Intellia Therapeutics

Corporate Overview

November 2026

KIM
Living with Hereditary Angioedema



Intellia Therapeutics' Legal Disclaimer

This presentation contains "forward-looking statements" of Intellia Therapeutics, Inc. ("Intellia", "we" or "our") within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements include, but are not limited to, express or implied statements about Intellia's beliefs and expectations regarding: our ability to successfully develop and commercialize nexiguran ziclumeran ("nex-z"), previously referred to as NTLA-2001, for the treatment of transthyretin ("ATTR") amyloidosis and lonvoguran ziclumeran ("lonvo-z"), previously referred to as NTLA-2002, for the treatment of hereditary angioedema ("HAE") to address the significant unmet needs of patients and prescribers in ATTR amyloidosis and HAE, respectively; our ability to achieve upcoming objectives, including successfully launching lonvo-z for the treatment of HAE following approval in the U.S. in the first quarter of 2027 and scaling field sales and reimbursement teams for lonvo-z, finalize pricing for lonvo-z, finalizing price and contracting strategy for lonvo-z; our ability to optimize the impact of our collaborations on our development programs, including our collaboration with Regeneron Pharmaceuticals, Inc. ("Regeneron") and our co-development program for ATTR amyloidosis, and to advance additional development candidates; our expectations regarding our uses of capital, expenses, and ability to fund operations at least into 2028; the potential commercial opportunities for our product candidates, including the value and market potential for our product candidates, including the potential of nex-z and lonvo-z to be single-dose treatments administered in an outpatient setting, the potential of lonvo-z to completely redefine HAE treatment and to reduce burden and generate value for patients, HCPs, payers and the overall healthcare system, and the potential of nex-z to transform the standard of care for ATTR amyloidosis, provide patients with consistently rapid, deep and durable TTR reduction, stability or improvement in the disease for most patients, improved quality of life, and reduced cardiovascular events and mortality; and our ability to leverage our CRISPR gene editing and other core technologies for pipeline expansion efforts and collaborations.

Any forward-looking statements in this presentation are based on management's current expectations and beliefs of future events, and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: risks related to our ability to successfully develop and commercialize lonvo-z, nex-z, or any of our other product candidates; risks related to Intellia's ability to protect and maintain its intellectual property position; risks related to Intellia's relationship with third parties, including our contract manufacturers, licensors and licensees; risks related to the ability of our licensors to protect and maintain their intellectual property position; uncertainties related to the authorization, initiation and conduct of preclinical and clinical studies and other development requirements for our product candidates, including uncertainties related to regulatory approvals to conduct clinical trials; risks related to the results of preclinical studies or clinical studies not being predictive of future results in connection with future studies; the risk that clinical trial results will not be positive; risks related to the development and advancement of CRISPR gene editing and other core technologies technologies for pipeline expansion and collaborations; risks related to Intellia's future financial condition and our ability to fund our operations; risks related to Intellia's collaborations with Regeneron or our other collaborations not continuing or not being successful; and risks related to Intellia's ability to execute its strategic plans, including completing pivotal clinical trials and commercial launch of its product candidates. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause Intellia's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in Intellia's most recent Annual Report of Form 10-K and Quarterly Report on Form 10-Q as well as discussions of potential risks, uncertainties, and other important factors in Intellia's other filings with the Securities and Exchange Commission. All information in this presentation is as of the date on its cover page, and Intellia undertakes no duty to update this information unless required by law.

Intellia THERAPEUTICS®

Our Vision: Leveraging CRISPR Gene Editing and Other Core Technologies to Transform the Lives of Patients



Treat patients at the **root cause of their disease**



Single dose treatment with potential for **durable benefit**



Reduce burden for the patient **and** the healthcare system



Optimal outcomes for patients

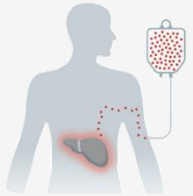
CRISPR: clustered regularly interspaced short palindromic repeats.

Intellia THERAPEUTICS®

Intellia is Leading a New Era of Medicine

Working diligently to bring the **first-ever *in vivo* CRISPR-based therapies** to patients living with severe diseases

600+ **Patients Dosed**
with Intellia's investigational *in vivo* CRISPR-based therapies

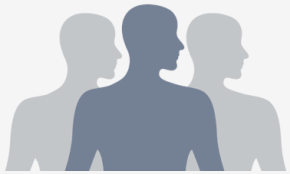


6+ **Years of Follow-Up**
in earliest dosed patients

1st **Positive Phase 3 Readout**
in hereditary angioedema (HAE)



2 **Additional Phase 3 Trials**
ongoing in transthyretin amyloidosis (ATTR-CM & PN)



6 Publications in The NEW ENGLAND JOURNAL of MEDICINE

AUG 5 **2021**	CRISPR-Cas9 *In Vivo* Gene Editing for Transthyretin Amyloidosis
JAN 31 **2024**	CRISPR-Cas9 *In Vivo* Gene Editing of *KLKB1* for Hereditary Angioedema
OCT 24 **2024**	CRISPR-Based Therapy for Hereditary Angioedema
NOV 16 **2024**	CRISPR-Cas9 Gene Editing with Nexiguran Ziclumeran for ATTR Cardiomyopathy
SEP 25 **2025**	Nexiguran Ziclumeran Gene Editing in Hereditary ATTR with Polyneuropathy
JUNE 13 **2026**	Lonvoguran Ziclumeran - *In Vivo* CRISPR Gene Editing in Hereditary Angioedema

CRISPR: clustered regularly interspaced short palindromic repeats; Cas9: CRISPR-associated protein 9; ATTR-CM: ATTR amyloidosis cardiomyopathy; ATTRv-PN: hereditary ATTR amyloidosis polyneuropathy; *KLKB1*: kallikrein B1.

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Intellia's Pipeline Advancing Toward Significant Near-Term Milestones

Program	Indication	Research/ Preclinical	Early-Stage Clinical	Late-Stage Clinical	BLA Submission	
Lonvo-z[1]	Hereditary Angioedema (HAE)					Intellia THERAPEUTICS
Nex-z[2]	Transthyretin Amyloidosis with Polyneuropathy (ATTRv-PN)					LEAD Intellia THERAPEUTICS REGENERON
	Transthyretin Amyloidosis with Cardiomyopathy (ATTR-CM)					LEAD Intellia THERAPEUTICS REGENERON
REGV131-LNP1265[3]	Hemophilia B					REGENERON
AVC-201 AVC-203	Acute Myeloid Leukemia (AML) B-cell malignancies					AVENCELL[4]
Other Ongoing Research Programs	Various					Intellia[5] THERAPEUTICS REGENERON AVENCELL kyverna

Lead refers to lead development and commercial party. 1. Lonvo-z (lonvoguran ziclumeran), formerly referred to as NTLA-2002. 2. Nex-z (nexiguran ziclumeran), formerly referred to as NTLA-2001; Regeneron shares in approximately 25% of worldwide development costs and commercial profits for the ATTR program and has an option to enter into a co-promotion agreement for the U.S. commercialization. 3. Hemophilia B is being advanced solely by Regeneron; Intellia is eligible for milestones and royalties. 4. AVC-201 and AVC-203 are wholly owned by AvenCell and utilize proprietary allogeneic cell engineering technology licensed from Intellia. 5. Intellia is advancing both wholly owned and partnered programs. ATTRv-PN: hereditary transthyretin amyloidosis with polyneuropathy.

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Key Objectives

Lonvo-z HAE

- Present topline Phase 3 HAELO data by mid-2026
- Present additional Phase 3 HAELO data at EAACI in June 2026
- Announce BLA acceptance by FDA in second half of 2026
- U.S. approval and commercial launch in first quarter of 2027

Nex-z ATTR

- Resume patient enrollment in Phase 3 MAGNITUDE trial in ATTR-CM
- Resume patient enrollment in Phase 3 MAGNITUDE-2 trial in ATTRv-PN
- Complete enrollment in MAGNITUDE-2 in second half of 2026

Existing cash resources expected to fund operations at least into 2028, excluding potential commercial revenues from lonvo-z and potential future term loan facility funding

ATTR: transthyretin amyloidosis; ATTR-CM: ATTR amyloidosis cardiomyopathy; ATTRv-PN: hereditary ATTR amyloidosis polyneuropathy; BLA: biologics license application; HAE: hereditary angioedema.

Lonvoguran Ziclumeran (lonvo-z) for Hereditary Angioedema

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HAE: A Rare and Debilitating Disease Often Diagnosed Early in Life

- Rare, genetic, and life-threatening disease
- Caused by a hereditary deficiency or dysfunction of the C1 inhibitor protein, leading to an imbalance in the kallikrein-kinin system and an overproduction of bradykinin
- Patients experience unpredictable, recurrent, painful and potentially life-threatening swelling attacks[1,2]
- Symptoms almost always apparent by puberty
- Average age of diagnosis in U.S.: ~20 years old[3]

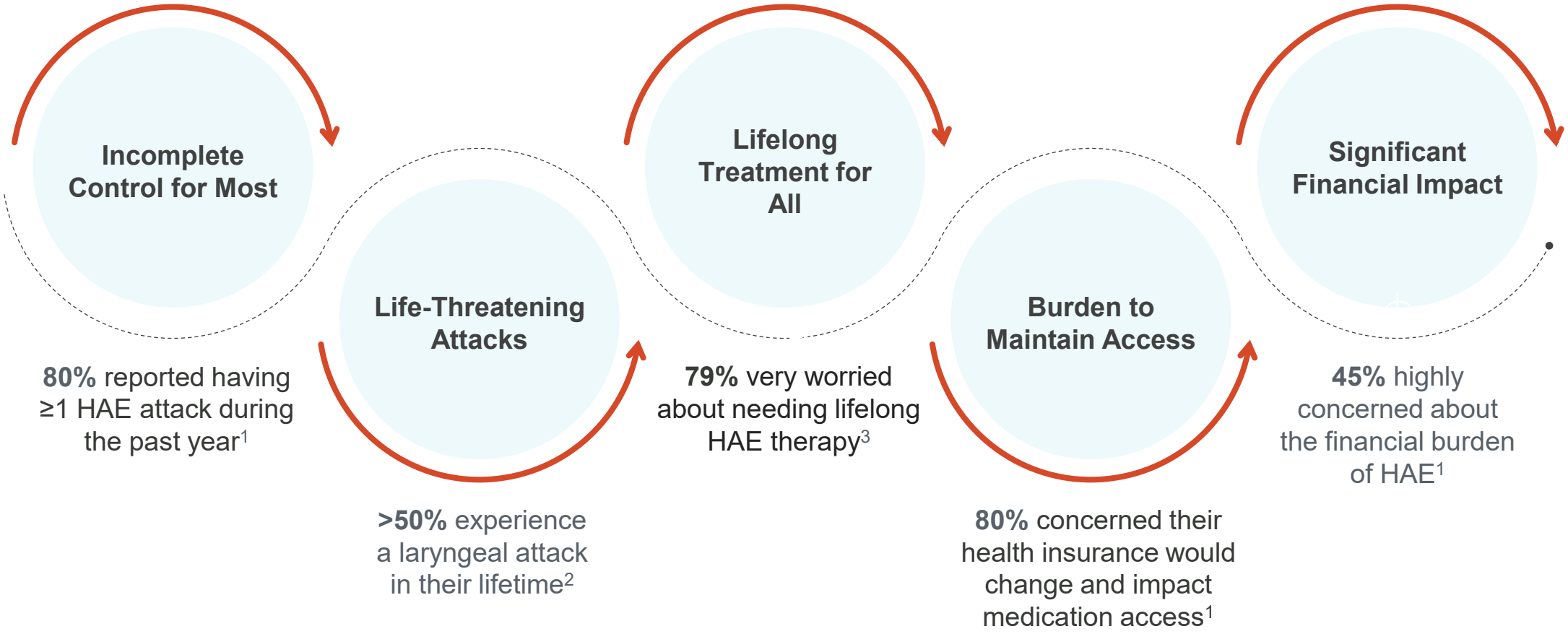


Photo source: U.S. Hereditary Angioedema Association. 1. Zuraw et al. *New England Journal of Medicine*, September 2008. 2. Busse and Christiansen, *New England Journal of Medicine*, March 2020. 3. Banerji A et al. *Annals of Allergy, Asthma & Immunology*, June 2020. HAE: hereditary angioedema.

