



## EXPLORER-CN Topline Data Results and Mavacamten China Commercial Opportunity Call

May 1, 2023

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**Yizhe Wang, Ph.D.**

Chief Executive Officer, LianBio



## Obstructive Hypertrophic Cardiomyopathy (oHCM)

Treatment and diagnosis in China today

*Zhuang Tian, M.D., Professor of Cardiology, Peking Union Medical College Hospital; EXPLORER-CN Investigator*



## Phase 3 EXPLORER-CN Topline Data Review

Clinical and regulatory update

*Michael Humphries, FRCP, Chief Scientific Advisor, LianBio*



## Mavacamten Potential

Clinical development strategy in other diseases of diastolic dysfunction

*Brianna Sun, Head of CV Medical, LianBio*



## Commercial Readiness Strategy

Mavacamten in oHCM

*Pascal Qian, Chief Commercial Officer and General Manager of China, LianBio*



## Q&A

*Yizhe Wang, Ph.D., Yi Larson, Pascal Qian, Michael Humphries*



**Mission:** To catalyze the development and accelerate availability of paradigm-shifting medicines for patients in China and major Asian markets

## Where We Started

- Vision to **accelerate patient access** to innovative medicines
- **Decrease the time** it has historically taken to bring new medicines into China
- Leverage newly available regulatory paths that **shorten timeline to approval**
- **Design and execute bespoke development strategies**, taking into account local clinical practice and local regulator considerations

## Where We Are

- First program in-licensed has met primary endpoint in **first pivotal trial**
- NDA accepted with **priority review** by China's National Medical Products Administration
- Designed clinical programs based on key endpoints to **support commercialization**
- Potential for mavacamten approval in China roughly **2 years after approval in the U.S.**



## HCM Diagnosis and Treatment in China Today

### Zhuang Tian, M.D.

- Professor of Cardiology, and Deputy Director of the Internal Medical Department, Peking Union Medical College Hospital
- Member of Chinese Society of Rare Diseases
- Member and Secretary of the Heart Failure Group of Chinese Society of Cardiology
- Member of the Standing Committee of the Clinical Pharmacy Branch of the Beijing Medical Association
- Deputy Director of the Cardiovascular Precision Medicine and Rare Diseases Group of the Fifth Committee of the Cardiovascular Physician Branch of the Chinese Medical Doctor Association
- China Executive Director of the Rare Disease Branch of the Research Hospital Association
- Expertise in the diagnosis and treatment of heart failure, cardiomyopathy, pulmonary hypertension and imaging studies such as echocardiography.
- Author of more than 60 papers and editor of 2 books
- Investigator, EXPLORER-CN

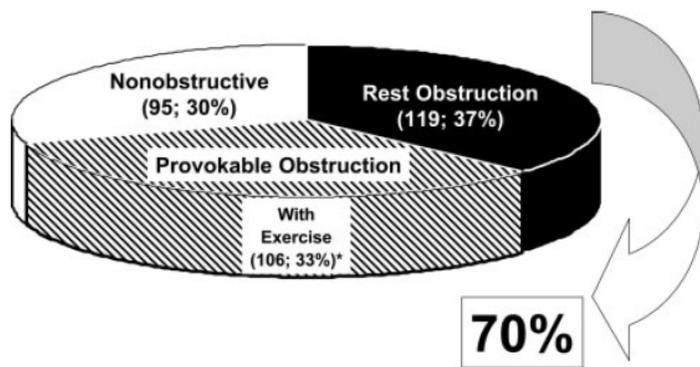
# Definition and Clinical Diagnosis of Hypertrophic Cardiomyopathy (HCM): Similar Between US and China

## HCM Clinical Definition<sup>1-3</sup>

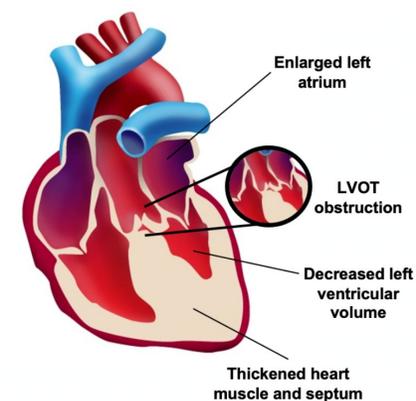
- ❑ HCM is a disease state in which morphologic expression is confined solely to the heart. It is characterized predominantly by **left ventricular hypertrophy (LVH)** in the absence of another cardiac, systemic, or metabolic disease capable of producing the magnitude of hypertrophy evident in a given patient and for which a **disease-causing sarcomere (or sarcomere-related) variant** is identified, or genetic etiology remains unresolved.

## HCM Clinical Diagnosis in Adults<sup>1-3</sup>

- ❑ A diagnosis of HCM can be established by imaging, with **echocardiography or cardiac magnetic resonance (CMR)** showing a maximal end-diastolic wall thickness **≥15 mm** anywhere in the left ventricle, in the absence of another cause of hypertrophy in adults. More limited hypertrophy (**13-14 mm**) can be diagnostic when present in family members of a patient with HCM or in conjunction with a positive genetic test.



Up to 70% of HCM patients have resting or provokable LVOT obstruction (LVOT gradient  $\geq 30$  mmHg)<sup>4</sup>

