Development and marketing agreement for ALN-PCS RNAi therapeutic program

The Medicines Company
Alnylam Pharmaceuticals

Feb 04 2013
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Companies:
The Medicines Company
Alnylam Pharmaceuticals

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

Details

Start date: Feb 03 2013
Industry sectors: Bigbiotech
Bigpharma
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
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.

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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

LICENSE AND COLLABORATION AGREEMENT

by and between

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ALNYLAM PHARMACEUTICALS, INC.

and

THE MEDICINES COMPANY

LICENSE AND COLLABORATION AGREEMENT

THIS LICENSE AND COLLABORATION AGREEMENT (this "Agreement"), effective as of February 3, 2013 (the "Effective Date"), by and between Alnylam Pharmaceuticals, Inc., a corporation organized and existing under the laws of the State of Delaware ("Alnylam") and, The Medicines Company, a corporation organized and existing under the laws of Delaware ("MedCo").

RECITALS:

WHEREAS, Alnylam owns or controls certain fundamental intellectual property relating to RNA interference, and is developing proprietary therapeutic products in the Field Targeting the human PCSK9 gene, including ALN-PCS02 and ALN-PCSc (all as defined below);

WHEREAS, MedCo desires to develop and commercialize such products in the Territory (as defined below);

WHEREAS, Alnylam desires to collaborate with MedCo in the further development of such products in the Territory as set forth herein; and

WHEREAS, Alnylam and MedCo believe that a license and collaboration for such purpose on the terms and conditions of this Agreement would be desirable.

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants herein contained, the Parties hereby agree as follows:

1. DEFINITIONS

Unless specifically set forth to the contrary herein, the following terms, whether used in the singular or plural, shall have the respective meanings set forth below:

1.1 [Intentionally Omitted].

1.2 "Acquired Party" has the meaning set forth in Section 6.7.

1.3 "Acquirer" has the meaning set forth in Section 6.7.

1.4 "Additional Alnylam In-Licenses" means the agreements set forth in Section C of Schedule D.

1.5 "Affiliate" means, with respect to a Person, any other Person which controls, is controlled by, or is under common control with the applicable Person. For purposes of this definition, "control" shall mean: (a) in the case of corporate entities, direct or indirect ownership of at least fifty percent (50%) of the stock or shares (or such lesser percentage which is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction) entitled to vote for the election of directors, or otherwise having the power to control or direct the affairs of such Person; and (b) in the case of non-corporate entities, direct or indirect ownership of at least fifty percent (50%) of the equity interest or the power to direct the management and policies of such non-corporate entities.

1.6 "ALN-PCS02" means the siRNA Product Controlled by Alnylam comprising the siRNA [**]) formulated in a lipid-based nanoparticle, as further described on Schedule A.

1.7 "ALN-PCSc" means an siRNA Product Controlled by Alnylam comprising an siRNA conjugated with a triantennary Ga1NAc molecule, as further described on Schedule B.

1.8 "Alnylam Collaboration IP" means (a) any improvement, discovery or Know-How, patentable or otherwise, first conceived or reduced to practice or, with respect to inventions and discoveries other than patentable inventions, otherwise identified, discovered, made or developed, solely by individuals who are employees, agents or consultants of Alnylam or its Affiliates and Controlled by Alnylam at any time during the Term, in each case in the conduct of the Collaboration, and (b) any Patent Rights which claim such improvements, discoveries or Know-How. Alnylam Collaboration IP excludes Alnylam's interest in Joint Collaboration IP. Patent Rights constituting Alnylam Collaboration IP are either Alnylam Core Technology Patent Rights or Alnylam Product-Specific Patent Rights, as the case may be.

1.9 "Alnylam Core Technology Patent Rights" means Patent Rights Controlled by Alnylam at any time during the Term that are reasonably necessary or useful to Develop, Manufacture or Commercialize Licensed Products, in each case other than Alnylam Product-Specific Patent
Rights and Patent Rights comprising Joint Collaboration IP. Alnylam Core Technology Patent Rights includes the Patent Rights set forth on Schedule C-1 and may include Patent Rights that constitute Alnylam Collaboration IP.

1.10 "Alnylam Indemnitees" has the meaning set forth in Section 10.1.

1.11 "Alnylam In-Licenses" means (a) the Existing Alnylam In-Licenses and (b) any agreement between Alnylam (or its Affiliates) and a Third Party entered into after the Effective Date pursuant to which Alnylam acquires Control of Know-How or Patent Rights that are reasonably necessary or useful to Develop, Manufacture or Commercialize Licensed Products in the Field in the Territory, but in the case of any such agreement described in clause (b), solely to the extent that such agreement is designated as an Alnylam In-License pursuant to Section 6.4.2.2.

1.12 "Alnylam Know-How" means Know-How Controlled by Alnylam at any time during the Term that is reasonably necessary or useful to Develop, Manufacture and/or Commercialize Licensed Products in the Field in the Territory.


1.14 "Alnylam Product-Specific Patent Rights" means Patent Rights Controlled by Alnylam at any time during the Term that solely claim (a) an siRNA Targeting the human PCSK9 gene contained in a Licensed Product, and pharmaceutical compositions thereof; (b) an siRNA Product or specific components thereof to the extent that such components are unique to said siRNA Products; (c) methods of using the compositions described in clause (a) or (b) above as a human therapeutic or prophylactic, or to Target the human PCSK9 gene, or to inhibit expression of human PCSK9, and foreign equivalents of such method claims; (d) methods and compositions directed to the synthesis or analysis of the compositions described in clause (a) or (b); or (e) Alnylam Collaboration IP that is applicable solely to a Licensed Product; provided, however, that (y) any such patents that include claims that are directed to subject matter applicable to siRNA or siRNA delivery in general will not be considered Alnylam Product-Specific Patent Rights but will be considered Alnylam Core Technology Patent Rights. Alnylam Product-Specific Patent Rights exclude Joint Collaboration IP, includes the Patent Rights set forth on Schedule C-2 and may include Patent Rights that constitute Alnylam Collaboration IP.

1.15 "Alnylam Technology" means, collectively, Alnylam Know-How, Alnylam Patent Rights, Alnylam Collaboration IP and Alnylam's interest in Joint Collaboration IP.

1.16 "Bankrupt Party" has the meaning set forth in Section 6.5.

1.17 "Breaching Party" has the meaning set forth in Section 12.2.2.

1.18 "Bulk Drug Product" means formulated Bulk Drug Substance in bulk form prior to filling and finishing.

1.19 "Bulk Drug Substance" means an siRNA (including chemical modifications and covalent conjugates) or other active ingredient in bulk form manufactured for use as an active pharmaceutical ingredient in a Licensed Product.

1.20 "Business Day" means a day on which banking institutions in Boston, Massachusetts, USA and Parsippany, New Jersey, USA are open for business, excluding any Saturday or Sunday.

1.21 "Calendar Quarter" means the respective periods of three (3) consecutive calendar months ending on March 31, June 30, September 30 and December 31 of each Calendar Year; provided, that (a) the first Calendar Quarter of the Term shall begin on the Effective Date and end on the first to occur of March 31, June 30, September 30 or December 31 thereafter and the last Calendar Quarter of the Term shall end on the last day of the Term, and (b) the first Calendar Quarter of a Royalty Term for a Licensed Product in a country shall begin on the First Commercial Sale of such Licensed Product in such country and end on the first to occur of March 31, June 30, September 30 or December 31 thereafter and the last Calendar Quarter of a Royalty Term shall end on the last day of such Royalty Term.

1.22 "Calendar Year" means each successive period of twelve (12) months commencing on January 1 and ending on December 31; provided, that (a) the first Calendar Year of the Term shall begin on the Effective Date and end on the first December 31 thereafter and the last Calendar Year of the Term shall end on the last day of the Term, and (b) the first Calendar Year of a Royalty Term for a Licensed Product in a country shall begin on the First Commercial Sale of such Licensed Product in such country and end on the first December 31 thereafter and the last Calendar Year of the Term shall end on the last day of such Royalty Term.

1.23 "Challenge" has the meaning set forth in Section 12.2.4.

1.24 "Challenging Party" has the meaning set forth in Section 12.2.4.