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Despite Available Treatments, Many Patients are Unable to Break the Chronic Cycle of Managing Their HAE

Patient-Reported Burdens

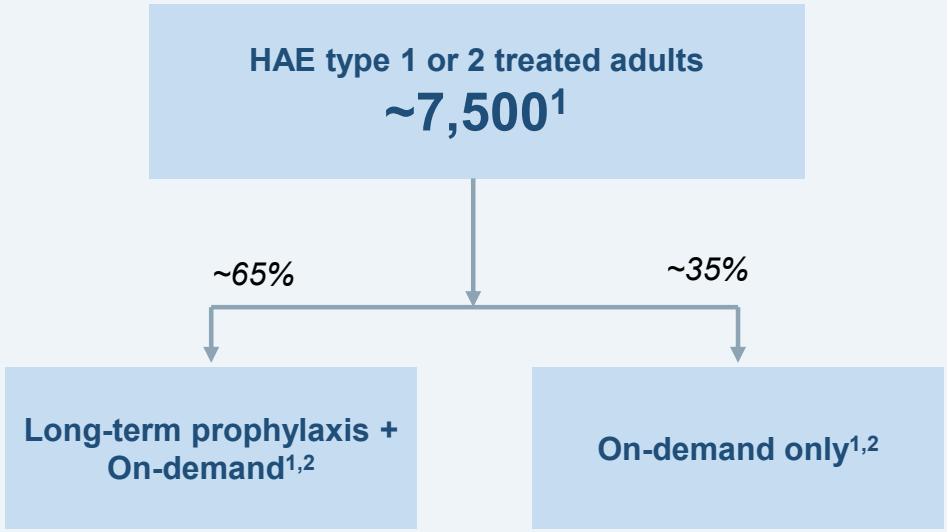


1. Busse et al. *Allergy Asthma Proc*. 2026 Mar 1;47(2):92-101. 2. Lumry WR, Settipane RA. *Allergy Asthma Proc*. 2020 Nov 1;41(Suppl 1):S08-S13. 3. Intellia Commissioned Market Research, October 2026 (Patients n=156). Interest: rating 4–5 on a 5-point interest scale. Worry about lifelong therapy: rating 5–7 on a 7-point agreement scale. HAE: hereditary angioedema.

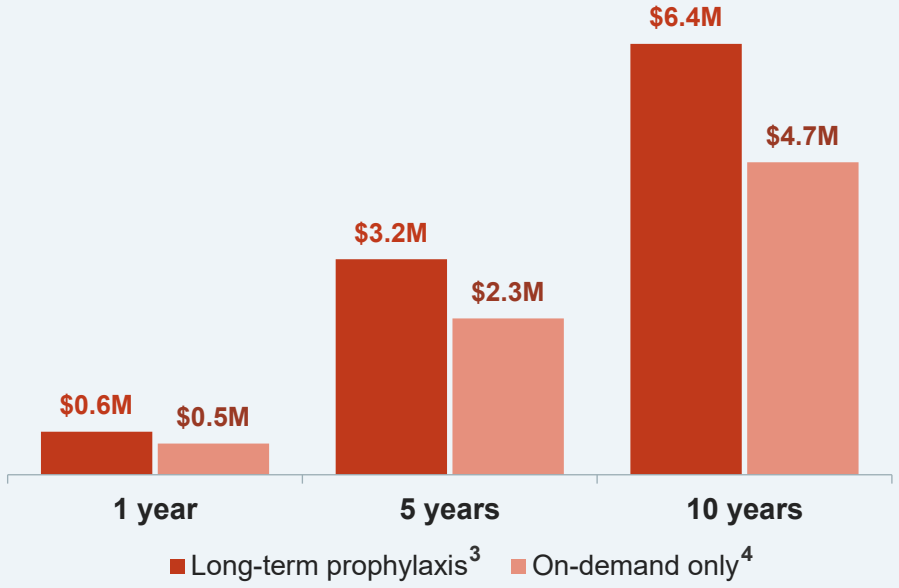
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About 7,500 U.S. Adults Are Treated for HAE, and a Single Patient on LTP Can Cost the U.S. Healthcare System >$6 Million Per Decade

U.S. TREATED ADULTS



PROJECTED CUMULATIVE COST PER PATIENT ($M)



Illustrative, per patient: LTP at ~$641K per year (95% CI: $560K-$737K); on-demand at the ~$465K midpoint of the ~$360K-$570K range. Costs held constant over time.

1. Population estimate: IQVIA LAAD+ 2018–2025. 2. Banerji A, et al. *Ann Allergy Asthma Immunol*ogy, June 2020; Anderson J, et al. *Advances in Therapy*, September 2026.
3. IQVIA PharMetrics® Plus retrospective claims analysis 2017-2022, commercially insured age 12+ LTP patients (n=210). 4. Range derived from 2 distinct studies: Castaldo et al. (2021). doi:10.2500/aap.2021.42.200127; Bernstein et al. (2020). doi:10.18553/jmcp.2019.19217. HAE: hereditary angioedema; LTP: long-term prophylaxis.

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Lonvo-z: A One-Time Therapy Unlike Any Other

DISRUPTIVE
TREATMENT APPROACH

A new modality that stands apart from past one-time treatments and chronic long-term prophylactics; aiming to **completely redefine HAE treatment**.

EMPOWERED
AND HIGHLY MOTIVATED PATIENTS

Patients with HAE are highly educated and have an outsized voice in their treatment. **Most report they would seek a one-time therapy**.

ADVANCING
TOWARD LAUNCH

Intellia has a **strong strategy and full team already in place**. Proactive work is well underway in anticipation of potential approval.

BENEFIT
FOR ALL

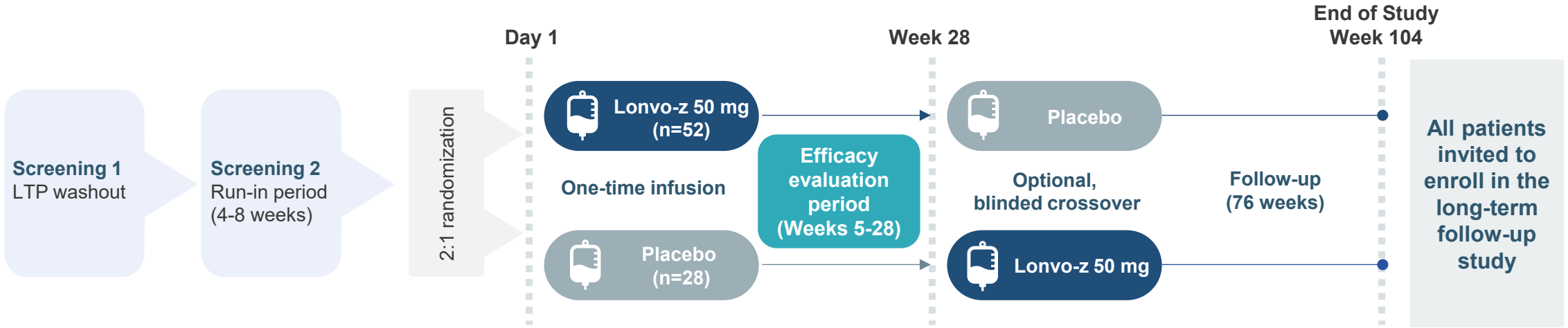
As a one-time treatment, lonvo-z could **reduce burden and generate value** for patients, HCPs, payers and the overall healthcare system.

HAE: hereditary angioedema; HCP: healthcare provider.

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A Placebo-Controlled, Double-Blind, Randomized Phase 3 Trial of Lonvo-z as a One-Time HAE Treatment

HAELO Clinical Trial



Stratification

Baseline number of investigator-confirmed HAE attacks per month from Screening 2 to Randomization

Primary Endpoint

Time-normalized number of investigator-confirmed HAE attacks from Weeks 5 through 28

Key Secondary Endpoints

- Time-normalized number of investigator-confirmed HAE attacks requiring on-demand treatment from Weeks 5 through 28
- Time-normalized number of moderate or severe investigator-confirmed HAE attacks from Weeks 5 through 28
- Investigator-confirmed HAE attack-free status from Weeks 5 through 28
- Change from baseline to Week 28 in AE-QoL Questionnaire total score

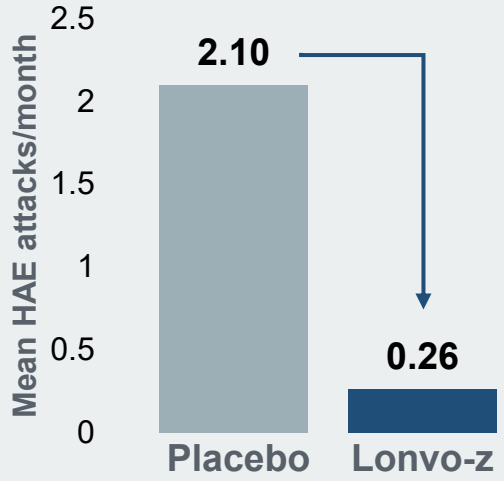
Pre-specified primary analysis when ≥60 patients reached Week 28

ClinicalTrials.gov: https://clinicaltrials.gov/study/NCT06634420. AE-QoL: Angioedema Quality of Life; EOS: end of study; HAE: hereditary angioedema; LTP: long-term prophylaxis; mg: milligram.

