Scientific Sessions

LONG-TERM EFFICACY AND SAFETY OF HRS/BHB-1893 IN PATIENTS WITH OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY: RESULTS FROM THE 52-WEEK EXTENSION PERIOD

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American Heart Association.

DISCLOSURES

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This study and presentation were funded by Jiangsu Hengrui Pharmaceuticals Co., Ltd. and Braveheart Bio, Inc.

Xueyi Wu has no conflicts of interest to declare

BACKGROUND

HRS/BHB-1893 is a selective, reversible, small-molecule cardiac myosin inhibitor (CMI) engineered for rapid onset of action, shallow effect on LVEF, and ease of use

CMIs have been shown to improve symptoms and exercise capacity in patients with oHCM

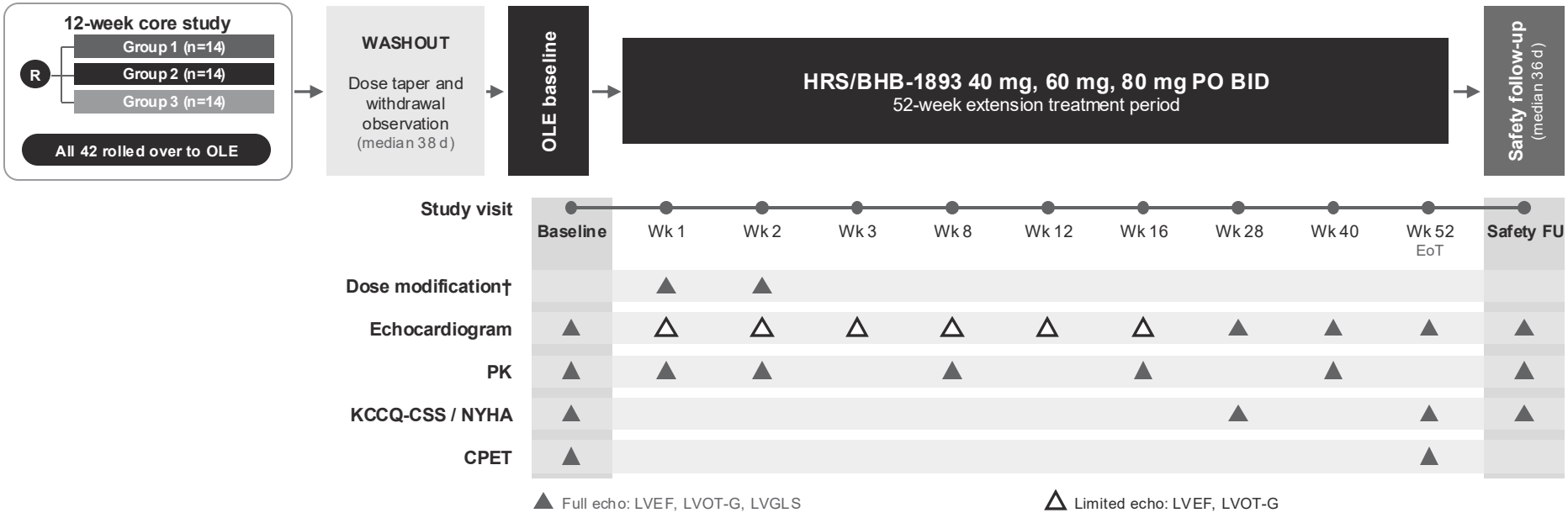
Current CMIs require **multi-step titration to reach an effective dose**, imposing substantial patient burden

This Phase 2 study evaluated the efficacy and safety of **multiple HRS/BHB-1893 dosing regimens** over the 52-week open-label extension (OLE)

CMI, cardiac myosin inhibitor; LVEF, left ventricular ejection fraction; oHCM, obstructive hypertrophic cardiomyopathy.

STUDY DESIGN

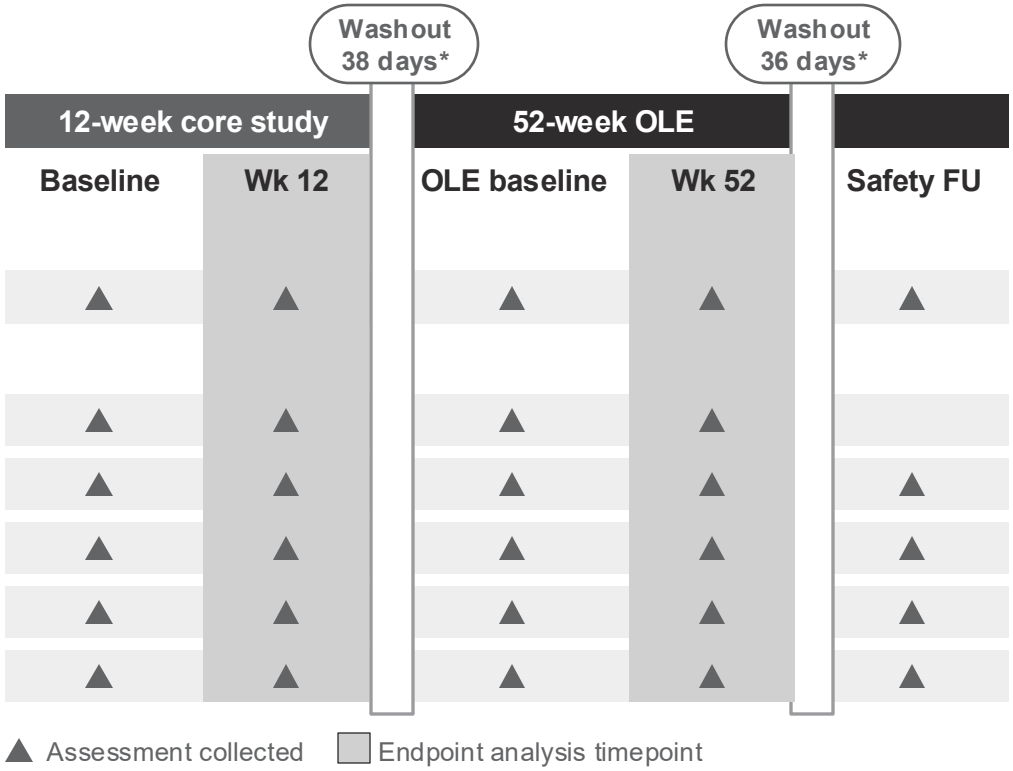
Adult patients with symptomatic oHCM who had resting LVOT-G ≥50 mmHg (or resting LVOT-G ≥30 mmHg and Valsalva LVOT-G ≥50 mmHg), LVEF ≥60%, and NYHA Class II-III were enrolled



