



**Long-term Safety and Tolerability
of Acoramidis (AG10) in
Symptomatic Transthyretin
Amyloid Cardiomyopathy: Updated
Analysis from an Ongoing Phase 2
Open-label Extension Study**

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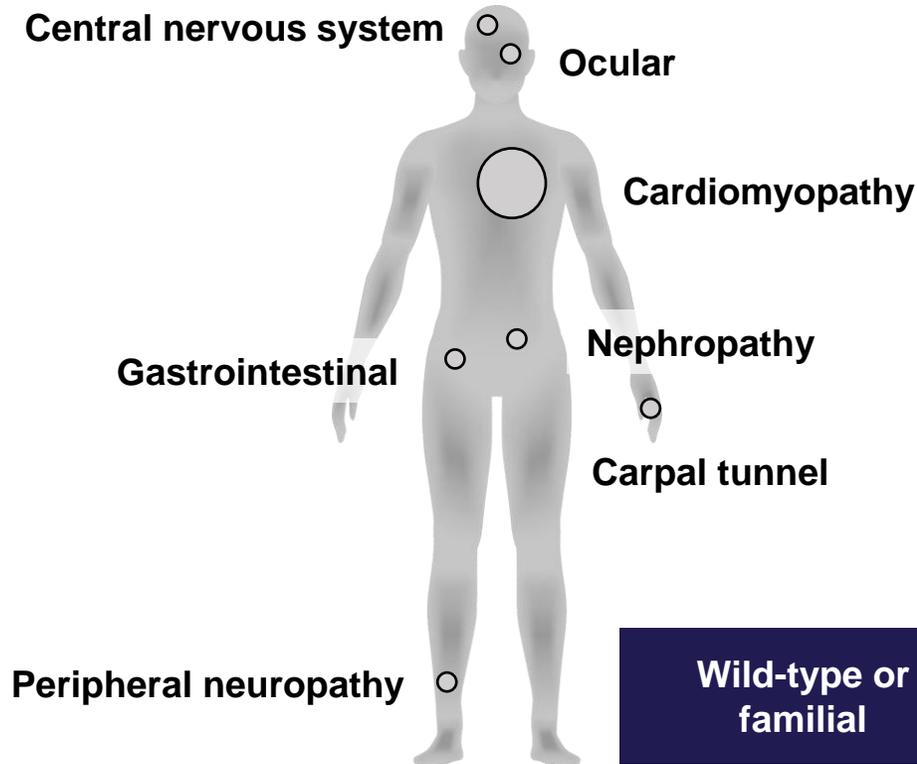


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Transthyretin (TTR) amyloidosis cardiomyopathy (ATTR-CM) is an emerging diagnostic and treatment priority

ATTR is a systemic disease



Growing awareness of undiagnosed ATTR:

10-13% of heart failure with preserved ejection fraction^{1,2,3}

7% of idiopathic bilateral carpal tunnel release⁴

5% of suspected hypertrophic cardiomyopathy*⁵

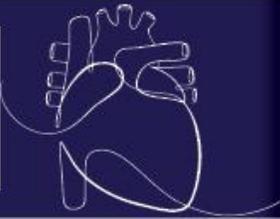
ATTR pathogenesis and therapeutic strategies:

- Instability of the TTR tetramer promotes dissociation and aggregation as amyloid plaques⁶
- Available therapies include TTR tetramer stabilizers, TTR knockdown agents (neuropathy only), and transplant
- Stabilizing mutation (T119M) protects against ATTR and was the basis for development of acoramidis⁷

