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Alnylam Presents Complete Results from Phase IIb Trial with ALN-RSV01, an Inhaled RNAi Therapeutic for the Treatment of Respiratory Syncytial Virus (RSV) Infection

– ALN-RSV01 Reduces Bronchiolitis Obliterans Syndrome (BOS) in RSV-Infected Lung Transplant Patients –

– Alnylam to Discuss Results with U.S. and European Regulatory Authorities and Communicate Future Development Plans at Year End –

Cambridge, Mass., September 4, 2012 – Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), a leading RNAi therapeutics company, announced today complete results from its Phase IIb trial with ALN-RSV01 for the treatment of respiratory syncytial virus (RSV) infection in lung transplant patients. The data were presented at the European Respiratory Society’s (ERS) Annual Congress held in Vienna, September 1-5, 2012. As reported previously, the study narrowly missed the primary endpoint of reduced day 180 BOS in an “intent-to-treat” (ITTc) analysis of confirmed RSV infected patients, but achieved statistically significant reductions in prospectively defined analyses of ITTc patients with their “last observation carried forward” (LOCF), and of ITTc patients treated “per protocol” (PP). At the ERS meeting, new results were presented on secondary endpoints and certain post-hoc analyses that support the efficacy of ALN-RSV01 in this setting. Further, and as reported earlier, ALN-RSV01 was found to be generally safe and well tolerated in the study. Alnylam plans to discuss these complete results with U.S. and European regulatory authorities, and communicate future development plans for ALN-RSV01 at year’s end.

“Our Phase IIb study results demonstrate that inhaled ALN-RSV01 reduces the incidence of new or progressive BOS in RSV-infected lung transplant patients. The complete results presented at the ERS meeting continue to show that ALN-RSV01 is associated with a significant treatment effect, including results of a multivariate logistic regression analysis where treatment with ALN-RSV01 showed an over eight-fold reduced risk in developing day 180 BOS. Further, we showed a statistically significant effect on the secondary endpoint of day 90 BOS, and demonstrated a particularly strong effect of over 80% in patients receiving ALN-RSV01 within five days of symptom onset,” said Akshay Vaishnaw, M.D., Ph.D., Executive Vice President and Chief Medical Officer of Alnylam. “Our plans are to discuss these results with U.S. and European regulatory authorities later this year and then communicate next steps, if any, for our ALN-RSV
program. In the meanwhile, we continue to execute on our ‘Alnylam 5x15’ product strategy with a focus on our transthyretin-mediated amyloidosis and hemophilia programs.”

“Community acquired respiratory infections, including RSV, represent a significant risk for lung transplant patients, as infection may be associated with the development of new or progressive BOS. Indeed, BOS is the leading cause of death in patients beyond the first year of transplantation,” said Jens Gottlieb, M.D., principal investigator, Hannover Medical School. “Amongst other study findings, ALN-RSV01 treatment shows a clinically meaningful effect on the incidence of day 180 BOS, and these results appear to be quite robust even in the context of concomitant therapies such as ribavirin and steroids. There is clearly an unmet medical need for an effective RSV therapy for lung transplant patients, and ALN-RSV01 holds considerable potential as an innovative therapeutic for the prevention RSV-induced BOS.”

As reported previously, the Phase IIb trial was an international multi-center, randomized, double-blind, placebo-controlled study of ALN-RSV01 in RSV-infected lung transplant patients. RSV infection in lung transplant patients represents a significant unmet medical need as it can lead to the development of new or progressive BOS, an irreversible fibro-occlusive pathology of the airways that is the biggest cause of chronic allograft dysfunction and mortality in lung transplant patients, with an approximately 50% mortality within five years of onset. The primary endpoint of the Phase IIb trial was the incidence of new or progressive BOS at 180 days. The trial enrolled 87 patients who were randomized in a one-to-one, ALN-RSV01-to-placebo ratio; a total of 33 sites participated from six countries. Based on central laboratory confirmation of RSV infection, a total of 44 patients were randomized to receive ALN-RSV01 and 33 patients were randomized to receive placebo, defining the overall intent-to-treat study cohort (ITTc). Data from the study show that ALN-RSV01 missed the primary endpoint of new or progressive BOS at 180 days in the ITTc population (p=0.058). However, ALN-RSV01 treatment was associated with a statistically significant reduction in the incidence of day 180 BOS in the prospectively defined LOCF (p=0.028) and PP (p=0.025) analyses. In all analyses, treatment with ALN-RSV01, as compared with placebo, was associated with a clinically meaningful reduction in the incidence of day 180 BOS with a treatment effect of greater than 50%.

