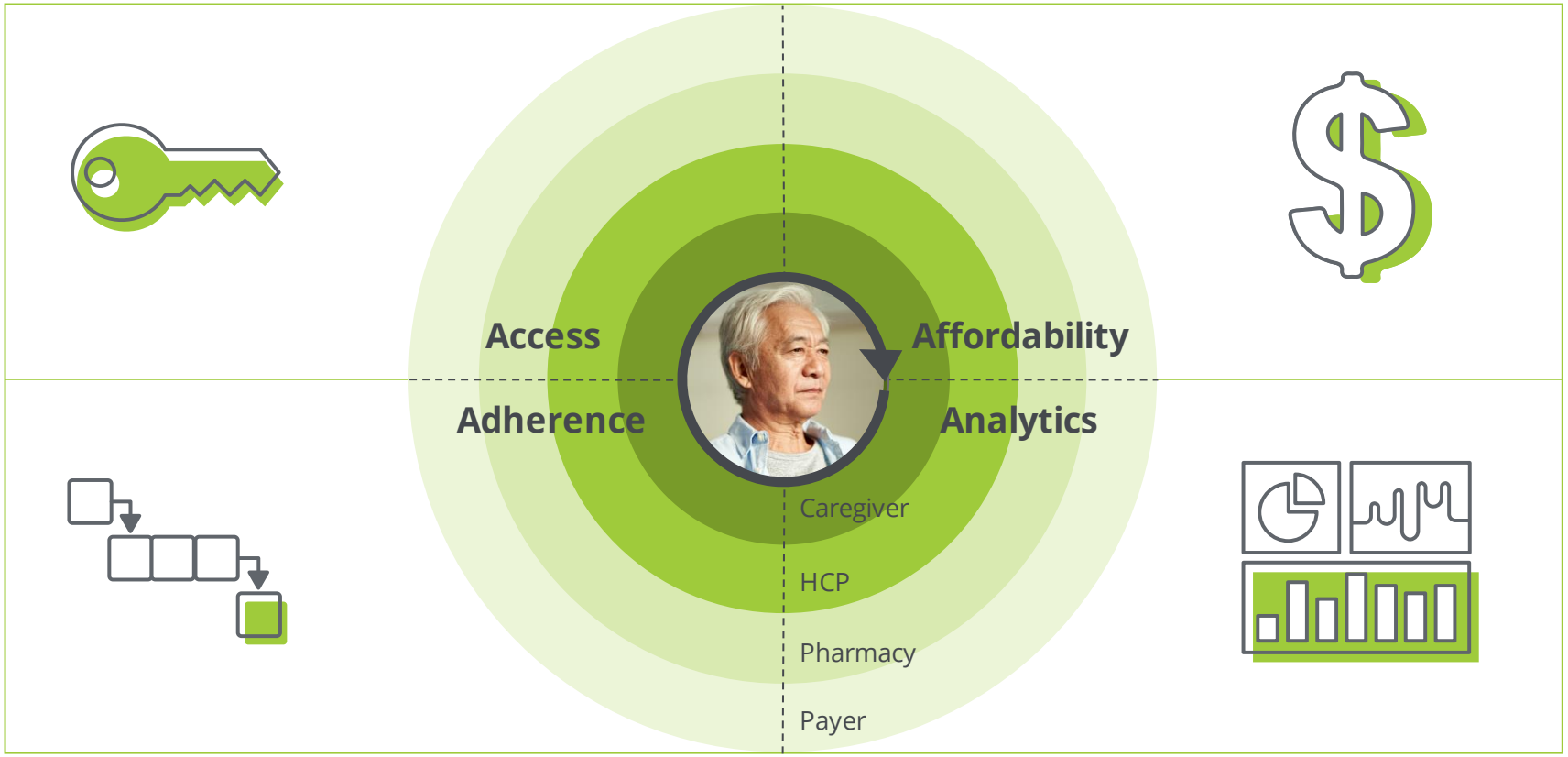


Evaluating Innovative Hub Models for Patient Services

Mix of:

High-touch support for patients and caregivers

Digital assistant for patient and HCP office staff



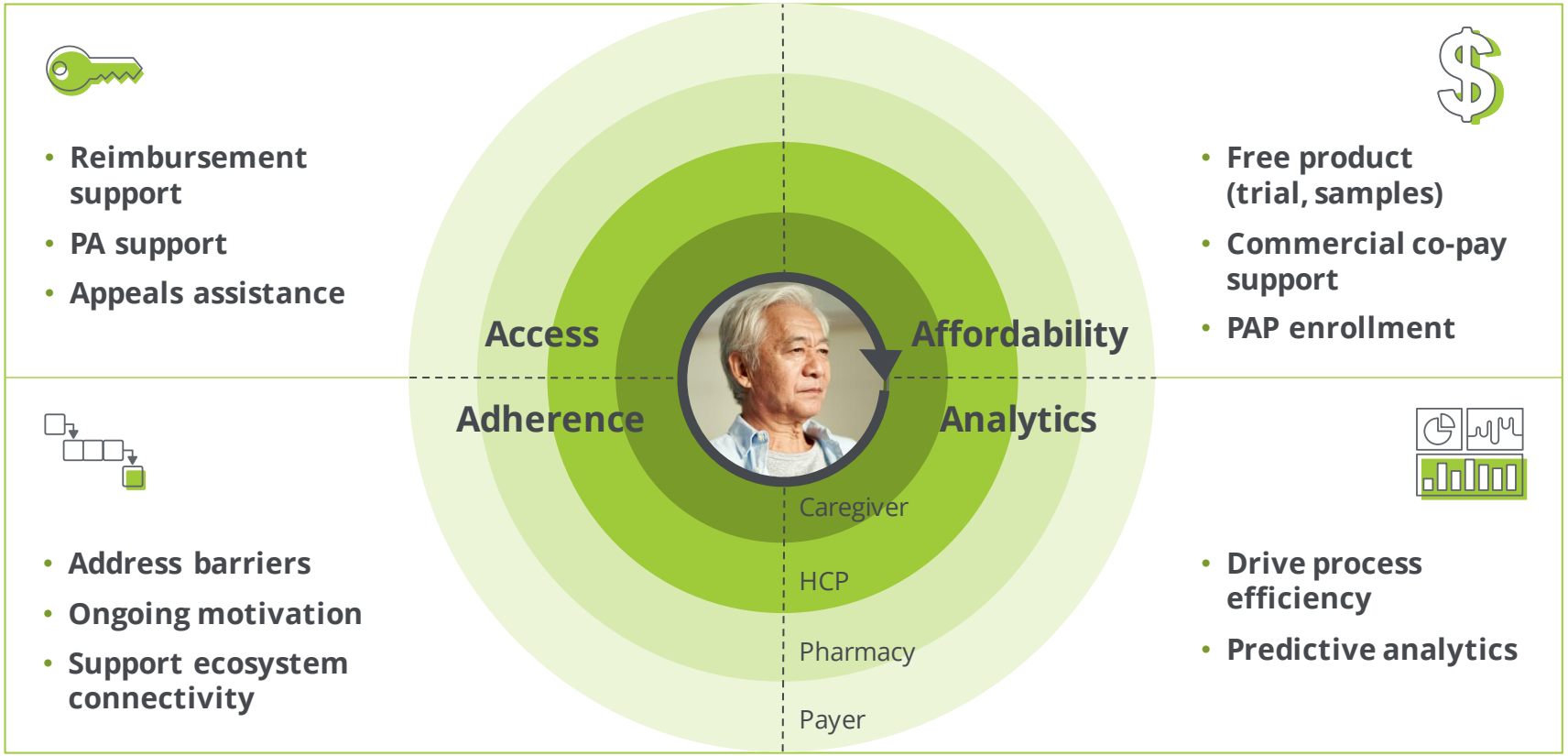
Evaluating Innovative Hub Models for Patient Services

Mix of:

High-touch support for patients and caregivers

Digital assistant for patient and HCP office staff

Help patients start and stay on *omecamtiv mecarbil* and eliminate barriers



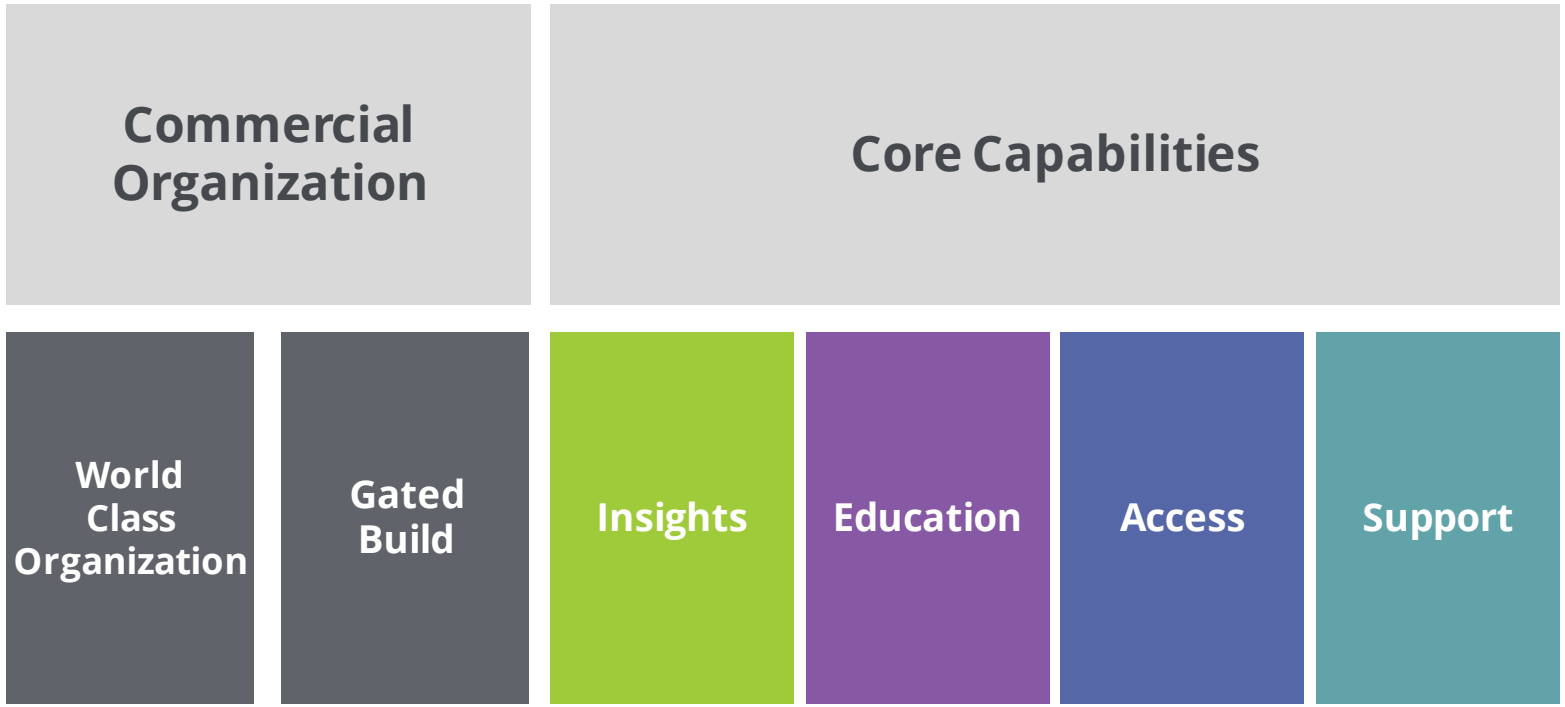
Realizing The Promise of *Omecamtiv Mecarbil*

Offering new hope for patients with worsening heart failure

Our Value Proposition

- **Addresses large unmet need**
- **OM is an add-on therapy for worsening HF patients**
- **Reduces hospitalization cost burden[1]**

Our GTM Approach



1. Felker GM. *ESC Heart Fail* 2021 Oral Presentation. Data based on post hoc analyses.

CHARTING THE COMMERCIAL COURSE

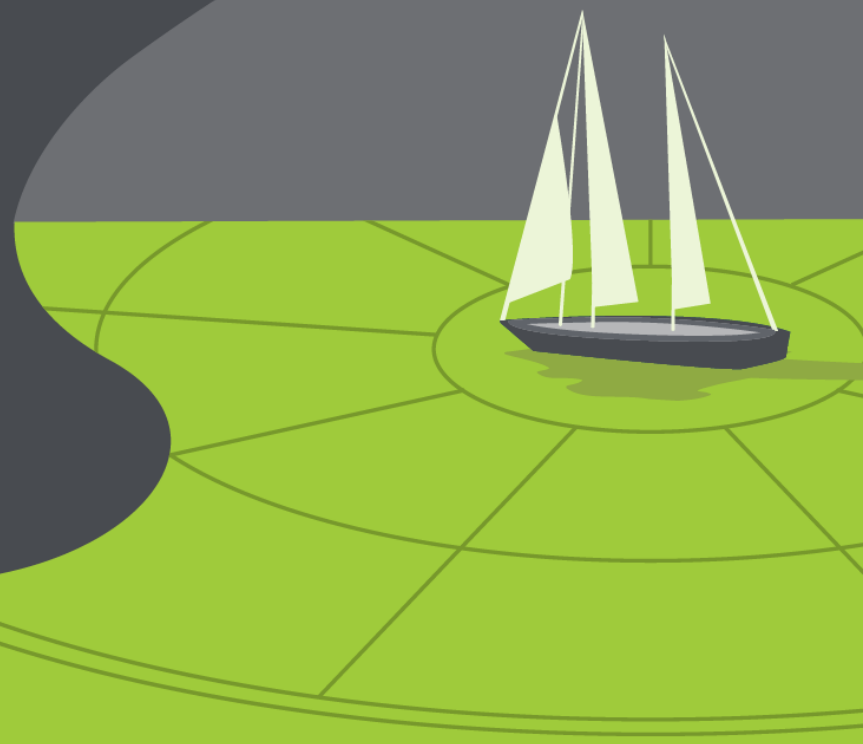
Analyst & Investor Day 2021

Cytokinetics

Q&A

To ask a question in the room, please raise your hand.