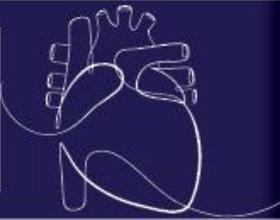
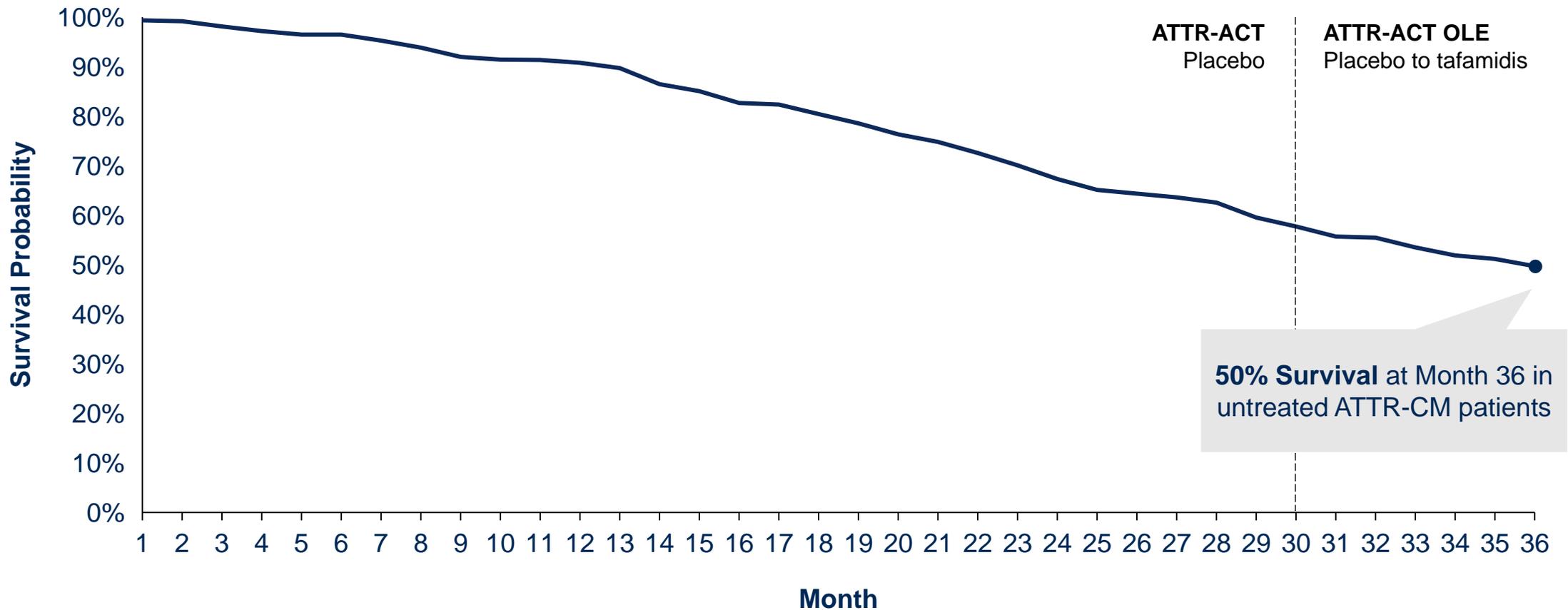
*Mutant TTR only, ^{99m}Tc=Technetium-99m; TAVR=transcatheter aortic valve replacement.

References: 1. Gonzalez-Lopez E, et al. *Eur Heart J* 2015. 2. Mohammed SF, et al. *JACC: Heart Failure* 2014. 3. Hahn VS, et al. *JACC* 2020. 4. Sperry BW et al. *JACC* 2018. 5. Damy T, et al. *Eur Heart J* 2015. 6. Sant'Anna R, et al. *Sci Rep*. 2017;7(44709):1-15. 7. Coelho T, et al. *Neuromuscul Disord*. 1996;6(1):S20.

