Development and marketing agreement for ALN-PCS RNAi therapeutic program

The Medicines Company
Alnylam Pharmaceuticals

Feb 04 2013
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Companies:
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Announcement date: Feb 04 2013
Deal value, US$m: 205 : sum of upfront and potential development and commercial milestone payments

Details

Industry sectors:
Bigbiotech
Bigpharma
Biotech
Pharmaceutical

Compound name: ALN-PCSsc
Asset type: Compound
Therapy areas: Cardiovascular » Hypercholesterolemia
Biological compounds
Peptides

Technology types:
Proteomics
RNA therapeutics
Small molecules
Development

Deal components:
Licensing
Marketing
Preclinical

Stages of development:
Phase I

Financials

Deal value, US$m: 205 : sum of upfront and potential development and commercial milestone payments
Upfront, US$m: 25 : sum of upfront payment
Milestones, US$m: 180 : sum of potential development and commercial milestone payments
Royalty rates, %: n/d : scaled double-digit royalties on global products sales of ALN-PCS products

Termsheet

The Medicines Company and Alnylam Pharmaceuticals they have formed an exclusive global alliance for the development and commercialization of Alnylam’s ALN-PCS RNAi therapeutic program for the treatment of hypercholesterolemia.

PCSK9 (proprotein convertase subtilisin/kexin type 9) is a protein that regulates low-density lipoprotein (LDL) receptor levels on hepatocytes; gain-of-function human mutations in PCSK9 are associated with hypercholesterolemia while loss-of-function mutations are associated with lower levels of LDL cholesterol and a reduced risk of cardiovascular disease.
ALN-PCS is a PCSK9 synthesis inhibitor that reduces intracellular and extracellular levels of PCSK9 resulting in lowered plasma levels of LDL-C.

The Medicines Company and Alnylam intend to collaborate on the advancement of the ALN-PCS program.

Alnylam’s ALN-PCS program includes ALN-PCS02 - an intravenously administered RNAi therapeutic which has completed a Phase I trial, and ALN-PCSsc - a subcutaneously administered RNAi therapeutic currently in pre-clinical development.

Alnylam will continue the program for an estimated one to two years to complete certain pre-clinical and Phase I clinical studies.

The Medicines Company is responsible for leading and funding development from Phase II forward and commercializing the ALN-PCS program if successful.

Under the terms of the agreement, The Medicines Company will make an upfront cash payment of $25 million to Alnylam.

Alnylam may also receive potential development and commercial milestone payments of up to $180 million.

Alnylam will be eligible to receive scaled double-digit royalties on global products sales of ALN-PCS products.

Press Release

The Medicines Company (MDCO) Buys Cholesterol Drug Rights From Alnylam Pharmaceuticals (ALNY) for Up to $205 Million

2/4/2013 7:10:37 AM

PARSIPPANY, N.J. & CAMBRIDGE, Mass.--(BUSINESS WIRE)-- The Medicines Company (MDCO) and Alnylam Pharmaceuticals, Inc. (ALNY), a leading RNAi therapeutics company, announced today that they have formed an exclusive global alliance for the development and commercialization of Alnylam’s ALN-PCS RNAi therapeutic program for the treatment of hypercholesterolemia.

“This new alliance unites two organizations with a shared culture and commitment to innovation. In my view and past experience, there could be no stronger partner for our ALN-PCS program than The Medicines Company, which has demonstrated industry-wide leadership in the advancement of cardiovascular medicines to patients and remarkable success in its strategy of in-licensing, developing, and commercializing breakthrough products,” said John Maraganore, Ph.D., Chief Executive Officer of Alnylam. “For Alnylam, this new partnership enables the advancement of ALN-PCS, an important program within our ‘Alnylam 5x15’ product development and commercialization strategy focused on RNAi therapeutics directed toward genetically validated targets. We believe that the ALN-PCS program holds great promise for the development of a significant therapeutic option for patients with hypercholesterolemia, and that the unique mechanism of action for ALN-PCS could provide a differentiated and potentially best-in-class strategy for PCSK9 antagonism.”

“Our focus on acute and intensive care medicine has led us to a leadership position with Angiomax® (bivalirudin) and potentially with cangrelor in the management of patients in extreme risk as a consequence of the rupture of their vulnerable coronary artery plaque at and around the time of acute coronary syndromes. Meantime, we have made progress with MDCO-216 (ApoA-1 Milano), a turbocharged form of HDL-C (‘good cholesterol’) which has the potential to modify disease through reverse cholesterol transport,” said Clive Meanwell, M.D., Ph.D., Chairman and Chief Executive Officer of The Medicines Company. “Now, this exciting collaboration with Alnylam - leaders in their field of RNAi - adds a second potentially disease modifying approach and more cutting edge technology to our portfolio. We have seen that PCSK9 gene silencing can substantially reduce LDL-cholesterol in patients and has epidemiological and disease mechanisms studies suggest this can further reduce the risks of the world’s number one killer, coronary artery disease. Clearly we see the complementarity of approaches which increase ‘good cholesterol’ (HDL-C) and decrease ‘bad cholesterol’ (LDL-C). We look forward to working with our colleagues at Alnylam for whom we have the greatest respect and admiration based upon earlier collaborations particularly around Angiomax, which was invented by John Maraganore.”