New study findings presented at the ERS meeting included results from key secondary endpoints and certain post-hoc analyses of data. As it pertains to key secondary endpoints, ALN-RSV01 treatment resulted in a statistically significant reduction in day 90 BOS as compared with placebo as measured in the ITTc population (p=0.044) with an overall effect size of 52%. Further, ALN-RSV01 showed an enhanced treatment effect size of 88% toward day 180 BOS in patients treated within five days from symptom onset (p=0.0095). Other secondary endpoints including viral parameters and symptom score were not significantly different between ALN-RSV01 and placebo. A number of post-hoc analyses were also performed. In a logistic regression analysis adjusting for multiple variables, treatment with ALN-RSV01 was found to be associated with a significantly reduced risk of developing day 180 BOS, with an odds ratio of 8.5 (95% confidence intervals of 1.7 and 41.7). Further, the effects of ALN-RSV01 on day 180 BOS persisted when controlled for the concomitant administration of pulse-dose steroids. A direct comparison of patients receiving ALN-RSV01 in the absence of ribavirin versus placebo patients receiving inhaled ribavirin, the current standard of care at some centers, showed that ALN-RSV01 was associated with a statistically significant reduction in new or progressive BOS at day
There was a similar incidence of reported adverse events in placebo (81%) and study drug (73.3%) treatment arms. Serious adverse events were also reported with similar incidence in patients receiving placebo (9.5%) and ALN-RSV01 (11%). In aggregate, the newly presented results support the conclusion that treatment of RSV-infected lung transplant patients with ALN-RSV01 is generally safe and well tolerated and associated with a decreased incidence of new or progressive BOS.

Alnylam’s RSV program is partnered with Cubist Pharmaceuticals in North America and the rest of the world outside of Asia, where the program is partnered with Kyowa Hakko Kirin Co., Ltd. These partners maintain certain opt-in rights for the development of ALN-RSV01.

**About Respiratory Syncytial Virus**
Respiratory syncytial virus (RSV) is a highly contagious virus that is the most common identified cause of lower respiratory tract infections in children under one year of age. The clinical manifestations of RSV infection depend on the patient’s age and health status. Older children and adults often have a milder course, with cold-like symptoms, while infants and immune-compromised patients can have a more severe illness that results in bronchiolitis, pneumonia and in some instances death. In the pediatric and adult populations, RSV accounts for more than 300,000 hospitalizations per year in the U.S. RSV infection in lung transplant patients represents an important unmet medical need. Lung transplant patients infected with RSV are at risk for both acute rejection and a bronchiolitis obliterans syndrome (BOS). BOS is a progressive inflammatory and fibrotic lesion of the small airways resulting in an irreversible loss of function in the transplanted lung, and is associated with approximately 50% mortality within five years. As a result, there is a significant need for novel therapeutics to treat patients who become infected with RSV.

**About RNA Interference (RNAi)**
RNAi (RNA interference) is a revolution in biology, representing a breakthrough in understanding how genes are turned on and off in cells, and a completely new approach to drug discovery and development. Its discovery has been heralded as “a major scientific breakthrough that happens once every decade or so,” and represents one of the most promising and rapidly advancing frontiers in biology and drug discovery today which was awarded the 2006 Nobel Prize for Physiology or Medicine. RNAi is a natural process of gene silencing that occurs in organisms ranging from plants to mammals. By harnessing the natural biological process of RNAi occurring in our cells, the creation of a major new class of medicines, known as RNAi therapeutics, is on the horizon. Small interfering RNA (siRNA), the molecules that mediate RNAi and comprise Alnylam’s RNAi therapeutic platform, target the cause of diseases by potently silencing specific mRNAs, thereby preventing disease-causing proteins from being made. RNAi therapeutics have the potential to treat disease and help patients in a fundamentally new way.