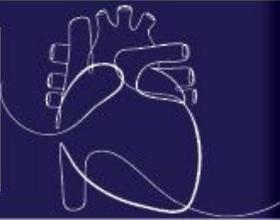
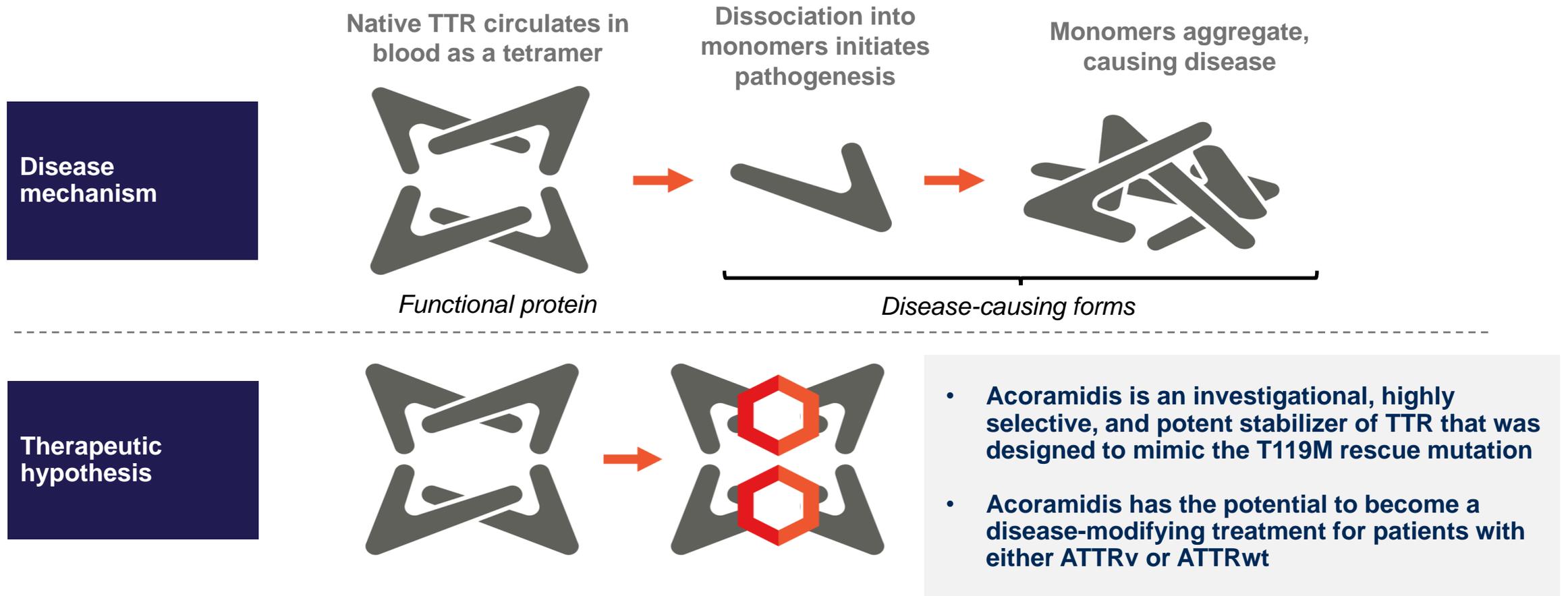
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ATTR-CM is a rapidly progressive and fatal disease