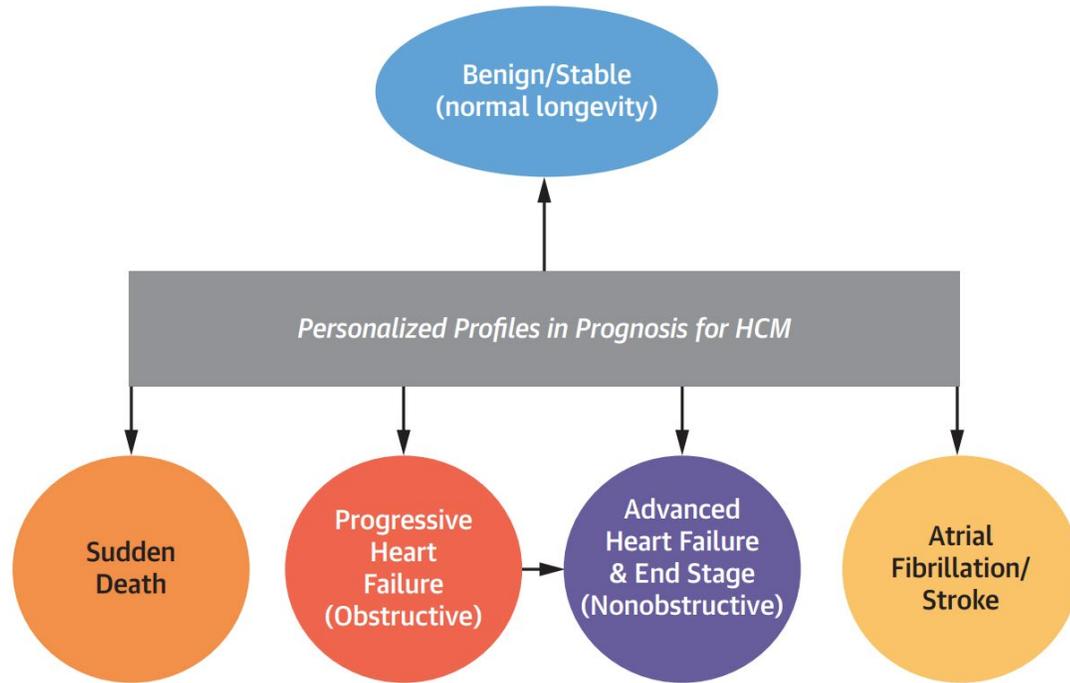


**Obstructive HCM (oHCM)**

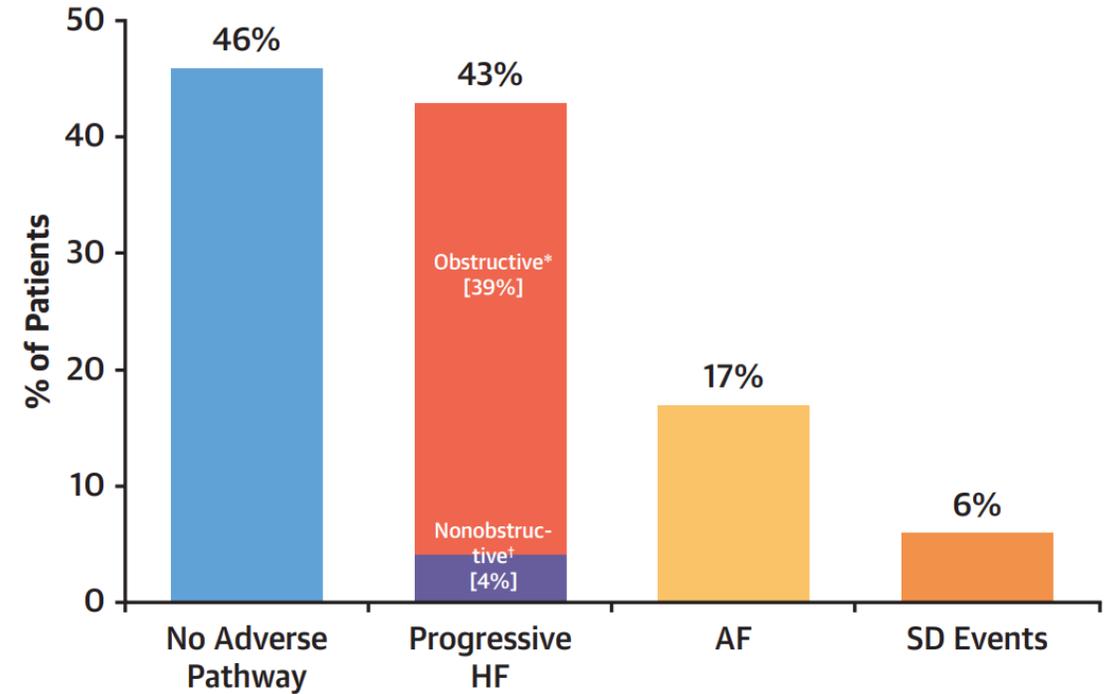
1. Circulation 2020;142:e558-e631
2. Clin J Heart Fail & Cardiomyopathy 2022;6:80-105
3. Chinese Circulation Journal 2023;38:1-33
4. Circulation 2006;114:2232-9