To ask a question online, type it into the tab on the left.



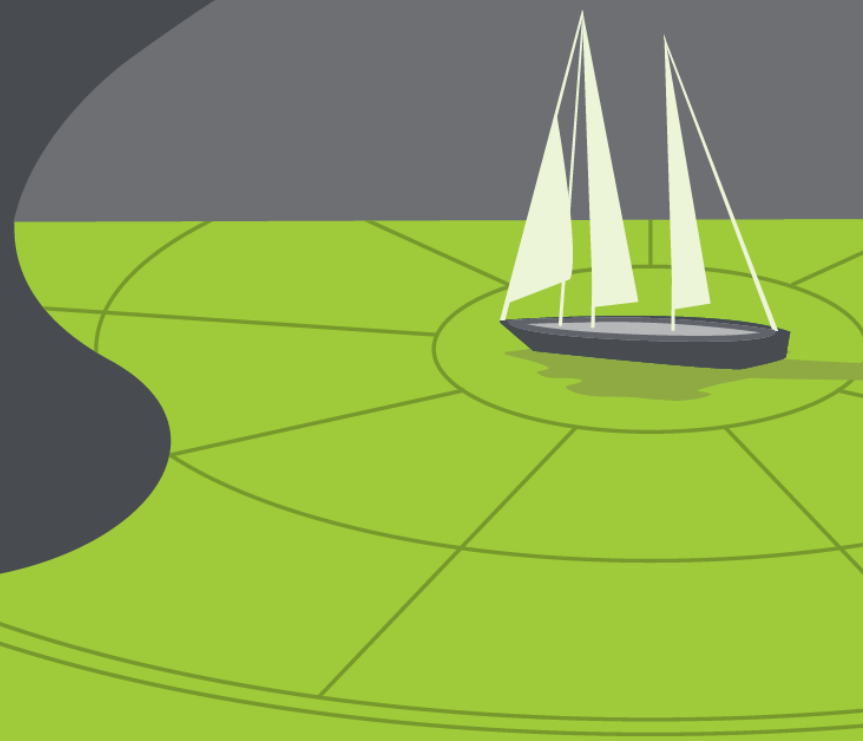
CHARTING THE COMMERCIAL COURSE

Analyst & Investor Day 2021

Cytokinetics

Break

2-5 minutes



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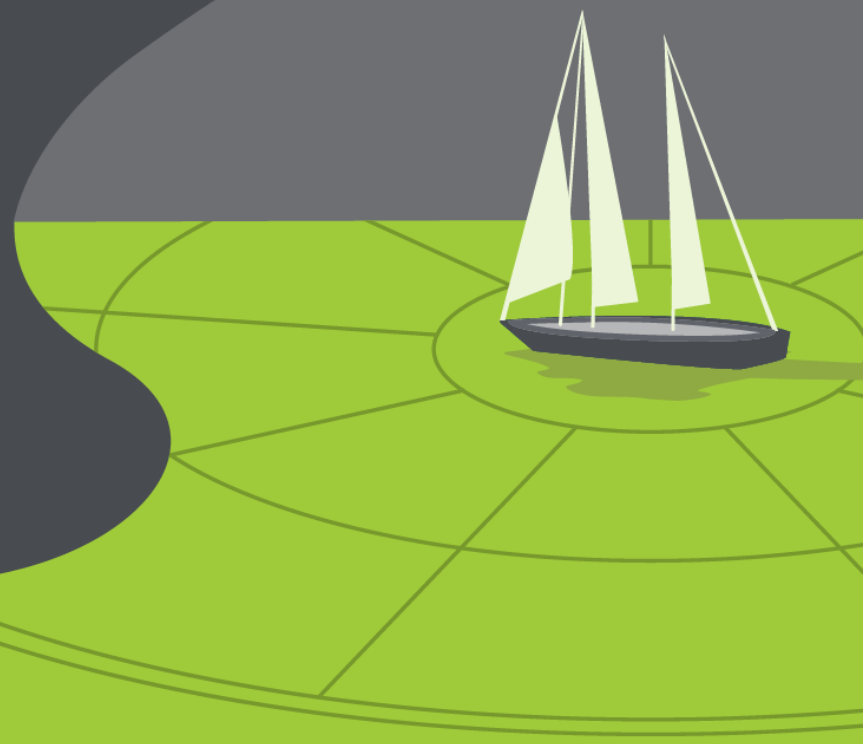
Cytokinetics

HCM Landscape

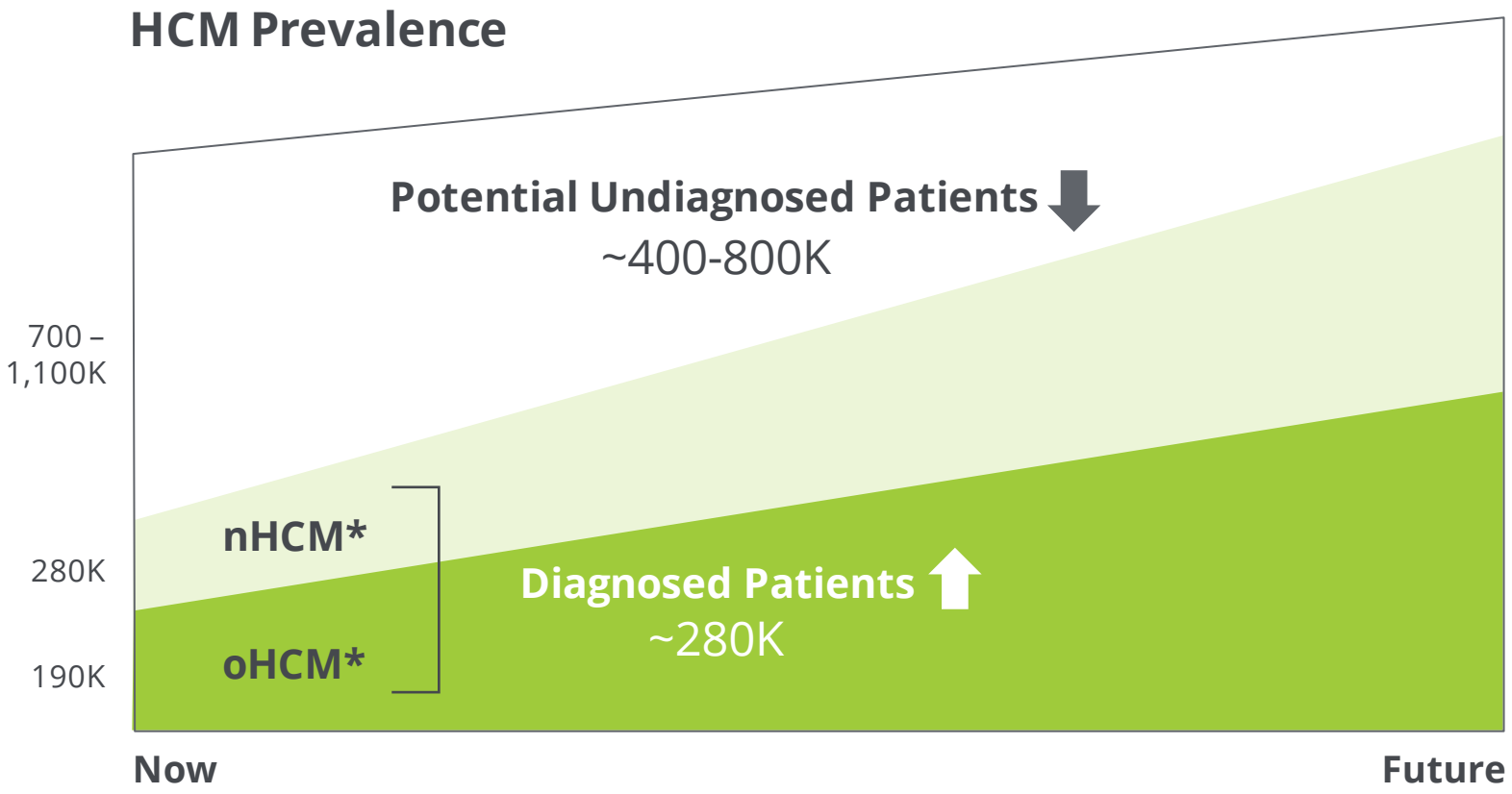
Andrew Callos, EVP, Chief Commercial Officer



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

Multiple Activities Under Way to Increase HCM Diagnosis

HCM market expected to grow significantly

Early Detection

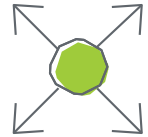
Academia and industry partnering to support early HCM detection (incl AI-based) and monitoring

Genetic Test Companies

Genetic testing companies raising awareness and driving testing for high-risk patients

Genetic tests Guidelines

Professional organizations and Academia revising HCM treatment guidelines given recent development in HCM

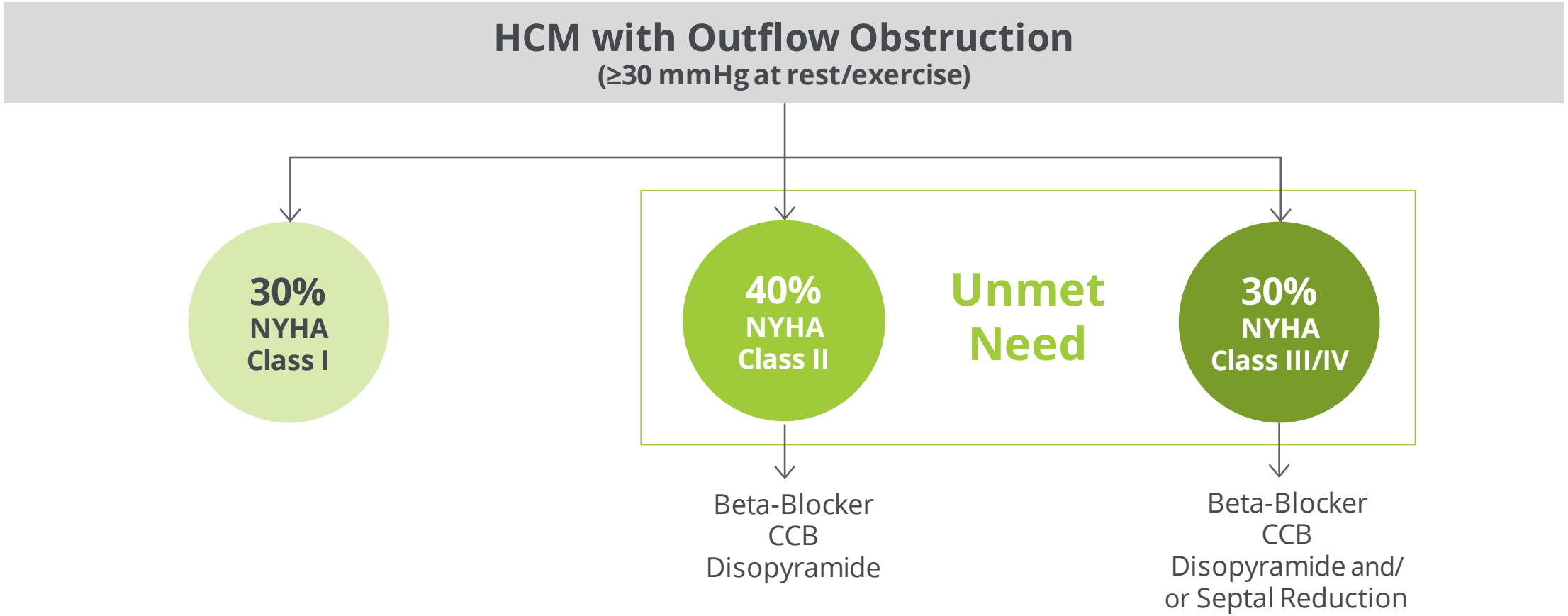


Raised Awareness From New Treatments

New treatment options and pharmaceutical companies starting to invest and educate more