1.25 "Change of Control" means, with respect to a Party, any of the following: (a) the sale or disposition of all or substantially all of the assets of such Party or its direct or indirect controlling Affiliate to a Third Party, other than to an entity of which more than fifty percent (50%) of the voting capital stock are owned after such sale or disposition by shareholders of such Party or its direct or indirect controlling Affiliate (in either case, whether directly or indirectly through any parent entity); or (b) (i) the acquisition by a Third Party, alone or together with any of its Affiliates, other
than an employee benefit plan (or related trust) sponsored or maintained by such Party or any of its Affiliates, of more than fifty percent (50%) of
the outstanding shares of voting capital stock of such Party or its direct or indirect controlling Affiliate, or

(ii) the acquisition, merger or consolidation of such Party or its direct or indirect controlling Affiliate with or into another Person, other than, in the
case of this clause (b), an acquisition or a merger or consolidation of such Person or its controlling Affiliate in which the holders of shares of
voting capital stock of such Person or its controlling Affiliate, as the case may be, immediately prior to such acquisition, merger or consolidation
will beneficially own, directly or indirectly, at least fifty percent (50%) of the shares of voting capital stock of the acquiring Third Party or the
surviving corporation in such acquisition, merger or consolidation, as the case may be, immediately after such acquisition, merger or
consolidation.

1.28"Clinical Study" means a Phase I Study, Phase II Study, Phase III Study, or Pivotal Study, as applicable; but excluding any Post-Approval
Studies.

1.29"Collaboration" means the activities of the Parties in the Development and Manufacture of Licensed Products under this Agreement and/or
the Development Supply Agreement.

1.28"Combination Product" has the meaning set forth in Section 1.89.

1.30"[**]" has the meaning set forth in Section 7.4.4.

1.31"Commercialization" or "Commercialize" means any and all activities directed to marketing, promoting, distributing, importing, exporting,
offering to sell and/or selling a product, including the conduct of Post-Approval Studies, and activities directed to obtaining pricing and
reimbursement approvals, as applicable.

1.32"Commercially Reasonable Efforts" means (a) with respect to the obligations of a Party under this Agreement that relate to the
Development, Manufacture or Commercialization of a Licensed Product, the carrying out of such obligations in a diligent, expeditious and
sustained manner using efforts and resources, including reasonably necessary personnel and financial resources, that biopharmaceutical
companies of comparable size and resources, that biopharmaceutical companies of comparable size and resources, typically devote to their own products of similar market potential at a
similar stage in development or product life, taking into account the following factors to the extent reasonable and relevant: issues of safety and
efficacy, product profile, competitiveness of such Licensed Product and alternative Third Party products (but not alternative products Controlled
by the Party to which the efforts obligation applies which are not Licensed Products) in the marketplace, the patent or other proprietary position
of such Licensed Product, the regulatory structure involved and the potential profitability of such Licensed Product marketed or to be marketed,
but excluding from consideration any financial considerations of MedCo to Alnylam under this Agreement; provided, however, that to the extent
the obligations of MedCo under this Agreement relate to the Development, Manufacture or Commercialization of a Licensed Product for China,
such efforts and resources shall instead be those that MedCo typically devotes to its own products of similar market potential at a similar stage in
development or product life, taking into account the factors set forth above; and (b) with respect to other obligations under this Agreement, the
carrying out of such obligations in a diligent, expeditious and sustained manner using efforts and resources, including reasonably necessary
personnel and financial resources, that biopharmaceutical companies of comparable size and resources typically devote to similar obligations.

1.33"Competitive Infringement" has the meaning set forth in Section 11.4.1.

1.34"Confidential Information" means with respect to a Party but subject to Section 8.1(a)(i)-(iv), any and all confidential or proprietary
information and data, including (with respect to Alnylam as the
disclosing Party) Alnylam Technology, (with respect to MedCo as the disclosing Party) MedCo Technology, and all other scientific, pre-clinical,
clinical, regulatory, manufacturing, marketing, financial and commercial information or data, whether communicated in writing or orally or by any
other method, which is provided by one Party to the other Party in connection with this Agreement. Alnylam Technology is Confidential
Information of Alnylam. MedCo Technology is Confidential Information of MedCo. Joint Collaboration IP is the Confidential Information of both
Parties, with each Party being considered both the disclosing Party and the receiving Party.

1.35"Control", "Controls" or "Controlled by" means, with respect to any Know-How, Patent Right or other intellectual property right and a Party,
the ability of such Party or its Affiliates (whether by ownership or license, other than pursuant to a license granted under this Agreement) to
assign, transfer, or grant access to, or a license or sublicense of, such item or right as provided for herein without violating the terms of any
agreement or other arrangement with any Third Party; provided that, with respect to rights to any Third Party Know-How, Patent Rights or other
intellectual property right that are licensed to, or otherwise obtained by, (i) a Party or its Affiliates pursuant to an agreement entered into by such
Party or any of its Affiliates after the Effective Date or (ii) Alnylam or its Affiliates pursuant to any Additional Alnylam In-License, such Third Party
Know-How, Patent Rights or other intellectual property right shall be deemed not to be under the Control of such Party or its Affiliates, or Alnylam
or its Affiliates, respectively, unless and until the agreement pursuant to which such rights are obtained becomes an In-License pursuant to
Section 6.4.2.

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1.36 “Costs” means (a) with respect to the Development, (i) the direct and documented out-of-pocket costs and expenses incurred by a Party or its Affiliates in conducting activities under the Transaction Agreements, and (ii) FTE Costs of internal personnel that are attributable or reasonably allocable to such activities, in each case as determined in accordance with GAAP, and (b) with respect to the supply of Licensed Product by Alnylam pursuant to Sections 5.1(a)(i) and (ii), the reasonable internal and external costs of Alnylam incurred in Manufacturing or having Manufactured such Licensed Product (i) to the extent that such Licensed Product is Manufactured by Alnylam, the fully allocated cost of Manufacture of such Licensed Product, consisting of direct material and direct labor costs, plus Manufacturing overhead attributable to such Licensed Product (including facilities start-up costs, all directly incurred Manufacturing variances and a reasonable allocation of related Manufacturing administrative and facilities costs for such Licensed Product, but excluding corporate administrative overhead and/or costs associated with excess capacity), all calculated strictly in accordance with GAAP consistently applied by Alnylam, and (ii) to the extent that such Licensed Product is Manufactured by a Third Party manufacturer, the actual fees paid by Alnylam to the Third Party for the Manufacture, supply and packaging of such Licensed Product and any reasonable costs, including direct labor costs, actually incurred by Alnylam in managing or overseeing the Third Party relationship.

1.37 “Cover,” “Covering” or “Covers” means, as to a product and Patent Rights, that, in the absence of a license granted under, or ownership of, such Patent Rights, the research, development, manufacture, use, offer for sale, sale, or importation of such product would infringe such Patent Rights or, as to a pending claim included in such Patent Rights, the research, development, manufacture, use, offer for sale, sale, or importation of such product would infringe such Patent Rights if such pending claim were to issue in an issued patent.

1.38 “Development,” “Developing” or “Develop” means the research and development of Licensed Products, including activities related to the generation, characterization, optimization, construction, expression, use and production of Licensed Products, any other research and development activities related to the testing and qualification of Licensed Products, including toxicology studies, statistical analysis and report writing, pre-clinical testing, Clinical Studies and regulatory affairs, product approval and registration activities, but excluding Post-Approval Studies.

1.39 “Development Costs Cap” has the meaning set forth in Section 2.3.1.

1.40 “Development Supply Agreement” has the meaning set forth in Section 5.1.

1.41 “Dispute” has the meaning set forth in Section 13.12.

1.42 “Effective Date” has the meaning set forth in the preamble.

1.43 “EMA” means the European Medicines Agency and any successor governmental authority having substantially the same function.

1.44 “EU” means the European Union, as its membership may be altered from time to time, and any successor thereto.

1.45 “[**]” has the meaning set forth in Section 7.4.4.

1.46 [Intentionally Omitted].

1.47 “Existing Alnylam In-Licenses” means (a) the Third Party agreements identified as such in Section A of Schedule D and (b) any Additional Alnylam In-License included within the definition of Existing Alnylam In-Licenses pursuant to Section 6.4.2.3.

1.48 “Existing Alnylam Third Party Agreements” means the Third Party agreements identified as such in Section B of Schedule D.

1.49 “Extra Early Development Costs” has the meaning set forth in Section 2.3.1.

1.50 “FDA” means the United States Food and Drug Administration and any successor governmental authority having substantially the same function.

1.51 “Field” means the treatment, palliation and/or prevention of all human diseases.