# Clinical Course of HCM: More than 50% HCM Patients will Experience Adverse Clinical Outcomes

## Chinese Patients Experience Same Adverse Clinical Pathways



Clinical profiles and prognostic pathways

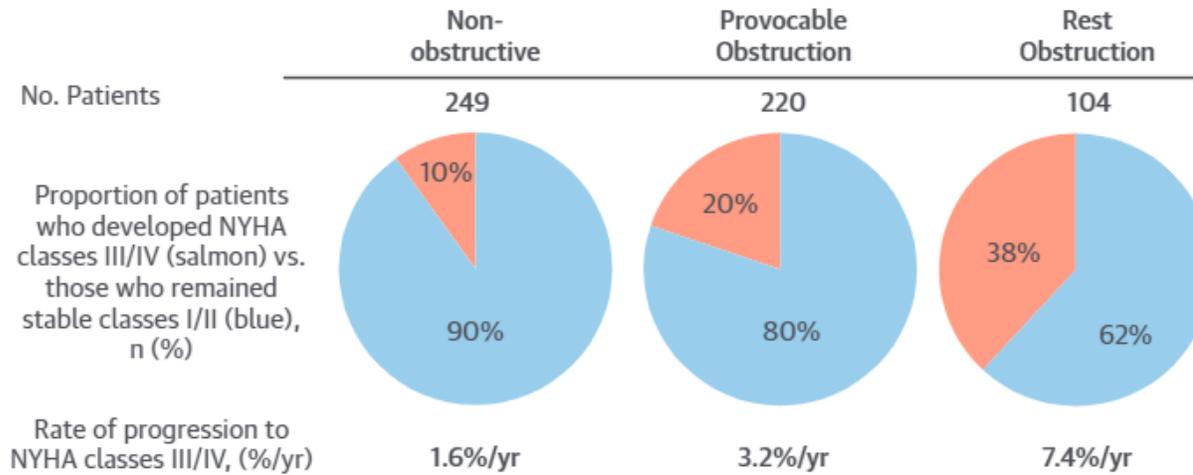


Percentage of HCM patients experiencing adverse clinical pathways

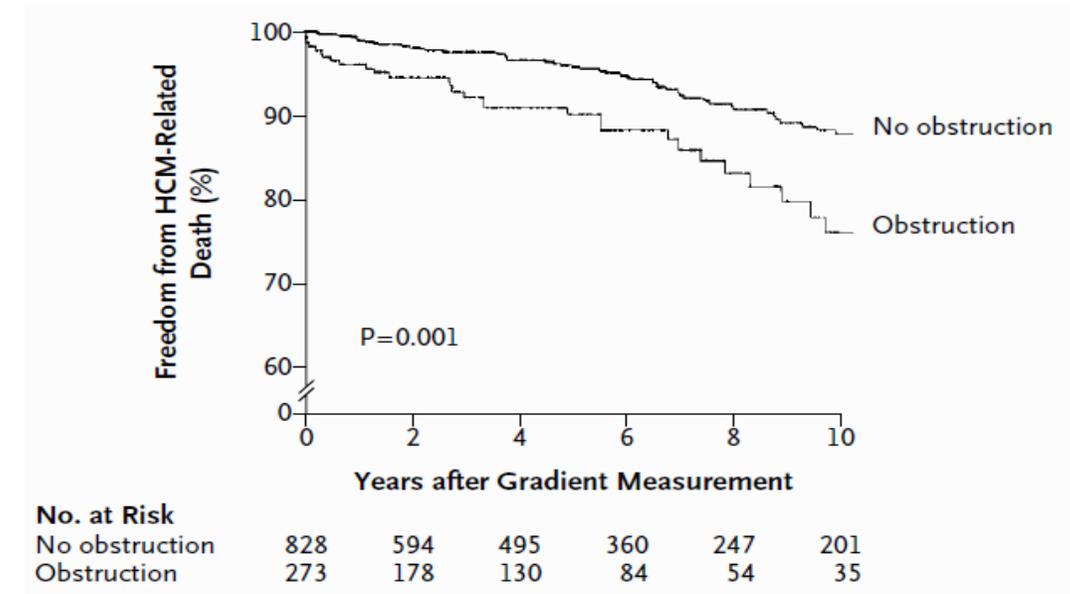
# Prognosis in oHCM Patients: Significantly Higher Risks of Severe Heart Failure and Death Compared with Nonobstructive Patients



Annual rate of progression to severe heart failure in oHCM is **3.2-7.4%**<sup>1</sup>



The risk of HCM-related death is **twice** that in non-obstructive HCM patients<sup>2</sup>



**LVOT obstruction is a strong, independent predictor of progression to severe heart failure and death<sup>2</sup>**

1. J Am Coll Cardiol 2016;67:1399-1409  
 2. N Engl J Med 2003;348:295-303



Treatment goals: relieving clinical symptoms, improving cardiac function, delaying disease progression, and reducing disease death<sup>1</sup>



## Obstructive HCM<sup>2</sup>

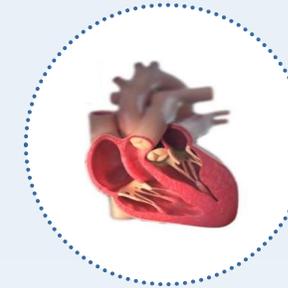
Avoid vasodilators and high-dose diuretics

Beta-blockade, verapamil/diltiazem

Disopyramide

Septal reduction therapy

Symptoms persist?



## Nonobstructive HCM (EF > 50%)<sup>2</sup>

Beta-blockade, verapamil/diltiazem

Diuretics

Symptoms persist?

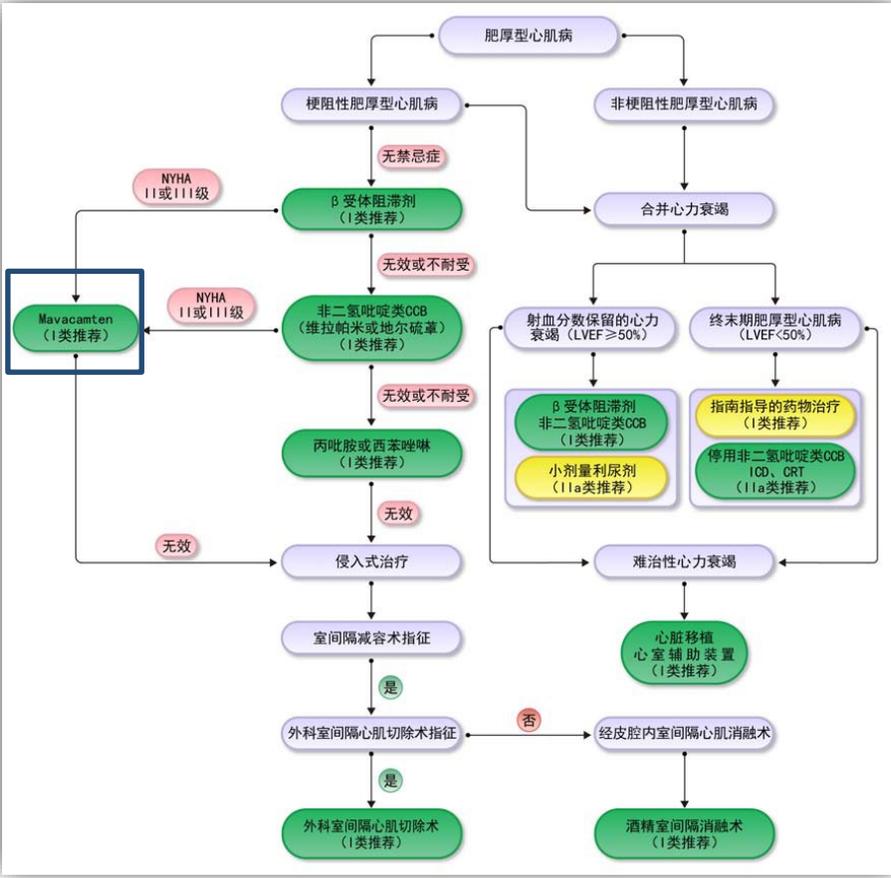
1. Clin J Heart Fail & Cardiomyopathy 2022;6:80-105

