**Co-development Programs**

the systemic delivery of RNAi therapeutics. that advancement of ALN-VSP into clinical development is our first systemically delivered RNAi therapeutic. We believe represents both Alnylam's first oncology program as well as and pharmacokinetics of this RNAi therapeutic. ALN-VSP and has begun enrolling patients in a multi-center, open feed tumors.

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**Clinical Programs**

Respiratory Syncytial Virus (RSV)

Respiratory syncytial virus infection, or RSV, is a serious respiratory infectious disease and the leading cause of pediatric hospitalizations in the U.S. (125,000 hospitalizations per year in the U.S.). RSV is also a major infectious disease in the elderly and in other adults with compromised immune systems (175,000 hospitalizations per year in the U.S.).

Alnylam’s lead program, ALN-RSV01, is being developed for the treatment of RSV infection. Since initiating this program in 2005, we have made rapid progress. Our RNAi therapeutic was designed to target the nucleocapsid “N” gene of the RSV genome, a gene that is critical for the replication of the virus. ALN-RSV01 silences the N gene, thereby reducing the virus’ ability to reproduce.

In early 2008, we presented data from our Phase II GEMINI study which showed a statistically significant decrease in infection rate in adults experimentally infected with RSV, demonstrating that ALN-RSV01 has antiviral activity in a disease setting. With these results, we believe we have demonstrated human proof of concept with an RNAi therapeutic — a first for the field.

In June 2009, along with our partner Cubist, we reported preliminary data from our Phase II study in adult lung transplant patients naturally infected with RSV. These results document for the first time the safety and tolerability inhaled ALN-RSV01 in naturally infected patients, which we consider an important step forward in the advancement of our overall ALN-RSV program.

The ALN-RSV program is partnered in Asia with Kyowa Hakko Kirin and in the rest of the world with Cubist Pharmaceuticals.

Liver Cancers

Primary liver cancer, or hepatocellular carcinoma, is one of the most common cancers worldwide with more than 600,000 patients diagnosed each year. Secondary liver cancer, also known as metastatic liver cancer, is cancer that spreads to the liver from solid tumors found elsewhere in the body with 500,000 patients diagnosed each year. Alnylam’s second clinical program is an RNAi therapeutic for the treatment of these devastating diseases.

ALN-VSP is comprised of two siRNAs, each targeting a separate gene involved in the disease pathways of liver cancer: kinesin spindle protein, or KSP, which is involved in cancer cell proliferation; and vascular endothelial growth factor, or VEGF, which is involved in the growth of new blood vessels that feed tumors.

Alnylam recently advanced ALN-VSP into human clinical trials and has begun enrolling patients in a multi-center, open label, dose escalation trial to evaluate the safety, tolerability, and pharmacokinetics of this RNAi therapeutic. ALN-VSP represents both Alnylam’s first oncology program as well as our first systemically delivered RNAi therapeutic. We believe that advancement of ALN-VSP into clinical development is demonstration of the significant progress we have made with the systemic delivery of RNAi therapeutics.

**Development Programs**

**Hypercholesterolemia**

Hypercholesterolemia is a condition characterized by very high levels of cholesterol in the blood which leads to an increased risk of cardiovascular disease – the leading cause of death in the U.S. Alnylam is developing ALN-PCS, an RNAi therapeutic to treat hypercholesterolemia. ALN-PCS targets proprotein convertase subtilisin/kexin type 9, or PCSK9, which has been identified as a key regulator of cholesterol metabolism in human genetics studies. Individuals with low levels of PCSK9 activity have significantly lower levels of LDL (or “bad”) cholesterol, and a statistically significant reduced risk of cardiovascular disease. In contrast, patients with PCSK9 mutations leading to excessive activity are afflicted with severe forms of hypercholesterolemia.

We believe that ALN-PCS, due to its novel mechanism of action, creates the opportunity to treat hypercholesterolemia in a way that current therapies, such as statin drugs, cannot. Since PCSK9 is considered “undruggable,” it is an ideal target for an RNAi therapeutic. We are very encouraged with the results from our pre-clinical studies with ALN-PCS, including demonstration of a greater than 50% reduction in levels of LDL cholesterol in non-human primates; these effects were durable for several weeks after just a single administration.

**TTR Amyloidosis**

Transthyretin (TTR) amyloidosis is a hereditary, systemic disease caused by mutations in the TTR gene. These mutations cause the abnormal protein to accumulate and damage organs and tissues, such as the peripheral nerves and heart. In its severest form, familial amyloidotic polyneuropathy caused by mutant TTR represents an orphan disease estimated to affect approximately 10,000 people worldwide. The disease is associated with significant morbidity and mortality and the only treatment option available is liver transplantation.

Alnylam is advancing ALN-TTR, an RNAi therapeutic for TTR amyloidosis, as one of our key development programs. Data from pre-clinical studies demonstrated that an RNAi therapeutic can silence the TTR gene and reduce production of this pathogenic trigger. These data suggest that treatment of TTR amyloidosis with an RNAi therapeutic may represent a promising alternative to liver transplantation for these patients.