CVRG market strategies heart failure 2Q 2021 and other sources on file

The *Unmet* Treatment Need in oHCM

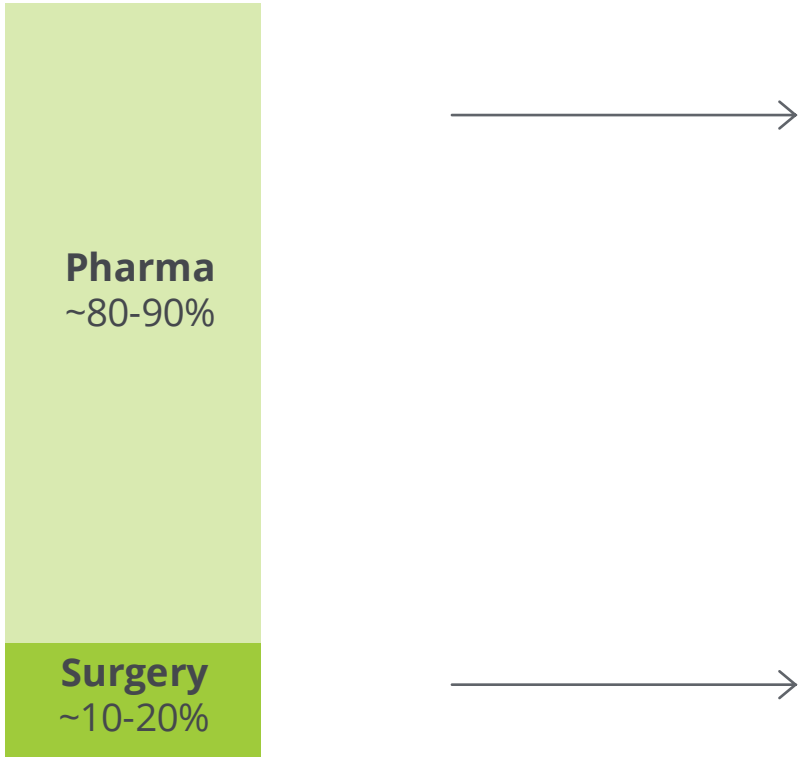


1.Maron BJ. Clinical Course and Management of Hypertrophic Cardiomyopathy. The New England Journal of Medicine. 2018 Aug;379(7):655-668. DOI: 10.1056/nejmra1710575. PMID: 30110588.
2.Maron BJ, Casey SA, Poliac LC, Gohman TE, Almquist AK, Aeppli DM. Clinical Course of Hypertrophic Cardiomyopathy in a Regional United States Cohort. *JAMA*. 1999;281(7):650–655. doi:10.1001/jama.281.7.650
3.Zaiser E, Sehnert AJ, Duenas A, Saberi S, Brookes E, Reaney M. Patient experiences with hypertrophic cardiomyopathy: a conceptual model of symptoms and impacts on quality of life. *J Patient Rep Outcomes*. 2020;4(1):102. Published 2020 Dec 1. doi:10.1186/s41687-020-00269-8

Current oHCM Treatments Have Significant Limitations

Current SOC does not address underlying disease

oHCM Treatment Options



Pharmacological

- Current Standard of Care
  - Beta Blockers
  - Calcium Channel Blockers
- Focus on symptom relief
- Results are often inadequate
- Indirect mechanisms of action
- Systemic side effects

Surgical

- Septal reduction therapy can reduce septal thickness and offer relieve
- Surgical myectomy is invasive and can carry risk
- Not always a permanent solution

SOC: Standard of care

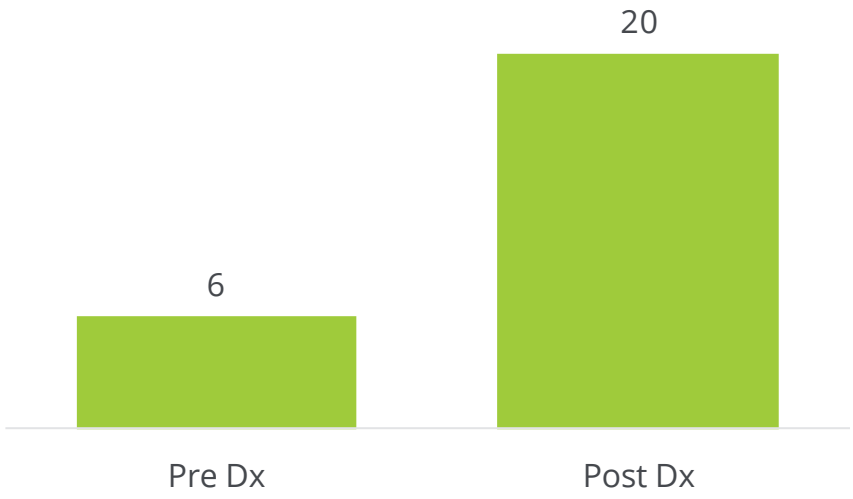
Also, Significant Cost Burden With Current Treatments

Total HCM-related costs increased by ~4x one year after diagnosis

Medical

Annual **medical costs more than doubled** following diagnosis

Cost Per Patient ($K)

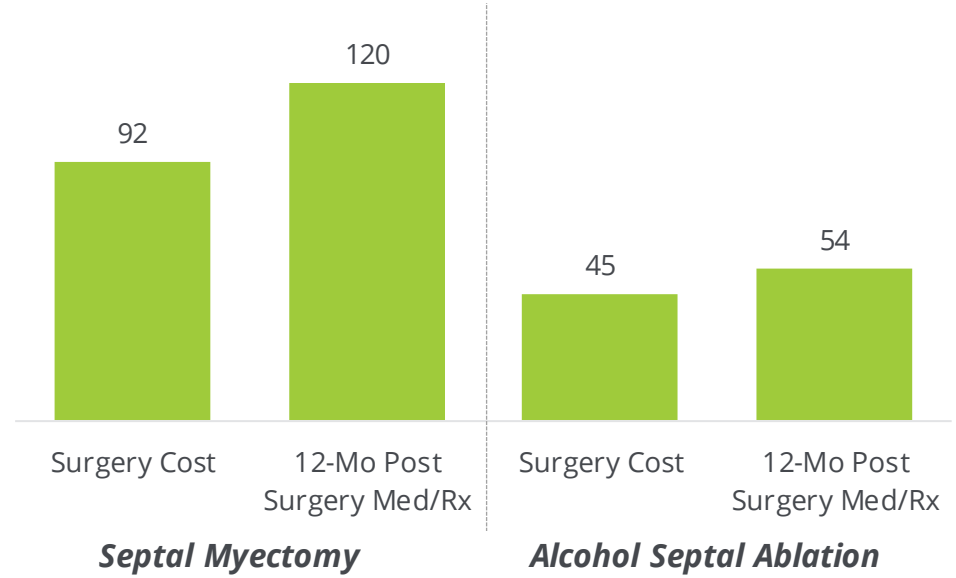


Butzner et al. 2021

Surgical

High **surgery costs** *as well as* **costs of medical and pharmacy costs post-procedure**

Cost Per Patient ($K)



Remaining Areas of Unmet Need in oHCM

Drugs that improve function and exercise capacity

Drugs that work in more severe patients

Drugs that can impact long term complications

Drugs that prevent HCM in Gene +ve patients

Drugs that provide reverse remodel benefit

Aficamten: A Next Generation Therapy

Key Attributes

No plasma monitoring

Reduce time to optimal dose

Widen therapeutic window

Fewer dose adjustments

Attributes may translate into

Accelerated Symptom Relief

Dose Optimization

Rapid Reversibility

Key Components of Aspirational Target Profile

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

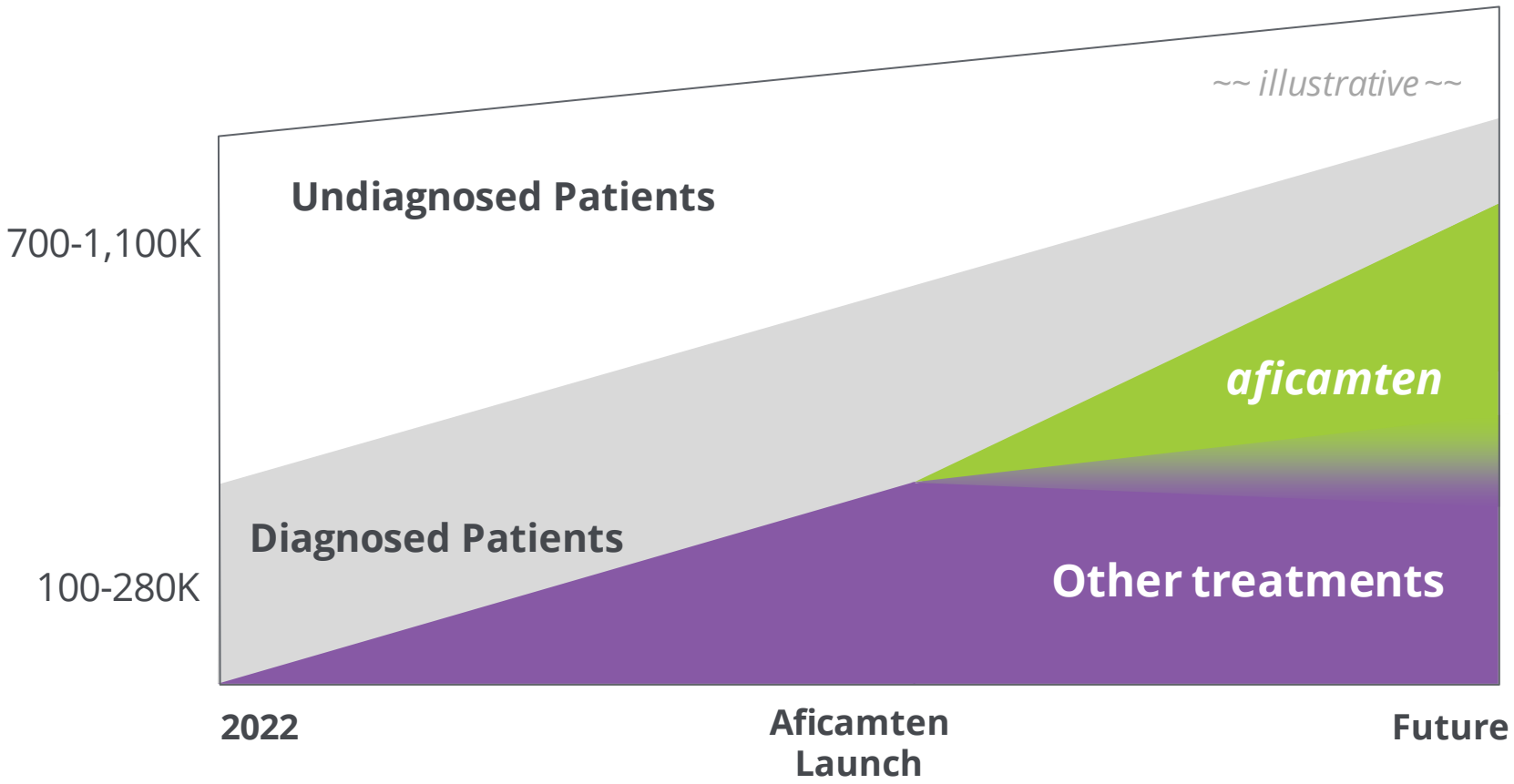
Dosing

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

Three Key Sources of Patients for *Aficamten*



Key sources of patients

Newly diagnosed

Therapy failures

Excluded patients

Aficamten: Value Proposition

Profile addresses ***all* oHCM patients regardless of severity** of disease or risk

No anticipated contraindications and ***minimal* drug interactions**

Addresses **largely *untapped* market,** potential of over 400K undiagnosed oHCM patients

Second generation treatment for newly diagnosed, therapy failures and excluded patients

