CENTOGENE and Alnylam Pharmaceuticals Launch a New Clinical Program Aimed at Revolutionizing the Diagnosis of Hereditary Transthyretin-Related Amyloidosis ("ATTRv")

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CAMBRIDGE, Mass. and ROSTOCK, Germany, and BERLIN and MUNICH, Germany, Dec. 08, 2020 (GLOBE NEWSWIRE) -- Centogene N.V. (Nasdaq: CNTG), a commercial-stage company focused on rare diseases that transforms real-world clinical and genetic data into actionable information for patients, physicians and pharmaceutical companies, and Alnylam Pharmaceuticals, Inc. ("**Alnylam**"), the leading RNAi therapeutics company, announced today the launch of a new joint clinical screening program: the genetic screening of the at-risk population for hereditary **T**ransthy**R**etin-related **AM**yloidosis and longitudinal **moni**toring of ***TTR*** positive subjects (the "**TRAMmoni*TTR* Study**").

The new TRAMmoni*TTR* Study is a follow-up to the preceding epidemiological analysis for hereditary **T**ransthy**R**etin-related **AM**yloidosis (the "**TRAM Study**" (NCT03237494)). Since 2017, 5,000 participants from Germany, Austria and Switzerland with polyneuropathy and/or cardiomyopathy of no obvious etiology have been screened for ATTRv as part of the TRAM Study. More than 1% of participants were eventually diagnosed with ATTRv, clinically characterized and regionally mapped.

The follow-up TRAMmoni*TTR* Study will include both symptomatic and asymptomatic *TTR* positive participants, who will be invited to take part in the longitudinal phase to monitor their clinical status. Using CENTOGENE´s metabolomics profiling platform, the Company has discovered and now characterizes novel ATTRv biomarkers. Such molecules are crucial to accelerate ATTRv diagnostics and treatment personalization. The monitoring of these biomarkers in *TTR* positive participants will support the validation process.

Prof. Peter Bauer, Chief Genomic Officer of CENTOGENE, said, "This is the first study where both symptomatic and asymptomatic *TTR* positive participants will be monitored for two years. This will allow us to validate our ATTRv biomarkers and later utilize them for treatment individualization."

Dr. Volha Skrahina, Director of Clinical Studies at CENTOGENE, added, "Within the initial TRAM Study, we were able to deliver truly valuable insights. More than 50 participants suffering from the known and treatable disease received the diagnosis. We will now proceed with the screening in TRAMmoni*TTR* in order to accelerate the diagnosis for those suffering and awaiting answers. This is crucial due to the progressive nature of the disease."

"We are excited about expanding our collaboration with CENTOGENE in its epidemiology and biomarker work through the initiation of a new clinical program (TRAMmoni*TTR*) focused on Hereditary Transthyretin-Related Amyloidosis," said Dr. Bernhard Kaumanns, VP Medical Affairs CEMEA (Canada, Europe, Middle East & Africa) at Alnylam. "This program will help to better understand diagnostic pathways and identify possible biomarkers to accelerate the diagnosis of this devastating disease. Equally important is the patient follow-up that this program provides; long term evidence-based data will be generated to improve the understanding of this disease under conditions of daily clinical practice."

About Hereditary Transthyretin-Related Amyloidosis ("ATTRv")

ATTRv is an autosomal dominant condition caused by a pathogenic variant in the *TTR* gene (Plante-Bordeneuve *et al.* 2011). The *TTR* gene is coding for transthyretin, formerly known as prealbumin. Transthyretin ("**Ttr**") is found primarily in the serum (secreted by the liver) and the cerebrospinal fluid (secreted by the choroid plexus), and functions as a carrier for the hormone thyroxine (T4) and retinol-binding protein (bound to retinol or vitamin A). The destabilization of the Ttr protein and the formation of misfolded Ttr proteins results in the transthyretin amyloidosis diseases. There are more than 150 *TTR* pathogenic variants described; the disease phenotype is *TTR* variant dependent (Ando *et al*. 2013, Rowczenio *et al*. 2014, Rowczenio *et al*. 2015).

On average, the diagnosis is delayed by 4–5 years, especially in non-endemic areas. Also, there is potential for misdiagnosis due to ATTRv´s clinical heterogeneity (Adams *et al*., 2016). The common misdiagnosis of ATTRv with polyneuropathy includes chronic inflammatory demyelinating polyradiculoneuropathy, idiopathic axonal polyneuropathy, lumbar spinal stenosis and, more rarely, diabetic neuropathy and AL amyloidosis (Koike *et al*., 2011; Adams *et al*., 2019).