†Scheduled dose modification at Wk 1 and Wk 2 of OLE; down-titration or temporary interruption permitted at any visit based on LVEF and Valsalva LVOT-G.
Database Lock: June 2026.

BID, twice daily; CPET, cardiopulmonary exercise test; EoT, end of treatment; FU, follow-up; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire Clinical Summary Score; LVGLS, left ventricular global longitudinal strain; LVEF, left ventricular ejection fraction; LVOT-G, left ventricular outflow tract gradient; NYHA, New York Heart Association; oHCM, obstructive hypertrophic cardiomyopathy; OLE, open-label extension; PK, pharmacokinetics; PO, oral administration; R, randomization; Wk, week.

STUDY ENDPOINTS



*Median washout duration. Database lock: June 2026. CPET, cardiopulmonary exercise test; FU, follow-up; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire Clinical Summary Score; LVOT-G, left ventricular outflow tract gradient; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; OLE, open-label extension; Wk, week. + endpoints for OLE were secondary / exploratory

BASELINE CHARACTERISTICS

	40-60-80 mg BID (N=14)	Core treatment baseline (N=42)	OLE Baseline (N=42)
Age, years, mean (SD)	51.5 (10.4)	51.5 (11.4)	-
Male, n (%)	9 (64.3)	26 (61.9)	-
Background therapy, n (%)			
Beta blockers	12 (85.7)	38 (90.5)	-
Calcium channel blockers	1 (7.1)	2 (4.8)	-
History of Atrial Fibrillation	2 (14.3)	2 (4.8)	-
Valsalva LVOT-G, mmHg, mean (SD)	107.2 (41.7)	100.4 (34.9)	115.1 (44.3)
Resting LVOT-G, mmHg, mean (SD)	80.3 (33.4)	72.5 (25.5)	93.3 (41.5)
LVEF, %, mean (SD)	69.3 (3.5)	69.9 (3.3)	71.5 (4.1)
pVO2, mL/kg/min, mean (SD)	17.5 (3.2)	18.4 (3.5)	17.1 (4.1)
NYHA class, n (%)			
Class I	0 (0.0)	0 (0.0)	2 (4.8)
Class II	14 (100.0)	40 (95.2)	38 (90.5)
Class III	0 (0.0)	2 (4.8)	2 (4.8)
KCCQ-CSS, mean (SD)	86.0 (12.9)	81.7 (13.5)	77.2 (15.1)

BID, twice daily; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire Clinical Summary Score; LVEF, left ventricular ejection fraction; LVOT-G, left ventricular outflow tract gradient; NYHA, New York Heart Association; OLE, open-label extension; pVO2, peak oxygen uptake; SD, standard deviation.