**About Alnylam Pharmaceuticals**
Alnylam is a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. The company is leading the translation of RNAi as a new class of innovative medicines with a core focus on RNAi therapeutics for the treatment of genetically defined diseases, including ALN-TTR for the treatment of transthyretin-mediated amyloidosis.
(ATTR), ALN-AT3 for the treatment of hemophilia, ALN-PCS for the treatment of severe hypercholesterolemia, ALN-HPN for the treatment of refractory anemia, and ALN-TMP for the treatment of hemoglobinopathies. As part of its “Alnylam 5x15™” strategy, the company expects to have five RNAi therapeutic products for genetically defined diseases in clinical development, including programs in advanced stages, on its own or with a partner by the end of 2015. Alnylam has additional partnered programs in clinical or development stages, including ALN-RSV01 for the treatment of respiratory syncytial virus (RSV) infection, ALN-VSP for the treatment of liver cancers, and ALN-HTT for the treatment of Huntington’s disease. The company’s leadership position on RNAi therapeutics and intellectual property have enabled it to form major alliances with leading companies including Merck, Medtronic, Novartis, Biogen Idec, Roche, Takeda, Kyowa Hakko Kirin, Cubist, Ascleatis, and Monsanto. In addition, Alnylam and Isis co-founded Regulus Therapeutics Inc., a company focused on discovery, development, and commercialization of microRNA therapeutics; Regulus has formed partnerships with GlaxoSmithKline and Sanofi. Alnylam has also formed Alnylam Biotherapeutics, a division of the company focused on the development of RNAi technologies for applications in biologics manufacturing, including recombinant proteins and monoclonal antibodies. Alnylam’s VaxiRNA™ platform applies RNAi technology to improve the manufacturing processes for vaccines; GlaxoSmithKline is a collaborator in this effort. Alnylam scientists and collaborators have published their research on RNAi therapeutics in over 100 peer-reviewed papers, including many in the world’s top scientific journals such as Nature, Nature Medicine, Nature Biotechnology, and Cell. Founded in 2002, Alnylam maintains headquarters in Cambridge, Massachusetts. For more information, please visit www.alnylam.com.

Alnylam Forward-Looking Statements
Various statements in this release concerning Alnylam’s future expectations, plans and prospects, including without limitation, statements regarding Alnylam’s views with respect to the potential for RNAi therapeutics, including ALN-RSV01, its plans to discuss the results of its ALN-RSV01 Phase IIb study with U.S. and European regulatory authorities later this year and thereafter, determine appropriate next steps for its ALN-RSV program, the rights of its partners to opt-in to the ALN-RSV01 study, and Alnylam’s expectations regarding its “Alnylam 5x15” product strategy, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, Alnylam’s ability to discover and develop novel drug candidates, successfully demonstrate the efficacy and safety of its drug candidates, including ALN-RSV01, the pre-clinical and clinical results for these product candidates, which may not support further development of such product candidates, actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials for such product candidates, obtaining, maintaining and protecting intellectual property, obtaining regulatory approval for products, competition from others using technology similar to Alnylam’s and others developing products for similar uses, and Alnylam’s ability to establish and maintain strategic business alliances and new business initiatives, as well as those risks more fully discussed in the “Risk Factors” section of its most recent quarterly report on Form 10-Q on file with the Securities and Exchange Commission. In addition, any forward-looking statements represent Alnylam’s views only as of today and should not be relied upon as representing its views as of any subsequent date. Alnylam does not assume any obligation to update any forward-looking statements.