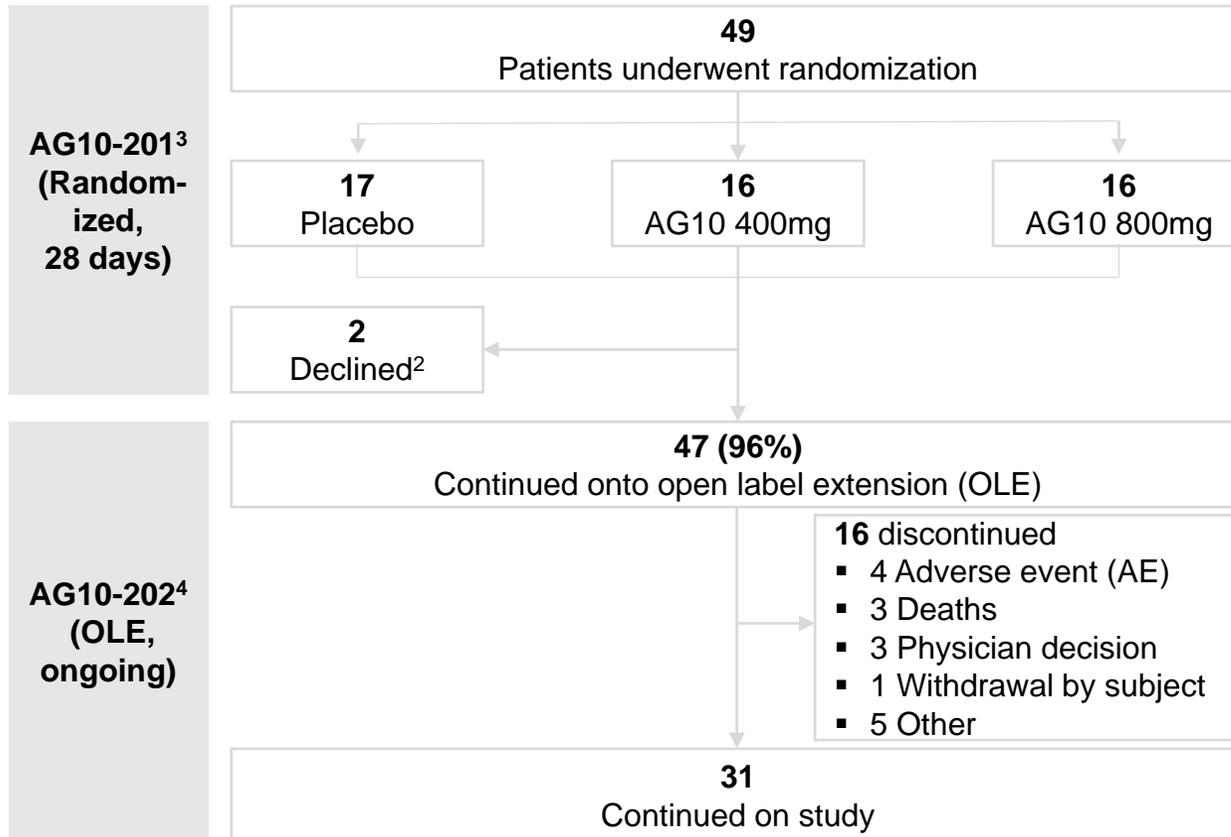


Acoramidis was designed to mimic a naturally occurring TTR variant that protects carriers from ATTR development



Acoramidis Phase 2 design

Schematic of acoramidis Phase 2 as of August 31, 2021¹



Patient selection and objectives

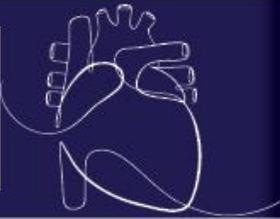
Selected inclusion criteria

- Established diagnosis of ATTR-CM
- NYHA class II or III symptoms
- ≥1 prior hospitalization for heart failure or clinical evidence of heart failure

Primary and secondary objectives

- Safety and tolerability
 - Pharmacokinetics
 - Pharmacodynamics
- Consort diagram reflects status of participants as of August 31, 2021 or study discontinuation
 - Overall, AEs with an outcome of death, cardiac transplant or transition to hospice were reported for 11 participants

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¹Median 38 months from initial Phase 2 randomization. Median 35 months on open-label acoramidis

²Both declined participation due to geographical constraints regarding study visits.

³Clinicaltrials.gov identifier: NCT03458130

⁴Clinicaltrials.gov identifier: NCT03536767

No safety signals of clinical concern identified in Phase 2 OLE

Summary of treatment-emergent adverse events

Number of participants (%)

Any treatment-emergent adverse event	47 (100)
Most common adverse events (≥ 9)	
Fall	21 (44.7)
Acute kidney injury	12 (25.5)
Cardiac failure congestive	10 (21.3)
Arthralgia	9 (19.1)
Cardiac failure acute	9 (19.1)
Constipation	9 (19.1)
Dyspnea	9 (19.1)
Fatigue	9 (19.1)

Summary of serious treatment-emergent adverse events

Number of participants (%)

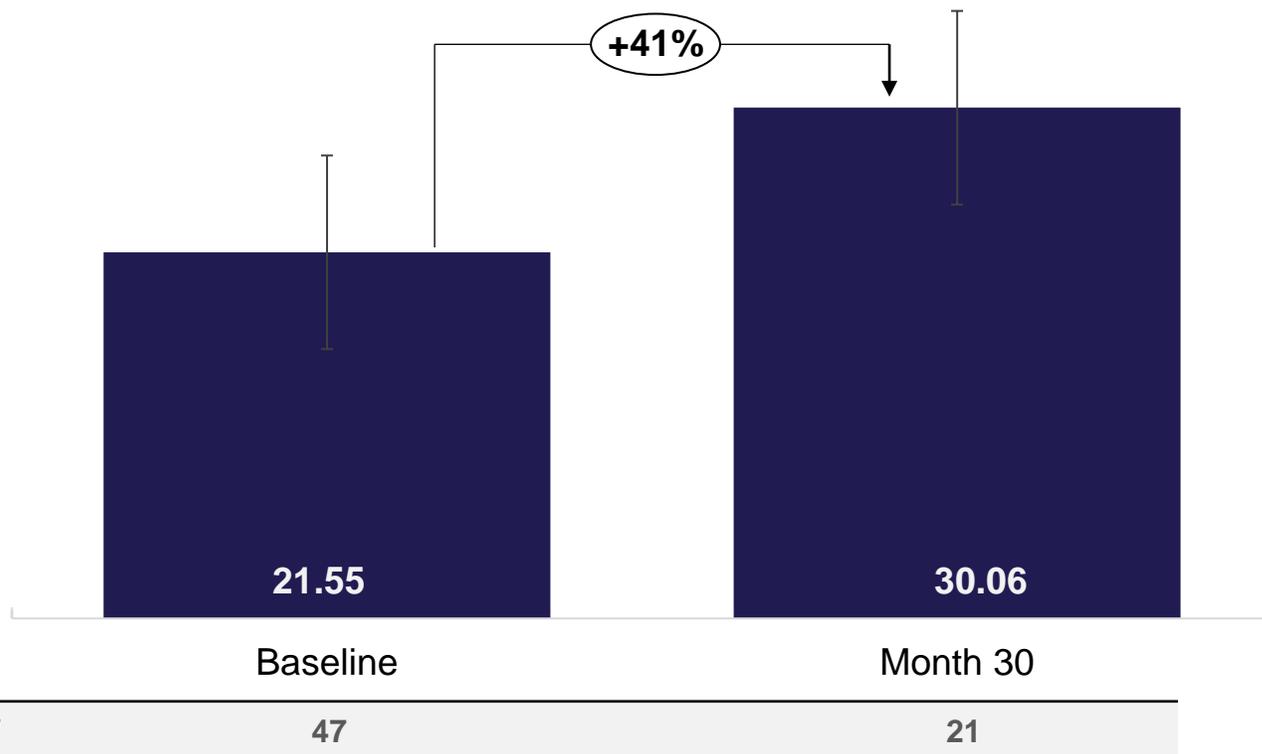
Any serious treatment-emergent adverse event	31 (66.0)
Most common serious adverse events (≥ 4)	
Cardiac failure acute	9 (19.1)
Acute kidney injury	7 (14.9)
Cardiac failure congestive	5 (10.6)
Fall	5 (10.6)
Cardiac failure	4 (8.5)
Cardiogenetic shock	4 (8.5)
Cardiorenal syndrome	4 (8.5)