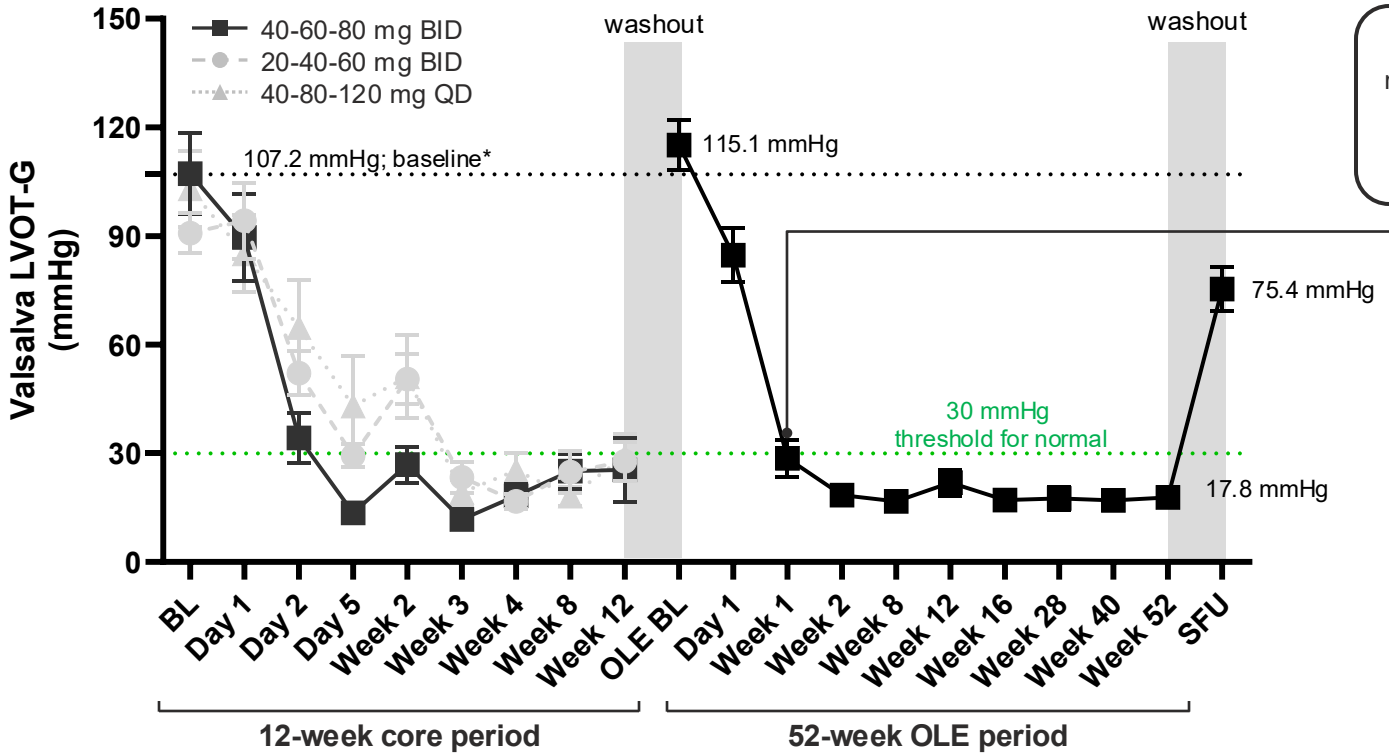
SIMPLIFIED DOSING OPPORTUNITY: MAJORITY SERVED BY 40 MG STARTING DOSE

Last Dose Level	Week 12 *BID Groups 1 & 2 (n=28)*	Week 52 *OLE 40-60-80 mg BID (n=42)*
20 mg BID	2 (7.1%)	2 (4.8%)
40 mg BID	**17 (60.7%)**	**24 (57.1%)**
60 mg BID	8 (28.6%)	8 (19.0%)
80 mg BID	1 (3.6%)	8 (19.0%)

Limited titration required given robust gradient response seen with 40 mg dose at Week 1

Database lock: June 2026. BID, twice daily; OLE, open-label extension.

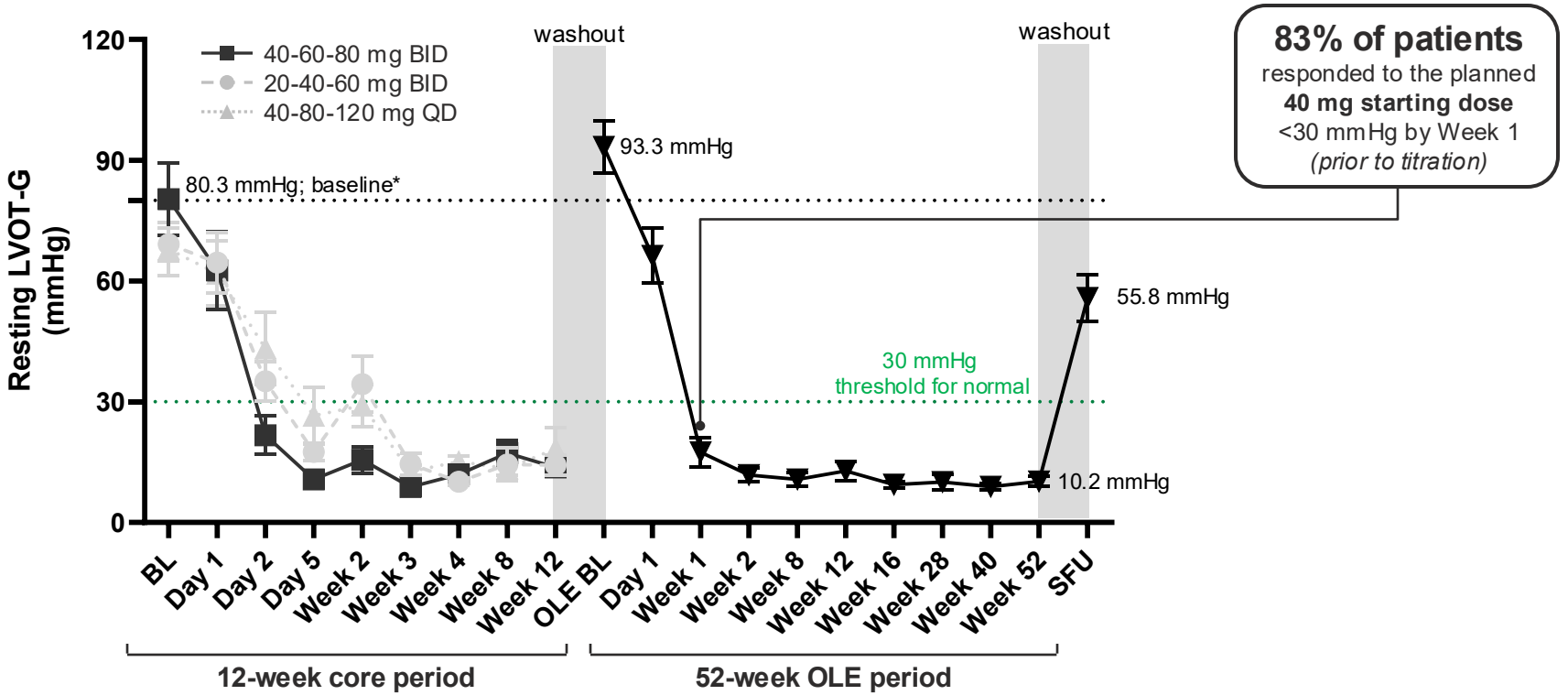
VALSALVA LVOT-G: RAPID AND DEEP REDUCTION MAINTAINED THROUGH WEEK 52



67% of patients
responded to the planned
40 mg starting dose
<30 mmHg by Week 1
(prior to titration)

Database lock: June 2026.
*Group 2. BID, twice daily; BL, baseline; LVOT-G, left ventricular outflow tract gradient; OLE, open-label extension; QD, once daily; SFU, safety follow-up.