2. Circulation 2020;142:e558-e631



Mavacamten is recommended in the latest China HCM guidelines

HCM patient advocacy group (肥厚型心肌病病友关爱之家) organized symposium on new modalities in the treatment of HCM



Treatment flow chart of oHCM\*

Clin J Heart Fail & Cardiomyopathy 2022;6:80-105  
 \* Mavacamten not approved in China at time of publication



## EXPLORER-CN Topline Data & Regulatory Update



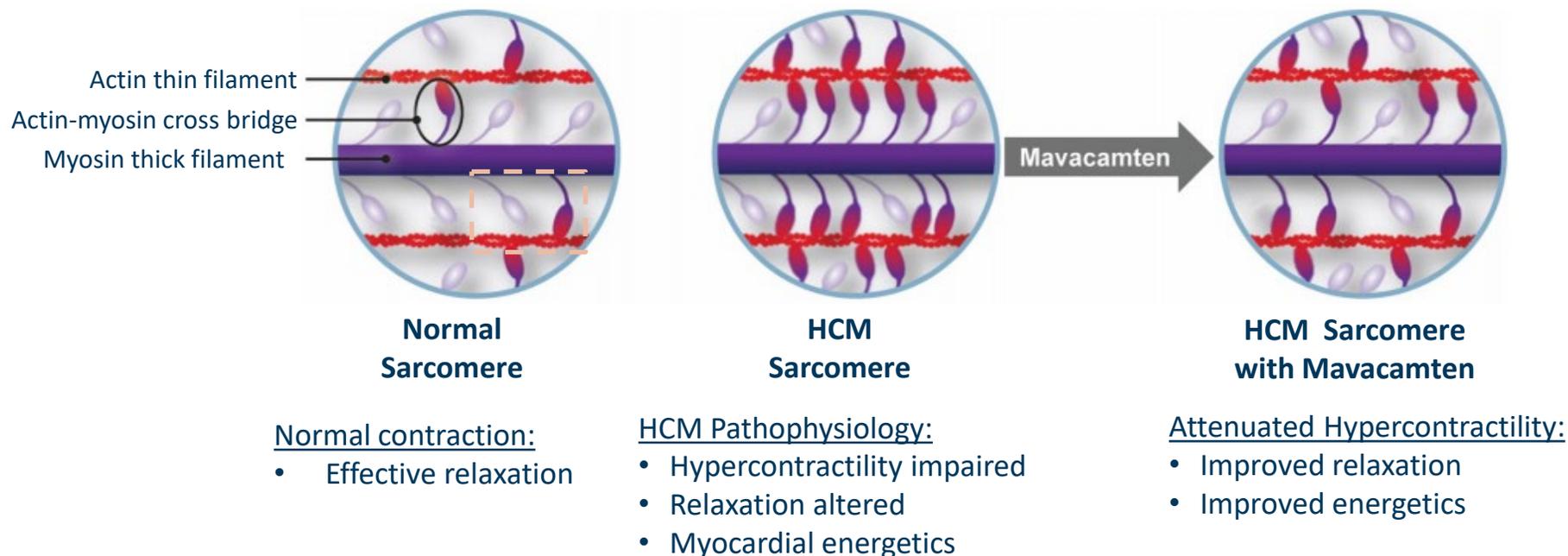
**Michael Humphries, FRCP**

Chief Scientific Advisor, LianBio

# Mavacamten: Precision Medicine Approach to Treating Diseases of Diastolic Dysfunction

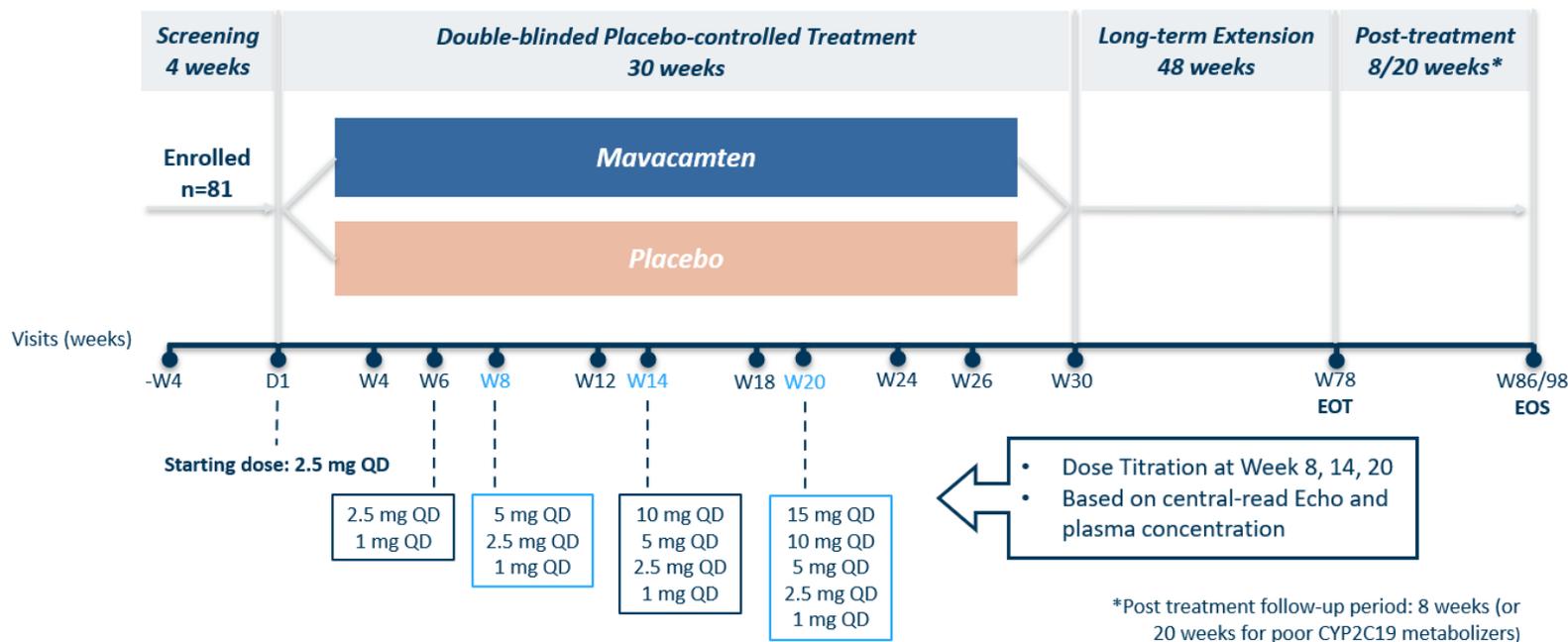
## Mechanism of Action

- Mavacamten is a first-in-class myosin inhibitor that targets the excessive contractility and impaired relaxation, myocardial energetics and compliance, with the intent of correcting the abnormal function of the hypertrophic cardiomyopathy (HCM) heart.
- **Primary mechanism** of mavacamten-mediated inhibition of cardiac myosin is the decrease of phosphate release from  $\beta$ -cardiac myosin-S1
- **Secondary mechanism** is the decrease in the number of actin-binding heads transitioning from the weakly to the strongly bound state, which occurs before phosphate release and may provide an additional method to modulate myosin function<sup>1</sup>