Acoramidis was generally well tolerated with a pattern of adverse events consistent with underlying disease, progression of disease, concurrent illnesses, and age of participants

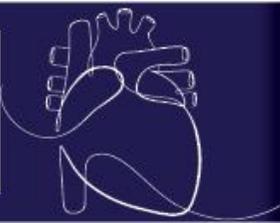
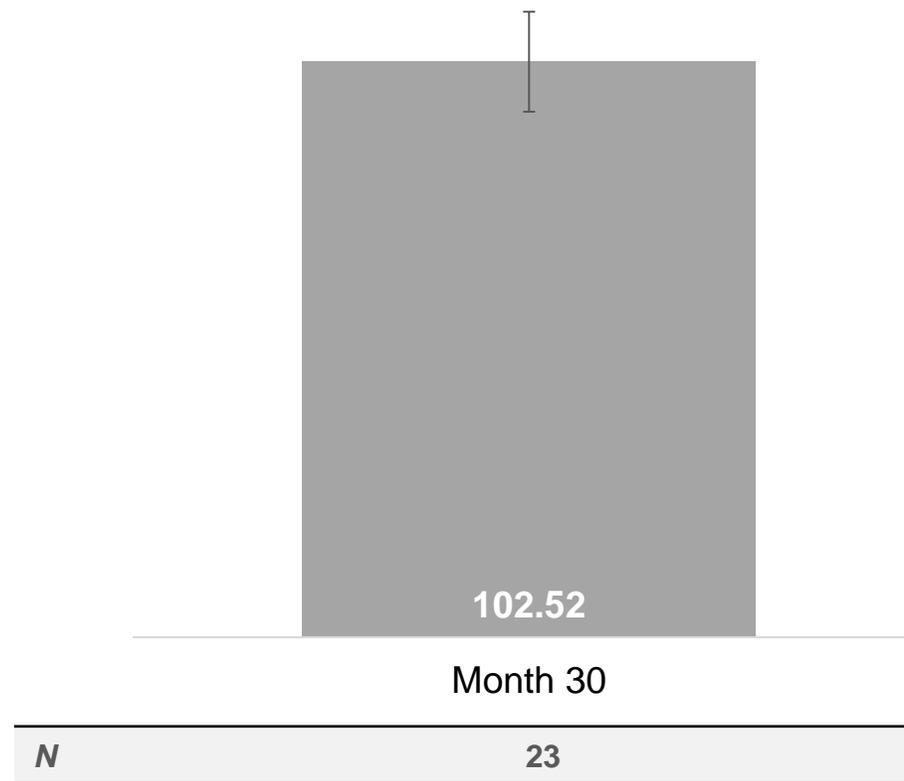


Acoramidis increased serum TTR levels and provided near-complete TTR stabilization

Serum TTR concentration
Mean +/- SD (mg/dL)