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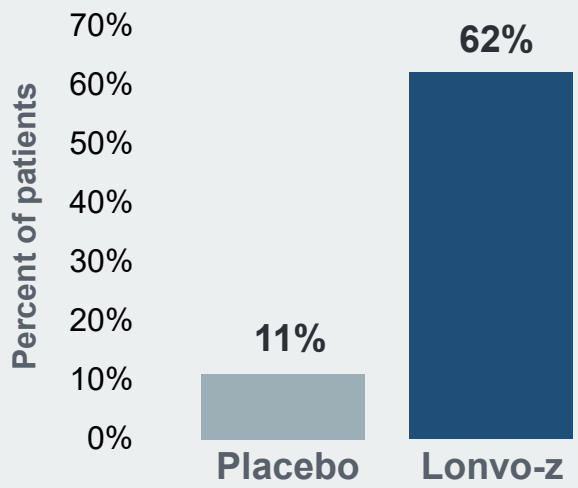
HAELO Trial Achieved its Primary and All Key Secondary Endpoints

Mean Attack-Rate Reduction Weeks 5 – 28 (Primary Endpoint)[1,2]



87% reduction
(95% CI: 78%-93%)
p<0.0001

Attack Free Weeks 5 – 28 (Key Secondary Endpoint)[2]



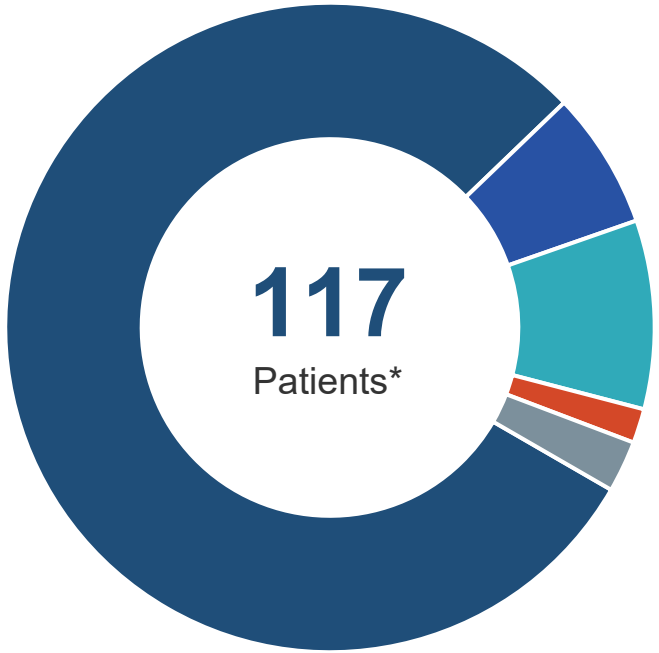
Odds Ratio 12.8
(95% CI: 3.5-47.6)
p<0.0001

All other key secondary endpoints were achieved with high statistical significance (p<0.0001)

Data cutoff: February 10, 2026. 1. Model-based HAE attack rate using a Poisson regression model with Pearson Chi-square scaling of standard error with treatment arm and baseline attack rate (> 3 vs ≤ 3 attacks/month) as covariates. 2. Includes assessments up to and including Week 28, or the latest assessment prior to the data cut-off date for patients who did not reach Week 28. CI: confidence interval; HAE: hereditary angioedema.

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Robust Experience with Lonvo-z: 117 Patients, Including Some with 4 Years of Follow-up



93 **Received one lonvo-z 50 mg dose**
in Phase 1/2 trial or Phase 3 HAELO trial

Integrated Phase 1/2/3 analysis

8 **Received placebo → lonvo-z 50 mg dose**
in Phase 3 HAELO trial (lonvo-z dose after Feb. 10 data cutoff)

11 **Received lonvo-z 25 → 50 mg doses**
in Phase 1/2 trial

2 **Received one lonvo-z 25 mg dose**
in Phase 1/2 trial

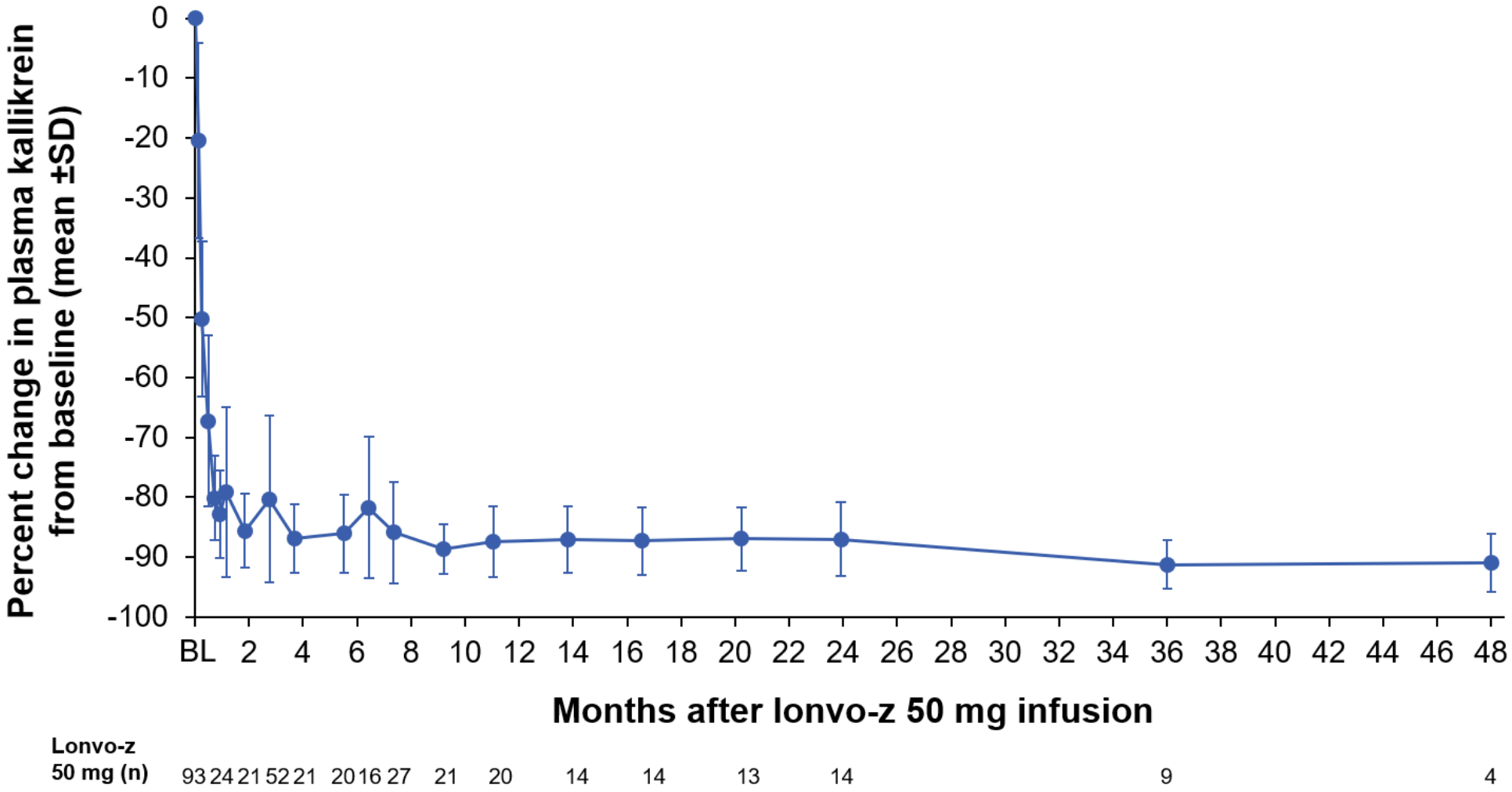
3 **Received one lonvo-z 75 mg dose**
in Phase 1/2 trial

Median total follow-up: 7.6 months (up to 4 years)

*June 26, 2026 (Phase 1/2); data cutoff date: February 10, 2026 (Phase 3); July 10, 2026 (LTFU: long-term follow-up). Mg: milligram.

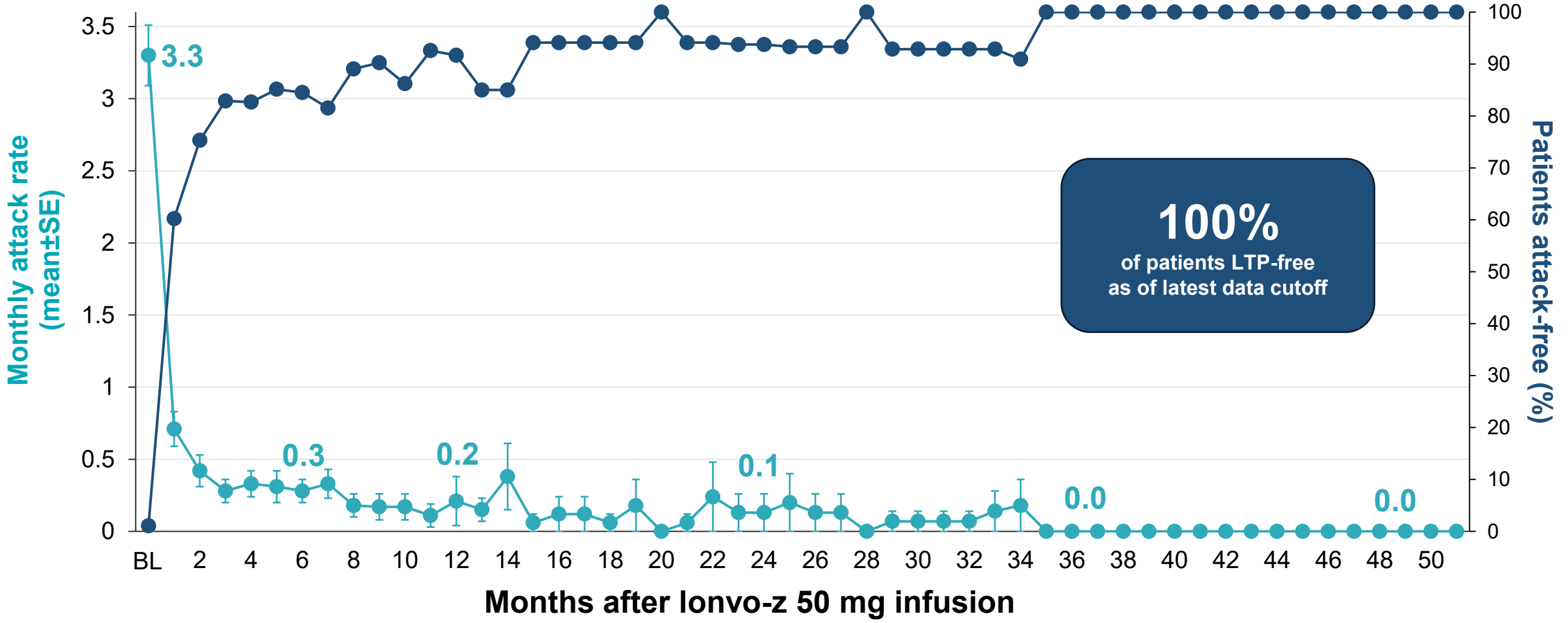
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Kallikrein Reduction Remains Deep and Durable with up to 4 Years Follow-up; No Waning of Effect



June 26, 2026 (Phase 1/2); data cutoff date: February 10, 2026 (Phase 3); July 10, 2026 (LTFU: long-term follow-up). BL: baseline; mg: milligram; SD: standard deviation.

Deep Attack-Rate Reduction and High Attack-Free Rate Maintained up to 4 Years After Lonvo-z 50 mg



Lonvo-z 50 mg (n)	93	93	81	76	75	74	71	65	64	41	29	27	24	20	20	17	17	17	17	17	17	17	17	16	16	15	15	15	14	14	14	14	14	14	11	10	9	9	9	9	7	4	4	4	4	4	4	4	4	4	4	4

June 26, 2026 (Phase 1/2); data cutoff date: February 10, 2026 (Phase 3); July 10, 2026 (LTFU: long-term follow-up). 31/32 patients treated with lonvo-z 50 mg remain in long-term follow-up. N shown represents the number of patients who have reached that time point. One month = 28 days. Timepoints with data from ≥3 patients are presented. BL: baseline; LTP: long-term prophylaxis; mg: milligram; SE: standard error.