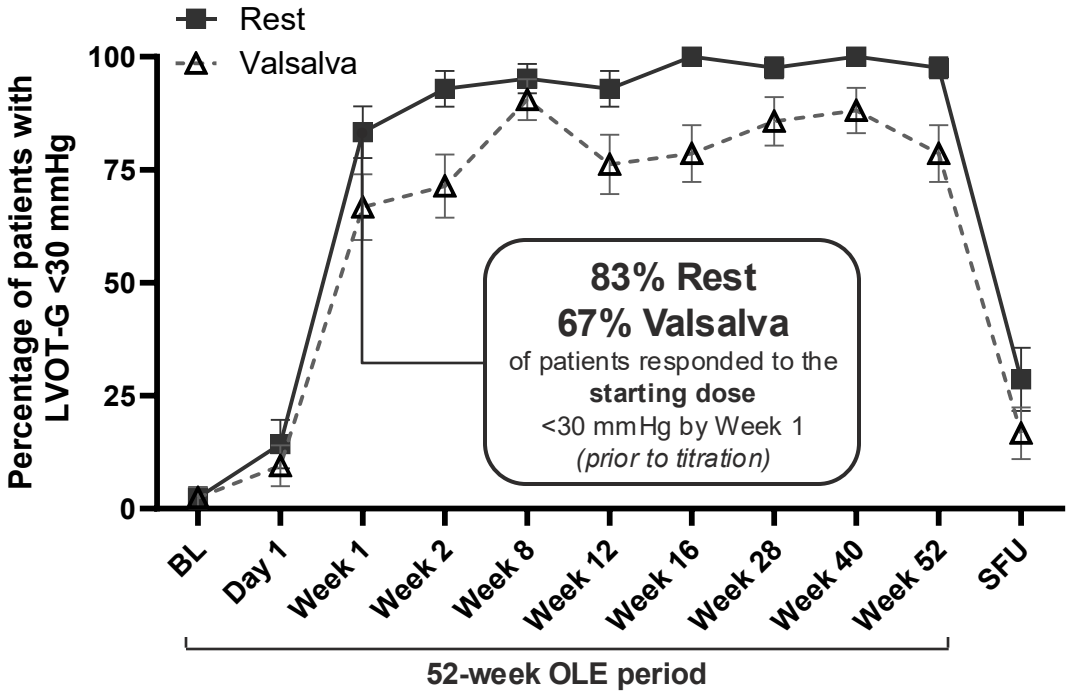
RESTING LVOT-G: RAPID REDUCTION WITH DURABLE RESPONSE THROUGH WEEK 52



83% of patients
responded to the planned **40 mg starting dose**
<30 mmHg by Week 1
(prior to titration)

Database lock: June 2026.
*Group 2. BID, twice daily; BL, baseline; LVOT-G, left ventricular outflow tract gradient; OLE, open-label extension; QD, once daily; SFU, safety follow-up.

90% OF PATIENTS ACHIEVED A VALSALVA LVOT-G <30 mmHg DURING 52 WEEKS OF TREATMENT



- Rapid normalization of gradient observed at both rest and Valsalva
- Responders seen as early as **Day 1**

Database lock: June 2026.
BL, baseline; LVOT-G, left ventricular outflow tract gradient; OLE, open-label extension; SFU, safety follow-up.

NT-PROBNP: RAPID AND DEEP REDUCTION

Partial return to baseline after 52 weeks of treatment

WEEK 12

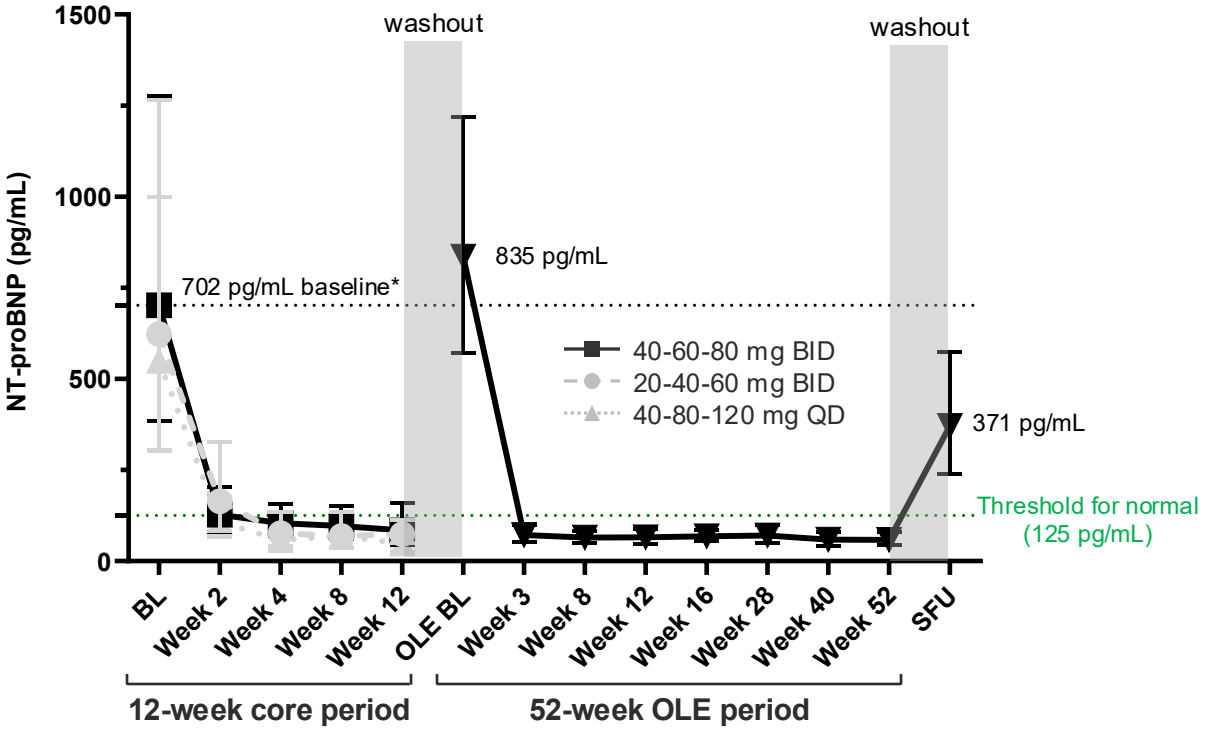
78.8% reduction

76.2% of patients normalized (<125 pg/mL)

