



Alnylam Announces Positive Initial Phase 1b Data for Brezosiran (ALN-HTT02) Demonstrating Deep and Durable Huntingtin Lowering in Huntington's Disease

Oct 23, 2026

- Initial Phase 1b results show mean reduction of cerebrospinal fluid mutant huntingtin of 60 to 64% at month 3 with individual reduction of up to 83% and encouraging safety and tolerability with potential for twice yearly dosing -
- Unique targeting approach reduces both mutant huntingtin and shorter mutant HTT1a-
- Placebo-controlled pivotal study planned for 2027, pending regulatory alignment -
- Alnylam to discuss Huntington's disease program at October 26 RNAi Roundtable -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- **Alnylam Pharmaceuticals, Inc.** (Nasdaq: ALNY), the leading RNAi therapeutics company, today reported positive initial Phase 1b clinical trial results for ALN-HTT02, an investigational RNAi therapeutic in development for the treatment of Huntington's disease, which will be developed under the International Nonproprietary Name (INN) brezosiran (bre-ZOH-sir-an). The data were presented in oral and poster presentations at the European Huntington's Disease Network (EHDN) Clinical Research Congress 2026 in Krakow,

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In the ongoing Phase 1b study, participants on single ascending intrathecal doses of brezosiran experienced robust, dose-dependent reductions of mutant huntingtin protein (mHTT) in cerebrospinal fluid (CSF), with target engagement demonstrated using two independent assays. Across the first five cohorts, dose-dependent reductions of CSF mHTT were observed, with a mean reduction from baseline of 60-64% at month 3 in the highest dose group evaluated to date, with a maximum individual reduction of 83%. The observed durability of mHTT-lowering shows the potential for a twice-yearly dosing paradigm in downstream development. The initial data include individuals followed for up to 12 months, during which an encouraging safety and tolerability profile has been observed with no dose-dependent increases in CSF inflammatory markers, CSF neurofilament light chain (NfL) or brain ventricular volume.

“The evidence suggesting that brezosiran has the potential to achieve robust and durable HTT-lowering, while maintaining an encouraging safety profile, is a very promising advance for this program at a time when there are still no approved disease-modifying therapies for Huntington disease,” said Dr. Blair R. Leavitt, MDCM, FRCPC, neurologist and Director of Research at the Centre for Huntington Disease at the University of British Columbia Hospital and a principal investigator on the Phase 1b study. “Brezosiran is designed to lower all forms of HTT, including full-length mutant HTT and the shorter mutant HTT1a, which a growing body of evidence suggests may play a key role in the progression of Huntington disease.”

All eligible Phase 1b study participants have the option to transition into a Ph1b open-label extension (OLE) study, receiving brezosiran once every six months for up to 36 months to evaluate long-term safety, sustained target engagement, and exploratory measures of disease progression. Alnylam plans to initiate a placebo-controlled pivotal study in 2027, pending regulatory alignment, to evaluate the ability of brezosiran to slow disease progression in adults with Huntington’s disease.

“The deep and durable mutant huntingtin lowering observed after a single dose, together with the encouraging safety profile seen to date, give us confidence to advance brezosiran into a pivotal study,” said Pushkal Garg, M.D., Chief Research and Development Officer at Alnylam. “We plan to evaluate our differentiated huntingtin-lowering approach in a rigorous placebo-controlled study to determine whether it can alter the course of Huntington’s disease. We are deeply grateful to the people living with Huntington’s disease, their families and caregivers, advocacy organizations,

investigators and clinical trial staff whose partnership makes this work possible.”

Brezosiran and the Phase 1b results will be featured as part of Alnylam’s 10th “RNAi Roundtable” series on October 26, 2026, at 10:00 a.m. ET. To register for the webcast or access replay details, please visit the Events and Presentations section of the Alnylam website at investors.alnylam.com.

To view Alnylam’s EHDN Clinical Research Congress 2026 presentations, please visit [Capella](#).

About the Phase 1b Study of Brezosiran (ALN-HTT02)

The Phase 1b trial is a randomized, double-blind, placebo-controlled, single ascending dose study evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics of brezosiran (ALN-HTT02). The ongoing study includes adult patients aged 25 to 70 years with genetically confirmed Huntington’s disease in HD-ISS Stage 2 or early Stage 3. Reported data include a total of 48 enrolled participants across five single-dose cohorts with doses increasing by no more than 3x when escalating to the next cohort (with an additional Dose 6 cohort (N=12) currently enrolling and yet to be evaluated). The Phase 1b single ascending dose (SAD) study is focused on assessing safety and tolerability as well as target engagement (HTT-lowering). The Phase 1b study is ongoing in Canada, Germany, and the United Kingdom, with patients receiving brezosiran every 6 months in the open-label extension (OLE).