**Huntington’s Disease**

Huntington’s disease is a severe neurodegenerative genetic disease that affects approximately 30,000 patients in the U.S., with an estimated 150,000 additional patients at significant risk of developing the disease in their lifetime. ALN-HTT, an RNAi therapeutic for the treatment of Huntington’s disease, is designed to silence the huntingtin gene, which is the genetic cause of the disease. We are developing ALN-HTT as a drug-device combination in collaboration with Medtronic, a company with unmatched expertise in delivering therapeutics directly to the central nervous system.

In pre-clinical studies, ALN-HTT was well tolerated following administration to the brain and was shown to silence the huntingtin gene. This also translated into a therapeutic effect in animal models, including improvement in motor behavior, a hallmark symptom of this debilitating and fatal disease. We are encouraged by these proof of concept results to date, and the potential they represent for patients that have no effective treatment options today.
RNAi and Alnylam’s Approach

The discovery of RNAi sparked a revolution in biology, representing a major breakthrough in understanding how genes are turned on and off in cells, and providing a completely new approach to drug discovery and development. RNAi has the potential to become the foundation for a whole new class of therapeutics that harness this natural mechanism to achieve high potency and specificity.

RNAi is mediated by small, double-stranded RNA molecules. One method to activate RNAi is with siRNAs, which are double-stranded RNAs that are targeted to a specific disease-associated gene. The siRNA molecules are used by the natural RNAi machinery in cells to cause highly targeted gene silencing.

Non-Exclusive Platform Alliances

Roche

In July 2007, Roche and Alnylam formed a strategic platform alliance, valued at approximately $1 billion, in which Roche obtains a non-exclusive license to Alnylam’s technology platform for developing RNAi therapeutics. The alliance will initially cover four therapeutic areas: oncology, respiratory diseases, metabolic diseases, and certain liver diseases. Alnylam and Roche will also collaborate on RNAi drug discovery for one or more disease targets in these therapeutic areas.

Takeda

In May 2008, Alnylam and Takeda formed a strategic platform alliance, valued at approximately $1 billion, that provides Takeda with broad, worldwide, non-exclusive access to and enablement with Alnylam’s RNAi therapeutics platform technology and intellectual property in the fields of oncology and metabolic disease, with the right to expand the number of therapeutic fields in the future. The agreement also includes the transfer of platform technology from Alnylam to Takeda, a collaboration and cross-license of delivery technologies between the two companies, and a drug discovery collaboration on certain RNAi therapeutic targets.

microRNA Programs

Regulus Therapeutics Inc.

Regulus Therapeutics is a leading microRNA therapeutics company. In September 2007 with Isis Pharmaceuticals, we formed Regulus to focus on the discovery, development, and commercialization of microRNA-based therapeutics. Regulus combines the strengths and assets of Isis’ and Alnylam’s technologies, know-how, and intellectual property with strong leadership from a focused management team and a world-class Scientific Advisory Board chaired by Nobel laureate David Baltimore and including key pioneers in the microRNA field. The company maintains facilities in Carlsbad, California. In April 2008, Regulus announced the first ever microRNA-focused strategic alliance with GlaxoSmithKline to discover, develop, and market novel microRNA-based therapeutics to treat inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. For more information, visit www.regulusrx.com.

In early 2008, we launched our “RNAi 2010” initiative focused on achieving major scientific, clinical, and business milestones by the end of 2010. We believe that execution on our “RNAi 2010” plan will continue to advance RNAi therapeutics as a transformative approach for new medicines and further our mission of building a leading biopharmaceutical company founded on RNAi.

Scientific Leadership

Alnylam expects to broaden its leadership and significantly expand the scope of delivery solutions for RNAi therapeutics. This will be achieved by the continued scientific leadership of Alnylam scientists and current academic and industry collaborators, but also by a significant external effort to form new delivery technology partnerships. Further, this effort will include the significant expansion of the range of tissues and cell types where the company aims to achieve efficient delivery of RNAi therapeutics with both direct and systemic delivery approaches.

Clinical Pipeline

Alnylam expects to have four or more RNAi therapeutic programs in clinical development. These include direct and systemic RNAi programs, Alnylam proprietary and 50-50 partnership programs, and siRNA and microRNA therapeutics.

New Business Collaborations

Based on our scientific, clinical, and intellectual property leadership, the company also expects to form four or more new major business collaborations. These are expected to include the completion of additional broad platform alliances similar to the company’s July 2007 partnership with Roche. Completion of these business collaborations is expected to provide the company significant resources and funding to advance Alnylam’s proprietary and 50-50 partnership pipeline programs.

NASDAQ: ALNY

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Various statements in this document regarding Alnylam Pharmaceuticals’ business which are not historical facts are forward-looking statements that involve risks and uncertainties. For a discussion of such risks and uncertainties, which could cause actual results to differ from those contained in the forward-looking statements, see “Risk Factors” in our most recent quarterly and annual reports on file with the SEC.