1.52 “Finished Product” means the finished product formulation of a Licensed Product, containing Bulk Drug Product, filled into unit packages (but excluding, in the case of supply by Alnylam or its Affiliates, any automated delivery device such as an “autoinjector”) for final labeling and packaging.

1.53 “First Commercial Sale” means, with respect to a Licensed Product in a country, the first sale by MedCo or its Related Parties for end use or consumption of such Licensed Product in such country after all Regulatory Approvals legally required for such sale have been granted by the Regulatory Authority of such country.

1.54 “FTE” means [**] hours of work devoted to or in support of the Development or Manufacture of a Licensed Product, that is carried out by one or more qualified scientific or technical employees or contract personnel of a Party or its Affiliates.
1.55“FTE Cost” means, for any period, the FTE Rate multiplied by the number of FTEs in such period; provided, however, that for purposes of such calculation, no individual may account for more than one FTE in any Calendar Year.

1.56“FTE Rate” means [*] U.S. Dollars ($[*]) per FTE, increased annually beginning on January 1, 2014 and thereafter on January 1 of each succeeding year by the percentage increase in the CPI as of December 31 of the then most recently ended calendar year over the level of the CPI on December 31, 2012. As used in this definition, “CPI” shall mean the Consumer Price Index - Urban Wage Earners and Clerical Workers, U.S. City Average, All Items, 1982-84 = 100, published by the United States Department of Labor, Bureau of Labor Statistics (or its successor equivalent index) in the United States.

1.57“GAAP” means generally accepted accounting principles as practiced in the United States or, to the extent applicable, IFRS (International Financial Reporting Standards).

1.58“Generic Competition” has the meaning set forth in Section 7.4.3.

1.59“Generic Product” means, with respect to a Licensed Product in a country, another pharmaceutical product that (a) is sold by a Third Party other than a Related Party of MedCo under license from Medco in such country, (b) is authorized for use in such country in one or more of the indications for which such Licensed Product has Regulatory Approval in such country, (c) contains the same active ingredient(s) as such Licensed Product or a bioequivalent thereof, and (d) was approved for sale in such country by reference to the same or a subset of the same information that was used for obtaining the Regulatory Approval for such Licensed Product in such country without such Third Party being granted a license to such information by MedCo or its Related Parties.

1.60“Governmental Authority” means any applicable government authority, court, tribunal, arbitrator, agency, legislative body, commission or other instrumentality of (a) any government of any country or territory, (b) any state, province, county, city or other political subdivision thereof or (c) any supranational body.

1.61“IND” means an Investigational New Drug application, Clinical Trial Application or similar application or submission for approval to conduct human clinical investigations filed with or submitted to a Regulatory Authority in conformance with the requirements of such Regulatory Authority.

1.62“Indemnitee” has the meaning set forth in Section 10.3.

1.63“Initial Development Budget” has the meaning set forth in Section 2.2.1.

1.64“Initial Development Plan” has the meaning set forth in Section 2.2.1.

1.65“In-Licenses” means, collectively, the Alnylam In-Licenses and the MedCo In-Licenses.

1.66“Joint Collaboration IP” means, collectively, (a) any improvement, discovery or Know-How, patentable or otherwise, first conceived or reduced to practice or, with respect to inventions and discoveries other than patentable inventions, otherwise identified, discovered, made or developed, jointly by individuals who are employee(s), agent(s) or consultant(s) of Alnylam or its Affiliates, on the one hand, and individuals who are employee(s), agent(s) or consultant(s) of MedCo or its Affiliates, on the other hand, in the conduct of the Collaboration, and (b) any Patent Rights which claim such improvements, discoveries or Know-How during the Term.

1.67“Joint Steering Committee” or “JSC” means the joint steering committee as more fully described in Section 4.1.

1.68“Know-How” means any biological materials and other tangible materials or intangible information, including inventions, practices, methods, protocols, formulas, knowledge, know-how, trade secrets, processes, assays, skills, experience, techniques, governmental or regulatory correspondence (including conversation logs), and results of experimentation and testing, including pharmacological, toxicological and pre-clinical and clinical test data and analytical and quality control data, patentable or otherwise.

1.69“Laws” means all applicable laws, statutes, rules, regulations, orders, judgments, injunctions, ordinances or other pronouncements having the binding effect of law of any Governmental Authority.

1.70“Lead Product” has the meaning set forth in Section 2.2.2.

1.71“Licensed Compound” has the meaning set forth in Section 1.89.

1.72“Licensed Product” means any siRNA Product, including ALN-PCS02 and ALN-PCSsc.

1.73“Licensing Party” has the meaning set forth in Section 6.4.2.2.

1.74“Licensor Party” has the meaning set forth in Section 12.2.4.
1.75"Losses" has the meaning set forth in Section 10.1.

1.76"Major Market Country" means the United States, the United Kingdom, France, Germany, Italy, Spain, Japan, or China.

1.77"Manufacturing" or "Manufacture" means, as applicable, all activities associated with the production, manufacture, processing, filling, finishing, packaging, labeling, shipping, and storage of a Licensed Product (including Bulk Drug Substance, Bulk Drug Product and Finished Product), including process and formulation development, process validation, stability testing, manufacturing scale-up, pre-clinical, clinical and commercial manufacture and analytical development, product characterization, quality assurance and quality control development, testing and release.

1.78"MedCo Collaboration IP" means (a) any improvement, discovery or Know-How, patentable or otherwise, first conceived or reduced to practice or, with respect to inventions and discoveries other than patentable inventions, otherwise identified, discovered, made or developed, solely by individuals who are employees, agents or consultants of MedCo or its Affiliates and Controlled by MedCo at any time during the Term, in each case in the conduct of the Collaboration or otherwise under this Agreement, and (b) any Patent Rights which claim such improvements, discoveries or Know-How. MedCo Collaboration IP excludes MedCo’s interest in Joint Collaboration IP.

1.79"MedCo Commercialization Plan" has the meaning set forth in Section 3.2.

1.80"MedCo Development Plan" has the meaning set forth in Section 2.2.3.

1.81"MedCo Improvements" means any improvement, discovery or Know-How, patentable or otherwise, that (a) is first conceived or reduced to practice, or with respect to inventions and discoveries other than patentable inventions, otherwise identified, discovered, made or developed, solely by individuals who are employees, agents or consultants of MedCo or its Affiliates in the course of conducting Development, Manufacturing or Commercialization activities with respect to Licensed Products under this Agreement, (b) is Controlled by MedCo or its Affiliates, and (c) constitutes (i) a new use or method of use of, or a new indication for, a Licensed Product, or (ii) an improvement that would otherwise be dominated by Alnylam Technology, including, as applicable, formulation technology. For clarity, MedCo Improvements excludes device technology for the administration of a pharmaceutical product to a human.

1.82"MedCo Indemnitees" has the meaning set forth in Section 10.2.

1.83"MedCo In-License" means any agreement between MedCo (or its Affiliates) and a Third Party pursuant to which MedCo Controls Know-How or Patent Rights that are reasonably necessary or useful for the Development, Manufacture and/or Commercialization of Licensed Products in the Territory, but solely to the extent, if any, that such agreement is designated as a MedCo In-License pursuant to Section 2.4(b).

1.84"MedCo Know-How" means Know-How in MedCo Collaboration IP and MedCo’s rights in Know-How comprising Joint Collaboration IP.


1.86"MedCo Technology" means, collectively, MedCo Know-How, MedCo Patent Rights, MedCo Collaboration IP and MedCo’s interest in Joint Collaboration IP.

1.87"MicroRNA Mimic" means a double-stranded or single-stranded oligonucleotide or analog thereof with a substantially similar base composition as a particular microRNA and which is designed to mimic the activity of such microRNA.

1.88"NDA" means a New Drug Application, Biologics License Application, Marketing Authorization Application or similar application or submission filed with a Regulatory Authority in a country or group of countries to obtain marketing approval for a biological, pharmaceutical or other therapeutic or prophylactic product in that country or in that group of countries.