Favorable Safety and Tolerability Data and No Long-Term Risks Observed with up to 4 Years of Follow-up

	Lonvo-z 50 mg (N=93) n (%)
Mean (range) duration of follow-up	7.6 (0.3-46.5) months
Any Treatment Emergent Adverse Event (TEAE)	82 (88)
TEAE Reported in >10% of Patients	
Infusion related reaction	51 (55)
Headache	18 (19)
Fatigue	17 (18)
Nasopharyngitis	15 (16)
Upper respiratory tract infection	13 (14)
Back pain	12 (13)
Grade 3 TEAE	2 (<1%)
Pulmonary embolism*	1 (<1%)
Perforated gangrenous appendicitis†	1 (<1%)
Serious Adverse Events (SAE)	2 (<1%)
Pulmonary embolism*	1 (<1%)
Perforated gangrenous appendicitis†	1 (<1%)

June 26, 2026 (Phase 1/2); data cutoff date: February 10, 2026 (Phase 3); July 10, 2026 (LTFU: long-term follow-up). *One event of Grade 3 pulmonary embolism was reported in a patient 12 months after lonvo-z 50 mg infusion. The patient had multiple risk factors which included recent COVID infection, ongoing history of smoking, and obesity. †One event of Grade 3 perforated appendicitis occurred in a patient 22 months after lonvo-z 50 mg infusion and was not considered treatment-related. Mg: milligram.

If Approved, Lonvo-z Could Ease Burdens for Patients, HCPs and Payers Alike

	Lonvo-z	Approved Chronic LTPs
Attack reduction	87%	44–89%
Attack- and treatment-free	62%	0%
Off prophylaxis at latest follow-up	100%	0%
Dosing frequency	One infusion, one time	13–365 doses per year
Ongoing access burden for all	One authorization, one time	1–2 reauthorizations per year
Cost profile for payers	Reduced long-term financial burden	Lifetime recurring costs

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Statistics above based on Phase 3 cross-trial comparison, for illustrative purposes only. HCP: healthcare provider; LTP: long-term prophylaxis.

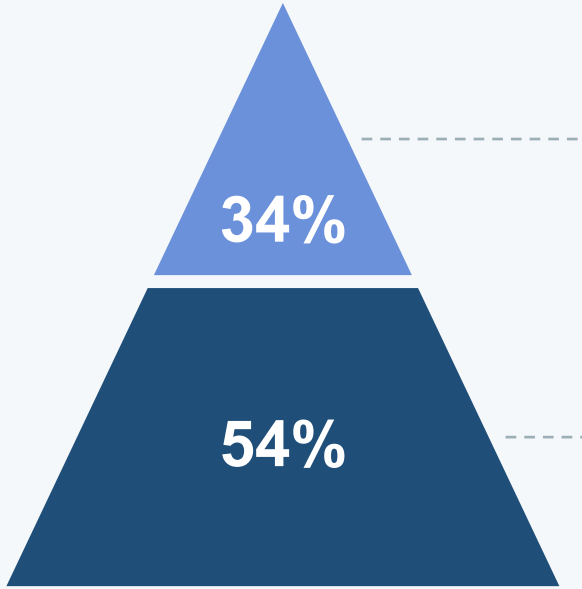
Strong Majority of Surveyed HCPs Would Prescribe Lonvo-z; Most to ≥50% of Their Patients

HCP RECEPTIVITY

88%

of HCPs would prescribe lonvo-z to **at least one patient**

PRESCRIBING OPPORTUNITY



EXPANSION OPPORTUNITY
Would prescribe to **<50% of patients** (n=51)

CORE PRESCRIBERS
Would prescribe to **≥50% of patients** (n=82)

TIME TO PRESCRIPTION

65%

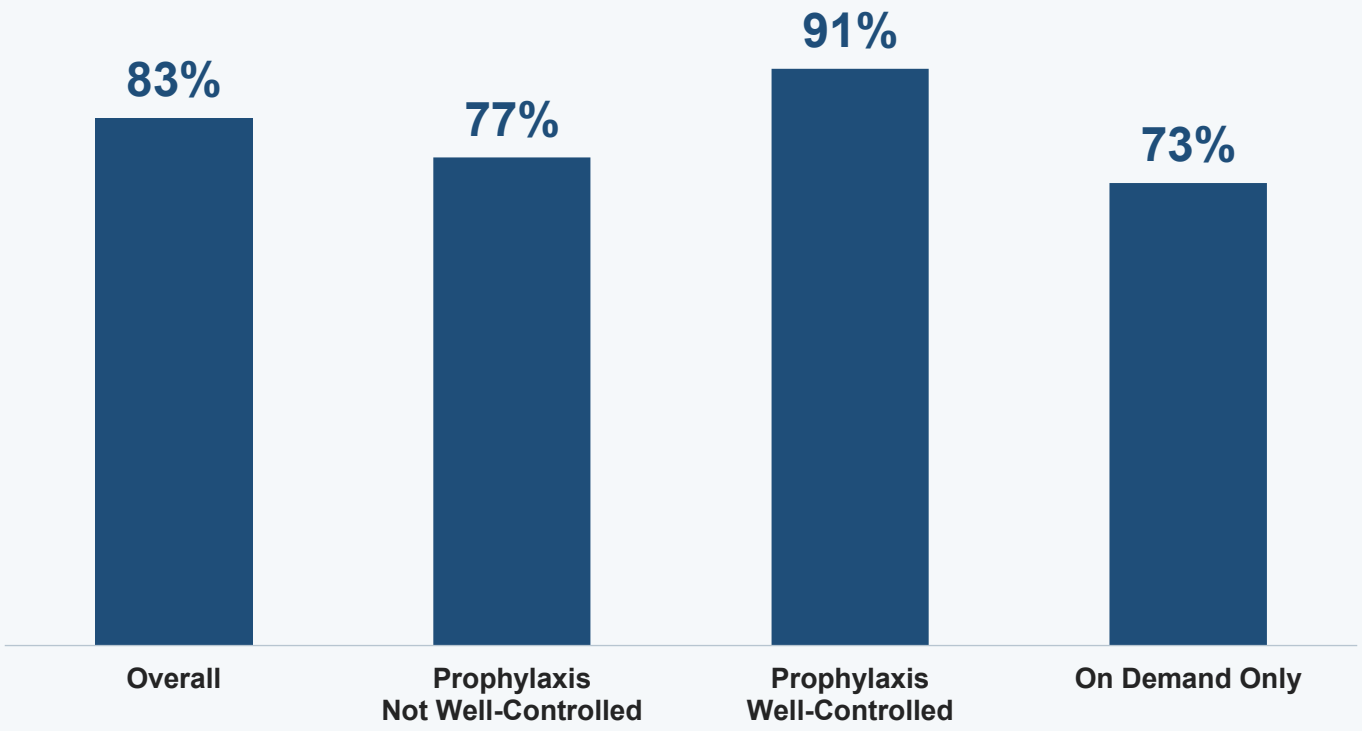
of HCPs would prescribe lonvo-z **within one year of approval**

Source: Intellia Commissioned Market Research, October 2026 (HCP n=151). HCP: healthcare provider.

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Most Surveyed Patients Would Ask About Lonvo-z, Regardless of Disease Control

% OF PATIENTS LIKELY / EXTREMELY LIKELY TO ASK ABOUT LONVO-Z[1]



SWITCHING HCPS

71%

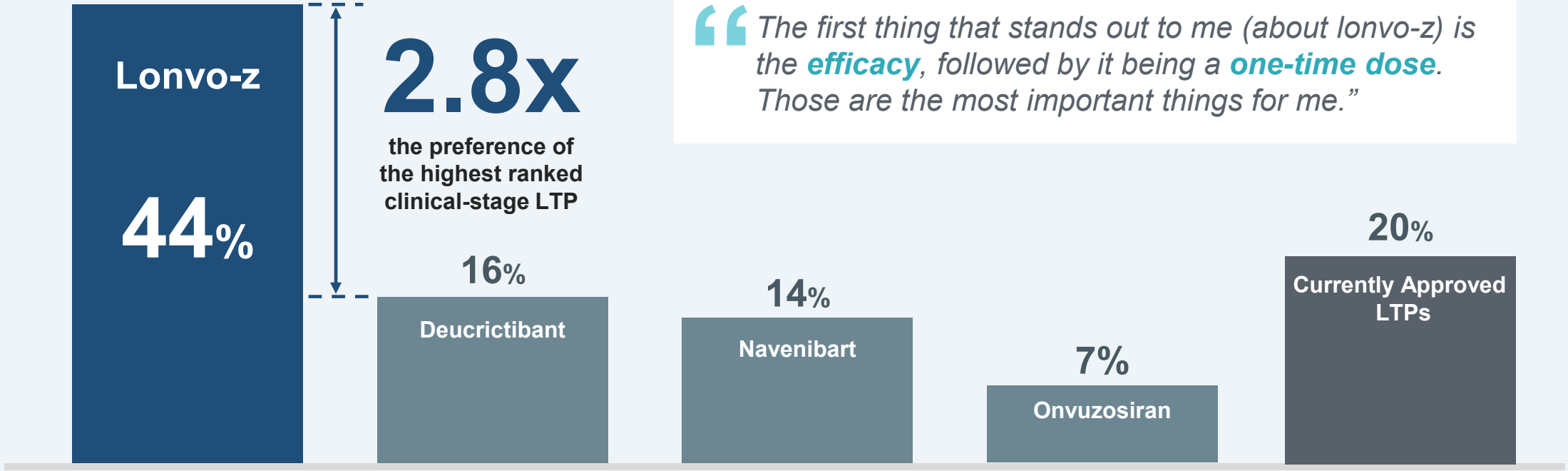
of patients **would seek a different HCP** if theirs can't prescribe lonvo-z

Source: Intellia Commissioned Market Research, October 2026 (Patients N= 156). 1. % of patients rating 5–7 (1=not at all likely; 4=somewhat likely; 7=extremely likely).
HCP: healthcare provider.

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Lonvo-z the Clear Preference Leader Among Approved and Clinical-Stage Products

% OF PATIENTS RANKING AN HAE PRODUCT / CANDIDATE AS THEIR FIRST CHOICE



*"The first thing that stands out to me (about lonvo-z) is the **efficacy**, followed by it being a **one-time dose**. Those are the most important things for me."*

Product options tested: Clinical-stage candidates lonvo-z, deucrictibant, navenibart and onvuzosiran; and 'currently approved LTPs'

Source: Intellia Commissioned Market Research, July 2026 (N=107). Pipeline products tested as blinded TPPs, based on latest publicly available data at time of study. HAE: hereditary angioedema; LTP: long-term prophylaxis.

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Lonvo-z BLA Under Review



REGULATORY REVIEW

Priority review granted

PDUFA GOAL DATE

MARCH 10, 2027

SEPTEMBER 3, 2026 FDA COMMUNICATION:

“We are not currently planning to hold an advisory committee to discuss this application.”

BLA: Biologics License Application; FDA: U.S. Food and Drug Administration; PDUFA: Prescription Drug User Fee Act.