In order to facilitate an early diagnosis, treatment choice and individualization, ATTRv biomarkers are critical.

About CENTOGENE

CENTOGENE engages in diagnosis and research around rare diseases transforming real-world clinical and genetic data into actionable information for patients, physicians and pharmaceutical companies. Our goal is to bring rationality to treatment decisions and to accelerate the development of new orphan drugs by using our extensive rare disease knowledge, including epidemiological and clinical data, as well as innovative biomarkers. CENTOGENE has developed a global proprietary rare disease platform based on our real-world data repository with over 3.6 billion weighted data points from approximately 570,000 patients representing over 120 different countries as of August 31, 2020.

The Company's platform includes epidemiologic, phenotypic and genetic data that reflects a global population, and also a biobank of these patients' blood samples. CENTOGENE believes this represents the only platform that comprehensively analyzes multi-level data to improve the understanding of rare hereditary diseases, which can aid in the identification of patients and improve our pharmaceutical partners' ability to bring orphan drugs to the market. As of August 31, 2020, the Company collaborated with over 40 pharmaceutical partners covering over 45 different rare diseases.

About Alnylam Pharmaceuticals

Alnylam (Nasdaq: ALNY) is leading 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 genetic, cardio-metabolic, hepatic infectious, and central nervous system/ocular diseases. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of a wide range of severe and debilitating diseases. Founded in 2002, Alnylam is delivering on a bold vision to turn scientific possibility into reality, with a robust RNAi therapeutics platform. Alnylam's commercial RNAi therapeutic products are ONPATTRO ® (patisiran), approved in the U.S., EU, Canada, Japan, Brazil and Switzerland, and GIVLAARI® (givosiran), approved in the U.S., EU, Brazil and Canada, and OXLUMO™ (lumasiran) approved in the U.S. and the EU. Alnylam has a deep pipeline of investigational medicines, including six product candidates that are in late-stage development. Alnylam is headquartered in Cambridge, MA.

Important Notice and Disclaimer

This press release contains statements that constitute "forward looking statements" as that term is defined in the United States Private Securities Litigation Reform Act of 1995, including statements that express the Company's opinions, expectations, beliefs, plans, objectives, assumptions or projections regarding future events or future results, in contrast with statements that reflect historical facts. Examples include discussion of our strategies, financing plans, growth opportunities and market growth. In some cases, you can identify such forward-looking statements by terminology such as "anticipate," "intend," "believe," "estimate," "plan," "seek," "project" or "expect," "may," "will," "would," "could" or "should," the negative of these terms or similar expressions. Forward looking statements are based on management's current beliefs and assumptions and on information currently available to the Company. However, these forward-looking statements are not a guarantee of our performance, and you should not place undue reliance on such statements. Forward-looking statements are subject to many risks, uncertainties and other variable circumstances, such as negative worldwide economic conditions and ongoing instability and volatility in the worldwide financial markets, the effects of the COVID-19 pandemic on our business and results of operations, possible changes in current and proposed legislation, regulations and govern-mental policies, pressures from increasing competition and consolidation in our industry, the expense and uncertainty of regulatory approval, including from the U.S. Food and Drug Administration, our reliance on third parties and collaboration partners, including our ability to manage growth and enter into new client relationships, our dependency on the rare disease industry, our ability to manage international expansion, our reliance on key personnel, our reliance on intellectual property protection, fluctuations of our operating results due to the effect of exchange rates or other factors. Such risks and uncertainties may cause the statements to be inaccurate and readers are cautioned not to place undue reliance on such statements. Many of these risks are outside of the Company's control and could cause its actual results to differ materially from those it thought would occur. The forward-looking statements included in this press release are made only as of the date hereof. The Company does not undertake, and specifically declines, any obligation to update any such statements or to publicly announce the results of any revisions to any such statements to reflect future events or developments, except as required by law.

For further information, please refer to the Risk Factors section in our Annual Report for the year ended December 31, 2019 on Form 20-F filed with the SEC on April 23, 2020, Form 6-K containing our financial results for the three months ended March 31, 2020, filed with the SEC on June 15, 2020 and other current reports and documents filed with the U.S. Securities and Exchange Commission (SEC). You may get these documents by visiting EDGAR on the SEC website at www.sec.gov.

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