WEEK 52

87.5% reduction

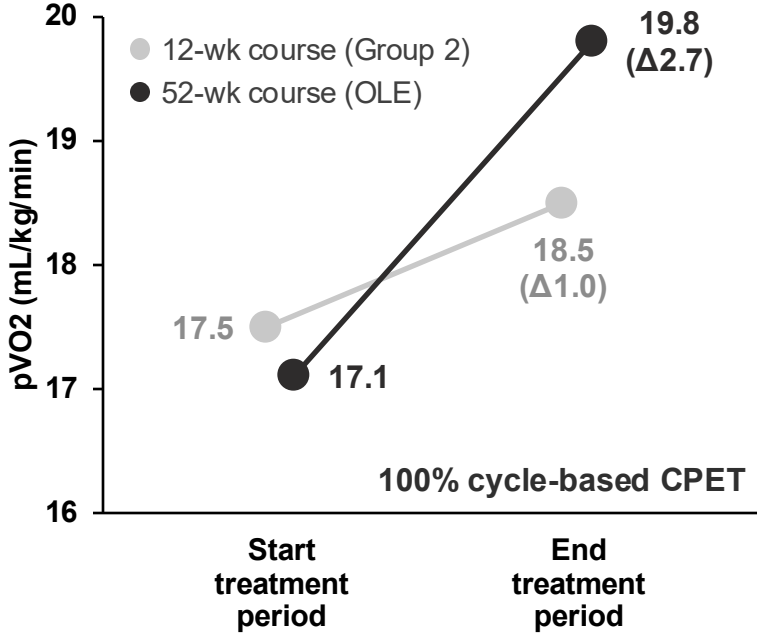
78.6% of patients normalized (<125 pg/mL)



Database lock: June 2026.

*Group 2. BID, twice daily; BL, baseline; NT-proBNP, N-terminal pro-B-type natriuretic peptide; OLE, open-label extension; QD, once daily; SFU, safety follow-up.

CPET IMPROVED FURTHER BY WEEK 52 IN BOTH PVO2 AND VE/VCO2



70% of patients
improved pVO2 by ≥1.5 mL/kg/min

50% of patients
improved pVO2 by ≥3.0 mL/kg/min

−4.1
VE/VCO2 improvement at Week 52

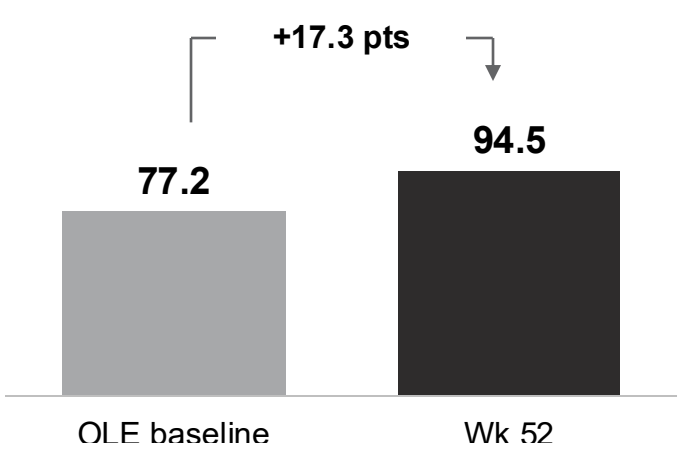
Early pVO2 improvements at Week 12 deepened by Week 52

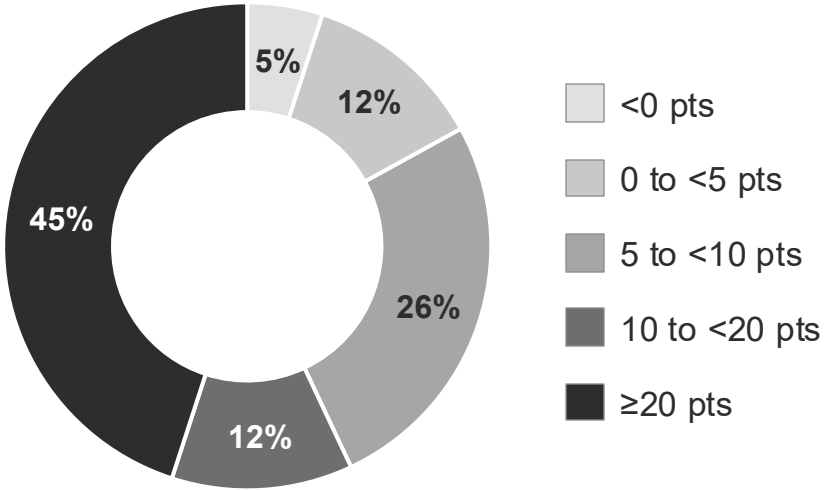
Database lock: June 2026. 12 wk = Group 2 (40-60-80 mg BID) baseline to Week 12 (N=14); 52 wk = 40-60-80 mg BID OLE baseline to Week 52 (N=40 with OLE BL CPET available). BID, twice daily; CPET, cardiopulmonary exercise test; OLE, open-label extension; pVO2, peak oxygen uptake; VE/VCO2, minute ventilation to carbon dioxide output ratio; Wk, week.