1.89"Net Sales" means, for any period and for any country in the Territory, the total aggregate amount billed during such period in such country by MedCo, its Affiliates and its Sublicensees in such country for all sales of the Licensed Products to Third Parties (other than to a Sublicensee of MedCo or its Affiliates) after deducting, if not previously deducted, from the amount invoiced or received, the following deductions to the extent actually applied or taken with respect to such sales of Licensed Products:

(a) discounts (including trade, cash and quantity discounts), cash and non-cash coupons, charge back payments and rebates granted to managed health care organizations or to federal, state and local governments, their agencies, and purchasers and reimbursers or to customers;

(b) actually granted credits, allowances, discounts to and chargebacks for claims, spoiled, damaged or outdated goods, rejections or returns of the Licensed Products, including Licensed Products returned in connection with recalls or withdrawals;

(c) taxes and duties paid, absorbed or allowed which are directly related to the sale of the Licensed Product;

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(d) actual freight and insurance costs incurred in transporting the Licensed Product to customers;

(e) discounts or rebates or other payments required by applicable Law, including any governmental special medical assistance programs;

(f) customs duties, surcharges and other governmental charges incurred in connection with the exportation or importation of the Licensed Product;

(g) fee-for-service wholesaler fees, GPO administrative fees, inventory management fees paid to wholesalers, and any similar fees reasonably allocated to the Licensed Product, to the extent consistent with the usual course of dealing of MedCo or the applicable Related Party for its products other than a Licensed Product;

(h) amounts that are written off as uncollectible in accordance with the accounting procedures of MedCo or the applicable Related Party, consistently applied; provided, that if any such written-off amounts are subsequently collected, such collected amounts shall be included in Net Sales in the period in which they are subsequently collected; and

(i) any other deduction to revenue that is not described above which is required to be recorded as an adjustment to gross revenue for financial reporting purposes.

Such amounts shall be determined from the books and records of MedCo or its Related Parties, maintained in accordance with GAAP, consistently applied.

If any Licensed Product is sold as a Combination Product (as defined below), the Net Sales from the Combination Product, for the purposes of determining milestones and royalties, shall be determined by multiplying the Net Sales of the Combination Product during the applicable Calendar Quarter, by the fraction, \( A/(A+B) \), where \( A \) is the average sale price of a Sole Compound Product (as defined below) when sold separately in finished form and \( B \) is the average sale price of the other active compounds or active ingredients included in the Combination Product when sold separately in finished form, in each case during the applicable Calendar Quarter or, if sales of both the Sole Compound Product and the other active compounds or active ingredients did not occur in such period, then in the most recent Calendar Quarter in which sales of both occurred. If such average sale price cannot be determined for both the Sole Compound Product and all other active compounds or active ingredients included in the Combination Product, Net Sales for the purposes of determining milestones and royalties shall be calculated by multiplying the Net Sales of the Combination Product by the fraction of \( C/(C+D) \) where \( C \) is the fair market value of the Sole Compound Product and \( D \) is the fair market value of all other active compounds or active ingredients included in the Combination Product. In such event, MedCo shall in good faith make a determination of the respective fair market values of the Sole Compound Product and all other active compounds or active ingredients included in the Combination Product, and shall notify Alnylam of such determination and provide Alnylam with MedCo's basis for such determination. If Alnylam in good faith does not agree with such determination, Alnylam shall give MedCo written notice of its disagreement within thirty (30) days after receiving the relevant report pursuant to Sections 7.3 or 7.4, and the provisions of Section 13.12 shall apply. “Licensed Compound” means an siRNA Product subject to a license granted by Alnylam to MedCo.

1.90 “Non-Acquired Party” has the meaning set forth in Section 6.7.

1.91 “Non-Bankrupt Party” has the meaning set forth in Section 6.5.

1.92 “Non-Breaching Party” has the meaning set forth in Section 12.2.2.

1.93 “Party” means MedCo and/or Alnylam.

1.94 “Patent Rights” means all patents (including all reissues, extensions, substitutions, confirmations, re-registrations, re-examinations, supplementary protection certificates and patents of addition) and patent applications (including all provisional applications, requests for continuation, continuations, continuations-in-part and divisionals) and all equivalents of the foregoing in any country of the world.

1.95 “Payee” has the meaning set forth in Section 7.9.1.

1.96 “Paying Party” has the meaning set forth in Section 7.9.1.
1.97"[*]" means the ["*"].

1.98"Person" shall mean any natural person, corporation, unincorporated organization, partnership, association, joint stock company, joint venture, limited liability company, trust, Governmental Authority, or any other entity.

1.99"Pharmacovigilance Agreement" has the meaning set forth in Section 2.6.3.

1.100"Phase I Completion" means ["*"].

1.101"Phase I Study" means a study in humans which provides for the introduction into humans of a product, conducted in healthy volunteers or patients, to obtain initial information on product safety, tolerability, pharmacological activity or pharmacokinetics, as more fully defined in 21 C.F.R. § 312.21(a) (or the equivalent thereof outside the United States).

1.102"Phase I/II Study" means a single study in humans that includes a Phase I Study and a Phase II Study.

1.103"Phase II Study" means a study in humans of the safety, dose ranging or efficacy of a product, as further defined in 21 C.F.R. § 312.21(b) (or the equivalent thereof outside the United States).

1.104"Phase III Study" means a study in humans of the efficacy and safety of a product, which is prospectively designed to demonstrate statistically whether such product is effective and safe for use in a particular indication in a manner sufficient (alone or together with one or more other such studies) to file an application for Regulatory Approval for such product, as further defined in 21 C.F.R. § 312.21(c) (or the equivalent thereof outside the United States).

1.105"Pivotal Study" means a controlled pivotal clinical study of a product that is prospectively designed to demonstrate statistically whether such product is effective and safe for use in a particular indication in a manner sufficient to obtain Regulatory Approval to market such product in a Major Market Country.

1.106"Post-Approval Study" means a clinical study of a Licensed Product initiated in a country after receipt of Regulatory Approval for such Licensed Product in such country.

1.107"Pre-Existing Affiliates" has the meaning set forth in Section 6.7.

1.108"Product Trademark(s)" means the trademark(s) and service mark(s) for use in connection with the distribution, marketing, promotion and sale of Licensed Products, and/or accompanying logos, trade dress and/or indicia of origin. Product Trademarks specifically excludes the corporate names and logos of the Parties and their Related Parties.

1.109"Regulatory Approval" means any and all approvals, licenses, registrations or authorizations of any Regulatory Authority that are necessary for the marketing and sale of a pharmaceutical product in a country or group of countries, including pricing and/or reimbursement approval in any country in which pricing and/or reimbursement approval is required by applicable Laws.

1.110"Regulatory Authority" means any applicable government regulatory authority involved in granting approvals for the Development, Manufacturing and/or Commercialization of any Licensed Product, including the FDA and the EMA.

1.111"Regulatory Lead" has the meaning set forth in Section 2.6.1.

1.112"Regulatory Exclusivity" means, with respect to a Licensed Product in a country, any exclusive marketing right, data exclusivity right, orphan drug designation, or another exclusive right which would prevent a Generic Product version of such Licensed Product from being marketed or sold in such country, conferred by any Governmental Authority with respect to such Licensed Product in such country, other than a Patent Right.

1.113"Related Party" means, with respect to a Party, such Party's Affiliates and permitted Sublicensees.

1.114"Royalty Term" has the meaning set forth in Section 7.4.2.

1.115"Sales Milestone" has the meaning set forth in Section 7.3.

1.116"Selection Date" has the meaning set forth in Section 2.2.2.

1.117"siRNA" means a double-stranded ribonucleic acid (RNA) composition designed to act primarily through an RNA interference mechanism that consists of either (a) two separate oligomers of native or chemically modified RNA that are hybridized to one another along a substantial portion of their lengths, or (b) a single oligomer of native or chemically modified RNA that is hybridized to itself by self-complementary base-pairing along a substantial portion of its length to form a hairpin.
1.118“siRNA Product” means an siRNA composition designed to Target the human PCSK9 gene through an RNA interference mechanism, and which is not a microRNA, microRNA antagonist or MicroRNA Mimic.

1.119“Sole Compound Product” has the meaning set forth in Section 1.89.

1.120“Sublicensing Party” has the meaning set forth in Section 6.4.1.2.

1.121“Sublicensee” means, with respect to MedCo or Alnylam, as the case may be, a Third Party to whom such Party grants a sublicense under any Alnylam Technology or MedCo Technology, respectively, to Develop, Manufacture or Commercialize a Licensed Product in the Field pursuant to Section 6.1.3 or Section 6.2.3, and, with respect to Alnylam, a Third Party to whom Alnylam grants a sublicense pursuant to Section 6.2.2 under any MedCo Improvements licensed to Alnylam pursuant to Section 6.2.2.