Nexiguran Ziclumeran (nex-z) for ATTR Cardiomyopathy (CM) and ATTR Polyneuropathy (PN)

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Transthyretin Amyloidosis (ATTR): Large and Growing Market with Significant Unmet Need

Severe, fatal, progressive disease with shortened life expectancy

- CM patients have debilitating shortness of breath, arrythmias, reduced mobility and quality of life, as well as a high rate of hospitalization
- Wild-type disease, the most common form, occurs with aging and manifests as heart failure; inherited TTR mutations lead to rapidly progressive heart failure and/or polyneuropathy
- 250,000 to 500,000 ATTR patients worldwide[1-4]; increasing rate of diagnosis due to an aging population and improved disease awareness
- PN presents as motor and sensory dysfunction, muscle wasting, weight loss, as well as autonomic neuropathy with severe GI symptoms

Despite available treatments, significant unmet need persists

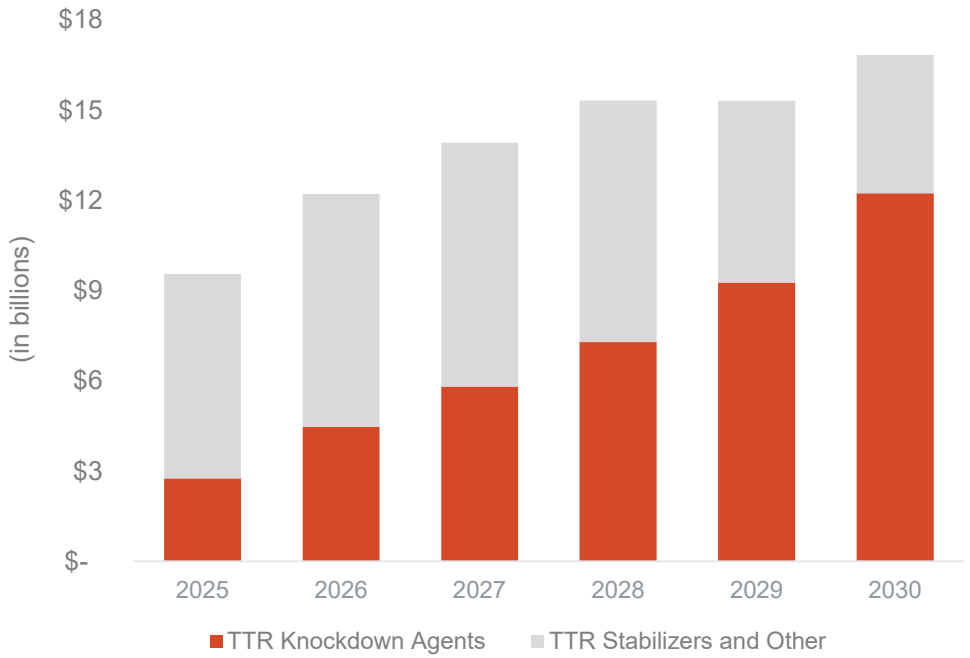
- Inconsistent and slow TTR lowering response observed with silencers[5]
- In Phase 3 trials of silencer or stabilizer therapies for CM, the annual rate of CV events or death is high at ~15% of enrolled patients in the first year[5,6]
- Even on existing therapies, CM patients have a marked decline in quality of life and functional capacity as measured by 6MWT[5,6]
- Treatment adherence due to frequent administration/polypharmacy remains an issue



1. Hawkins et al, Annals of Medicine, 2015. 2. Maurer et al, Circulation: Heart Failure, 2019. 3. Nativi-Nicolau et al, ESC Heart Failure, 2021. 4. Gillmore et al, American Heart Association Scientific Sessions, 2022. 5. Fontana et al, NEJM, 2024. 6. Gillmore et al, NEJM, 2024. CM: cardiomyopathy; CV: cardiovascular; GI: gastrointestinal; PN: polyneuropathy; TTR: transthyretin; 6MWT: 6-Minute Walk Test.

Seeking to Meet Patient and Provider Needs in a Large and Growing ATTR Market

Global ATTR market projected to reach **~$16.8B dollars by 2030**[1]



Patients want a **highly effective** therapy **and freedom** from chronic treatment[2]

*"It would be incredible to have a **one-time therapy**. This would get rid of the mental energy and anxiety I get from going to infusion centers."*

U.S. ATTRv-PN Patient

*"My number one wish would be a **cure**."*

U.S. ATTR-CM Patient

*"This treatment could help me get my life back. I would feel more comfortable going back to work knowing there is a **permanent treatment**."*

UK ATTR-CM Patient

If approved, nex-z would enter a large and growing market with a strong potential value proposition

1. Consensus analyst forecasts per FactSet (Dec. 2025). 2. Intellia commissioned ATTR patient and caregiver interviews (n=46). 3. Intellia commissioned physician quantitative survey (n=232) based on nex-z target product profile. ATTR-CM: ATTR amyloidosis cardiomyopathy; ATTRv-PN: hereditary ATTR amyloidosis polyneuropathy; B: billion; TTR: transthyretin.

REGENERON Intellia THERAPEUTICS®

Nex-z: Potential to Transform the ATTR Amyloidosis Treatment Paradigm

DISRUPTIVE
TREATMENT APPROACH

One-time treatment that stands apart from chronic stabilizers and silencers; aiming to **redefine ATTR treatment** and negate the need for ongoing dosing.

LARGE AND GROWING
PATIENT POPULATION

Up to 500,000 ATTR-CM patients worldwide with **diagnosis rapidly increasing** and additional opportunity to address unmet needs in ATTR-PN.

DISEASE-REVERSING
POTENTIAL

Deep and durable TTR reduction observed for 3 years clinically; **disease stability or improvement** observed in most Phase 1 PN and CM patients.

RAPIDLY ADVANCING
PHASE 3 CLINICAL TRIALS

Significant progress advancing enrollment in MAGNITUDE trial in CM; **enrollment in MAGNITUDE-2 trial in PN completed in 3Q26**.

ATTR amyloidosis: transthyretin amyloidosis; CM: cardiomyopathy; HCP: healthcare provider; PN: polyneuropathy.

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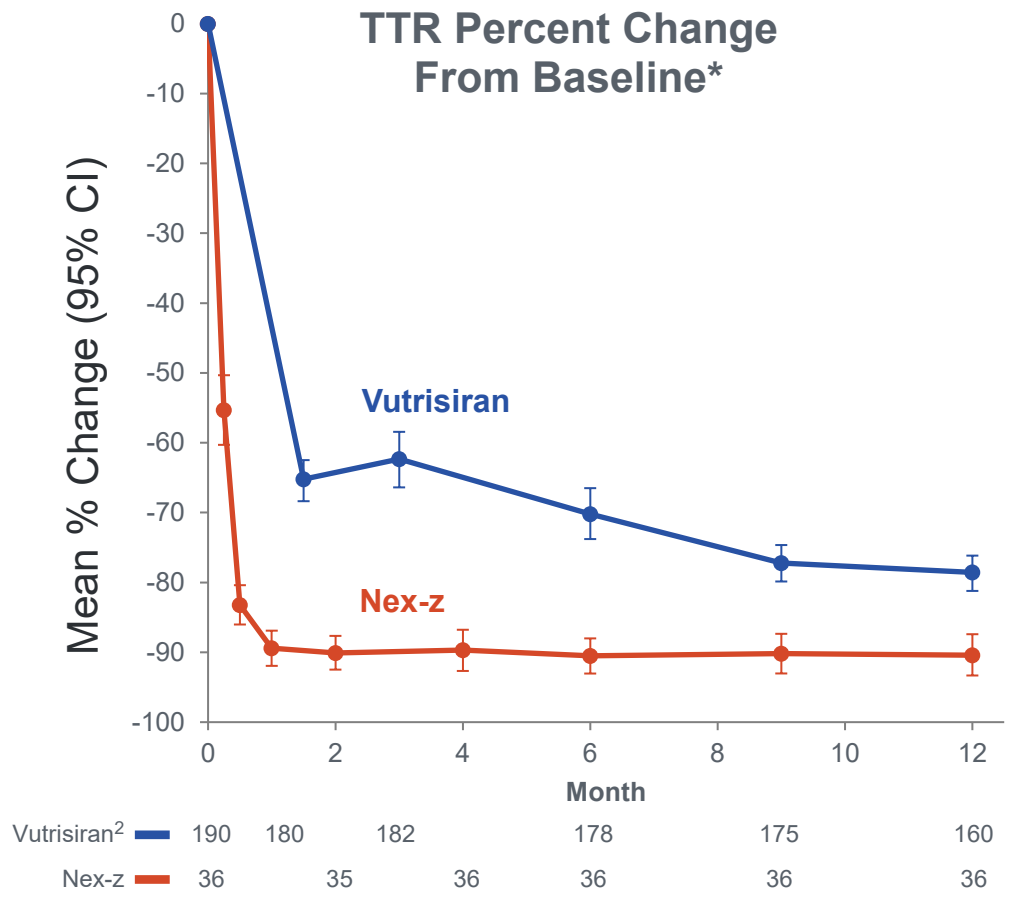
Nex-z has the Potential to Transform the Standard of Care for ATTR Amyloidosis

- First and only investigational therapy that **targets the *TTR* gene**, to reduce production of TTR protein at its source
- Potential to provide patients with:
  - Consistently rapid, deep and durable TTR reduction
  - Stability or improvement in disease measures
  - Improved quality of life
  - Reduced CV events and mortality
- Nex-z is being developed as a **one-time IV infusion** administered in an **outpatient setting**



Based on interim nex-z Phase 1 data as of data cutoff August 21, 2024. Studies are ongoing to assess this investigational product. ATTR amyloidosis: transthyretin amyloidosis; CV: cardiovascular; IV: intravenous.

Nex-z Led to Consistent Rapid, Deep and Durable Reductions in Serum TTR: Cross-Trial Comparison to Vutrisiran TTR Profile from HELIOS-B



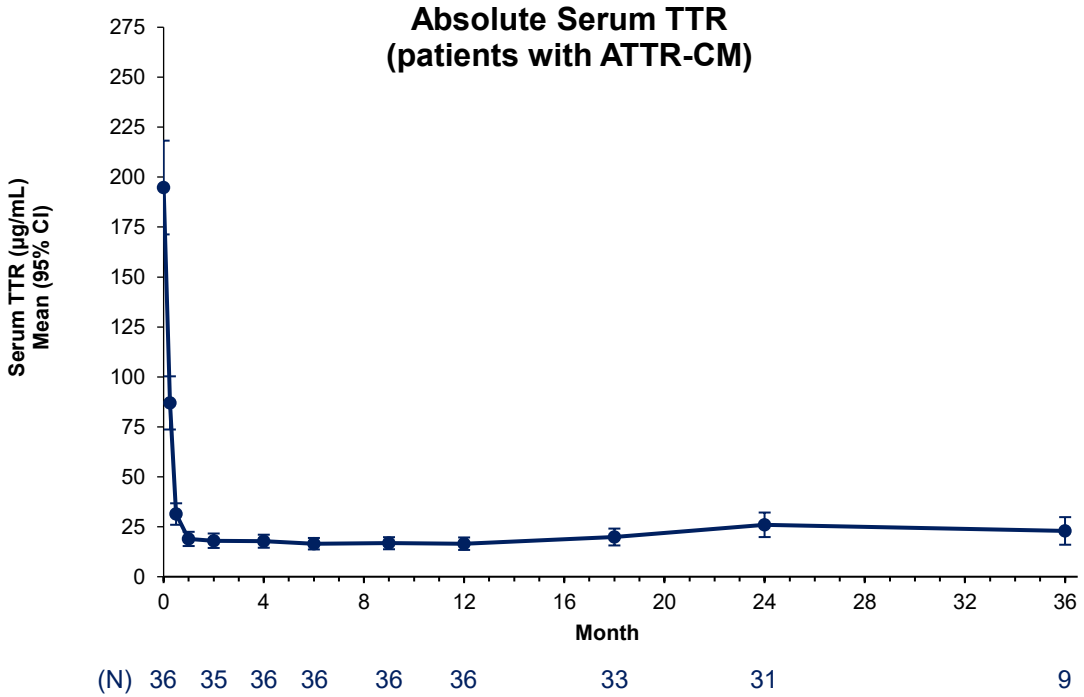
Research has shown a correlation between deeper reductions in TTR and increased clinical benefit[1-5]