# EXPLORER-CN Study Design

## A Phase III, Randomized, Double-Blinded, Placebo-Controlled Study



**Key inclusion criteria:**

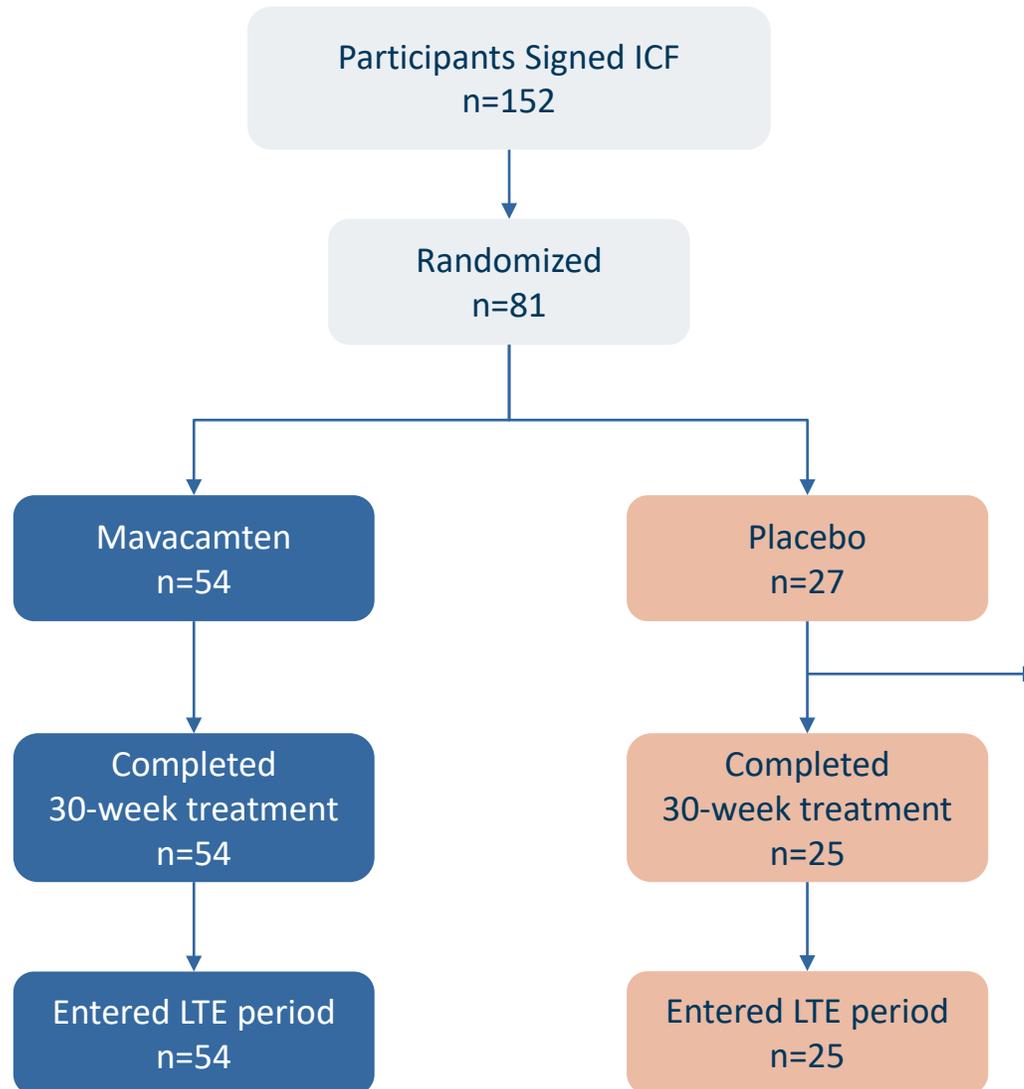
- Aged 18 years or older
- Diagnosed with obstructive hypertrophic cardiomyopathy
- Body weight > 45 kg
- LVEF  $\geq$  55% at rest
- Resting or Valsalva LVOT peak gradient ( $\geq$ 50 mmHg) at screening

**Primary endpoint:**

- Change from baseline to week 30 in Valsalva LVOT gradient

**Secondary endpoints:**

- Change from baseline in resting LVOT peak gradient
- Proportion of participants achieving Valsalva LVOT peak gradient <30 mmHg
- Proportion of participants achieving Valsalva LVOT peak gradient <50 mmHg
- Proportion of participants with  $\geq$ 1 NYHA class improvement from baseline
- Change from baseline in KCCQ-CSS
- Change from baseline in NT-proBNP
- Change from baseline in cardiac troponin
- Change from baseline in LVMI evaluated by CMR



**12** Clinical sites enrolled patients

**81** Participants enrolled

**100%** Completed 30-week treatment in the mavacamten group

- Discontinued (n=2)
- n=1 withdrawal by subject
  - n=1 other (COVID-19)

