Alnylam Announces Health Canada Approval of AMVUTTRA® (vutrisiran), the First and Only RNAi Therapeutic for the Treatment of Cardiomyopathy in Adult Patients with ATTR Amyloidosis

MISSISSAUGA, ON, December 16, 2025 - Alnylam Canada ULC is pleased to announce that Health Canada has issued a Notice of Compliance (NOC) authorizing AMVUTTRA® (vutrisiran) for the treatment of cardiomyopathy in adult patients with wild-type or hereditary transthyretin-mediated amyloidosis (wtATTR or hATTR amyloidosis).[1] The approval broadens the indication for AMVUTTRA®, which now becomes the first and only RNAi therapeutic authorized by Health Canada for the treatment of both the cardiomyopathy manifestations of TTR amyloidosis and stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin-mediated amyloidosis.[2]

Cardiomyopathy with wtATTR or hATTR amyloidosis (also referred to as ATTR-CM) is a devastating, progressive and ultimately fatal condition affecting over 300,000 people worldwide.[3,4] In Canada, the disease is under-recognized and under-diagnosed as symptoms tend to be associated with other conditions.[5] There is no cure for ATTR-CM, which is caused by the deposition of misfolded transthyretin (TTR) fibrils (malformed proteins) that build up primarily in your heart and elsewhere in the body. This makes it harder for the heart to pump blood throughout the body, which can cause irreversible damage, and lead to heart failure.[6] Life expectancy for patients with ATTR-CM is currently two to five years after diagnosis, highlighting the importance of early and accurate detection to slow disease progression.[7]

"AMVUTTRA® represents a major advance in the treatment of TTR amyloid cardiomyopathy, and the HELIOS-B trial clearly demonstrated its ability to significantly reduce cardiovascular events, slow functional decline, and improve survival," said Dr. Diego Delgado, Cardiologist in the Division of Cardiology and Cardiac Transplantation at the University Health Network. "Patients experienced fewer hospitalizations, better quality of life, and most importantly, lived longer—making AMVUTTRA® a powerful tool to transform how we manage this condition in practice. As a Canadian principal investigator in the HELIOS-B trial, I'm encouraged that these proven clinical benefits are now accessible to Canadians living with TTR amyloid cardiomyopathy."

The Health Canada approval was based on positive results from the pivotal HELIOS-B Phase 3 study – a randomized, double-blind, placebo-controlled, multicenter, global trial that enrolled adult patients with wtATTR or hATTR amyloidosis with cardiomyopathy. Patients were randomized 1:1 to receive 25 mg of AMVUTTRA® administered subcutaneously once every 3 months, or matching placebo. Randomization was stratified by baseline tafamidis use, ATTR disease type, and by baseline severity of disease and age. At baseline, 40% of patients were receiving treatment with tafamidis. The primary efficacy endpoint was the composite outcome of all-cause mortality and recurrent cardiovascular (CV) events (CV hospitalizations and urgent heart failure visits) during the double-blind treatment period of up to 36 months, evaluated in the overall population and in the monotherapy population (defined as patients not receiving tafamidis at study baseline). In the overall and monotherapy populations, AMVUTTRA® led to significant reductions in the risk of all-cause mortality and recurrent CV events as compared to placebo in the overall and monotherapy populations of 28.2% and 32.8%, respectively. Mortality in the overall and monotherapy populations was significantly reduced by 35.5% and 34.5%, respectively, through 42 months in a pre-specified secondary endpoint analysis which included the double-blind period plus six months of survival data in all patients. Results from the subgroup analysis for the primary composite endpoint favoured AMVUTTRA® across all prespecified subgroups in the overall population and the monotherapy population. In HELIOS-B, the nature, frequency, and severity of adverse events in patients treated with AMVUTTRA® were similar to placebo; one patient developed anti-drug antibodies.[8] Detailed results from the HELIOS-B study were published in *The New England Journal of Medicine*.