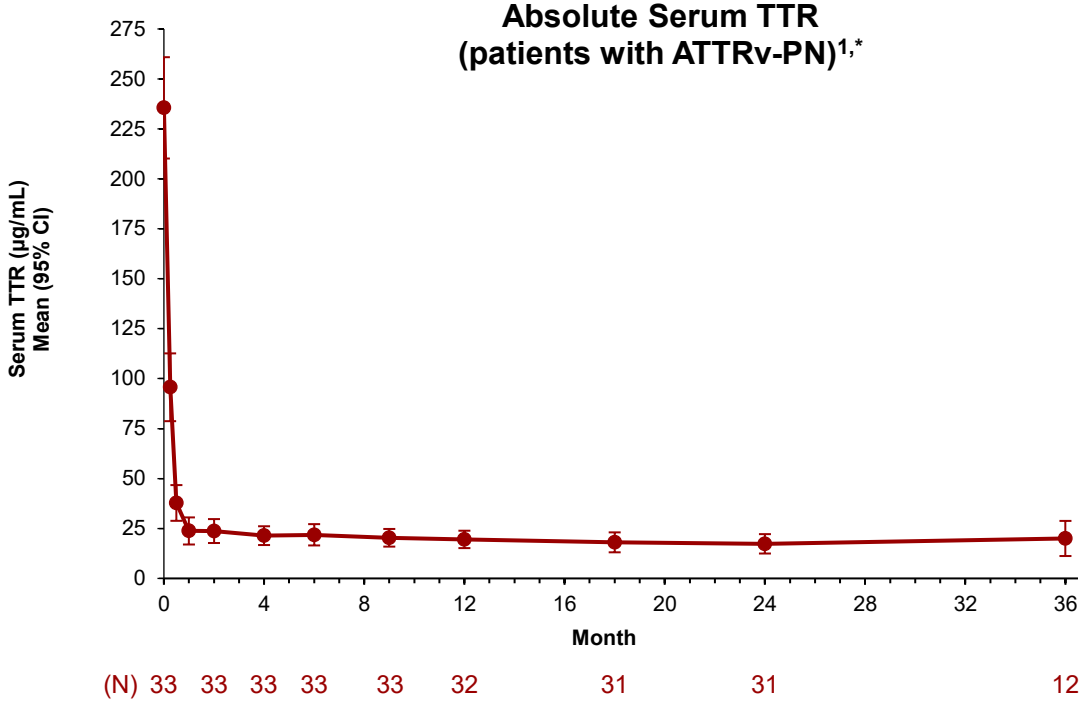
*This graphic includes data from distinct clinical trials with their own enrollment criteria and methodologies. Cross-trial comparisons have inherent limitations and should be interpreted with caution. Vutrisiran data digitized from HELIOS-B: Fontana et al, NEJM, 2024. Nex-z data from: Gillmore et al. NEJM, 2024. 1. Gillmore JD, et al. Lancet, 2001. 2. Lachmann HJ, et al. Br J Haematol, 2003. 3. Palladini G, et al. J Clin Oncol., 2012. 4. Lachmann HJ, et al. NEJM, 2007. CI: confidence interval; TTR: transthyretin.

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Phase 1 Clinical Data: One-time Nex-z Dose Led to Consistent, Rapid, Deep and Durable Serum TTR Reduction

American Heart Association. Scientific Sessions
November 7-10, 2025 | Scientific Sessions
November 8-10, 2025 | Exhibits
Ernest N. Morial Convention Center | New Orleans, LA





From *The New England Journal of Medicine*, Gillmore JD, et al, Nexiguran ziclumeran gene editing in hereditary ATTR with polyneuropathy, Volume 393, Page no. 1375-1386. Copyright © 2025 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Across patients with ATTR-CM and ATTRv-PN, durable reductions in serum TTR have been observed for up to 36 months (n=21)

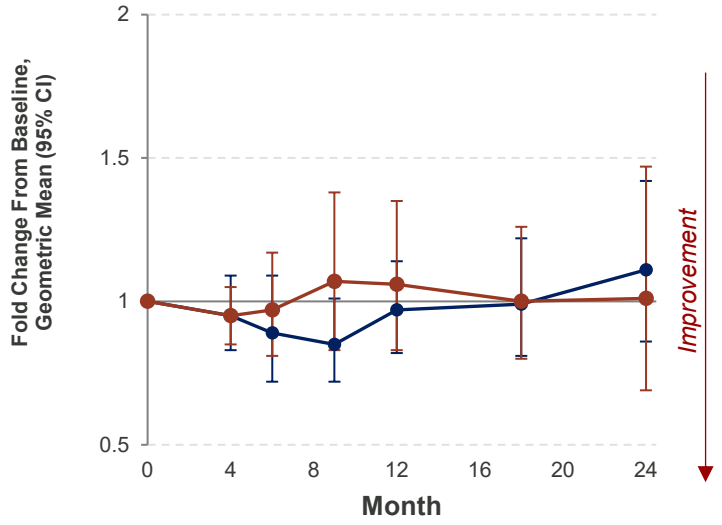
Data cutoff date: August 23, 2025. Data at Month 36 collected from patients who entered the long-term follow-up safety monitoring study (data-cutoff date: August 21, 2025). Changes in N from total population (N=36) reflect patient death (n=2), withdrawal (n=1), or missing assessment. * Results shown for patients with ATTRv-PN who received nex-z at a dose > 0.1 mg/kg. 1. Gillmore D, et al. NEJM, 2025. ATTR-CM: ATTR amyloidosis with cardiomyopathy; ATTRv-PN: hereditary transthyretin amyloidosis with polyneuropathy; CI: confidence interval; TTR: transthyretin.

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Phase 1 ATTR-CM Clinical Data: Improvement/Stabilization of Disease Progression Maintained Regardless of NYHA Class

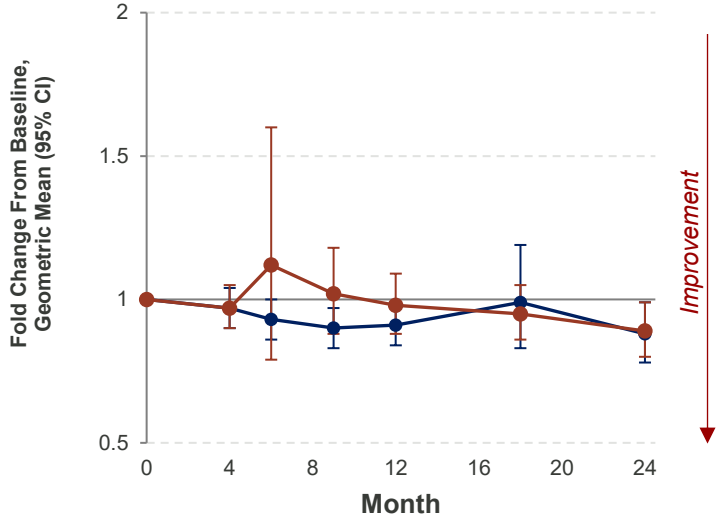
American Heart Association. Scientific Sessions
November 7-10, 2025 | Scientific Sessions
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Ernest N. Morial Convention Center | New Orleans, LA

NT-proBNP



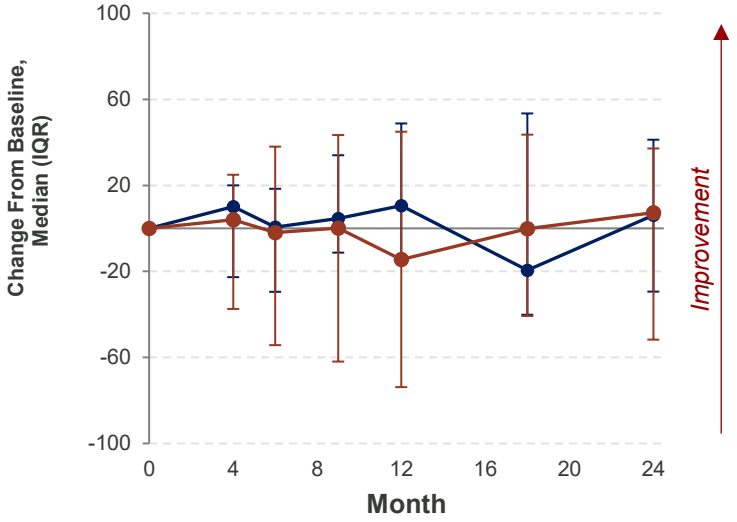
(N)	18	17	18	18	18	16	17
(N)	18	17	18	18	18	16	14

hs-Troponin T



(N)	18	17	18	18	18	16	17
(N)	18	17	18	18	18	16	14

6MWT Distance (meters)



(N)	18	17	18	18	18	17	15
(N)	18	16	16	14	17	12	12

NYHA class I/II — NYHA class III

Data cutoff date: August 23, 2025. Changes in N from total population (N=36) reflect patient death (n=2), withdrawal (n=1), or missing assessment. ATTR-CM: ATTR amyloidosis cardiomyopathy; CI: confidence interval; hs: high sensitivity; IQR: interquartile range; NT-proBNP: N-terminal pro-B-type natriuretic peptide; NYHA: New York Heart Association. 6MWT: 6-Minute Walk Test.

REGENERON Intellia THERAPEUTICS®

Phase 1 ATTR-CM Safety Summary

American Heart Association. Scientific Sessions
November 7-10, 2025 | Scientific Sessions
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Event	n (%)
At least one AE	36 (100)
AEs occurring in ≥15% of patients	
Cardiac failure	13 (36)
COVID-19	8 (22)
Upper respiratory tract infection	7 (19)
Atrial fibrillation	6 (17)
Urinary tract infection	6 (17)
Treatment-related AEs in ≥5% of patients	
Infusion-related reaction	5 (14)
Aspartate aminotransferase increased	2 (6)
Any AE leading to treatment discontinuation	0
Any SAE*	15 (42)
SAEs occurring in ≥5% of patients	
Cardiac failure	8 (22)
Acute myocardial infarction	2 (6)
Cardiac failure congestive	2 (6)
Atrial flutter	2 (6)
Urinary tract infection	2 (6)
Pneumonia	2 (6)
Any event leading to death**	4 (11)

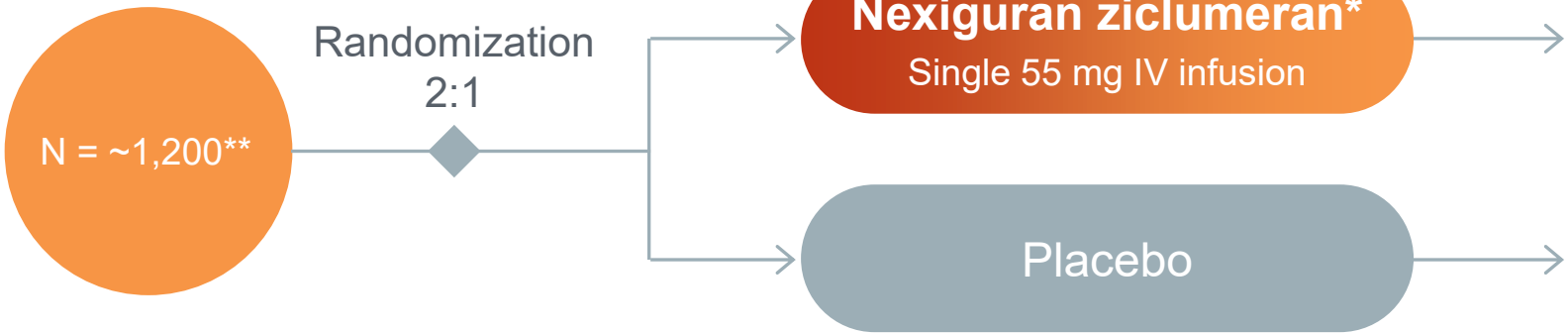
In this Phase 1 Trial

- Nex-z was generally well tolerated with IRRs being the most frequent related AE
- In the first 8 weeks post-dose, all liver enzyme elevations were transient, generally mild and no elevation was above Grade 2
- Two patients had AST elevations assessed by investigators as related to nex-z
  - One case occurred on Day 1 and the other case occurred on Day 22 post-dose
  - These elevations peaked at Grade 2 and resolved within approximately 10 days without medical intervention

Data cutoff date: August 23, 2025. *In addition, 1 patient in the long-term follow-up had unrelated serious adverse events. **One death was due to ischemic heart disease on Day 506, one due to decompensated heart failure on Day 675, one due to decompensated congestive heart failure on Day 790, and one due to heart failure, cardiac amyloidosis, and hypertension on Day 1204; all were unrelated to treatment. At each level of summarization (any event and preferred term), subjects reporting more than one adverse event are counted only once. AE: adverse event; AST: aspartate aminotransferase; ATTR-CM: ATTR amyloidosis cardiomyopathy; IRR: infusion-related reaction; SAE: serious AE.