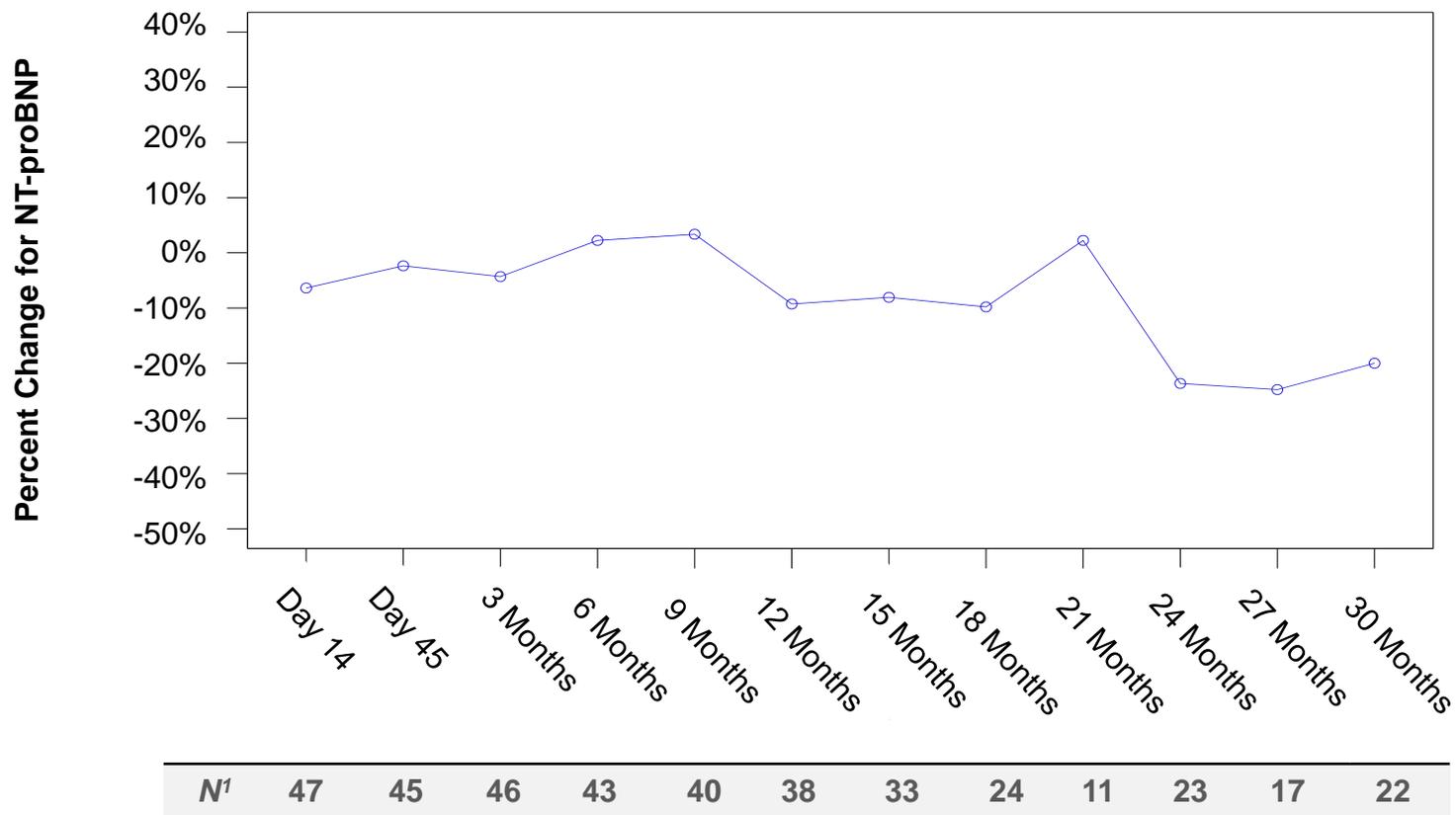


TTR stabilization by FPE¹
Mean +/- SD (%)

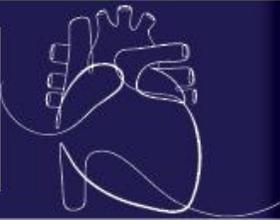


Median NT-proBNP was stable or improving at all time points beyond Month 12

Median Change for NT-proBNP by Visit



- At Month 30, median change from baseline was -437 pg/mL [-950, 316]
- At Month 30, 15/22 (68%) participants had NT-proBNP levels below their baseline¹



Summary of acoramidis Phase 2 OLE results

1

Safety and tolerability

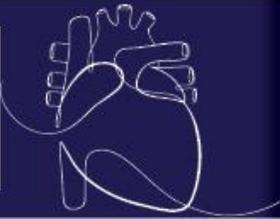
- Adverse event profile consistent with baseline disease severity and progression
- No signals of concern observed with median participation of 38 months