	Mavacamten (n=54)	Placebo (n=27)
Age, years, mean (SD)	52.4 (12.1)	51.0 (11.8)
Sex, n (%)		
Male	41 (75.9)	17 (63.0)
Female	13 (24.1)	10 (37.0)
BMI, mean (SD)	25.17 (3.46)	26.11 (3.58)
NYHA Class, n (%)		
Class II	44 (81.5)	18 (66.7)
Class III	10 (18.5)	9 (33.3)
Background HCM therapy, n (%)		
β blocker	48 (88.9)	24 (88.9)
Calcium channel blocker	4 (7.4)	2 (7.4)
Other	2 (3.7)	1 (3.7)

Echocardiographic parameters, mean (SD)	Mavacamten (n=54)	Placebo (n=27)
Resting LVOT peak gradient, mmHg	74.62 (35.05)	73.41 (32.23)
Valsalva LVOT peak gradient, mmHg	106.78 (43.23)	99.79 (41.10)
LVEF, %	77.80 (6.89)	77.00 (6.73)
Maximum LV wall thickness, mm	22.87 (4.93)	24.34 (6.35)
Left atrial volume index, mL/m <sup>2</sup>	43.33 (12.15)	47.47 (14.75)

LV, left ventricular; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; SD, standard deviation

### Topline Safety Summary\*

- Mavacamten demonstrated a safety profile consistent with past studies, with no new safety signals observed
- Incidence of treatment-emergent adverse events (TEAEs) on mavacamten arm similar to placebo arm
- All treatment-emergent serious adverse events (TESAEs) considered not related to study drug
- No cases of heart failure or death

### Protocol-Driven Temporary Treatment Discontinuation

Criteria	Mavacamten (n=54)	Placebo (n=27)
Resting LVEF <50% by core Laboratory	0	0
Pre-dose plasma drug concentration ≥1000 ng/mL	1 (1.9%)	0
Both	0	0

- 1 participant in the mavacamten group had dose interruption due to pre-dose plasma drug concentration ≥1000 ng/mL. The LVEF was normal and study medication was later resumed.
- No participant had temporary treatment discontinuation or dose interruption due to LVEF <50%

\*Full safety data to be presented at an upcoming medical meeting

- Mavacamten demonstrated a statistically significant improvement in Valsalva LVOT gradient from baseline to week 30 with a LSM difference of -70.29 mmHg compared to placebo (p <0.001)
- Data illustrates improvement in Valsalva LVOT gradient in mavacamten group compared to placebo group as early as 4 weeks and sustained through the study period

	Mavacamten (n=54)	Placebo (n=27)	LSM Difference <sup>^</sup> (95% CI)	p-value
Change from baseline to Week 30 in Valsalva LVOT peak gradient, mmHg, mean (SD)	-57.93 (45.61)	20.65 (46.45)	<b>-70.29</b> <b>(-89.64, -50.94)</b>	<b>&lt;0.001</b>

<sup>^</sup> Model estimated least-square mean differences were reported for continuous variables  
 CI, confidence interval; LSM, least squares mean; LVOT, left ventricular outflow tract; SD, standard deviation;

- Mavacamten demonstrated treatment benefit across all pre-specified secondary endpoints

Secondary Endpoints*	Mavacamten (n=54)	Placebo (n=27)	Difference (95% CI)^	Nominal p-value**
Change from baseline to Week 30 in Resting LVOT peak gradient, mmHg, mean (SD)	-51.45 (35.99)	6.38 (34.36)	-54.99 (-69.13, -40.86)	<0.001
Proportion of participants achieving a Valsalva LVOT peak gradient <30 mmHg at Week 30, n (%)	26 (48.1)	1 (3.7)	0.41 (0.24, 0.57)	<0.001
Proportion of participants achieving a Valsalva LVOT peak gradient <50 mmHg at Week 30, n (%)	32 (59.3)	2 (7.4)	0.47 (0.30, 0.64)	<0.001
Proportion of participants with at least 1 class improvement in NYHA functional classification from baseline to Week 30, n (%)	32 (59.3)	4 (14.8)	0.39 (0.20, 0.58)	<0.001
Change from baseline to Week 30 in KCCQ-CSS, LSM (SE)	4.99 (2.06)	-5.25 (2.75)	10.24 (4.35, 16.13)	<0.001
Change from baseline to Week 30 in LVMI (CMR), mean (SD)***	-26.37 (21.06)	4.43 (14.42)	-30.80 (-41.55, -20.05)	<0.001

\*Due to China HGRAC regulations, biomarker data are not shown. These data will be presented at an upcoming medical meeting

^ Model estimated least-square mean differences were reported for continuous variables

\*\*P-values shown for descriptive purposes only, not multiplicity-adjusted

\*\*\* CMR set: mavacamten n=39, placebo n=19

CMR, cardiac magnetic resonance; LVMI, left ventricular mass index; LVOT, left ventricular outflow tract; NYHA, New York Heart Association; SD, standard deviation; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire-Clinical Summary Score; LSM, least squares mean

- **EXPLORER-CN met the study's primary endpoint with high statistical significance ( $p < 0.001$ )**
  - Mavacamten showed a significant and **clinically important improvement** in change from baseline to Week 30 in Valsalva LVOT peak gradient by a LSM difference of -70.29 mmHg compared to placebo.
- **Mavacamten showed improvements versus placebo from baseline to Week 30 in all secondary endpoints, including:**
  - Change from baseline in resting LVOT peak gradient
  - Proportion of participants achieving Valsalva LVOT peak gradient  $< 30$  mmHg
  - Proportion of participants achieving Valsalva LVOT peak gradient  $< 50$  mmHg
  - Proportion of participants with  $\geq 1$  NYHA class improvement from baseline
  - Change from baseline in KCCQ-CSS
  - Change from baseline in LVMI evaluated by CMR
- **Mavacamten demonstrated a safety profile consistent with past studies**
  - There were no new safety signals observed in Chinese patients with oHCM
- **No participant had temporary treatment discontinuation or dose interruption due to LVEF  $< 50\%$**