1.122“Sublicensor Party” has the meaning set forth in Section 6.4.1.2.

1.123“Target” or “Targeting” means, with respect to an siRNA and a target gene, that such siRNA antagonizes the expression of the messenger RNA of such target gene, and with respect to a product and a target gene, that such product contains an siRNA that antagonizes the expression of the messenger RNA of such target gene.

1.124“Term” has the meaning set forth in Section 12.1.

1.125“Territory” means all countries of the world.

1.126“Third Party” means an entity other than the Parties and their Affiliates.

1.127“Third Party License Payment” means royalties, upfront fees, milestones or other amounts payable under an In-License.

1.128“Transaction Agreements” means, collectively, this Agreement, the Development Supply Agreement, any quality agreement between the Parties with respect to the supply of Licensed Product and the Pharmacovigilance Agreement.

1.129“United States” means the United States of America and its territories, possessions and commonwealths.

1.130“Valid Claim” means a claim of: (a) an issued and unexpired Patent Right, which claim has not been (i) revoked or held unenforceable, unpatentable or invalid by a decision of a court or other governmental agency of competent jurisdiction, which is not appealable or has not been appealed within the time allowed for appeal, or (ii) abandoned, disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer or otherwise, or (b) a patent application that has been pending less than [**] from the date of filing of the earliest patent application from which such patent application claims priority, which claim has not been cancelled, withdrawn or abandoned, or finally rejected by an administrative agency action from which no appeal can be taken.

2. DEVELOPMENT COLLABORATION

2.1Overview. Prior to the Effective Date, Alnylam has been engaged in the Development of Licensed Products. Under this Agreement, the Parties will collaborate in the further Development of Licensed Products, with Alnylam retaining all responsibility for the Development of Licensed Products until Phase I Completion as set forth in the Initial Development Plan, and MedCo assuming all other responsibility for the Development of Licensed Products. Initially the Collaboration will include the Development of both ALN-PCS02 and ALN-PSCsc in parallel. In accordance with the process described below, the Parties intend to select one of ALN-PCS02 or ALN-PSCsc for ongoing Development prior to the initiation of IND-enabling studies described in the Initial Development Plan.

2.2Development Plans.

2.2.1Initial Global Development Plan. The Development activities to be undertaken by Alnylam with respect to Licensed Products in the Territory prior to Phase I Completion will be set forth in a written workplan and timetable (the “Initial Development Plan”), which plan includes the Development activities to be undertaken (and all of which will be conducted by Alnylam) with respect to Licensed Products prior to Phase I Completion, and an estimated budget for such Development activities (“Initial Development Budget”). A draft of the Initial Development Plan is attached hereto as Schedule E. Alnylam shall submit an update to the Initial Development Plan for review and approval by the JSC of any material modifications or updates within forty-five (45) days of the Effective Date and thereafter on at least a semi-annual basis. The JSC shall have the right to modify the Initial Development Plan during such review and approval but only to the extent consistent with the budget and timelines contained in the Initial Development Plan attached hereto as Schedule E or as otherwise agreed by the Parties.

2.2.2Selection of Lead Product. Within thirty (30) days after the Selection Date (as defined below), the JSC shall designate one of ALN-PCS02 and ALN-PSCsc as the product to continue to Develop under the Collaboration (the designated product, the “Lead Product”). “Selection Date” means [**].
2.2.3 MedCo Development Plan. The global Development activities to be undertaken with respect to Licensed Products by MedCo, or, to the extent agreed upon by the Parties in writing, by Alnylam following Phase I Completion, will be set forth in a rolling [*] written workplan and timetable (the “MedCo Development Plan”) to be prepared, subject to JSC approval, by MedCo. Within [*] days after filing of the IND for the Lead Product in accordance with the Initial Development Plan, MedCo shall provide the initial MedCo Development Plan to the JSC for review and approval. The MedCo Development Plan shall subsequently be updated by MedCo from time to time and no less frequently than twice per Calendar Year, subject to JSC approval.

2.3 Responsibilities for Development Activities.

2.3.1 Initial Development Plan. Alnylam shall be responsible for the global Development of Licensed Products and all Development activities with respect thereto through Phase I Completion as set forth in the Initial Development Plan. Alnylam shall be responsible for one hundred percent (100%) of all Costs for the Development activities that are conducted by Alnylam for the Licensed Products in the Territory.

pursuant to the Initial Development Plan up to a total of (a) [*] dollars ($[*]), prior to the receipt by Alnylam of the Milestone Payment in Section 7.2(a)(i), or (b) [*] ($[*]), upon receipt by Alnylam of the Milestone Payment in Section 7.2(a)(i) (such amount in (a) or (b), the relevant “Development Costs Cap”); provided, however, that, Alnylam shall also bear any Costs for Development activities conducted by Alnylam pursuant to the Initial Development Plan that exceed such amount to the extent such excess Costs [*]. MedCo shall be responsible for all Costs with respect to Development activities for the Licensed Product pursuant to the Initial Development Plan that (a) are conducted by Alnylam, (b) are in excess of the then-applicable Development Costs Cap, and (c) are approved by the JSC (the “Extra Early Development Costs”).

2.3.2 MedCo Development Plan. MedCo shall be responsible for all Development activities with respect to Licensed Products under the MedCo Development Plan and, as and to the extent mutually agreed by the Parties in writing, Alnylam will assist MedCo in such Development activities under the MedCo Development Plan. MedCo shall be responsible for one hundred percent (100%) of all costs and expenses with respect to such Development activities that are conducted by or on behalf of MedCo and, if agreed upon in writing by the Parties, all Costs with respect to such Development activities that are conducted by Alnylam after Phase I Completion pursuant to the MedCo Development Plan.

2.3.3 Development and Certain Supply Costs. Within thirty (30) days following the end of each Calendar Quarter in which Costs are incurred by Alnylam under the Initial Development Plan or the MedCo Development Plan or pursuant to Section 5.1(a), Alnylam shall prepare and deliver to MedCo a quarterly report summarizing such Costs incurred during such period. Alnylam shall submit any additional information reasonably requested by MedCo related to such Costs included in its report within [*] Business Days after its receipt of such request. Alnylam shall issue concurrently an invoice to MedCo for any Extra Early Development Costs incurred by Alnylam and/or any Costs incurred by Alnylam pursuant to the MedCo Development Plan in conducting activities to be conducted by Alnylam as agreed upon in writing by the Parties, and MedCo shall pay all amounts within [*] days after its receipt of the invoice. Alnylam and its Affiliates shall keep complete and accurate records in sufficient detail to enable the payments payable hereunder to be determined. Commencing after Alnylam first issues such an invoice, MedCo shall have the right to audit the records of Alnylam with respect to any such Costs included in such reports, in accordance with Section 7.5.

2.4 Diligence.

(a) After the JSC’s selection of the Lead Product, MedCo will use Commercially Reasonable Efforts to (i) Develop at least one Licensed Product and obtain Regulatory Approval of at least one Licensed Product in each Major Market Country and (ii) subject to Section 2.3.2, perform the Development activities under the MedCo Development Plan.

(b) Alnylam will use Commercially Reasonable Efforts to perform the Development activities under the Initial Development Plan and, subject to Section 2.3.2, those activities under the MedCo Development Plan which Alnylam has agreed in writing to undertake; provided, however, that except as expressly provided in this Agreement or otherwise agreed to in writing by Alnylam, in no event will Alnylam be required to perform any activities under the Initial Development Plan or the MedCo Development Plan with respect to Licensed Products that would require Alnylam to incur Costs in excess of the then-applicable Development Costs Cap, unless paid or payable by MedCo as Extra Early Development Costs. Alnylam will be excused from its obligation to perform its affected Development and Manufacturing obligations with respect to Licensed Products under the Transaction Agreements during any period of time with respect to which Alnylam cannot perform such obligations to the extent that, (i) Alnylam becomes aware that the performance of such obligations would infringe Patent Rights that MedCo Controls and are reasonably necessary for such performance by Alnylam, and (ii) Alnylam is not protected by any safe harbor provisions with respect to claims that it would infringe such Patent Rights. The Parties agree to promptly discuss in good faith a mutually agreed resolution to such a situation. If the Parties agree in writing that MedCo will grant Alnylam a license or sublicense under such Patent Rights, then unless otherwise agreed by the Parties in writing, such Patent Rights will be considered MedCo Patent Rights, and if such Patent Rights are licensed to MedCo or its Affiliate by a Third Party, such sublicense shall be subject to the relevant license agreement to MedCo or its Affiliate from such Third Party and such agreement shall be designated a MedCo In-License.