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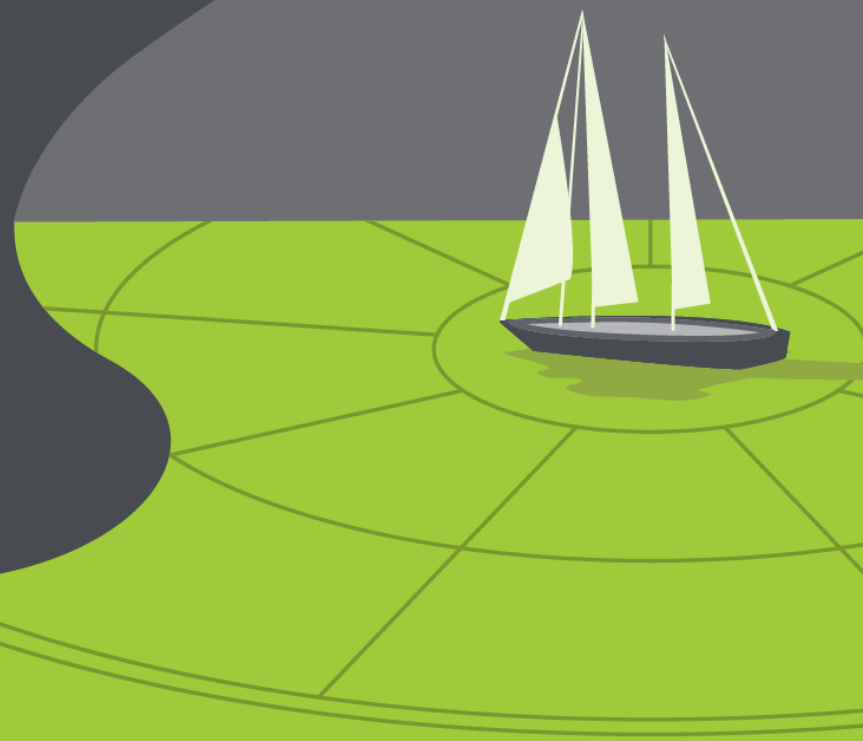
Aficamten:

Potential Next-In-Class Therapy

Steve Heitner, M.D., Senior Medical Director, Clinical Research Cardiovascular



Aficamten: Leveraging Pharmacology for Clinical Practice

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

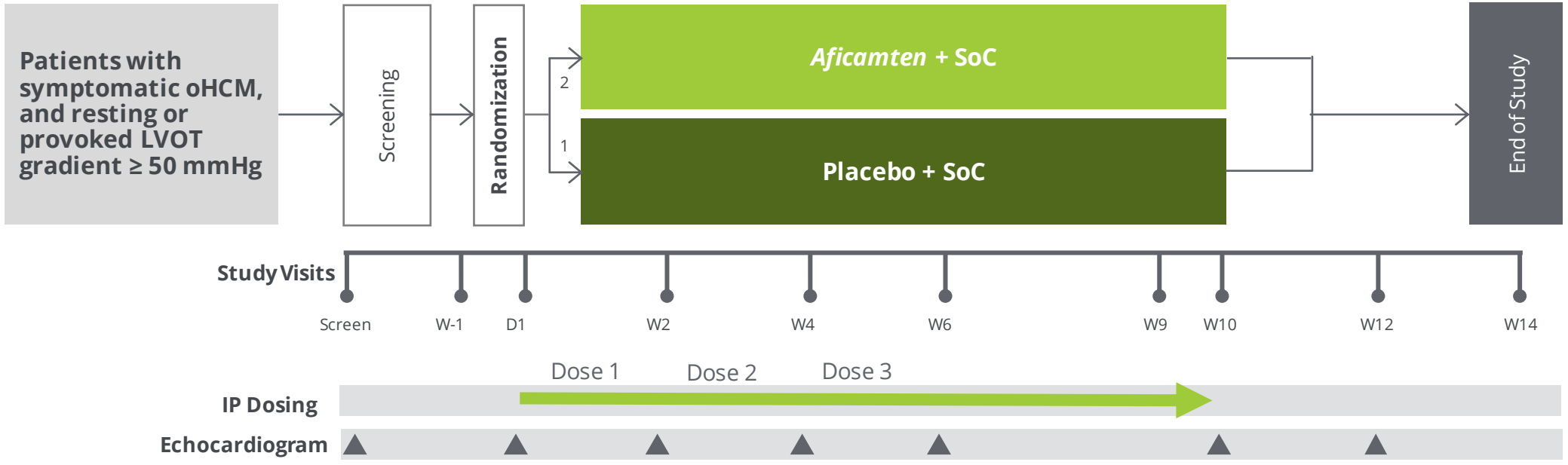
No off-target effects and use in combination with β-blockers, CCB, Disopyramide, and/or Ranolazine

Rapid Reversibility

Washout of pharmacodynamic effect within 2 weeks

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

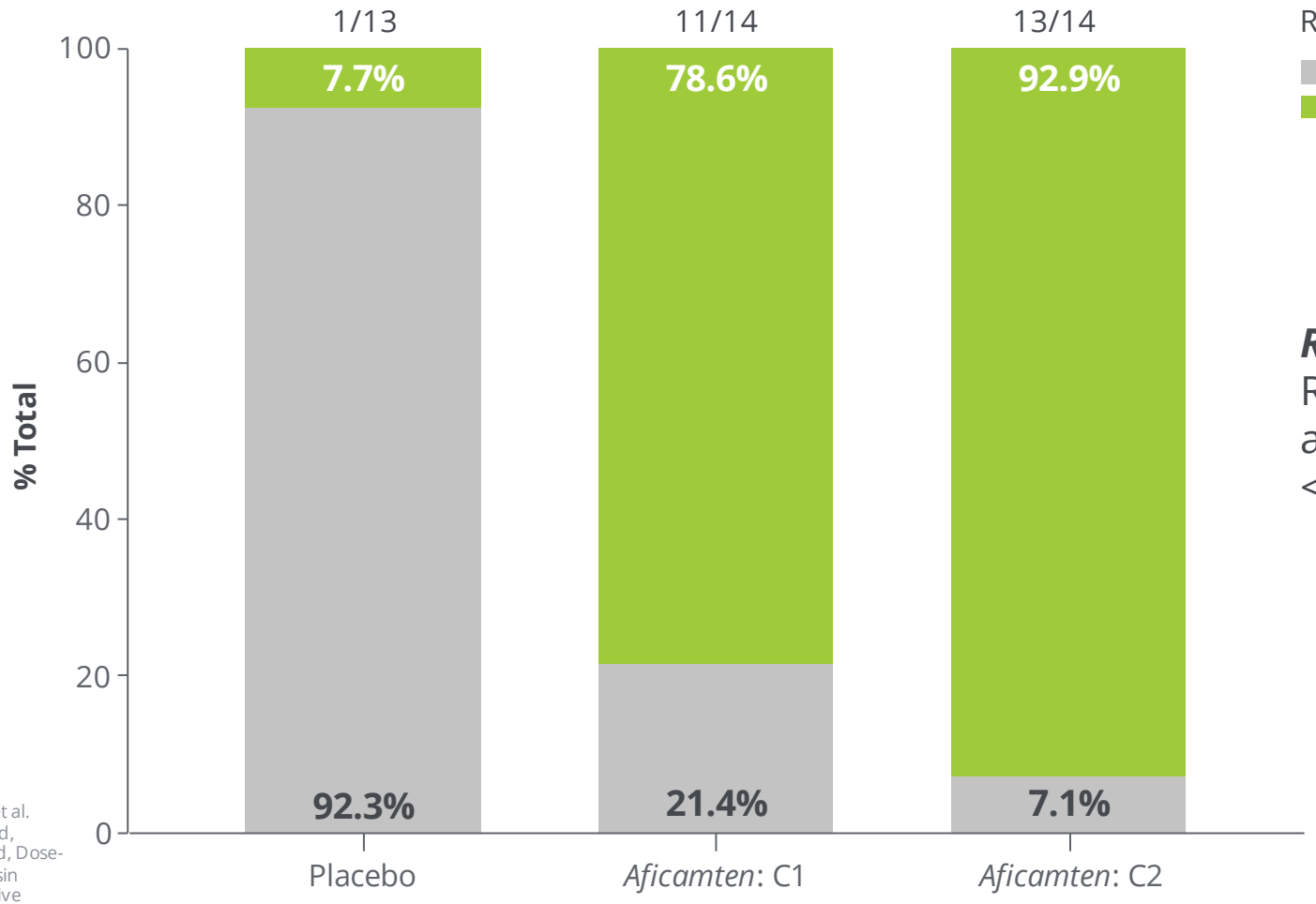
Baseline Characteristics

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"

High Response Rates on Treatment with *Aficamten*

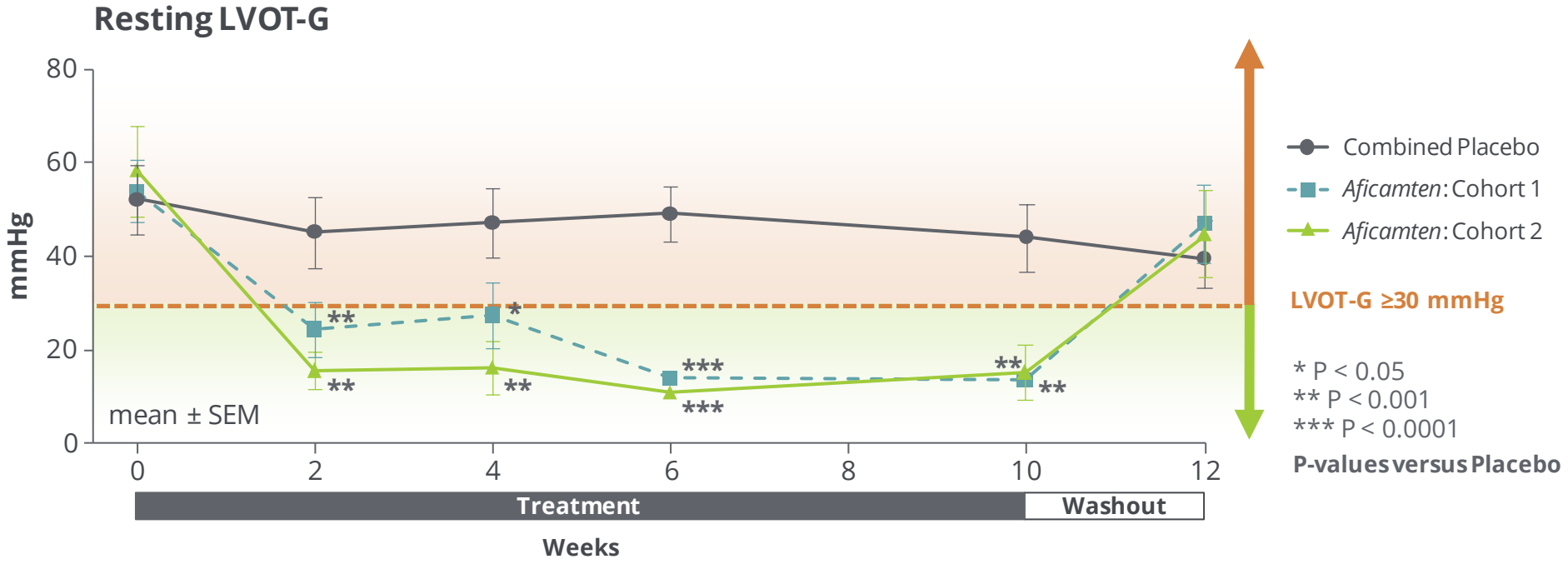


Responder Definition:
Resting LVOT-G <30 mmHg and post-Valsalva LVOT-G <50 mmHg at Week 10

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: Efficacy

Resting Left Ventricular Outflow Tract Gradient (LVOT-G)