PCSK9 (proprotein convertase subtilisin/kexin type 9) is a protein that regulates low-density lipoprotein (LDL) receptor levels on hepatocytes; gain-of-function human mutations in PCSK9 are associated with hypercholesterolemia while loss-of-function mutations are associated with lower levels of LDL cholesterol and a reduced risk of cardiovascular disease. ALN-PCS is a PCSK9 synthesis inhibitor that reduces intracellular and extracellular levels of PCSK9 resulting in lowered plasma levels of LDL-C. MDCO-216 is a naturally occurring variant of a protein found in high-density lipoprotein, or HDL. It is a reverse cholesterol transport agent designed to reduce atherosclerotic plaque burden development and thereby reduce the risk of adverse thrombotic events.

Under this alliance, The Medicines Company and Alnylam intend to collaborate on the advancement of the ALN-PCS program. Alnylam’s ALN-PCS program includes ALN-PCS02 - an intravenously administered RNAi therapeutic which has completed a Phase I trial, and ALN-PCSsc - a subcutaneously administered RNAi therapeutic currently in pre-clinical development. Alnylam will continue the program for an estimated one to two years to complete certain pre-clinical and Phase I clinical studies. The Medicines Company is responsible for leading and funding development from Phase II forward and commercializing the ALN-PCS program if successful. Under the terms of the agreement, The Medicines Company will make an upfront cash payment of $25 million to Alnylam. Alnylam may also receive potential development and commercial milestone payments of up to $180 million. Alnylam will be eligible to receive scaled double-digit royalties on global products sales of ALN-PCS products.
Alnylam has completed a Phase I trial of ALN-PCS02 in healthy volunteer subjects with elevated baseline LDL-C. Results showed that administration of a single intravenous dose of drug, in the absence of concomitant lipid-lowering agents such as statins, resulted in statistically significant and durable reductions of PCSK9 plasma levels of up to 84% and lowering of LDL-C of up to 50%. ALN-PCS02 was shown to be generally safe and well tolerated in this study and there were no serious adverse events related to study drug administration. Alnylam has also presented pre-clinical data from its ALN-PCSsc program demonstrating potent knockdown of the PCSK9 target gene with an ED50 of less than 0.3 mg/kg after a single subcutaneous dose.

“Cardiovascular disease remains the leading cause of mortality worldwide, with elevated LDL-C a major modifiable risk factor. New strategies are needed to dramatically and rapidly reduce LDL-C and prevent acute cardiovascular events that result from the rupture of cholesterol rich plaque when patients are at their most vulnerable,” said Daniel J. Rader, M.D., professor of Medicine and chief, Division of Translational Medicine and Human Genetics, at the Perelman School of Medicine at the University of Pennsylvania. “As a key regulator of the LDL receptor, liver-expressed PCSK9 is one of the most important and best validated new targets in molecular medicine for the treatment of hypercholesterolemia. The ALN-PCS data generated to date are very encouraging and I look forward to continued clinical studies that highlight the unique mechanistic approach of PCSK9 synthesis inhibitors.”

Dr. Rader serves as a member of Alnylam’s Scientific Advisory Board and as a consultant on Alnylam’s ALN-PCS program, and Alnylam and Dr. Rader collaborate on research for which Alnylam provides materials.

About Hypercholesterolemia

Hypercholesterolemia is a condition characterized by very high levels of cholesterol in the blood which is known to increase the risk of coronary artery disease, the leading cause of death in the U.S. Some forms of hypercholesterolemia can be treated through dietary restrictions, lifestyle modifications (e.g., exercise and smoking cessation) and medicines such as statins. However, a large proportion of patients with hypercholesterolemia are not achieving target LDL-C goals with statin therapy, including genetic familial hypercholesterolemia patients, acute coronary syndrome patients, high-risk patient populations (e.g., patients with coronary artery disease, diabetics, symptomatic carotid artery disease, etc.) and other patients that are statin intolerant. Severe forms of hypercholesterolemia are estimated to affect more than 500,000 patients worldwide, and as a result, there is a significant need for novel therapeutics to treat patients with hypercholesterolemia whose disease is inadequately managed by existing therapies.

About ALN-PCS

ALN-PCS is a systemically delivered RNAi therapeutic targeting the gene proprotein convertase subtilisin/kexin type 9 (PCSK9), a target validated by human genetics that is involved in the metabolism of low-density lipoprotein cholesterol (LDL-C, or “bad” cholesterol). ALN-PCS therapies are PCSK9 synthesis inhibitors that lower levels of both intracellular and extracellular PCSK9, thereby phenocopying the human genetics observed in loss of function or null human PCSK9 mutations (N. Engl. J. Med. (2006) 354:1264-1272; Am. J. Hum. Genet. (2006) 79: 514-523). PCSK9 synthesis inhibition through an RNAi mechanism has the potential to lower tissue and circulating plasma PCSK9 protein levels resulting in higher LDL receptor levels in the liver, and subsequently lower LDL-C levels in the blood stream. Lower LDL-C is associated with a decreased risk of cardiovascular disease, including myocardial infarction and stroke.

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 The Medicines Company

The Medicines Company (MDCO) provides medical solutions to improve health outcomes for patients in acute and intensive care hospitals worldwide. These solutions comprise medicines and knowledge that directly impact the survival and well being of critically ill patients.

Filing Data

Not available.

Contract

Not available.