2.5 Records and Reports.

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2.5.1 Prior to the date that is [**] days after Phase I Completion, Alnylam shall prepare and deliver to the JSC a quarterly written report summarizing Alnylam’s Development activities for Licensed Products performed to date (or updating such report for activities performed since the last such report submitted hereunder, as applicable). Within [**] days after Phase I Completion Alnylam shall deliver to the JSC a final report of Alnylam’s Development activities for the Licensed Products. After Phase I Completion, MedCo shall prepare and deliver to the JSC, by no later than each [**] (for the period ending December 31 of the prior Calendar Year), written reports summarizing Development activities for Licensed Products performed to date (or updating such report for activities performed since the last such report submitted hereunder, as applicable), with Alnylam providing to MedCo, in accordance with the MedCo Development Plan, written reports summarizing Alnylam’s activities (if any) under the MedCo Development Plan. Each Party will provide the members of the JSC with written copies of all materials they intend to present at a JSC meeting. The JSC may also request at any time specific material data or information related to Collaboration activities or that a written report be prepared in advance of any meeting summarizing certain material data and information arising out of the conduct of the Collaboration activities, and the Party or appropriate committee to whom such request is made shall promptly provide to the other Party or JSC such report, data or information.

2.5.2 Each Party will maintain scientific records, in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes, which will fully and properly reflect all work done and results achieved in the performance of the Development activities with respect to Licensed Products by such Party. Each Party will have the right, during normal business hours and upon reasonable notice, to inspect and copy (or request the other Party to copy) all records of the other Party maintained in connection with the work done and results achieved in the performance of such Development activities, but solely to the extent access to such records is necessary for such Party to exercise its rights under this Agreement. All such records, and the information disclosed therein, will be maintained as Confidential Information by the recipient Party in accordance with Article 8.

2.6 Regulatory Matters.

2.6.1 Regulatory Filings and Interactions. Alnylam shall be the “Regulatory Lead” with respect to Licensed Products through Phase I Completion and MedCo shall be the Regulatory Lead with respect to Licensed Products thereafter. Except as otherwise provided in the Initial Development Plan or Section 2.6.2, (a) each Party will own the INDs, the NDAs and related regulatory documents submitted to the applicable Regulatory Authorities by it with respect to Licensed Products and (b) the Regulatory Lead will, as to Licensed Products, (i) oversee, monitor and coordinate all regulatory actions, communications and filings with, and submissions to, each Regulatory Authority, (ii) be responsible for interfacing, corresponding and meeting with each Regulatory Authority, and (iii) be responsible for maintaining all regulatory filings. Alnylam will promptly notify the JSC in writing of all material communications received by it from Regulatory Authorities regarding the Licensed Products and of all filings and submissions made by it to Regulatory Authorities regarding the Licensed Products; provided, however, that after Phase I Completion, Alnylam shall not communicate with any Regulatory Authority regarding any Licensed Product without MedCo’s prior written consent, except as required by Law or as requested or required by a Regulatory Authority. MedCo shall provide Alnylam with written notice of (x) all filings and submissions for Regulatory Approval regarding any Licensed Product in the Territory in a timely manner; and (y) all Regulatory Approvals obtained or denied and the filing of any IND for any Licensed Product within fifteen (15) days after such event; provided, however, that in all circumstances except as required by Law, MedCo shall inform Alnylam of such event prior to public disclosure of such event by MedCo.

2.6.2 IND Transfer; Right of Reference. Upon MedCo’s written request Alnylam will use Commercially Reasonable Efforts to promptly transfer to MedCo, at Alnylam’s expense, Alnylam’s IND for the Lead Product after Phase I Completion, and any other Alnylam Know-How reasonably requested by MedCo with respect to any such IND. During the Term, each Party will have the right to reference the other Party’s INDs, NDAs and other filings with and submissions to Regulatory Authorities with respect to Licensed Products for the purpose of conducting its Development activities under the Initial Development Plan and the MedCo Development Plan, and in the case of MedCo, to otherwise obtain Regulatory Approval of Licensed Products in the Territory.

2.6.3 Pharmacovigilance. Within [**] months after the Effective Date, the Parties will develop and agree in writing upon a pharmacovigilance agreement (“Pharmacovigilance Agreement”) that will include safety data exchange procedures governing the coordination of collection, investigation, reporting, and exchange of information concerning any adverse experiences, and any product quality and product complaints involving adverse experiences, related to Licensed Products, sufficient to enable each Party to comply with its legal and regulatory obligations.

2.7 Information Exchange. Prior to Phase I Completion, Alnylam shall provide, and shall have its Affiliates provide, to MedCo, without additional compensation, all material Know-How Controlled by Alnylam and/or its Related Parties (as applicable) relating to Licensed Products, including copies of (a) pre-clinical and clinical safety and efficacy data, (b) protocols and investigator brochures, and (c) regulatory filings, that are reasonably necessary or useful for MedCo (or its Related Parties) to perform its obligations or exploit its rights under this Agreement with respect to such Licensed Products. Promptly after Phase I Completion and on an ongoing basis throughout the Term, as requested by the JSC and to the extent not already provided to MedCo, Alnylam shall provide, and shall have its Affiliates provide, to MedCo, without additional compensation, all material Alnylam Know-How that relates to the Licensed Products, including copies of (i) pre-clinical and clinical safety and efficacy data, (ii) protocols and investigator brochures and (iii) regulatory filings, in each case that are reasonably necessary or useful for MedCo (or its Related Parties) to perform its obligations or exploit its rights under this Agreement with respect to such Licensed Products. The transfer of Alnylam Know-How reasonably necessary or useful for the Manufacture of Licensed Products by Alnylam and its Affiliates to MedCo will also be subject to the provisions of Section 5.2 and the Development Supply Agreement.

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2.8 Third Parties. The Parties shall be entitled to utilize the services of Third Party contract research and contract manufacturing organizations to perform their respective Development and Manufacturing activities under this Agreement; provided, that (a) each Party shall ensure that such Third Parties it utilizes operate in a manner consistent with the terms of this Agreement and (b) each Party shall remain at all times fully liable for its responsibilities under this Agreement. Each Party shall ensure that any agreements with such Third Parties shall include confidentiality and non-use provisions that are no less stringent than those set forth in Section 8.1 of this Agreement and shall use Commercially Reasonable Efforts to obtain ownership of, and/or a fully sublicensable license under and to, any Know-How and Patent Rights that are developed or used by such Third Parties in the performance of such agreement and are reasonably necessary or useful to Develop, Manufacture and/or Commercialize Licensed Products in the Field.

3. COMMERCIALIZATION OF THE LICENSED PRODUCTS

3.1 Responsibility and Diligence. As between the Parties, MedCo shall have the sole right and be solely responsible, at its expense, for all Commercialization activities relating to Licensed Products in the Field in the Territory. MedCo shall use Commercially Reasonable Efforts, through itself or its Related Parties, to Commercialize at least one Licensed Product in the Field in at least each Major Market Country after receipt of Regulatory Approval of such Licensed Product in the Field in such Major Market Country.

3.2 MedCo Commercialization Plan. No less than [**] months in advance of the reasonably expected first Regulatory Approval in the Territory with respect to a Licensed Product, and on an annual basis thereafter, MedCo shall prepare and deliver to Alnylam, a written non-binding plan that summarizes the Commercialization activities to be undertaken with respect to Licensed Products in the Territory in the next Calendar Year and, to the extent commercially reasonable, MedCo's plans to obtain further Regulatory Approvals and Commercialize Licensed Products in countries in the Territory in which MedCo is not then Commercializing Licensed Products, and the dates by which such activities are targeted to be accomplished (the “MedCo Commercialization Plan”). The MedCo Commercialization Plan shall subsequently be updated and modified by MedCo, from time to time and no less frequently than once per Calendar Year.

3.3 Advertising and Promotional Materials. MedCo will be responsible for the creation, preparation, production, reproduction and filing with the applicable Regulatory Authorities, of relevant written sales, promotion and advertising materials relating to Licensed Products for use in the Territory. All such promotional materials will be compliant with all Laws, and substantially consistent with the MedCo Commercialization Plan. To the extent permitted by Law, MedCo and its Related Parties shall use Commercially Reasonable Efforts to include Alnylam's (or its designee's) name with reasonable prominence on Licensed Product promotional materials related to the Licensed Product in the Territory in acknowledgement of Alnylam's contributions to the Licensed Product.