About Brezosiran (ALN-HTT02)

Brezosiran (ALN-HTT02) is an investigational, intrathecally administered RNAi therapeutic in development for the treatment of Huntington’s disease (HD), which utilizes Alnylam’s proprietary C16 conjugate platform for delivery to the central nervous system. Brezosiran targets exon 1 of the huntingtin (HTT) mRNA transcript — a differentiated targeting strategy designed to reduce the production of all forms of the huntingtin protein, including full-length mutant HTT and the shorter mutant HTT1a, both of which may be important contributors to disease progression. This program is being developed by Alnylam in collaboration with Regeneron Pharmaceuticals. The safety and efficacy of brezosiran have not been evaluated or established by the U.S. Food and Drug Administration or any other health authority.

About Huntington’s Disease

Huntington’s disease (HD) is an autosomal dominant, progressively fatal neurodegenerative disorder caused by an expanded CAG repeat in exon 1 of the huntingtin (HTT) gene. The accumulation of toxic mutant huntingtin proteins drives disease progression, resulting in widespread neuronal loss, motor dysfunction, cognitive decline, and psychiatric symptoms. HD typically presents in adults aged 30 to 50 and relentlessly progresses over 15 to 20 years. More than one hundred thousand individuals are living with symptomatic disease globally, with many gene-positive individuals and family members and caregivers impacted. There are currently no approved disease-modifying therapies capable of slowing, halting, or reversing HD progression.

About RNAi

RNAi (RNA interference) is a natural cellular process of gene silencing that has become an important and clinically validated platform for drug development. Its discovery was recognized with the award of the 2006 Nobel Prize for Physiology or Medicine. By harnessing RNAi, Alnylam pioneered a new class of medicines known as RNAi therapeutics. Small interfering RNA (siRNA), the molecules that mediate RNAi and comprise Alnylam’s therapeutic platform, function upstream of today’s medicines by potently silencing messenger RNA (mRNA) – the genetic precursors – that encode for disease-causing or disease pathway proteins, thus preventing them from being made. RNAi therapeutics have been used to treat hundreds of thousands of patients worldwide, demonstrating the impact of



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breakthroughs and six approved medicines. Alnylam has medicines available in more than 70 countries and a rapidly expanding and robust pipeline, in addition to consistently being recognized as an exceptional workplace and socially responsible organization. The Company is executing on its Alnylam 2030 strategy to accelerate innovation and scale impact to transform human health. For more information, please visit www.alnylam.com or follow Alnylam on [X](#), [LinkedIn](#), [Facebook](#), [Instagram](#), or [YouTube](#).

Alnylam Forward-Looking Statements

This press release contains forward-looking statements. Forward-looking statements include statements regarding Alnylam's expectations, beliefs, goals, plans or prospects including, without limitation, statements regarding the potential efficacy or safety of brezosiran for the treatment of Huntington's disease, including the potential for brezosiran to slow the progression of Huntington's disease and to alter the course of Huntington's disease; the potential for brezosiran to achieve robust and durable mutant HTT lowering while maintaining an encouraging safety profile with twice yearly dosing; the potential development timelines of brezosiran, including the potential for Alnylam to commence a placebo controlled clinical trial of brezosiran for the treatment of Huntington's disease in 2027; and Alnylam's ability to execute on its *Alnylam 2030* strategy to accelerate innovation and scale impact to transform human health. Actual results and future plans may differ materially from those indicated by these forward-looking statements as a result of various important risks, uncertainties and other factors, including, without limitation, risks and uncertainties relating to: Alnylam's ability to successfully execute on its *Alnylam 2030* strategy; Alnylam's ability to successfully launch, market and sell Alnylam's approved products globally; Alnylam's ability to discover and develop novel drug candidates and delivery approaches and successfully demonstrate the efficacy and safety of its product candidates; the pre-clinical and clinical results for Alnylam's product candidates; actions or advice of regulatory agencies and Alnylam's ability to obtain and maintain regulatory approval for its product candidates, as well as favorable pricing and reimbursement; delays, interruptions or failures in the manufacture and supply of Alnylam's marketed products or its product candidates; obtaining, maintaining and protecting intellectual property; Alnylam's ability to manage its growth and operating expenses through disciplined investment in operations;

Alnylam's ability to maintain strategic business collaborations; Alnylam's dependence on third parties for the development and commercialization of certain products; the outcome of litigation and government investigations; the risk of future litigation and government investigations; and unexpected expenditures; as well as those risks and uncertainties more fully discussed in the "Risk Factors" filed with Alnylam's 2025 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC), as may be updated from time to time in Alnylam's subsequent Quarterly Reports on Form 10-Q, and in other filings that Alnylam makes with the SEC. Alnylam explicitly disclaims any obligation, except to the extent required by law, to

update any forward-looking statements.

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