SIGNIFICANT IMPROVEMENT IN KCCQ WITH LARGE PROPORTION OF PATIENTS ≥20PT IMPROVEMENT

+17.3
Point improvement in KCCQ-CSS

45%
of patients with ≥20 pt improvement at Week 52



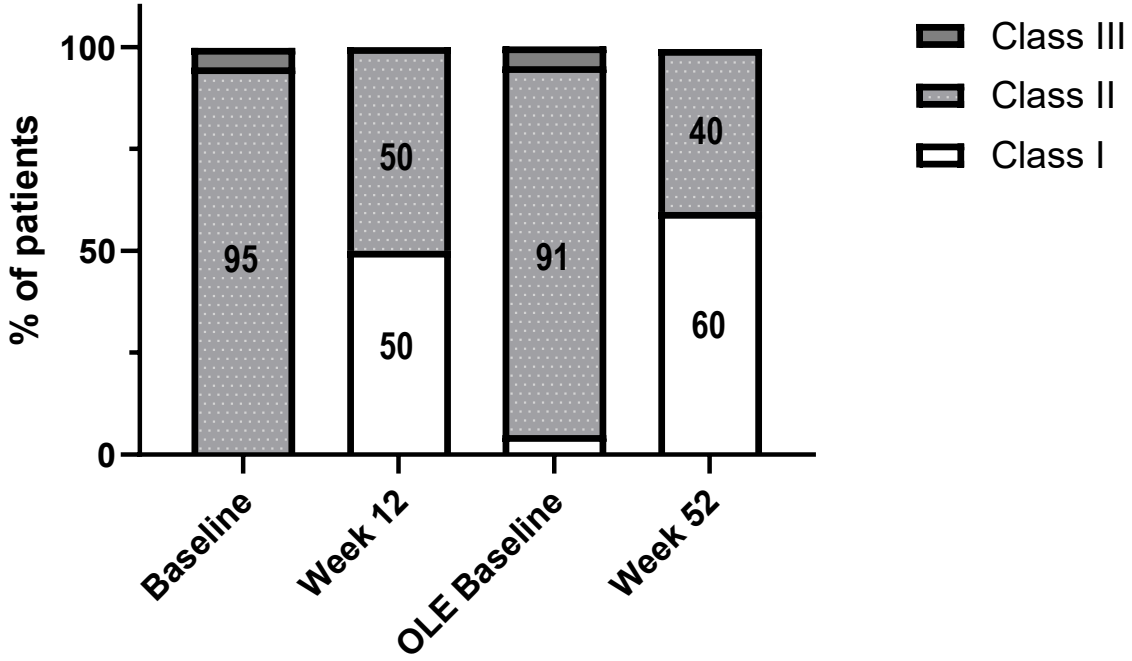


Database lock: June 2026. N=42, KCCQ-CSS values are means. KCCQ, Kansas City Cardiomyopathy Questionnaire; KCCQ-CSS, KCCQ Clinical Summary Score; OLE, open-label extension; Wk, week.

60% OF PATIENTS REACHED NYHA CLASS I BY WEEK 52

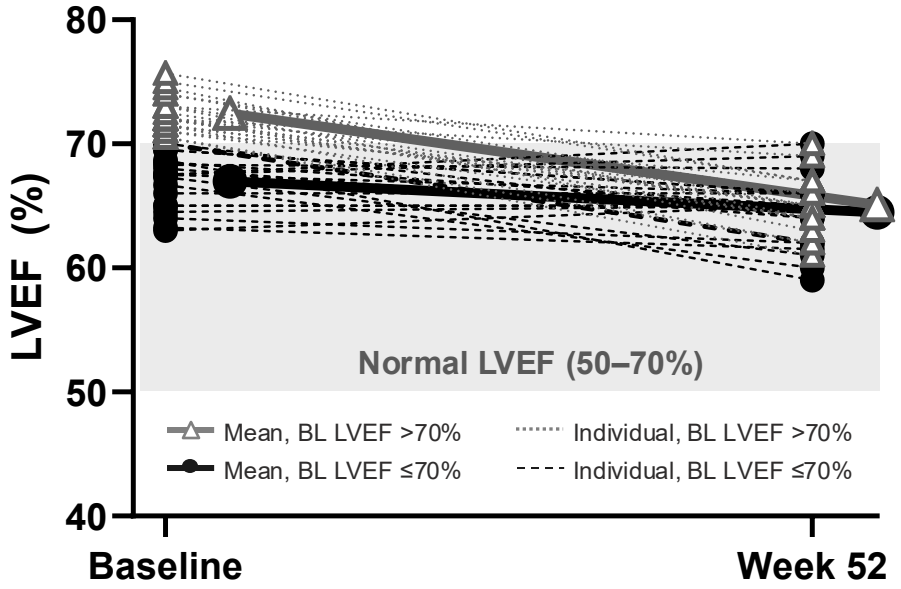
NYHA improvement
seen at Week 12 continues at Week 52

55%
improved by ≥1 NYHA class at 52 weeks



Database lock: June 2026. NYHA, New York Heart Association; OLE, open-label extension.