3.4 Reporting Obligations. MedCo shall prepare and deliver to Alnylam, by no later than each [**] following the first Regulatory Approval of a Licensed Product in the Field in the Territory (for the period ending December 31 of the prior Calendar Year), written reports summarizing MedCo's Commercialization activities for Licensed Products performed to date (or updating such report for activities performed since the last such report submitted hereunder, as applicable). In addition, MedCo shall provide Alnylam with written notice of the First Commercial Sale of each Licensed Product in the Territory within [**] days after such event; provided, however, that in all circumstances except as required by Law, MedCo shall inform Alnylam of such event prior to public disclosure of such event by MedCo. MedCo shall also provide such other information to Alnylam as Alnylam may reasonably request with respect to MedCo's Commercialization activities with respect to Licensed Products.

3.5 Sales and Distribution. MedCo and its Related Parties shall have the sole right and shall be responsible for the pricing of Licensed Products, booking sales, warehousing and distribution of Licensed Products in the Territory. Moreover, MedCo and its Related Parties shall have the sole right and shall be solely responsible for handling all returns of commercialized Licensed Product, as well as all aspects of Licensed Product order processing, invoicing and collection, distribution, inventory and receivables, in the Territory.

3.6 Recalls, Market Withdrawals or Corrective Actions. In the event that any Regulatory Authority issues or requests a recall or takes a similar action in connection with the Licensed Product in the Territory, or in the event MedCo determines that an event, incident or circumstance has occurred that may result in the need for a recall or market withdrawal in the Territory, MedCo shall, within [**] hours after it receives such information from such Regulatory Authority or makes such determination, advise Alnylam thereof by telephone, facsimile or e-mail.

3.7 Commercialization Expenses. As between the Parties, MedCo shall bear all costs and expenses incurred in connection with the Commercialization of Licensed Products in the Territory.

4. COLLABORATION MANAGEMENT

4.1 Joint Steering Committee. The Parties hereby establish a joint steering committee (the “JSC”) to facilitate the Collaboration as follows:

4.1.1 Composition of the Joint Steering Committee. The Development of Licensed Products hereunder shall be conducted under the direction of the JSC, which shall comprise [**] representatives of MedCo and [**] representatives of Alnylam. Each Party shall appoint its respective
representatives to the JSC from time to time, and may substitute one or more of its representatives, in its sole discretion, effective upon notice to
the other Party of such change. Each Party shall have at least one JSC representative who is a senior employee (vice president level or above),
and all JSC representatives shall be employees of the relevant Party and have appropriate expertise and ongoing familiarity with the
Collaboration. Additional non-voting representatives or consultants may from time to time, by mutual consent of the Parties, be invited to attend
JSC meetings, subject to all representatives (including the designated voting representatives) and consultants undertaking confidentiality
obligations in a written agreement (which may have been executed prior to the Effective Date) that are substantially comparable to the
requirements of Section 8.1. All proceedings for the JSC shall take place in English. Each Party shall bear its own expenses relating to
attendance at such meetings by its representatives.

4.1.2 JSC Chairperson. The JSC chairperson shall be an employee of Alnylam prior to Phase I Completion and an employee of MedCo
thereafter. The JSC chairperson's responsibilities shall include (a) scheduling meetings at least once per Calendar Quarter, but more frequently
if the JSC determines it necessary; (b) setting agendas for meetings with solicited input from other members; (c) coordinating the delivery of draft
minutes to the JSC for review and final approval; and (d) conducting meetings, including ensuring that objectives for each meeting are set and
achieved. The JSC chairperson shall have no greater authority on the JSC than any other representative of the JSC.

4.1.3 JSC Responsibilities. The JSC shall have the following responsibilities with respect to the Collaboration:

(a) reviewing reports and updates provided by Alnylam regarding the Development of Licensed Products under the Initial Development Plan,
including material modifications and updates to the Initial Development Plan provided by Alnylam in accordance with Section 2.2.1, providing
Alnylam with feedback regarding same and approving such updates and modifications to the Initial Development Plan in accordance with
Section 2.2.1;

(b)[**];

(c) approving Extra Early Development Costs in accordance with Section 2.3.1(c);

(d) reviewing reports and updates provided by MedCo regarding the Development of Licensed Products in the Territory, including reviewing and
approving the MedCo Development Plan and updates thereto in accordance with Section 2.2.3;

(e) ensuring coordination between the Parties with respect to Development activities in the Territory for Licensed Products under the MedCo
Development Plan (to the extent the Parties have agreed in writing that Alnylam should perform any such activities), and regulatory and
pharmacovigilance requirements and matters to the extent necessary for the Parties to perform their duties or exercise their rights hereunder
and for the Parties to comply with the Pharmacovigilance Agreement and the requirements of Law and Regulatory Authorities, respectively;

(f) regularly assessing the progress of Alnylam in its conduct of the Initial Development Plan and the progress of MedCo in its conduct of the
MedCo Development Plan, against the respective timelines contained therein;

(g) reviewing Alnylam Technology that would be reasonably helpful to MedCo's Development of Licensed Products and determine which of such
Alnylam Technology should be transferred to MedCo; and

(h) performing such other activities as the Parties agree in writing shall be the responsibility of the JSC.

For purposes of clarity, the JSC shall not have the authority to modify the terms of this Agreement.

4.1.4 Meetings. The first JSC meeting shall be held within [**] months after the Effective Date, and the JSC shall thereafter meet in accordance
with a schedule established by mutual written agreement of the Parties, but no less frequently than [**] per Calendar Quarter, with the location
for such meetings alternating between Alnylam's and MedCo's US facilities (or such other locations as are mutually agreed by the Parties).
Alternatively, the JSC may meet by means of teleconference, videoconference or other similar communications equipment, but at least [**]
meetings per Calendar Year shall be conducted in person.

4.2 Appointment of Subcommittees, Project Teams and Collaboration Managers. The JSC shall be empowered to create such subcommittees of
itself and project teams as it may deem appropriate or necessary. Each such subcommittee and project team shall report to the JSC, which shall
have authority to approve or reject recommendations or actions proposed thereby subject to the terms of this Agreement. The provisions of
Sections 4.1.1 and 4.1.4 shall apply to each subcommittee, mutatis mutandis, unless otherwise determined by the JSC.

4.3 Minutes. A secretary shall be appointed for each meeting and shall prepare minutes of the meeting, which shall provide a description in
reasonable detail of the discussions held at the meeting and a list of any actions, decisions or determinations approved by the JSC. The JSC
secretary shall have no greater authority on the JSC than any other representative of the JSC.

4.4 Decision-Making.
4.4.1 With respect to decisions of the JSC, the representatives of each Party shall have collectively one vote on behalf of such Party. For each meeting of the JSC, at least one (1) representative of each Party shall constitute a quorum and each Party shall use Commercially Reasonable Efforts to have its representative(s) participate in each JSC meeting. Action on any matter may be taken at a meeting, by teleconference, videoconference or by written agreement. The JSC shall attempt to resolve any and all disputes before it for decision by consensus.

4.4.2 If the JSC is unable to reach a consensus with respect to a dispute for a period in excess of [**] days, then the dispute shall be submitted to the Chief Executive Officers of Alnylam and MedCo for resolution.

4.4.3 If such escalated dispute cannot be resolved for a period in excess of [**] days, then:

[**].

4.4.4 Notwithstanding the foregoing, MedCo may not exercise its final decision-making authority (i) to require Alnylam to undertake obligations beyond those for which it is responsible, or forgo any rights, under this Agreement, (ii) to cause Alnylam to incur any Costs above the then-applicable Development Costs Cap with respect to which MedCo has not otherwise agreed to reimburse Alnylam under this Agreement, (iii) to require Alnylam to take or decline to take any action that would result in a violation of any Law or any agreement with any Third Party or the infringement of intellectual property rights of Third Parties, (iv) in a manner that excuses MedCo from any of its obligations specifically enumerated under this Agreement, or (v) to expand or narrow the responsibilities of the JSC.

4.5 Dissolution of JSC. The JSC shall be dissolved upon the First Commercial Sale of the last Licensed Product that is expected to be Developed in the Territory; provided, that after the fifth (5th) anniversary of the Effective Date Alnylam shall have the right, but not the obligation, to dissolve the JSC. Upon the dissolution of the JSC, MedCo shall have the sole rights and authority to take any action that had been within the JSC’s purview.