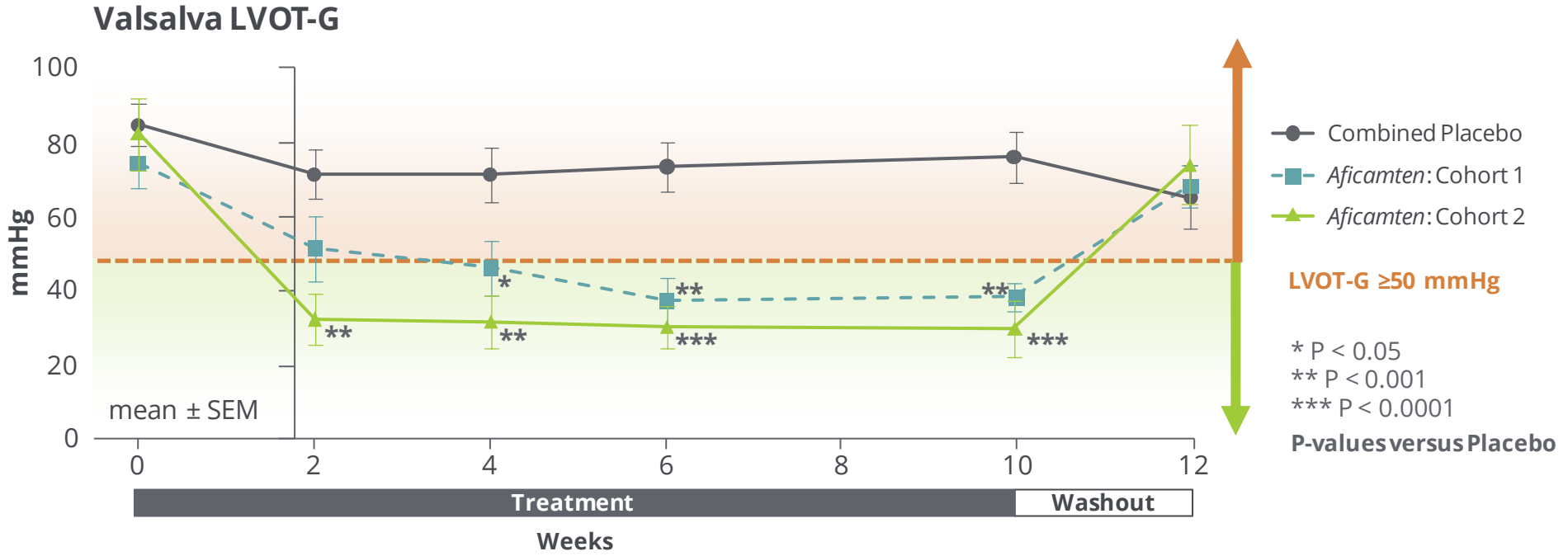


Mean ± SEM	Resting LVOT-G (mmHg)				
	Baseline	*Week 2*	*Week 4*	*Week 6*	*Week 10*
Placebo (n = 13)	52.1	45.0	47.1	49.0	44.0
Cohort 1 (n = 14)	53.8	24.3	27.3	13.9	13.4
p-value vs placebo	-	0.007	0.025	<0.0001	0.0003
Cohort 2 (n = 14)	58.2	15.5	16.1	10.9	15.1
p-value vs placebo	-	0.0002	0.0006	<0.0001	0.0004

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: Efficacy

Valsalva LVOT-G

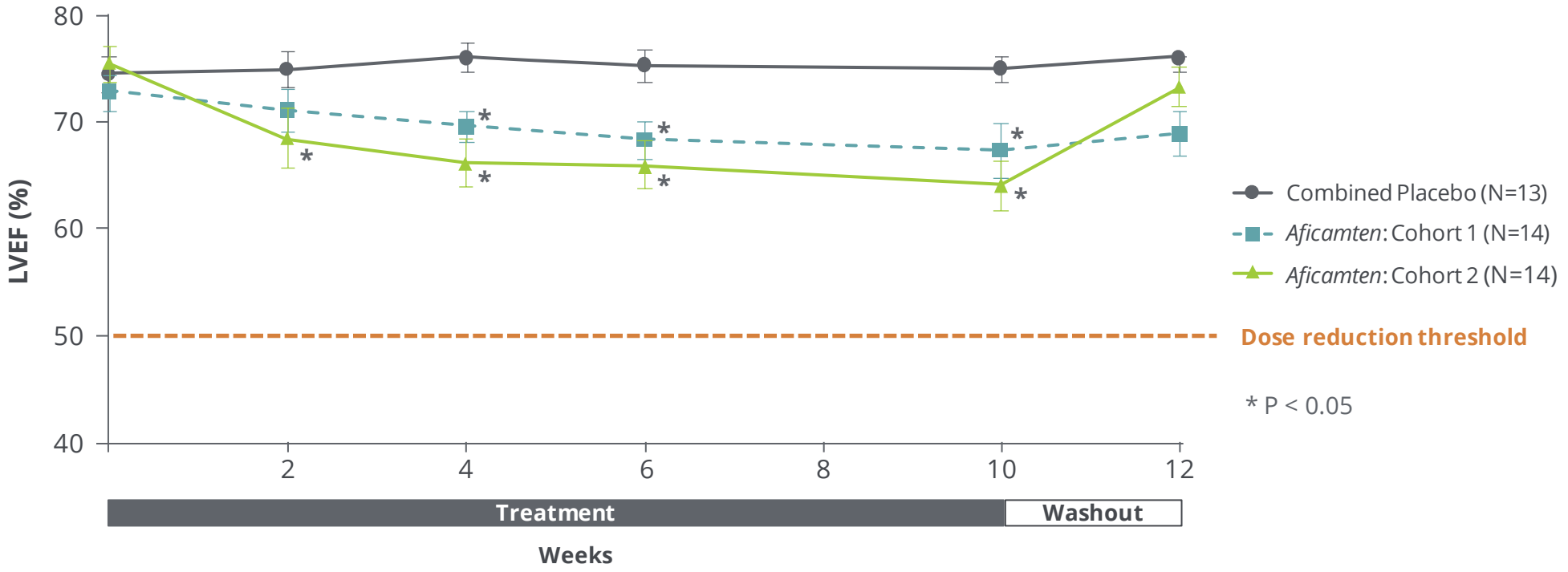


Mean ± SEM	Valsalva LVOT-G (mmHg)				
	Baseline	*Week 2*	*Week 4*	*Week 6*	*Week 10*
Placebo (n = 13)	84.6	71.3	71.3	73.4	76
Cohort 1 (n = 14)	74.4	51.3	46.1	37.1	38.1
p-value vs placebo	–	0.097	0.038	0.0003	0.001
Cohort 2 (n = 14)	82.3	32.3	31.5	30.3	29.8
p-value vs placebo	–	0.0005	0.0005	<0.0001	<0.0001

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: Efficacy

Changes in Left Ventricular Ejection Fraction over Study Period



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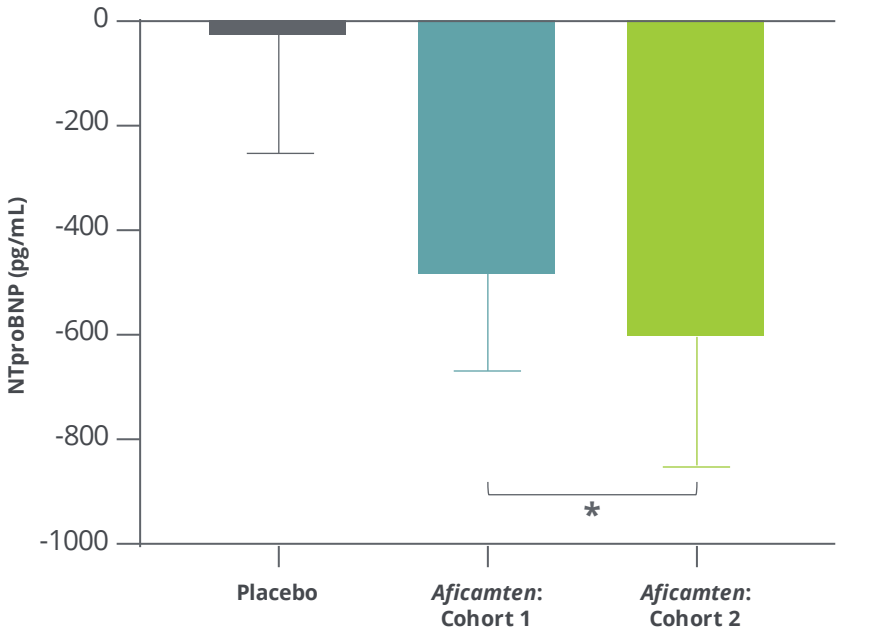
Change from Baseline in NT-proBNP & NYHA Class

Change from Baseline NT-proBNP to Week 10

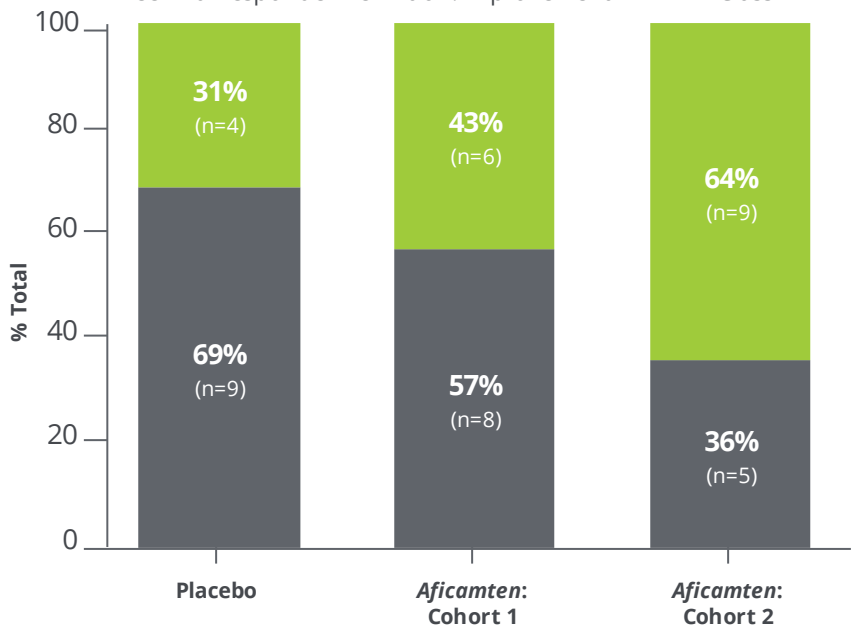


*** P = 0.003 for Pooled Cohort 1 & 2 vs. Placebo**

- 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: Safety Data

- **2 SAEs reported in Cohort 1 and none in Cohort 2**
  - Stress Cardiomyopathy: 55-year-old female assigned to Placebo, with associated cardiogenic shock after IP discontinuation at end of treatment (Week 10).
  - Back Pain: 50-year-old male assigned to *aficamten* (dose 5 mg at the time of SAE, and max dose 15 mg) visited Emergency Room for exacerbation of preexisting musculoskeletal back pain.
- **No SAEs reported that resulted in early termination**
- **No treatment-related serious adverse events**
- **No imbalance in adverse events between *aficamten* and placebo treated arms**

- **No patients met the "stopping criteria" of LVEF < 40%**
- **No treatment interruptions or discontinuations**
- **Treatment Emergent Adverse Events**
  - Placebo 85% of participants
  - *Aficamten* 88% of participants
- **LVEF < 50% (Cohort 2 only)**
  - 1 patient (baseline EF = 58%) underwent per-protocol dose reduction at Week 4 and had LVEF return above 50% (max dose 20 mg)
  - 1 patient (baseline EF = 70%) had LVEF 49.3% at Week 10 (max dose 20 mg; no dose changes) and LVEF returned to baseline at the end of study (Week 12)

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

Enrollment complete in Cohort 3

	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

Open Label Extension Trial

REDWOOD HCM OLE

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

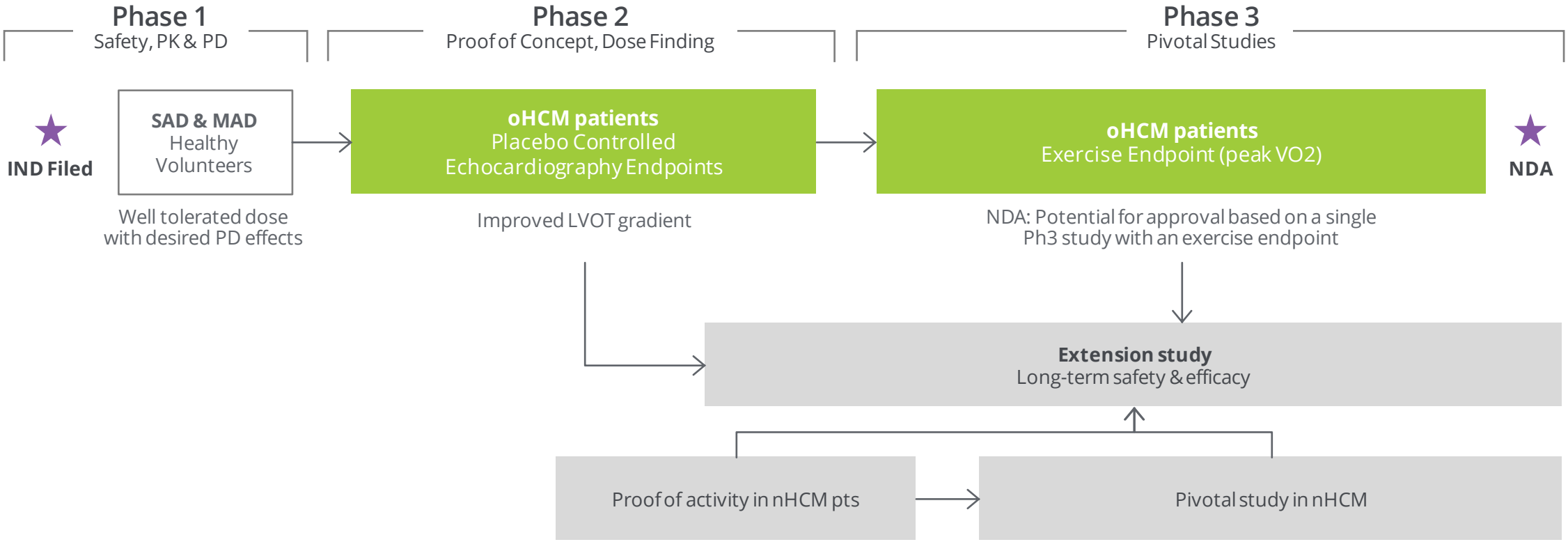
- Primary endpoint: incidence of AEs & LVEF <50
- Secondary endpoints: measures of long-term effects of *aficamten* on LVOT-G; assessments of steady-state pharmacokinetics.
  - Cardiac MRI sub-study to assess changes in cardiac morphology, function and fibrosis
- Individually optimized dose starts at 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

