Alnylam Receives Positive Reimbursement Recommendation From The Canadian Agencies For Drugs And Technology In Health (CADTH) For Use Of AMVUTTRA® For The Treatment Of Hereditary Transthyretin-mediated (hATTR) Amyloidosis In Adults

AMVUTTRA has demonstrated its potential to halt or reverse the deterioration of neuropathy with subcutaneous administration once every three months[1]

MISSISSAUGA, ON., April 4, 2024 - Alnylam Canada ULC is pleased to announce that AMVUTTRA® (vutrisiran injection) has now received a positive recommendation for reimbursement from the Canadian Agency for Drugs and Technologies in Health (CADTH). In October 2023, AMVUTTRA was authorized for sale in Canada for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis).[2]

"This positive recommendation is very important for improving quality of life and outcomes for Canadian patients living with hATTR amyloidosis," said Colleen Coxson, Country General Manager, Alnylam Canada ULC. "AMVUTTRA addresses the underlying cause of the condition, rapidly knocking down[3] toxic TTR* in the body and quickly controlling the disease to avoid irreversible damage. We look forward to continuing to work to expand access and coverage to deliver shared value for provinces and patients."

hATTR amyloidosis is an inherited, progressively debilitating, and often fatal disease caused by mutations in the TTR gene.[4] Mutations in the TTR gene cause abnormal amyloid proteins to accumulate and damage body organs and tissue, such as the peripheral nerves and heart, resulting in peripheral sensory-motor neuropathy, autonomic neuropathy, and/or cardiomyopathy.[3] hATTR amyloidosis represents a major unmet medical need, affecting approximately 50,000 people worldwide. The median survival is 4.7 years following diagnosis, with a reduced survival (3.4 years) for patients with cardiomyopathy.[3]

The positive recommendation for reimbursement was supported by the results of the HELIOS-A Phase 3 study, a global, randomized, open-label, multicentre study to evaluate the efficacy and safety of AMVUTTRA in adult patients with hATTR amyloidosis. Based on the study, AMVUTTRA significantly improved the signs and symptoms of hATTR amyloidosis, with an average of 50 percent of patients experiencing an arrest or reversal of their polyneuropathy symptoms.[5]

Full details on the recommendation are available on the CADTH website.[6]

About AMVUTTRA® (vutrisiran injection)[2]

AMVUTTRA is an RNAi therapy designed to silence a specific messenger RNA (mRNA) by blocking the production of the wild-type and variant transthyretin (TTR) protein before it is produced. AMVUTTRA utilizes Alnylam's GalNAc conjugate delivery platform and Enhanced Stabilization Chemistry (ESC), designed to increase potency and metabolic stability by allowing quarterly subcutaneous administration.

About HELIOS-A Phase 3 Study

HELIOS-A is a global, randomized, open-label, multicentre, Phase 3 study that evaluated the efficacy and safety of AMVUTTRA in a diverse group of hATTR patients with stage 1 or stage 2 polyneuropathy. The results of the HELIOS-A study were published in *Amyloid* in July 2022.

In the HELIOS-A study, the drug met the primary endpoint and all secondary endpoints of the study at both 9 months and 18 months. During the HELIOS-A 18-month treatment period, the most frequently occurring adverse reactions (≥10%) reported in patients treated with AMVUTTRA were pain in extremity (14.8%) and arthralgia (10.7%); none of the adverse reactions resulted in discontinuation of treatment.. Vutrisiran demonstrated an

improvement in the mean change from baseline in the modified neuropathy impairment score + 7 (mNIS+7) at 9 months (the primary endpoint), compared to external placebo data from the landmark APOLLO Phase 3 patisiran study.

*hATTR amyloidosis is caused by deposit of toxic misfolded TTR proteins.

About RNAi
RNAi (RNA interference) is a natural cellular gene silencing process that represents one of the most promising and rapidly advancing frontiers in biology and drug development today. Its discovery has been heralded as "a scientific breakthrough that occurs about once every ten years," and was recognized with the award of the 2006 Nobel Prize in Physiology or Medicine.

About Alnylam Pharmaceuticals
Alnylam (Nasdaq: ALNY) is leading the translation of RNA interference (RNAi) into a new class of innovative medicines with the potential to transform the lives of people affected by rare genetic, cardio-metabolic, hepatic infectious, and central nervous system (CNS)/ocular diseases. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful and clinically validated approach to the potential treatment of a wide range of serious and debilitating diseases. Founded in 2002, Alnylam is pursuing a bold vision to turn scientific possibilities into reality with a robust RNAi therapeutics platform. Alnylam has developed licensed RNAi therapeutics for the treatment of hATTR amyloidosis, acute hepatic porphyria, primary hyperoxaluria type 1 and primary hypercholesterolemia/mixed dyslipidemia. Alnylam has a broad pipeline of investigational drugs, including six product candidates that are in late-stage development. Alnylam is executing its "Alnylam P5x25" strategy to deliver transformative medicines in rare and common diseases that benefit patients worldwide through sustainable innovation and exceptional financial performance, resulting in a leading biotech profile. Alnylam is headquartered in Cambridge, MA. Alnylam Canada is headquartered in Mississauga, Ontario with established operations since June 2018.

###

Media Contacts:
Proof Strategies
Kendra Stephenson
kstephenson@getproof.com mailto:X@getproof.com
289-894-0828

[1] *Amyloid.* 2023 Mar;30(1):1-9. doi: 10.1080/13506129.2022.2091985. Epub 2022 Jul 23 https://www.tandfonline.com/doi/full/10.1080/13506129.2022.2091985 Accessed March 4, 2024
[2] AMVUTTRA Product Monograph. October 17, 2023
[3] Coelho T, Adams D, Silva A, et al. Safety and efficacy of RNAi therapy for transthyretin amyloidosis. N Engl J Med. 2013;369(9):819-829. doi:10.1056/NEJMoa1208760
[4] *The American Journal of Managed Care* https://www.ncbi.nlm.nih.gov/pubmed/28978215/ Accessed March 4, 2024.
[5] *Amyloid.* 2023 Mar;30(1):1-9. doi: 10.1080/13506129.2022.2091985. Epub 2022 Jul 23 https://www.tandfonline.com/doi/full/10.1080/13506129.2022.2091985 Accessed March 4, 2024
[6] https://www.cadth.ca/vutrisiran Accessed March 4, 2023