MAGNITUDE
CLINICAL TRIAL

A Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate Nexiguran Ziclumeran (nex-z)* in Patients with ATTR Amyloidosis with Cardiomyopathy (ATTR-CM)



Primary Endpoint

- Composite endpoint of CV-related mortality and CV-related events

Key Secondary Endpoints

- Serum TTR
- KCCQ-OS score

Key Eligibility Criteria:

- Adult patients with diagnosis of either hereditary or wild-type ATTR-CM
- NYHA Class I – III
- NT-proBNP baseline ≥ 600 pg/mL

Stratification:

- NAC stage
- TTR genotype: wild-type vs. mutant
- Concomitant tafamidis use vs. no tafamidis

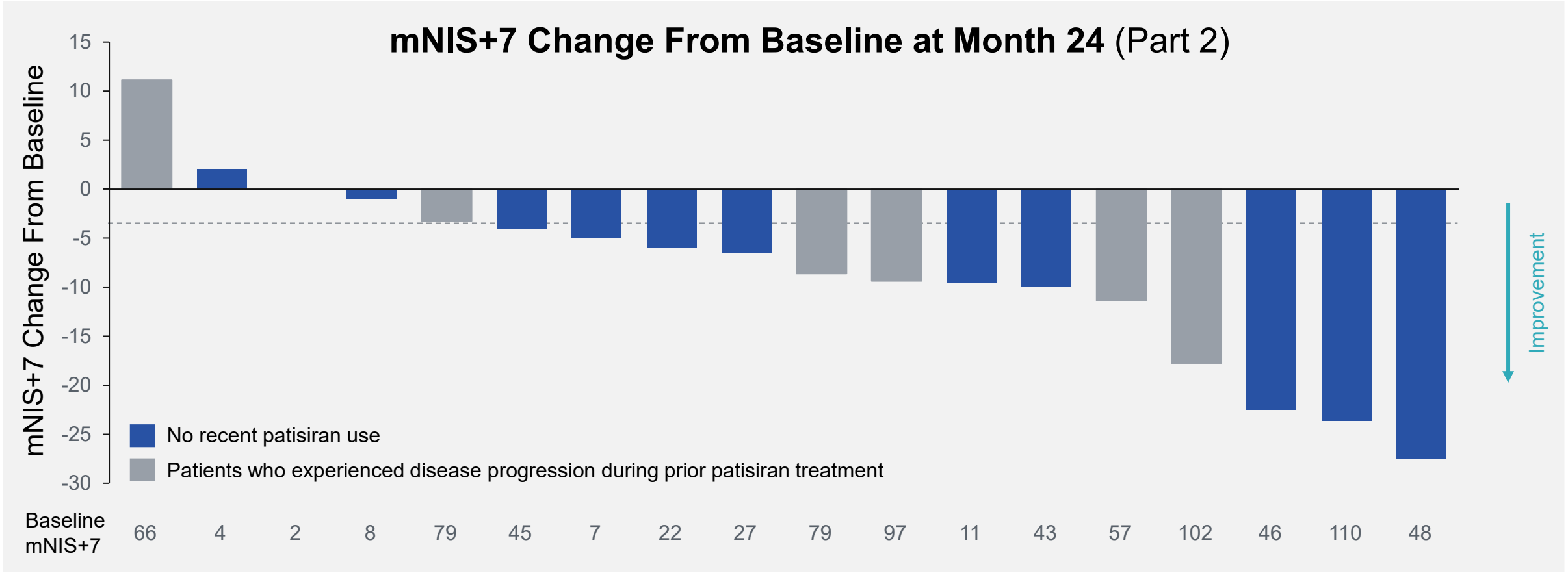
Trial Duration:

- Dependent on occurrence of pre-specified number of CV events and a minimum of 18 months follow-up
- Majority of patients are expected to have ≥ 30 months of follow-up for the primary analysis

Clinicaltrials.gov ID: NCT06128629. *Formerly referred to as NTLA-2001. **Subject to health authority review. CV: Cardiovascular; TTR: Transthyretin; KCCQ-OS: Kansas City Cardiomyopathy Questionnaire-Overall Summary; NHYA: New York Heart Association; NT-proBNP: N-terminal-pro-B-type natriuretic peptide; NAC: National Amyloidosis Centre.

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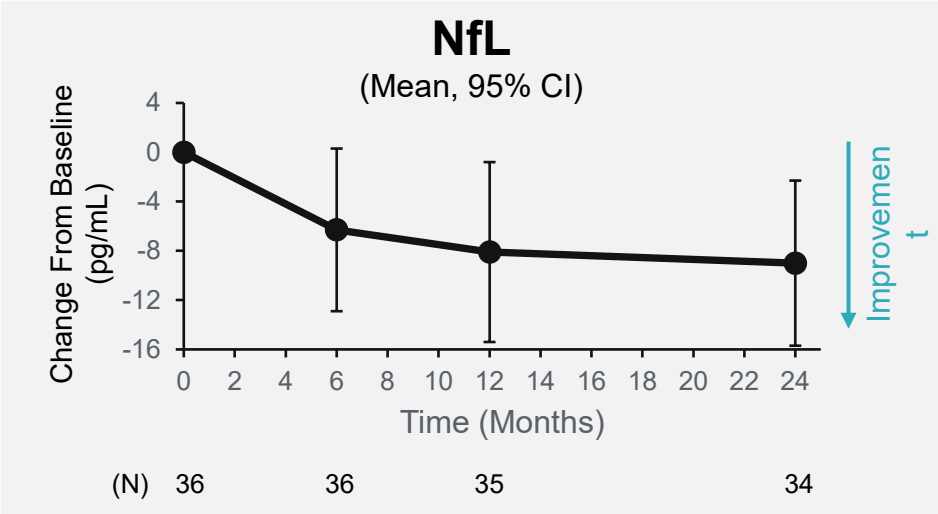
At Month 24, Majority of Patients With ATTRv-PN Experienced Improvements in mNIS+7

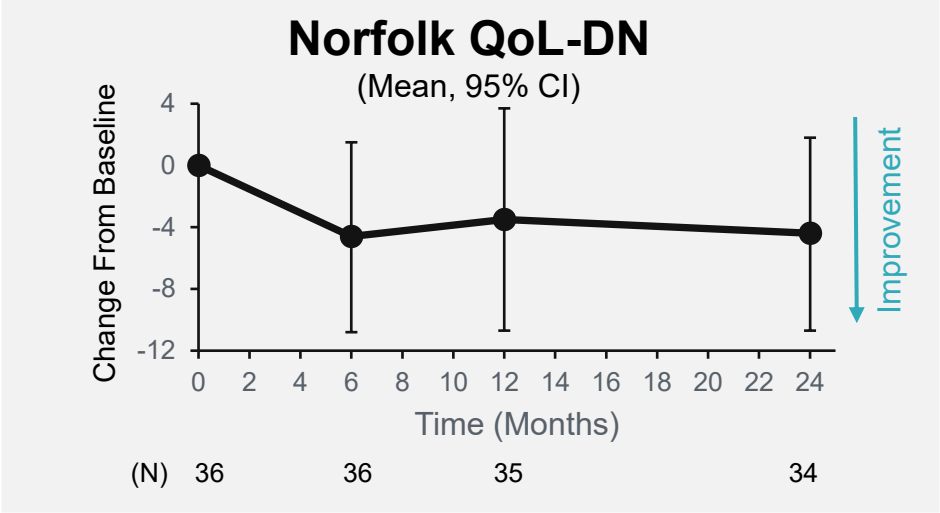


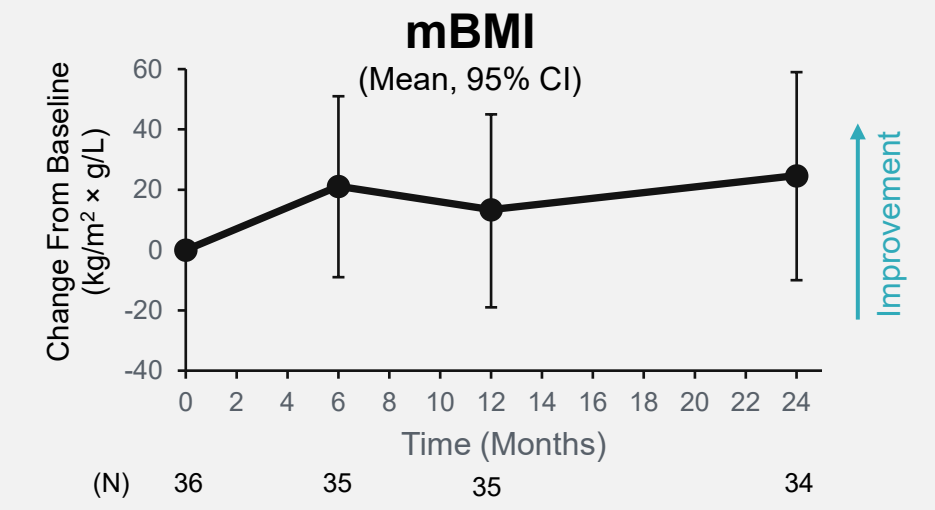
- The mean change in mNIS+7 at Month 24 was -8.5 points
- 13/18 (72%) patients had improvements in mNIS+7 which exceeded the clinically meaningful threshold of a ≥4-point reduction[1]

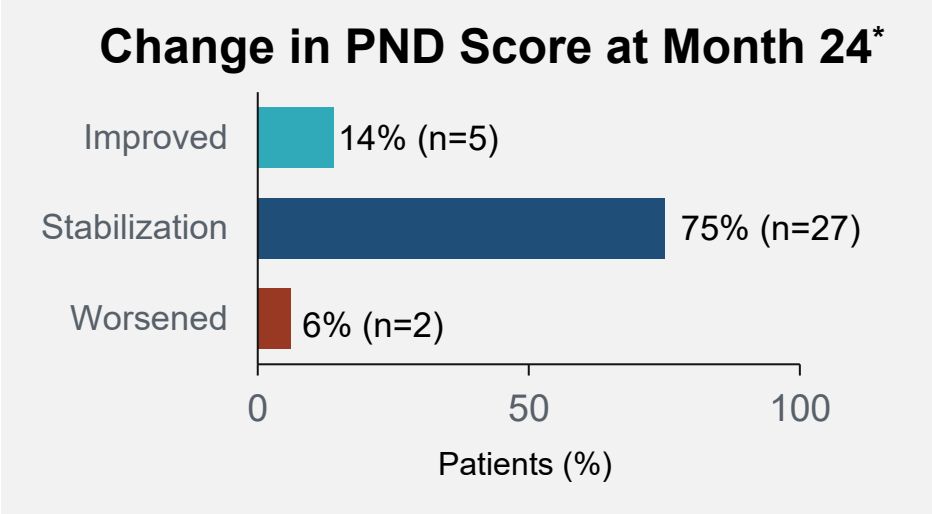
Data cutoff date: April 11, 2025. Gillmore JD, et al. NEJM, 2025. Copyright © 2025 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society. Dotted line indicates cutoff for clinically meaningful improvement (Folkvaljon F, et al. Muscle Nerve, 2025). 1. mNIS+7 ranges from 0 to 304, with higher values indicating increased impairment. ATTRv-PN: hereditary ATTR amyloidosis polyneuropathy; mNIS+7: modified neuropathy impairment score +7.