"People with transthyretin amyloid cardiomyopathy and other forms of amyloidosis are often misdiagnosed since symptoms can mirror more common heart and other conditions. As a result, the path to diagnosis can be a long, arduous journey. It is critical that a timely and accurate diagnosis is made not only for the individual experiencing symptoms but also for their loved ones," said Anne Marie Carr, Founder & CEO, Hereditary Amyloidosis Canada. "The Health Canada approval of this therapy is a game-changer for those living with this devastating fatal disease; AMVUTTRA offers hope for an improved quality of life and extended survival, which is why we encourage the government to provide access to it as quickly as possible."

AMVUTTRA® is an RNAi therapeutic that specifically targets variant and wild-type TTR messenger RNA.[9] By interfering with TTR production, AMVUTTRA® substantially decreases deposition of misfolded TTR fibrils, which form amyloid deposits and cause irreversible cardiovascular damage and premature death in patients with ATTR-CM.[10]

“This milestone underscores our commitment to pioneering the research and development of RNAi therapeutics, particularly for transthyretin amyloidosis where patients face a difficult prognosis,” said Colleen Coxson, Country General Manager, Alnylam Canada ULC. “AMVUTTRA works differently than other therapies approved in Canada, by silencing TTR production at its source. We are excited to bring this novel therapy to Canada, and our next priority is to work with the provinces and private payers to ensure broad access for patients across the country.”

About AMVUTTRA® (vutrisiran)
AMVUTTRA® (vutrisiran) suppresses variant and wildtype transthyretin (TTR), addressing the underlying cause of transthyretin (ATTR) amyloidosis. Administered via subcutaneous injection once every three months, AMVUTTRA® is approved and marketed in more than 15 countries for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN) in adults. It has been approved in the EU, Japan, the United States (U.S.), Brazil, United Arab Emirates (UAE), United Kingdon (UK) and Switzerland for the treatment of the cardiomyopathy of wild-type or hereditary ATTR amyloidosis in adults.

About the HELIOS-B Study[11]
HELIOS-B is a global, randomized, double-blind, placebo-controlled clinical trial that evaluated the efficacy and safety of AMVUTTRA® in adult patients with wtATTR or hATTR amyloidosis with cardiomyopathy.

In the HELIOS-B study, AMVUTTRA® met all 10 pre-specified primary and secondary endpoints across both the overall and monotherapy populations. These included statistically significant reductions in all-cause mortality and recurrent cardiovascular events, as well as significant improvements in functional capacity (6-minute walk test), health status and quality of life (Kansas City Cardiomyopathy Questionnaire), and heart failure symptoms and severity (NYHA class). The safety profile of AMVUTTRA® in HELIOS-B was consistent across all subgroups studied including age, sex, race, geographic region, type of ATTR amyloidosis (hATTR or wtATTR), baseline tafamidis use, and NYHA class.

About RNAi
RNAi (RNA interference) is a natural cellular process of gene silencing that represents one of the most promising and rapidly advancing frontiers in biology and drug development today.[12] Its discovery has been heralded as “a major scientific breakthrough that happens once every decade or so,” and was awarded the 2006 Nobel Prize for Physiology or Medicine.[13] By harnessing the natural biological process of RNAi occurring in our cells, a new class of medicines known as RNAi therapeutics is now a reality. Small interfering RNA (siRNA), the molecules that mediate RNAi and comprise Alnylam’s RNAi

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.[14] This is a revolutionary approach with the potential to transform the care of patients with genetic and other diseases.

About Alnylam Pharmaceuticals
Alnylam (Nasdaq: ALNY) has led the translation of RNA interference (RNAi) into a whole new class of innovative medicines with the potential to transform the lives of people afflicted with rare and prevalent diseases with unmet need. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach yielding transformative medicines. Since its founding in 2002, Alnylam has led the RNAi Revolution and continues to deliver on a bold vision to turn scientific possibility into reality. Alnylam has a deep pipeline of investigational medicines, including multiple product candidates that are in late-stage development. Alnylam is executing on its "*Alnylam P*^{5}*x25*" strategy to deliver transformative medicines in both rare and common diseases benefiting patients around the world through sustainable innovation and exceptional financial performance, resulting in a leading biotech profile. Alnylam is headquartered in Cambridge, MA. Alnylam Canada ULC is headquartered in Mississauga, Ontario with established operations since June 2018.

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