# Regulatory Status in Asia and Key Anticipated Program Milestones



## \*Data Included in China NDA Package

Global pivotal Phase 3 EXPLORER-HCM trial data

Phase 1 pharmacokinetics study of mavacamten in healthy Chinese volunteers

Blinded preliminary safety data from Phase 3 EXPLORER-CN trial



## Mavacamten Potential in Other Diseases of Diastolic Dysfunction



**Brianna Sun**

Cardiovascular Medical Head, LianBio

# Non-Obstructive Hypertrophic Cardiomyopathy (nHCM)

## Disease overview

- nHCM has no significant LVOT obstruction (e.g., <30 mmHg) at rest or with provocation
- Driven by diastolic impairment due to the enlarged and stiffened heart muscle
  - ~1/3 of HCM patients have nHCM

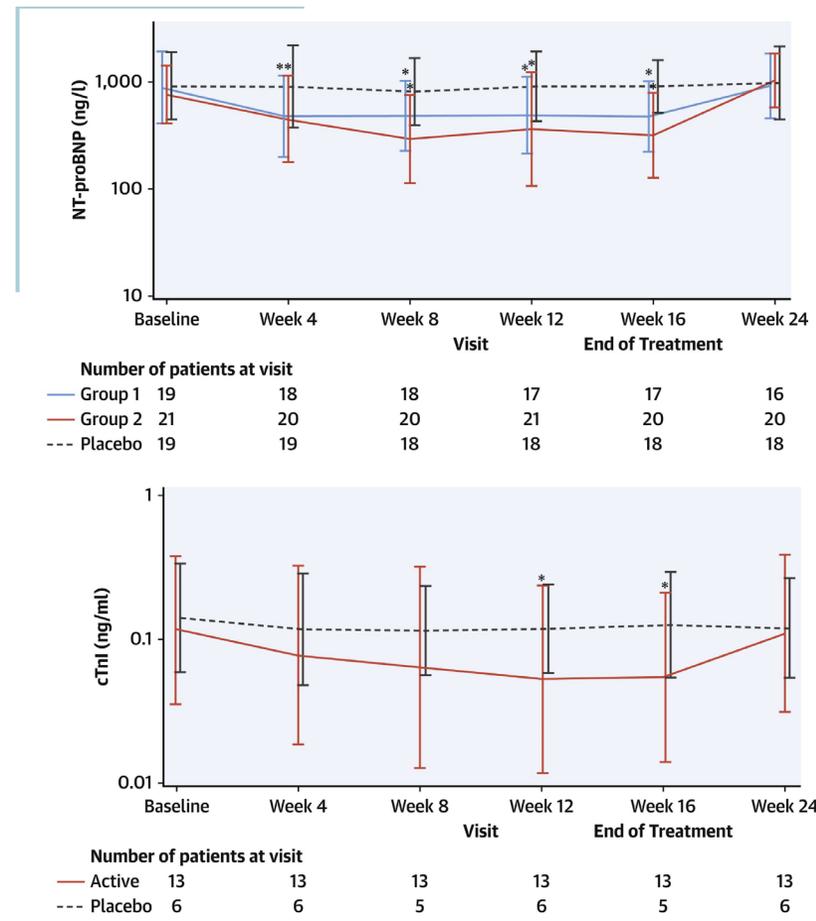
## Mavacamten treatment rationale

- By altering the contractile mechanics of the cardiomyocyte, mavacamten may have the potential to reduce cardiac filling pressures and improve symptoms associated with non-obstructive HCM

## Development pathway

- BMS initiated a Phase 3 trial of mavacamten in nHCM, ODYSSEY-HCM, in 2022

## Phase 2 MAVERICK-HCM Trial<sup>1</sup>



1. J Am Coll Cardiol. 2020 Jun 2;75(21):2649-2660

LVOT, left ventricular outflow tract; NT-proBNP, N-terminal pro-B-type natriuretic peptide; cTnI, cardiac troponin I

- Physiologic benefits demonstrated with dose dependent reduction in serum levels of NT-proBNP and cTnI, suggesting improvement in cardiac wall stress and myocardial injury



# Heart Failure with Preserved Ejection Fraction (HFpEF)

## Disease overview

- HFpEF is a disease in which the heart's ability to pump blood through the body is decreased due to the inability of the ventricle to fully relax and fill with blood
- At a cellular level, cardiac myocytes in patients with HFpEF are thicker and shorter than normal myocytes, and collagen content is increased

## Mavacamten treatment rationale

- In a subset of HFpEF patients, the underlying cause of symptoms is similar to nHCM, and we believe mavacamten has the potential to address underlying pathophysiology in this subset of HFpEF patients
  - LV diastolic dysfunction
  - Left atrial enlargement
  - Elevated LV filling pressure
  - Myocardial injury & fibrosis
  - LV hypertrophy
  - Abnormal myocardial energetics

## Development pathway

- BMS Phase 2a EMBARK-HFpEF trial of mavacamten in HFpEF patients with elevated NT-proBNP ongoing (NCT04766892)
  - Study designed to assess safety, tolerability, and preliminary efficacy of mavacamten on biomarker levels in participants with HFpEF and elevation of NT-proBNP with or without elevation of cTnT

- There are approximately 3.7 million HFpEF patients in China
- Approximately 10-20% of HFpEF patients share similar pathophysiology with nHCM
- Mavacamten may have the potential to treat the underlying pathophysiology

NT-proBNP, N-terminal pro-B-type natriuretic peptide;  
cTnT, cardiac troponin T



## Mavacamten China Market Opportunity



### **Pascal Qian**

Chief Commercial Officer and General Manager of China,  
LianBio



## HCM Epidemiology

- There are **1.1-2.8 million potential HCM patients** in China with 0.2%<sup>1</sup> prevalence rate
- oHCM contributes 67% of overall HCM patients and nHCM contributes 33% of overall HCM patients

## Diagnosis Opportunity

- Diagnosis rate in China is estimated at ~20%, with the potential for improvement through disease education campaigns
- Current standard diagnostic process needs to be improved including the application of provocation echo

## Treatment Opportunity

- No currently available therapy treats underlying disease
- Reach patients across China by leveraging COEs