Aficamten: Clinical Development Plan for HCM

Engaging regulatory authorities to inform Phase 3

Type C and end-of-phase 2 meetings with FDA occurred in Q3; Plans underway to start Phase 3 trial in Q4



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

Introducing SEQUOIA-HCM

SEQUOIA-HCM: Strategic Objectives

In patients with symptomatic, uncontrolled oHCM treated with *aficamten*, demonstrate:

- **Robust improvement in exercise capacity** using gold standard methodology
- Parallel alleviation of heart failure **symptoms and improvement in QoL**
- High level of **achievement of target LVOT gradients**
- Individualized, **rapid dose optimization**
- Ease of **echocardiographic-guided dose titration** – no PK-guided dosing
- **Functional and pharmacodynamic benefits** associated with:
  - Structural evidence of cardiac reverse remodeling
  - Good safety and tolerability profile
  - Maintenance of normal LVEF
  - Minimal dose interruptions
- **Favorable benefit-risk profile** on top of good SoC – BBs, CCBs, disopyramide

SEQUOIA-HCM: Key Entry Criteria

- Males and females between 18 and 85 years of age, inclusive, at screening
- Body mass index <35 kg/m^2
- Diagnosed with oHCM per the following criteria:
    - Has LV hypertrophy and non-dilated LV chamber in the absence of other cardiac disease AND
    - Has end-diastolic LV wall thickness as measured by the echocardiography core laboratory of ≥15 mm in one or more myocardial segments
- Has resting LVOT-G ≥30 mmHg and post-Valsalva LVOT G ≥50 mmHg during screening as determined by the echocardiography core laboratory
- LVEF ≥60% at screening as determined by the echocardiography core laboratory
- NYHA Functional Class II or III at screening
- Exercise performance <80% predicted on screening CPET
- Patients on beta-blockers, verapamil, or diltiazem should have been on stable doses for >6 weeks prior to randomization and anticipate remaining on the same medication regimen during the trial

SEQUOIA-HCM: Endpoints

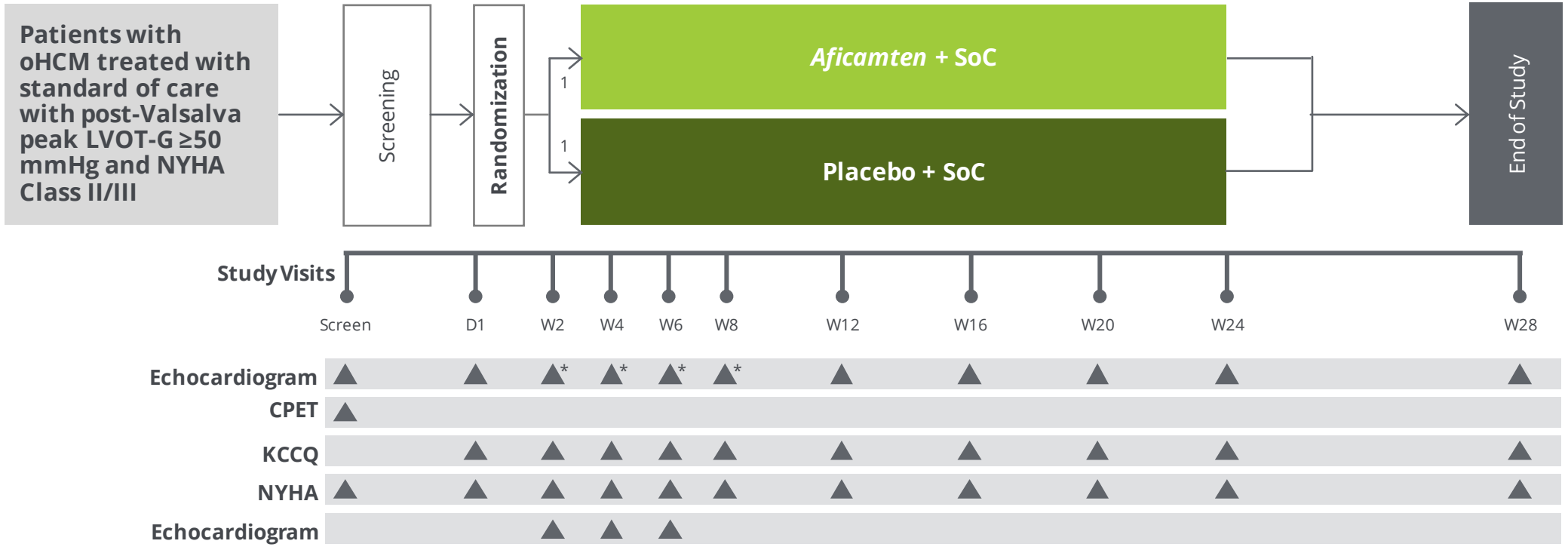
Phase 3 Clinical Trial Expected to Open for Enrollment in Q4 2021

Primary Objectives and Endpoints	
Exercise capacity in patients with oHCM	Δ pVO_2 by CPET from baseline to Week 24
Secondary Objectives and Endpoints	
To evaluate the effect on health status	Δ in KCCQ from baseline to Week 12 and Week 24
To evaluate the effect on NYHA FC	Proportion of patients with ≥1 class improvement in NYHA FC from baseline to Week 12 and Week 24
To evaluate the effect on post-Valsalva LVOT-G	Change in post-Valsalva LVOT-G from baseline to Week 12 and Week 24 & Proportion of patients with post-Valsalva LVOT-G <30 mmHg
To evaluate the effect on exercise capacity	Change in total workload during CPET from baseline to Week 24

pVO_2 = Peak oxygen uptake; KCCQ = Kansas City Cardiomyopathy Questionnaire Score; NYHA FC = New York Heart Association Functional Class; LVOT-G = Left Ventricular Outflow Tract Gradient; CPET = Cardiopulmonary Exercise Testing

SEQUOIA-HCM: Phase 3 Trial Design

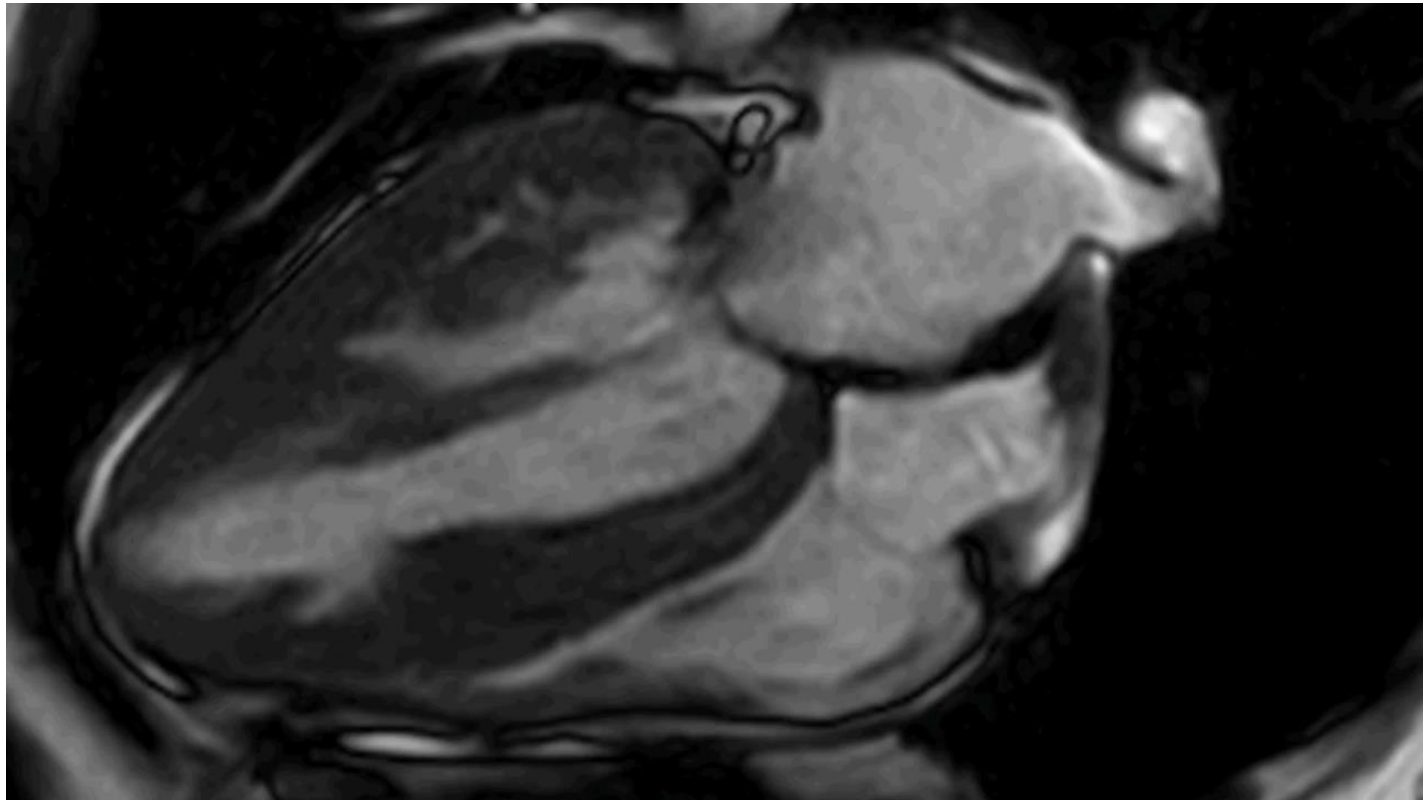
Individualized dose up-titration based on echocardiography: LVEF ≥55%, Post-Valsalva LVOT-G ≥30 mmHg

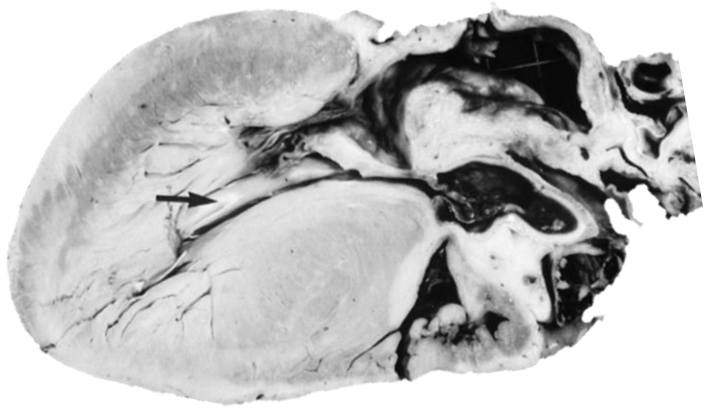


Dose Options (Dose optimization completed by Week 8)			
5 mg QD	10 mg QD	15 mg QD	20 mg QD