HRS/BHB-1893 MOVED LVEF INTO THE NORMAL RANGE FROM A HYPERCONTRACTILE BASELINE



Baseline LVEF >70%

73% → 65%

BL Wk 52

Baseline LVEF ≤70%

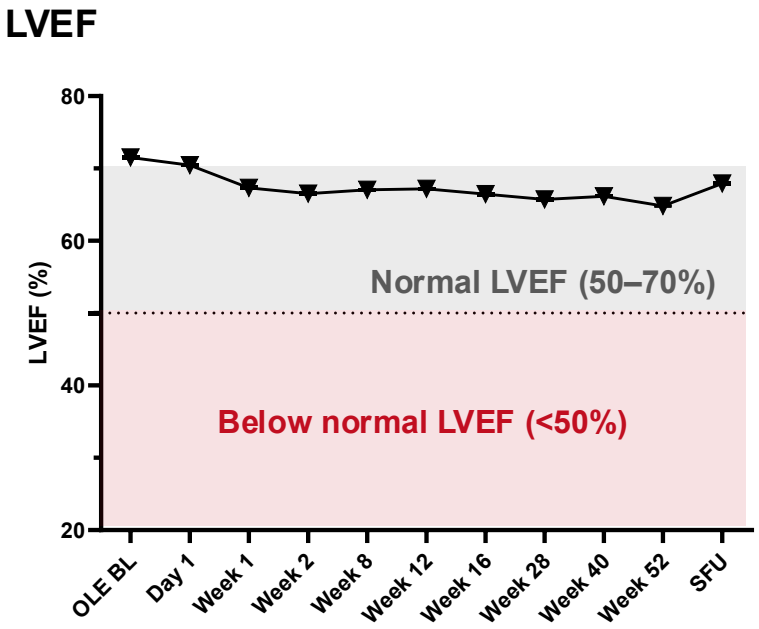
67% → 64%

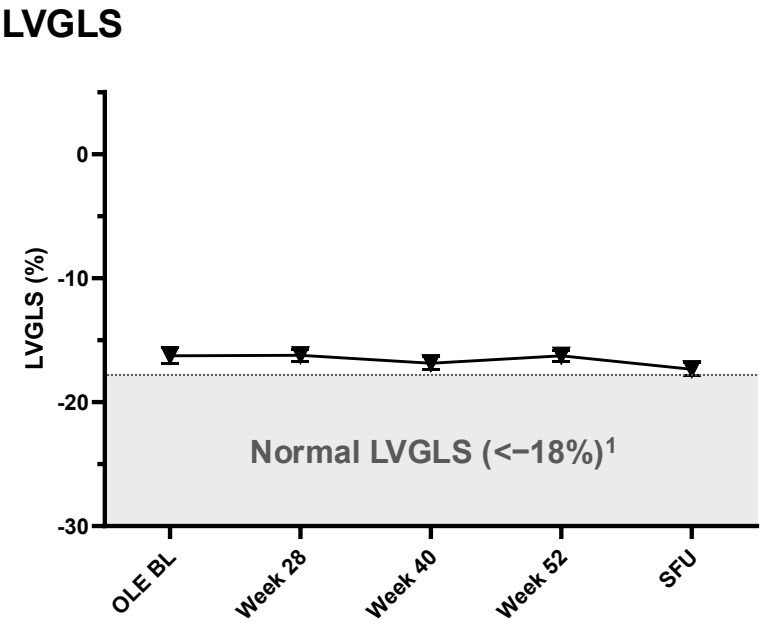
BL Wk 52

Two patients with transient LVEF <50% (48% and 49% site-measured), both resumed on lower dose

Database lock: June 2026. BL, baseline; LVEF, left ventricular ejection fraction; Wk, week.

LVEF NORMALIZED WITH STABLE LVGLS INDICATING STABLE SYSTOLIC FUNCTION

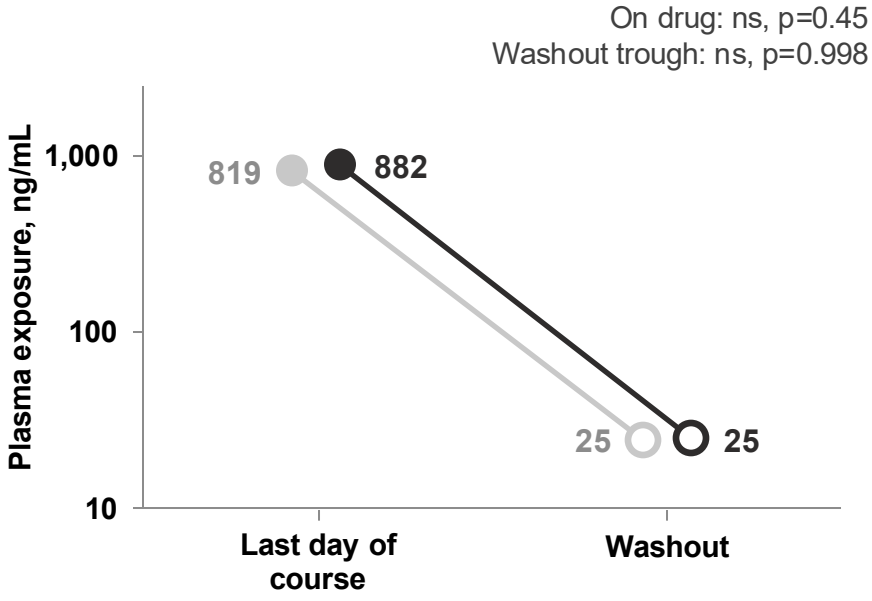




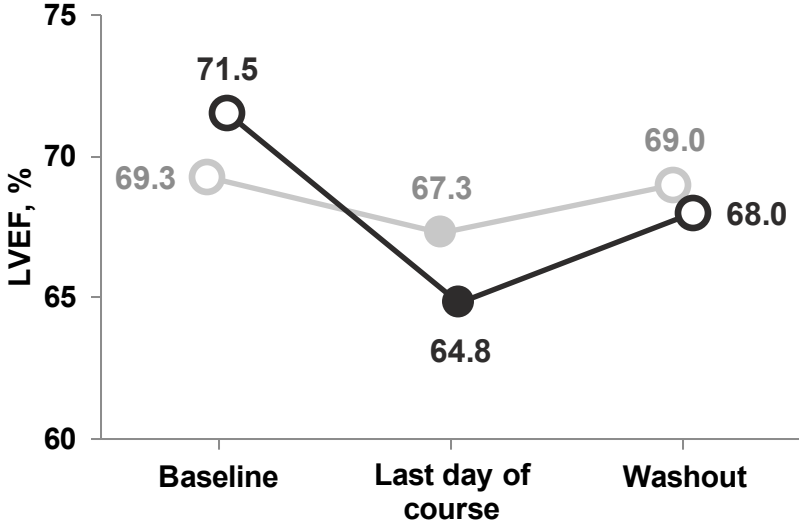
Database lock: June 2026. BL, baseline; LVEF, left ventricular ejection fraction; LVGLS, left ventricular global longitudinal strain; OLE, open-label extension; SFU, safety follow-up. 1. ASE/EACVI. Clinical applications of strain echocardiography: a clinical consensus statement. J Am Soc Echocardiogr. 2025.