  
**\$500M**  
**Peak Year Sales**  
*(w. additional indications)*

- oHCM
- nHCM
- HFpEF



120,000-180,000 diagnosed oHCM patients today with potential to reach 300,000 diagnosed oHCM patients



Efficient coverage through phased approach

~400 level III hospitals:  
~20% diagnosed patients

Launch

~1,500 Level II/III hospitals:  
(2,000 prescriber ~55% diagnosed patients)

Self-Pay

~3,000 Level II/III hospitals:  
(7,000 prescribers ~80% diagnosed patients)

Post-NRDL

~13,000 Level I/II/III hospitals: ~100% diagnosed patients



HCM COE Build



中国心血管健康联盟  
Chinese Cardiovascular Association  
Lianbio

- Partnership with Chinese Cardiovascular Association
- Leverage existing infrastructure of heart failure COE
- Lead by top KOLs who built heart failure COE



- Steering Committee
- Pilot wave



- Build standardized diagnosis and treatment

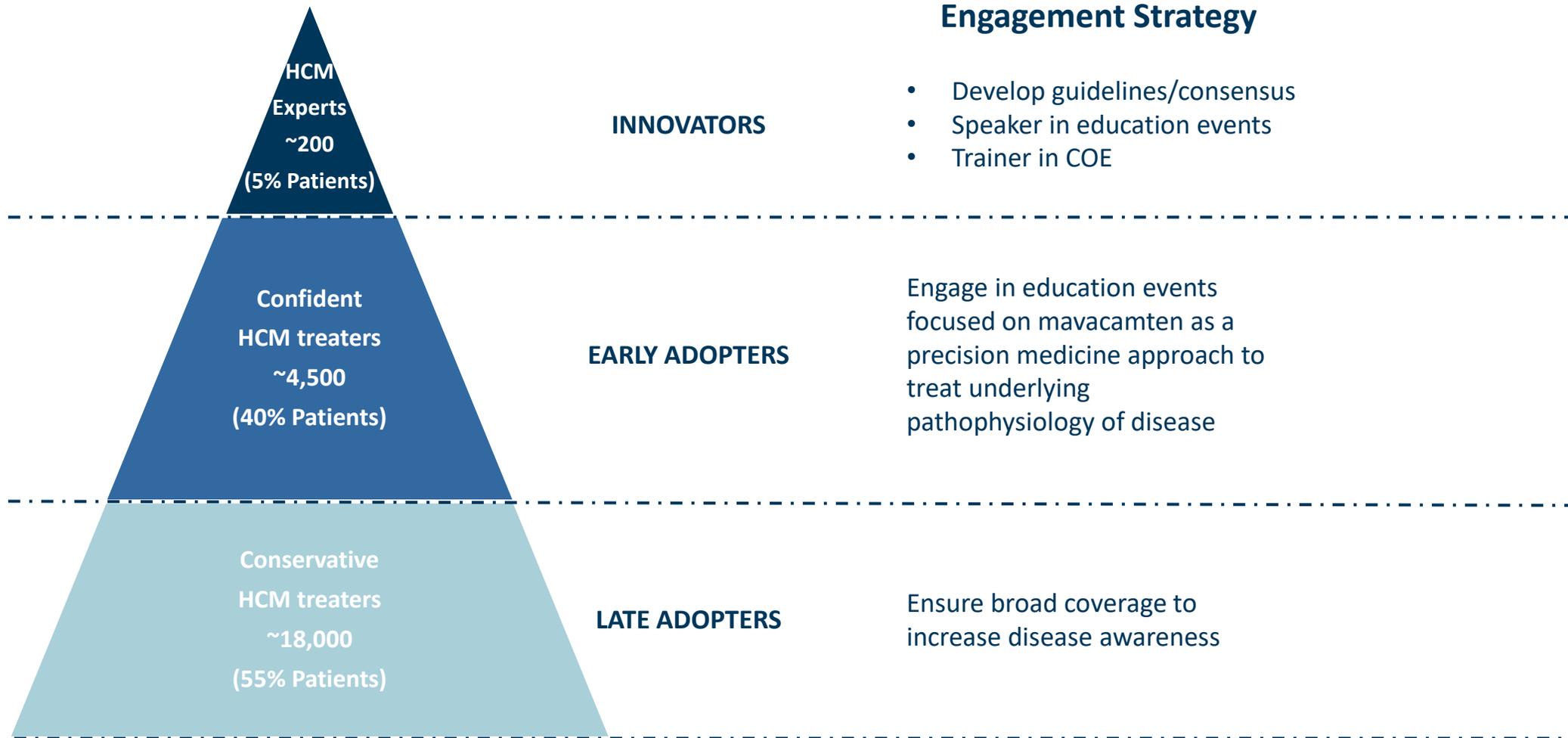


- Maximize Mavacamten uptake through standardized treatment

# There are Approximately 75,000 Cardiologists in China, 30% Currently Treat HCM



## Physician segmentation



# Positioning Mavacamten for Successful China Launch

LianBio vision: Establish myosin inhibitor class as the **new standard of care** for oHCM by maximizing mavacamten's value as the only **treatment targeting the underlying pathophysiology of disease**

## SHAPE

### Market Leadership

- Improve diagnosis
- Establish mavacamten as standard of care in oHCM

## REACH

### Optimize Patient Access

- Gain NRDL entry

## GROW

### Grow the HCM Market

- Improve the disease awareness

## BUILD

### Organization and Infrastructure

- Execute industry-leading commercial strategy

Collaboration with China Cardiovascular Association, Largest local cardiovascular medical society



Support Cardiovascular Foundation to develop the 1st HCM patient management and education platform



Collaboration with top institutions for mavacamten pricing and access strategy

**中山大學**  
SUN YAT-SEN UNIVERSITY

**北京大學**  
PEKING UNIVERSITY

- Mavacamten pharmacoeconomic project
- oHCM burden of disease project



## Q&A

### Company management available for Q&A

- Yizhe Wang, Ph.D., CEO
- Yi Larson, CFO
- Pascal Qian, CCO and General Manager of China
- Michael Humphries, FRCP, Chief Scientific Advisor



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