* Focused echocardiogram

CMR Sub-Study: Exploratory Objectives, Endpoints



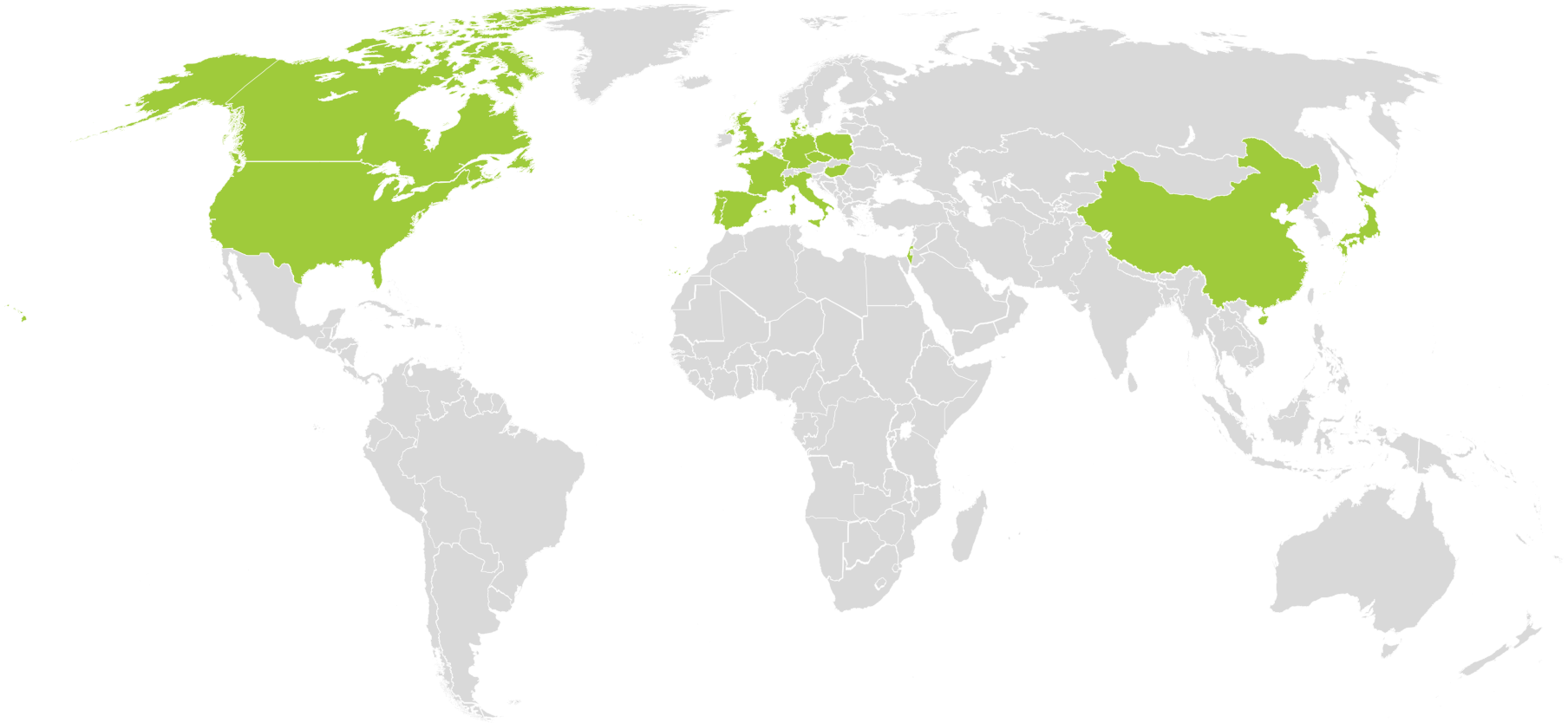


Cardiac Magnetic Resonance
Serial imaging gives us the highest definition images that can non-invasively quantify:

- Cardiac structure
- Cardiac function
- Tissue composition

Aficamten: SEQUOIA-HCM

Trial On Track to Start by Year End



Probable Sites	
US	35
Canada	2
Italy	10
France	7
Germany	9
Czech Republic	2
Denmark	3
Hungary	1
Netherlands	3
Poland	3
Portugal	2
Spain	5
UK	3
Israel	5
China	~8
Japan	TBD

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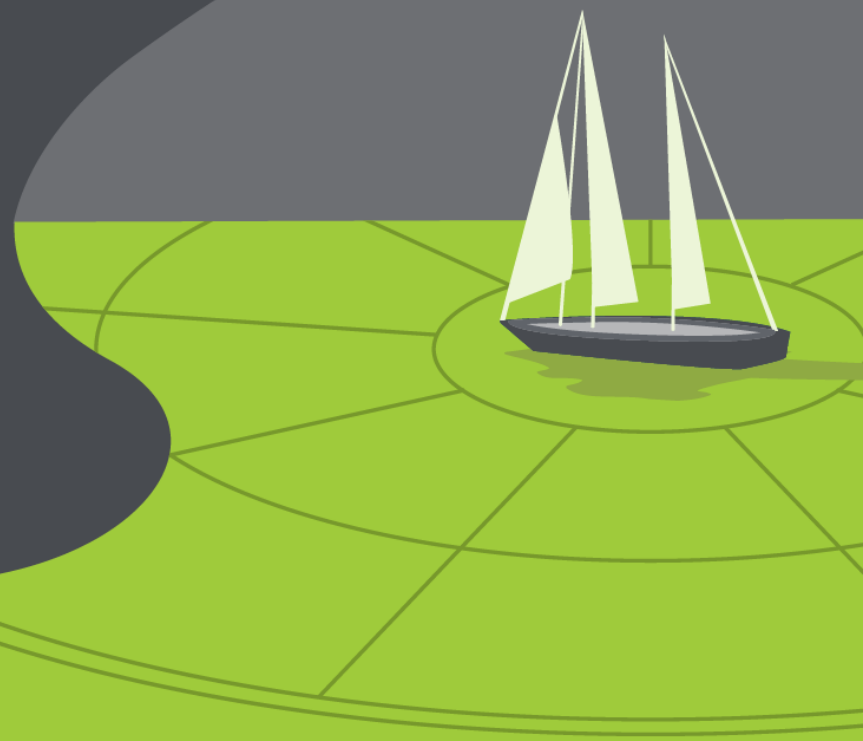
Franchise Strategy

Andrew Callos, EVP, Chief Commercial Officer



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 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 claims

Significant GTM Synergies Between *OM, 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**

Commercializing *Aficamten* Leverages Launch Build-Out

***Omecamtiv mecarbil* launch build-out …**		**… enables *aficamten* commercialization**
Internal	Commercial **leadership** Scalable **organization** design **Marketing & analytics** **Field teams** **Medical Affairs** incl. MSLs **Systems** and business **processes**	→ ☑ **Further build on** commercial capabilities put in place by 2025
External	**Relationships** with cardiologists and payers **Partnership** with patient advocates **Reputation** in cardiovascular	→ ☑ Accelerate **CV franchise leadership** through relationships and partnerships

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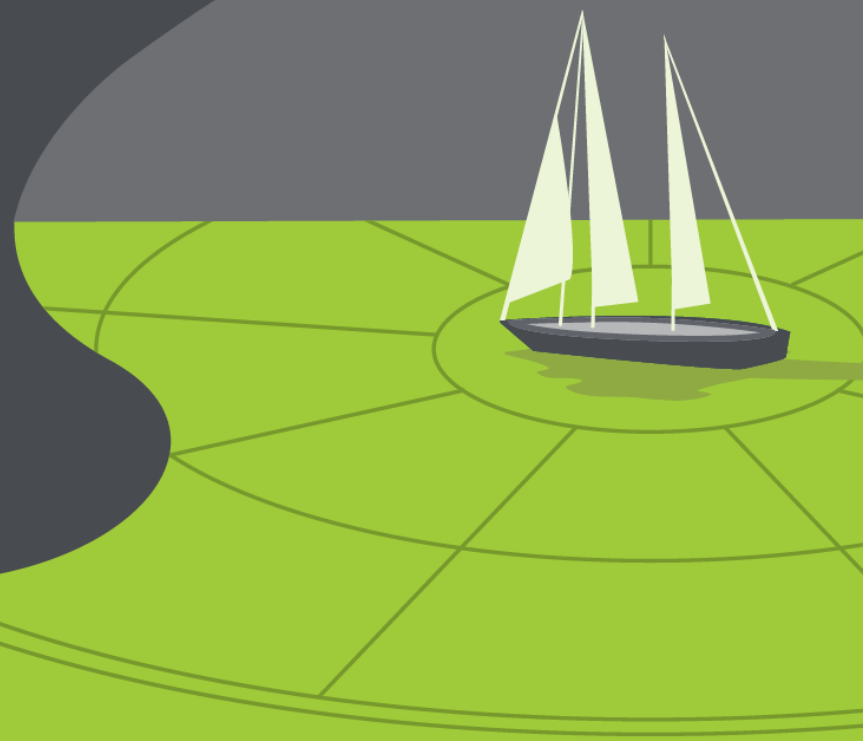
Financial Foundation & Corporate Development

Ching Jaw, CFO



For Investors Only

Current Financial Summary

Cash on Hand to EOY

~$600M*

Est. cash balance @ YE21

Debt

~$183M

Term loan plus convertible debt

2021 Guidance

~$195 - 215M

Est. net cash utilization for 2021

Cash Runway

~3 YRs**

Est. cash runway @ YE21

*Excludes potential proceeds from business development and structured financing transactions in 2H21
**Based on 2021 spending guidance of $195-$215M

Building Cytokinetics' Business on Solid Financials, Deals

Balanced approach to raising capital through equity raise and non-equity capital;

Pursue corporate partnerships to leverage partners' strength in complimentary geographies

Strong Balance Sheet	Current cash balance of more than $650M (~ 3years of runway based on 2021 guidance); $45M term loan; $138M convertible debt well above conversion price
Business Development	Pursuing licensing partnership(s) for *omecamtiv mecarbil* in Asia and Europe
Structured Financing	Raising non-equity dilutive capital through royalty monetization and structured debt

Financing History

As of 6/30/2021, with proceeds from 7/23/21 offering

in millions

	As of 6/30/2021	Financing	Equity	Upfront Cash, Option, & Milestones	R&D Reimbursement	Total
Investors	Private Investors (VCs)		$116			$116
	IPO		$94			$94
	Public Post-IPO/Other		$906			$906
	Term Loan	$45				$45
	Convertible Debt (net)*	$120.5				$120.5
		$165.5	**$1,116**			**$1,281.5**
Strategic Partners & Grants	RTW/Ji Xing		$50	$113		$163
	Astellas		$10	$130	$103	$243
	Amgen		$43	$145	$60	$248
	Royalty Pharma		$10	$90	–	$100
	GSK		$24	$22	$33	$79
	AstraZeneca		–	–	$2	$2
	MyoKardia		–	–	$2	$2
	Global Blood		–	–	$2	$2
	Grants (ALS Assoc/NINDS/other)		–	$6	–	$6
			$137	**$506**	**$202**	**$845**

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

Capital raised: combination of strategic partners and investors

We Are Aware of Investor Concern Regarding CV Launches

Overestimating market potential

Company A believed its product would be used by up to 2M patients at peak in the US and **guided the Street to use an unrealistic launch analogue**. Overconfidence & ungated spending may have driven too aggressive investment strategy

Failure to learn from others' experience

Company D and E struggled to launch into genericized and competitive markets underscoring the need to **focus to highly concentrated and specialized customer segments**

Overly aggressive deployment of sales force and marketing expenses

Company B **too quickly hired more than 300 reps**, believing its sales force could cover the top 4 deciles of targets based on market research and projected sales uptake. When sales expectations failed to realize, the fixed cost size of the investment exceeded its net cash inflows

Better to focus to markets with high morbidity/mortality and high economic burden

Company C commercialized a new medicine absent compelling pharmacoeconomic rationale. **HEOR drives payer response**

Under-prepared for slower product adoption

Company F **failed to raise sufficient capital** in anticipation of the increased net cash burn associated with increasing operating expenses and delayed reimbursement

Gating Commercial Spending to Achieve Profitability

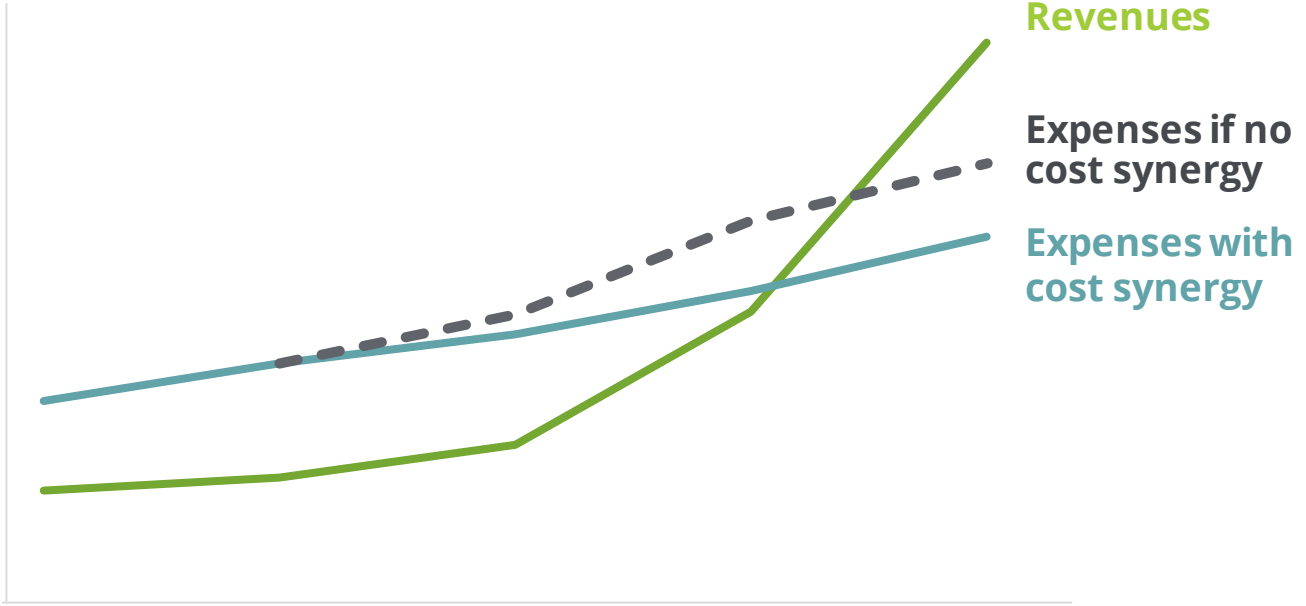
Omecamtiv Mecarbil → ***Aficamten***

Gate commercial investments to milestones:

- NDA submission
- NDA filing by the FDA
- NDA approval
- Sales thresholds

Leverage overlap of hospital and physician bases between treatment of worsening HF and HCM:

- Field force synergies
- Improved brand margins through cost savings
- Achieve brand profitability sooner



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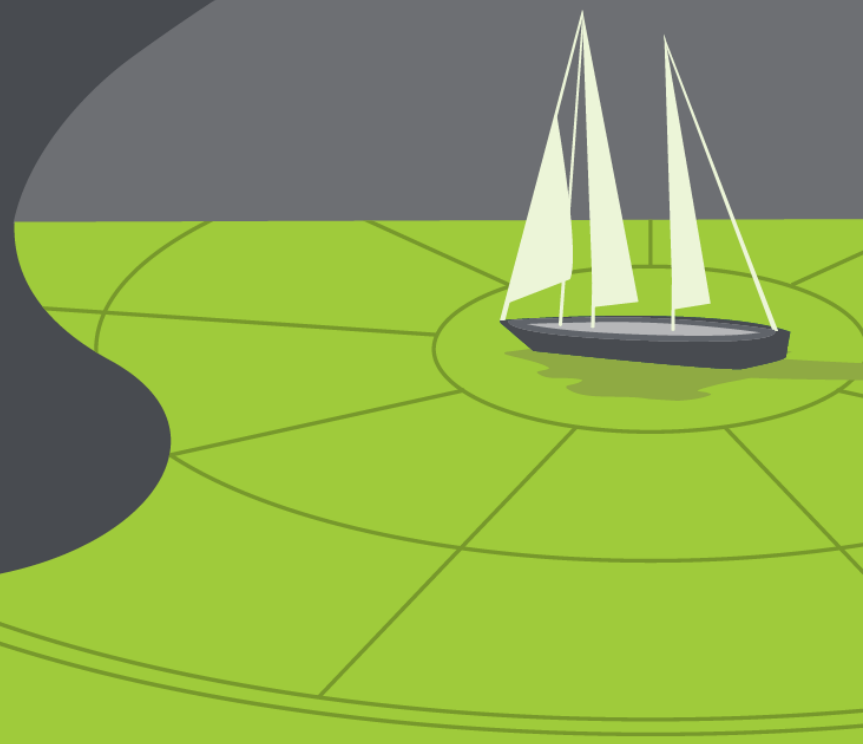
Q&A

To ask a question in the room, please raise your hand.

To ask a question online, type it into the tab on the left.



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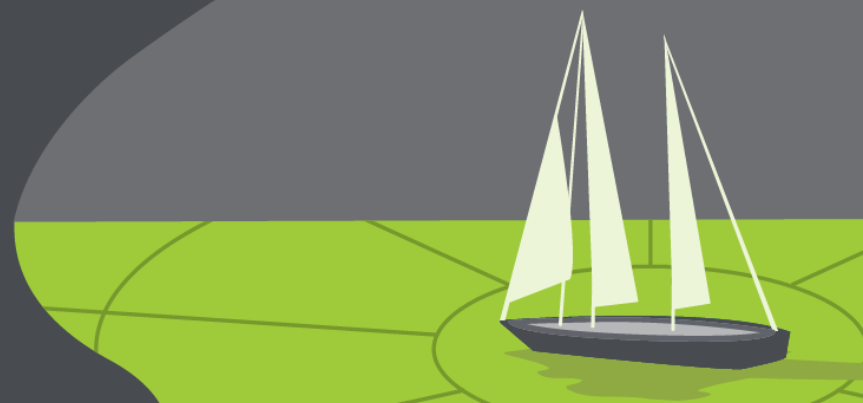
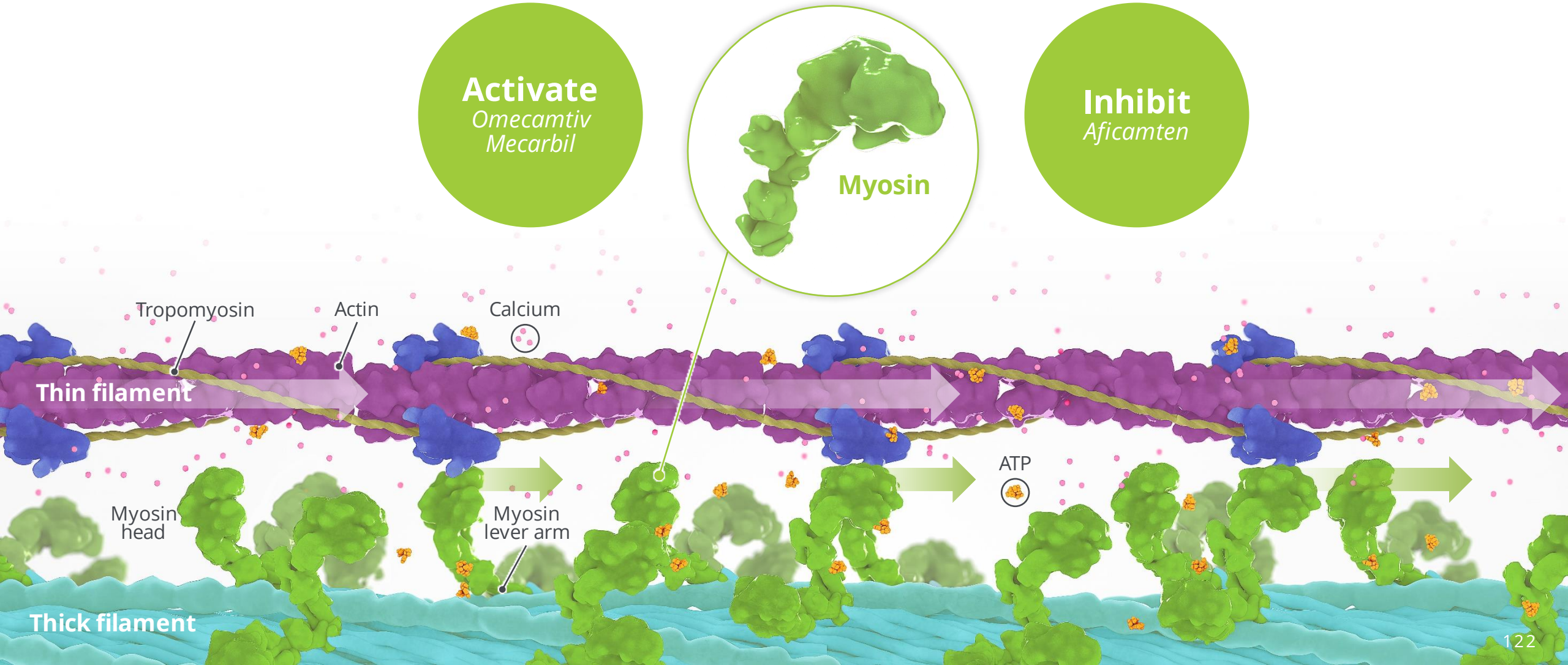
Closing Remarks

Robert Blum, President & CEO

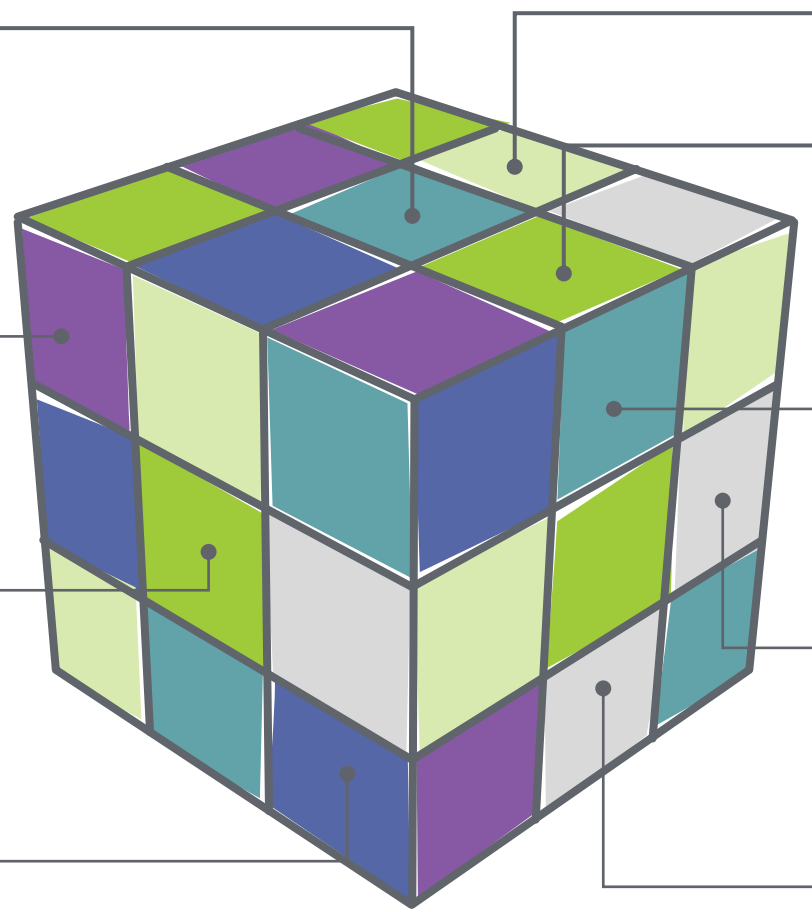


One Molecular Target Supports Emerging CV Franchise



Building a Cardiovascular Franchise

- Gated Investment Tied to Key Milestones
- Uncommon Franchise Strategy Opportunity
- Overlapping Physician, Hospital, Payor Customer Segments
- Compelling HEOR and Pharmacoeconomics
- High Clinical, Economic Burden
- Growing Prevalence with Aging Demographics
- Continued Life Cycle Management, Expanded Development



- Diversified Access to Additional Capital
- Major Public Policy Visibility
- Tractable to Lean Sales/Marketing Structure
- Big Pharma Investing in Market/Category Expansion
- Potential for High ROI with Layered Cash Flows
- Concentrated CV Specialty Care
- Add-on Complement to Standard of Care
- Strong Biological, Pharmacological Rationale

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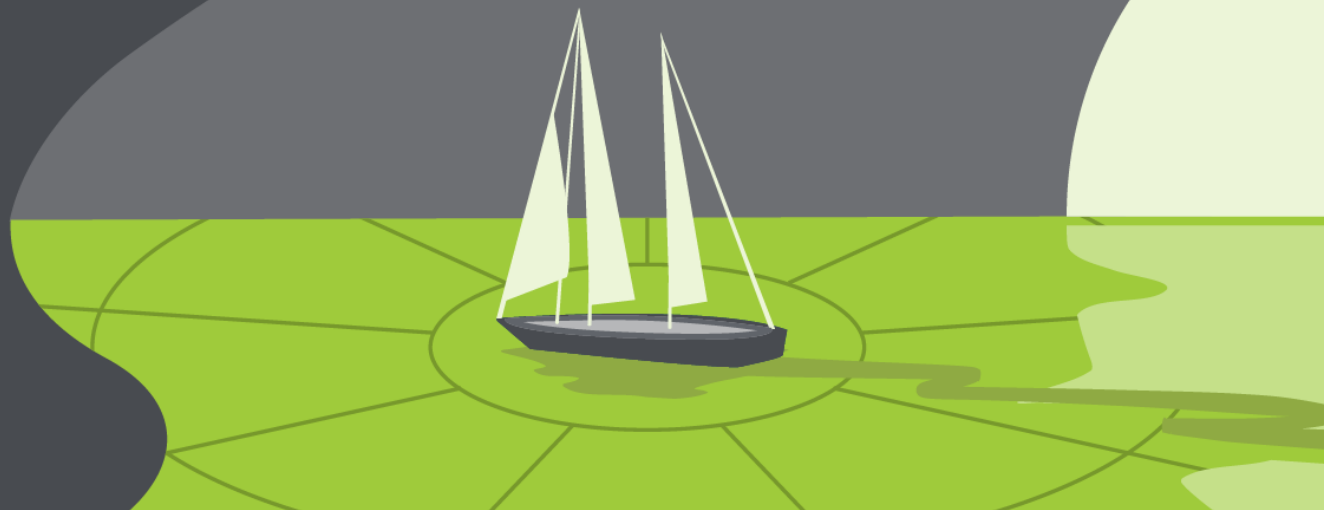

Boxed lunches available to go

Recording and slides to be made available online at cytokinetics.com