DRUG WAS CLEARED DURING WASHOUT AFTER BOTH COURSES; LVEF RETURNED TO BASELINE

A Plasma drug exposure by course



B LVEF by course



12-wk course (Group 2) 52-wk course (pooled OLE)

Database lock: June 2026. A: Welch t-tests from summary stats: Group 2 Wk 12 (n=14) vs pooled OLE Wk 40 (n=42); OLE Wk 1 (n=39) vs SFU (n=41). Trough SEM 18.1 and 9.8. B: Mean LVEF; filled markers on drug, open markers off drug. Baseline: Group 2 (n=14) and OLE baseline (n=42), as in baseline characteristics. LVEF, left ventricular ejection fraction; ns, not significant; OLE, open-label extension; SEM, standard error of the mean; SFU, safety follow-up; Wk, week.

PARTIAL RETURN TO BASELINE AFTER 52 WEEKS, CONSISTENT WITH REVERSE REMODELING

C LVOT-G and NT-proBNP after washout

Valsalva LVOT-G



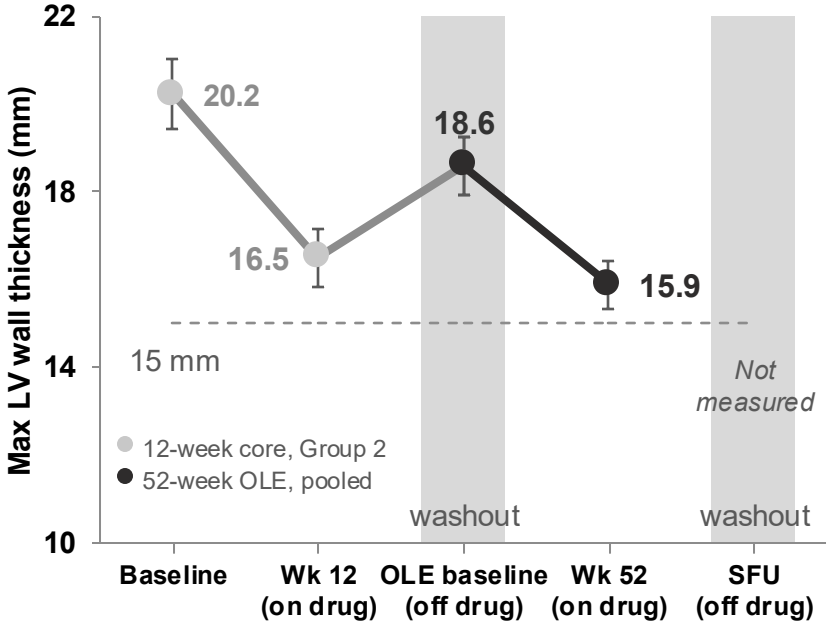
Rest LVOT-G



NT-proBNP



D Max LV wall thickness over time



Database lock: June 2026. C: Group means. Baseline, Group 2 core baseline; post 12-wk washout, OLE baseline; post 52-wk washout, SFU. **p<0.01, ***p<0.001, post 12-wk vs post 52-wk washout (Welch test; NT-proBNP on log scale); exploratory, unadjusted. D: Group means ± SEM. n: Group 2 baseline 13, Wk 12 12; pooled OLE baseline 38, Wk 52 36. No wall thickness measured at SFU. LV, left ventricular; LVOT-G, left ventricular outflow tract gradient; NT-proBNP, N-terminal pro-B-type natriuretic peptide; OLE, open-label extension; SEM, standard error of the mean; SFU, safety follow-up; Wk, week.

SAFETY

Treatment with HRS/BHB-1893 was well-tolerated with no on-treatment severe or serious AEs

n (%)	12-Week Core Period (n = 42)	52-Week Extension Period (n = 42)
Any TEAEs	**34 (81.0)**	**38 (90.5)**
Mild	31 (73.8)	33 (78.6)
Moderate	3 (7.1)	4 (9.5)
Severe	0	1 (2.4)[a]
Any TRAEs	**12 (28.6)**	**12 (28.6)**
Mild	12 (28.6)	12 (28.6)
Moderate	0	0
Severe	0	0
Any TEAE leading to permanent study drug discontinuation	0	0
Any TEAE leading to study drug interruption and/or dose reduction	0	2 (4.8)
Any Serious TEAE	0	1 (2.4)[b]
AESI: LVEF <50%	0	2 (4.8)

Database lock: June 2026. [a]Severe TEAE of platelets decreased occurred during washout. [b]Serious TEAE of chest discomfort occurred during washout. AE, adverse event; AESI, adverse event of special interest; LVEF, left ventricular ejection fraction; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

CONCLUSIONS

- **Large improvement in measures of feel and function** including NYHA class, KCCQ, pVO2, VE/VCO2, with longer time on therapy
- **Consistent with reverse remodeling after 52 weeks of treatment:** LVWT reduced through Week 52; LVOT-G and NT-proBNP partly returned to baseline after washout
- **Simple dosing:** most patients remained on the 40 mg starting dose; high complete gradient response rate at Week 1
- **LIONHEART-HCM**, a global Phase 3 trial in oHCM is open and enrolling

KCCQ, Kansas City Cardiomyopathy Questionnaire; LVOT-G, left ventricular outflow tract gradient; LVWT, left ventricular wall thickness; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; oHCM, obstructive hypertrophic cardiomyopathy; VE/VCO2, minute ventilation to carbon dioxide output ratio; pVO2, peak oxygen uptake.

THANK YOU

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