2

Cardiac biomarkers

- Sustained stabilization of TTR demonstrated by increased serum concentrations and ex vivo assays
- Median NT-proBNP was stable or declining at all time points beyond Month 12

Phase 2 OLE data and ongoing participation through 3 years support further development of acoramidis in ATTR-CM; evaluation in a Phase 3 trial is ongoing (ATTRibute-CM)



ATTRibute-CM Phase 3 design includes primary endpoints at Month 12 and Month 30

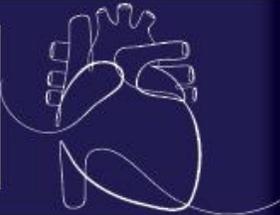
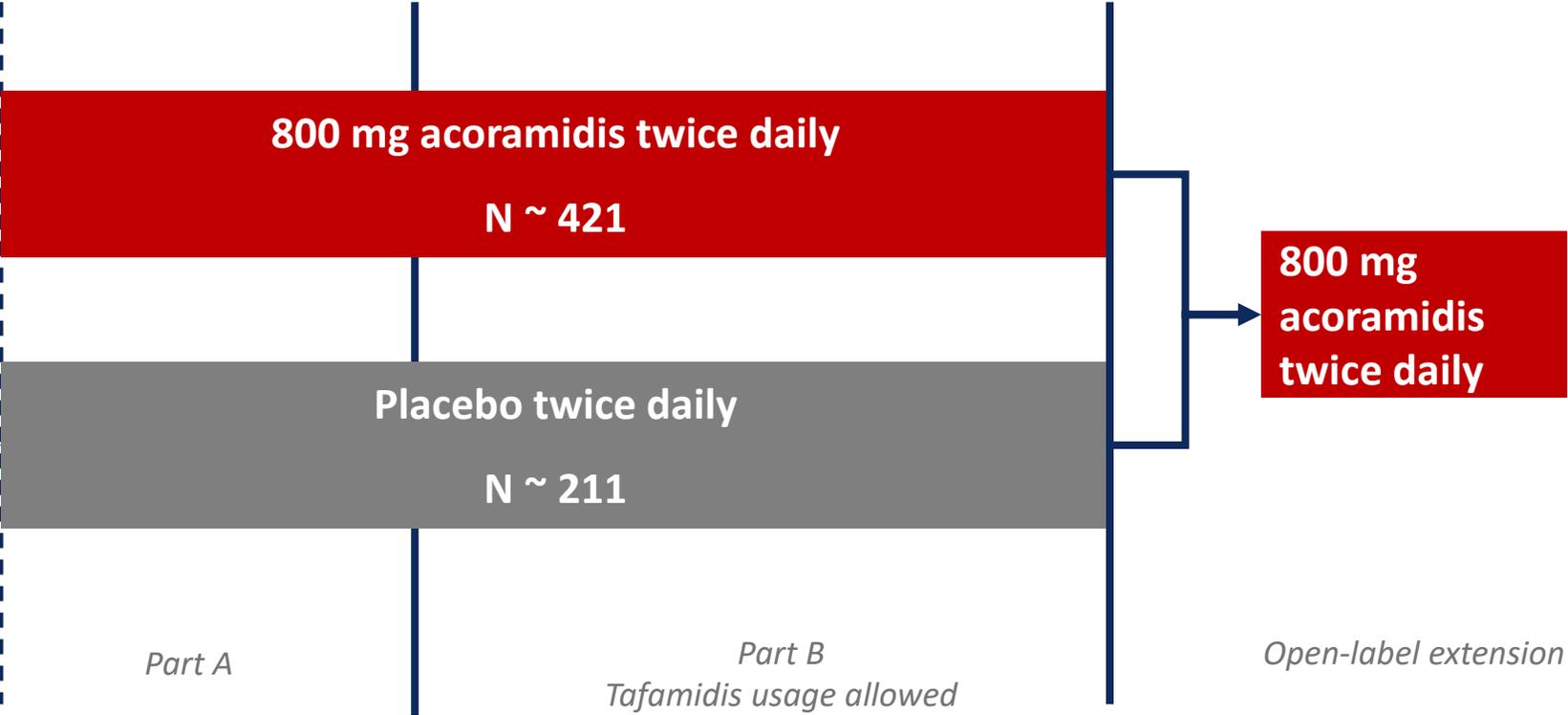
Key inclusion criteria