Multiple ATTRv-PN Disease-Related Clinical Measures Show Stability or Improvement Through Month 24









Data cutoff date: April 11, 2025. Gillmore JD, et al. NEJM, 2025. Copyright © 2025 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society. Norfolk QoL-DN total score ranges from -4 to 136, with lower scores indicating better QoL. * Improvement, No Change, or Worsened in PND score is relative to the measurement at baseline. PND score were missing for 2 patients at Month 24. In the patient who died and the patient who discontinued, PND score remained unchanged from baseline at the last available assessment, Month 6 and Month 12, respectively. ATTRv-PN: hereditary ATTR amyloidosis polyneuropathy; mBMI: modified body mass index; NfL: neurofilament light chain; Norfolk QoL-DN: Norfolk Quality of Life-Diabetic Neuropathy questionnaire; PND: Polyneuropathy Disability; QoL: quality of life.

Safety Summary in Patients with ATTRv-PN Treated with Nex-z

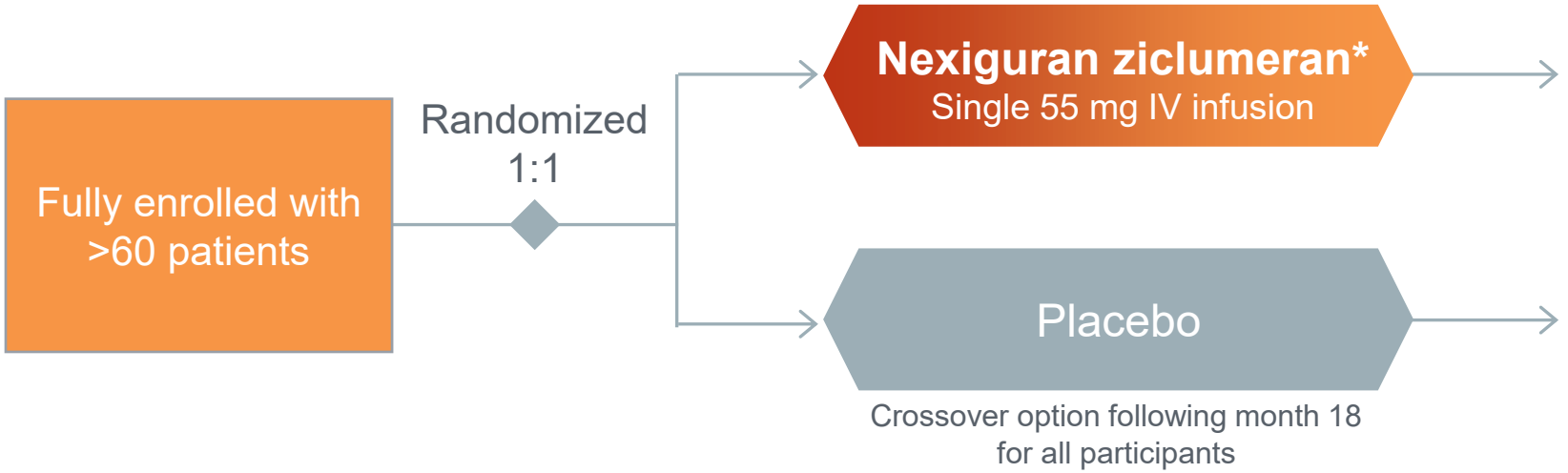
Safety Events	All Patients (N=36) n (%)
At least 1 AE	36 (100)
AEs occurring in ≥15% of patients	
IRR	21 (58)
Headache	10 (28)
Diarrhea	8 (22)
Thyroxine decreased	8 (22)*
AST increased	6 (17)**
Any serious AE	11 (31)
Treatment-related SAEs	3 (8)†
Death	1 (3)‡

- All patients received the intended dose of nex-z
- All IRRs were Grade ≤2 and resolved
- Three patients had ALT and/or AST elevations >5× ULN
  - No symptoms, changes in hepatic synthetic function, prolonged prothrombin time, or clinical sequelae; Hy's Law criteria were not met
  - Onset occurred 24 to 35 days following infusion and all returned to normal levels without intervention within 31 to 58 days
  - Two patients received an 80 mg dose and one patient received a 55 mg dose (selected as the Phase 3 dose)
- The safety profile in patients with prior disease progression on patisiran was comparable to the overall study population

Data cutoff date: April 11, 2025. Gillmore JD, et al. NEJM, 2025. Copyright © 2025 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society. *Not accompanied by thyroid-stimulating hormone elevation or symptoms of hypothyroidism. No patient had clinical hypothyroidism or TSH elevation. **3 patients had Grade ≥3 liver enzyme elevations. †One patient had grade 3 vomiting lasting 12 days, another had grade 2 ileus (Days 2-4), and the third patient had esophageal adenocarcinoma (Day 513) and prostate cancer (Day 610). This third patient had multiple risk factors for esophageal adenocarcinoma, including older age of 73 years, occupational chemical exposure including asbestos, a long history (>15 years) of smoking, heavy alcohol use, gastroesophageal reflux and recently diagnosed Barrett's esophagus. ‡One patient died from sudden cardiac death associated with cardiac amyloidosis at Month 9, not considered treatment-related. AE: adverse event; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ATTRv-PN: hereditary ATTR amyloidosis polyneuropathy; IRR: infusion-related reaction; ULN: upper limit of normal.

MAGNITUDE-2 CLINICAL TRIAL

A Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate Nexiguran Ziclumeran (nex-z)* in Patients with Hereditary ATTR Amyloidosis with Polyneuropathy (ATTRv-PN)



Primary Endpoints

- Change from baseline in mNIS+7 at month 18 and serum TTR at day 29

Key Secondary Endpoints

- Change from baseline in Norfolk QOL-DN, mBMI and serum TTR and absolute serum TTR at month 18

Key Eligibility Criteria:

- Adult patients with diagnosis of ATTRv-PN
- NIS 10 – 130
- PND score of ≤ 3B
- Naïve to silencers; washout of stabilizers

Stratification:

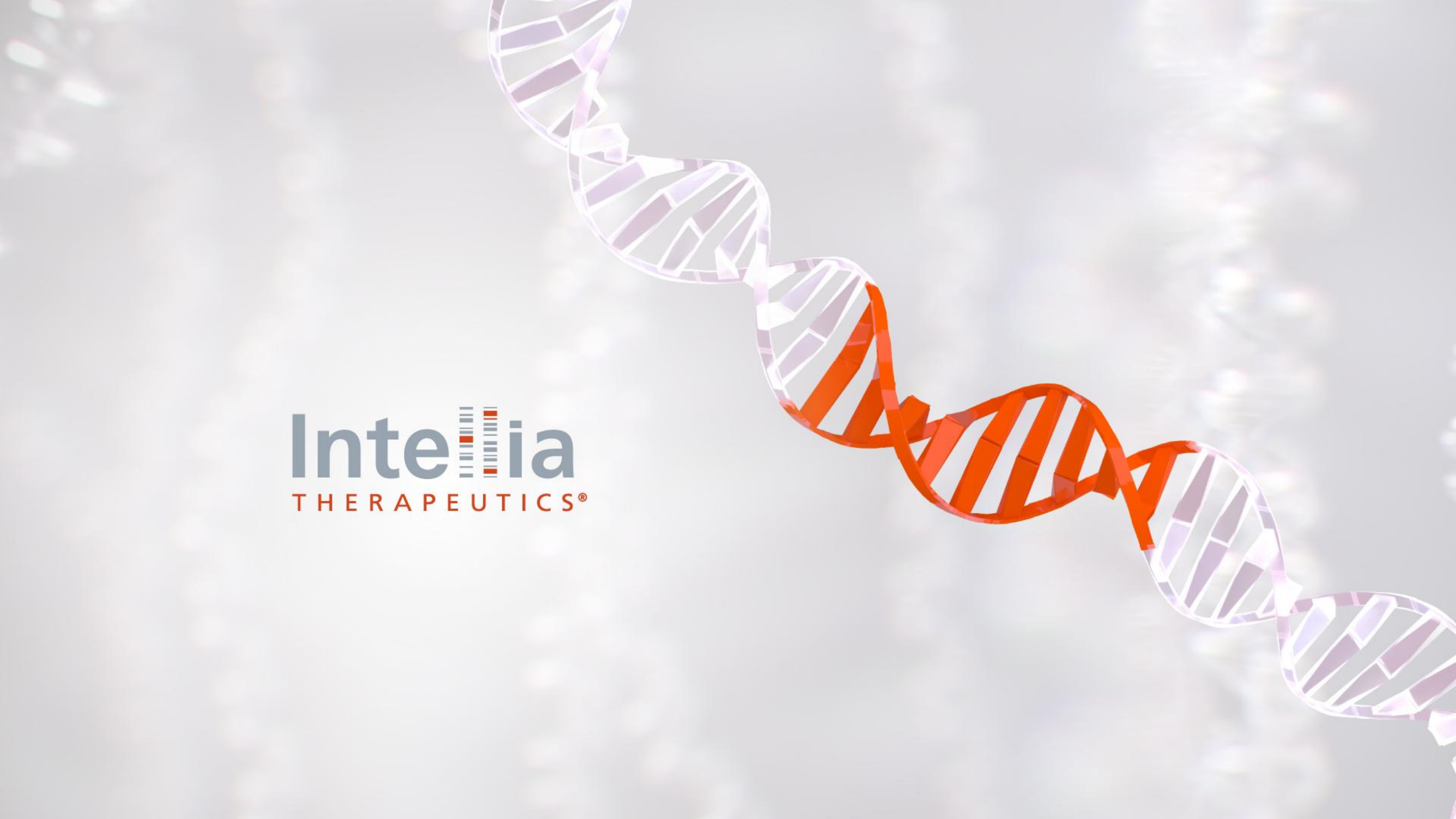
- NIS <50 vs. ≥ 50
- *TTR* genotype: early onset V30M vs others

Trial Duration:

- All patients must complete the month 18 visit

Clinicaltrials.gov ID: NCT06672237. *Formerly referred to as NTLA-2001. mNIS+7: Modified Neuropathy Impairment Score +7; TTR: Transthyretin; NIS: Neuropathy Impairment Score; PND: Polyneuropathy Disability; Norfolk QOL-DN: Quality of Life-Diabetic Neuropathy; mBMI: Modified Body Mass Index.

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