- Subjects with diagnosed ATTR-CM (WT or mutant)
- NYHA Class I-III
- ATTR-positive biopsy or ^{99m}Tc scan
- Light chain amyloidosis excluded if diagnosis by ^{99m}Tc

Screening and randomization

12-month endpoints:
Primary: Change in 6MWD
Key secondary: Change in KCCQ

30-month endpoints:
Primary: Hierarchical composite including all-cause mortality and CV-related hospitalizations
Key secondary: Change in 6MWD, KCCQ



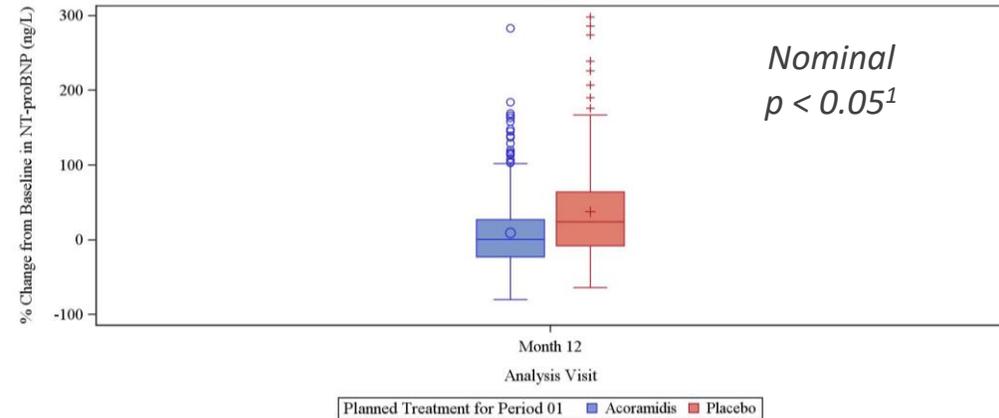
6MWD = six-minute walk distance; ^{99m}Tc = Technetium labeled pyrophosphate (PYP); CV= cardiovascular; KCCQ = Kansas City Cardiomyopathy Questionnaire; NYHA = New York Heart Association.
 Source: Clinicaltrials.gov identifier: NCT03860935

Summary of Month 12 results

Based on data available at Month 12, acoramidis demonstrated relative to placebo:

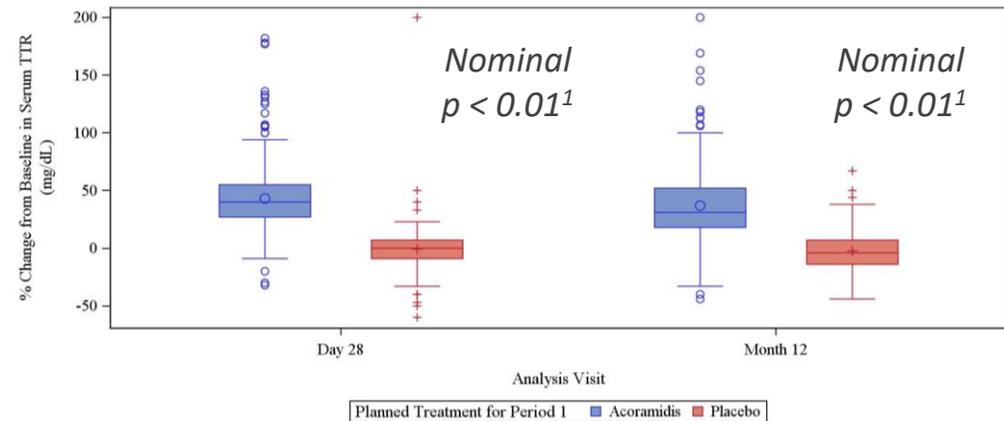
- No improvement in 6MWD
- ✓ Positive improvement in KCCQ-OS
- ✓ Positive reduction in NT-proBNP
- ✓ Positive improvement in serum TTR
- ✓ No safety signals of clinical concern

Percent change from baseline in NT-proBNP²



Note: to facilitate a focused review of the vast majority of the data, outliers greater than 300% change from baseline are not included in this plot.

Percent change from baseline in serum TTR²



Note: to facilitate a focused review of the vast majority of the data, outliers greater than 200% change from baseline are not included in this plot.

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Source: BridgeBio press release published 12/27/2021

¹Inference analysis (p-value) based on absolute change from baseline between groups

² Modified intent-to-treat (mITT) population defined as all randomized subjects who have received at least one dose of IMP and have at least one post baseline efficacy evaluation. mITT population pre-specified to exclude subjects with baseline eGFR < 30 mL/min/1.73 m²

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