5. MANUFACTURE AND SUPPLY OF THE LICENSED PRODUCT

5.1 Responsibilities for Licensed Product Supply.

(a) Alnylam will be solely responsible for (i) obtaining supply of Finished Product reasonably required for the conduct of Alnylam’s obligations under the Initial Development Plan through Phase I Completion, and (ii) supplying MedCo with the quantity of Finished Product reasonably required for the first Phase II Study of the Lead Product conducted under the MedCo Development Plan (which, for clarity, may be the Phase II Study portion of a Phase I/II Study of the Lead Product initiated pursuant to the Initial Development Plan), in each case at Alnylam’s expense for the Costs of such Licensed Product, but only to the extent that such Costs, when added to the Development Costs incurred by Alnylam pursuant to the Initial Development Plan, do not exceed the then-applicable Development Costs Cap, unless paid or payable by MedCo as Extra Early Development Costs.

(b) MedCo will have the sole right and responsibility to Manufacture and supply Licensed Product for Development and Commercialization in the Territory under the MedCo Development Plan (except that Alnylam shall be responsible for supplying Licensed Product as described in clause (a)(ii) above), subject to the successful completion of the transfer of Alnylam Know-How to MedCo or its designated Third Party(ies) contract manufacturers pursuant to Section 5.3 and the Development Supply Agreement.

5.2 Development Supply Agreement. Within [**] months after the Effective Date, the Parties will negotiate in good faith and enter into a supply and technical transfer agreement (the “Development Supply Agreement”) pursuant to which Alnylam will (a) subject to the terms of Section 5.3, promptly provide MedCo or Third Party contract manufacturer(s) selected by MedCo and reasonably acceptable to Alnylam with Alnylam Know-How reasonably necessary or useful for the Manufacture of the Bulk Drug Substance, Bulk Drug Product and Finished Product, as the case may be, and shall make available its personnel on a reasonable basis to consult with MedCo with respect thereto, all at MedCo’s expense for the Costs reasonably incurred by Alnylam in connection with such technology transfer activities; and (b) supply Finished Product to MedCo as set forth in Section 5.1(a)(ii). The terms and conditions of the Development Supply Agreement shall be commercially reasonable and consistent with industry standards, as well as, if applicable, Alnylam’s agreements with its Third Party contract manufacturers.

5.3 Technology Transfer. Subject to the terms of the Development Supply Agreement, as soon as reasonably practicable, but in no event later than the fifth (5th) anniversary of the Effective Date, Alnylam shall initiate a technology transfer to MedCo, or to its Third Party manufacturer(s) of Licensed Product, selected by MedCo and reasonably acceptable to Alnylam, of Alnylam Know-How that is reasonably necessary or useful for the Manufacture of the Licensed Product, and shall make available its personnel on a reasonable basis to consult with MedCo or such Third Party manufacturer(s) with respect thereto, at MedCo’s expense, including the Costs reasonably incurred by Alnylam in connection with such technology transfer activities. MedCo shall reimburse Alnylam such Costs incurred with respect to such Manufacturing technology transfer within [**] days after receipt of an invoice therefor. Alnylam and its Affiliates shall keep complete and accurate records in sufficient detail to enable the payments payable hereunder to be determined. Alnylam shall not be required to perform technology transfer to more than one Third Party manufacturer for each stage of the Licensed Product supply chain (i.e., Bulk Drug Substance, Bulk Drug Product and Finished Product). Promptly after MedCo’s written request, Alnylam shall use Commercially Reasonable Efforts to assign to MedCo any manufacturing agreement between Alnylam and a Third Party that is solely related to the manufacture of Licensed Products. Such assignment shall be subject to the terms and conditions of such agreement, including any required consents of such Third Party and MedCo’s written agreement to assume all the obligations of Alnylam under such agreement to be undertaken after such assignment, but Alnylam shall remain solely responsible for its...
obligations under such agreement arising prior to such assignment. Except as provided in the immediately preceding sentence, MedCo shall be solely responsible for contracting with such Third Party manufacturer (and any other Third Party manufacture to whom Alnylam has initiated technology transfer as set forth in this Section 5.3) for the supply of such Licensed Product and Alnylam shall have no obligations under such agreement between MedCo and such Third Party manufacturer. Alnylam shall use Commercially Reasonable Efforts to obtain any such consent in a form reasonably acceptable to MedCo.

5.4 Additional Licensed Product Supply. MedCo agrees to consider, and the Parties agree to discuss in good faith, the manufacture and supply of Bulk Drug Substance, Bulk Drug Product and/or Finished Product by Alnylam (or its designee) to MedCo for MedCo's further Development activities and/or for Commercial sale in the Territory; provided, however, that nothing in the foregoing sentence shall be construed to require the Parties to agree to such an arrangement.

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6. LICENSES

6.1 License Grants to MedCo.

6.1.1 Development and Commercialization License. Subject to the terms and conditions of this Agreement, including Section 6.1.4, Alnylam hereby grants MedCo a non-transferable (except as provided in Section 13.1), sublicenseable (subject to Section 6.1.3), exclusive license under Alnylam Technology to Develop and Commercialize Licensed Products in the Field in the Territory. Such license shall be royalty-bearing for the Royalty Term applicable to each Licensed Product in each country in the Territory, and, after the expiration of the Royalty Term applicable to such Licensed Product in such country, shall convert to a fully paid-up, irrevocable, perpetual, non-exclusive, sublicenseable (subject to Section 6.1.3) license to Develop and Commercialize such Licensed Product in the Field in such country.

6.1.2 Manufacturing License. Subject to the terms and conditions of this Agreement, including those set forth in Article 5 and Section 6.1.4, Alnylam hereby grants MedCo a non-transferable (except as provided in Section 13.1), sublicenseable (subject to Section 6.1.3), worldwide, royalty-bearing, exclusive license under Alnylam Technology to Manufacture Licensed Products for Development of Licensed Products after Phase I Completion and for Commercialization in the Field in the Territory. Such license shall be royalty-bearing for the Royalty Term applicable to each Licensed Product in each country in the Territory, and, after the expiration of the Royalty Term applicable to such Licensed Product in such country, shall convert to a fully paid-up, irrevocable, perpetual, non-exclusive, sublicenseable (subject to Section 6.1.3) license to Manufacture such Licensed Product for Development of Licensed Products after Phase I Completion and for Commercialization in the Field in such country.

6.1.3 Sublicensing Terms.

(a) MedCo shall have the right to sublicense any of its rights under Section 6.1.1 and 6.1.2 to any of its Affiliates or to any Third Party without the prior written consent of Alnylam, subject to the requirements of this Section 6.1.3, except that Alnylam's prior written consent shall be required for any sublicense to a Third Party of either (i) all or substantially all of MedCo's rights under this Agreement, or (ii) all or substantially all of MedCo's rights to Develop and Commercialize Licensed Products in the United States.

(b) Each sublicense granted by MedCo pursuant to this Section 6.1.3 shall be subject to the terms and conditions of this Agreement and shall contain terms and conditions consistent with those in this Agreement. MedCo shall promptly provide Alnylam with a copy of the fully executed sublicense agreement covering any Commercialization sublicense granted hereunder, and each such sublicense agreement shall contain the following provisions: (i) a requirement that the Sublicensee comply with confidentiality and non-use provisions that are no less stringent than Section 8.1 with respect to Alnylam's Confidential Information; provided, however, that if such sublicense agreement contains a sublicense of Licensed Product sales rights, such sublicense agreement shall also contain the following provisions: (x) a requirement that the Sublicensee submit applicable sales or other reports to MedCo to the extent necessary or relevant to the reports required to be made or records required to be maintained under this Agreement; and (y) the audit requirement set forth in Section 7.5; and (ii) subject to Section 6.4, any other provisions applicable to a Sublicensee required under any Alnylam In-License or necessary to allow Alnylam or its Affiliates to comply with its obligations thereunder, to the extent that MedCo had been made aware of such provisions prior to entering into such sublicense, including any such provision regarding diligence, insurance, indemnification, confidentiality, reporting, audits, publication, data sharing or regulatory matters.

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(c) If MedCo becomes aware of a material breach of any sublicense by a Sublicensee of the rights granted to MedCo under this Section 6.1, MedCo shall promptly notify Alnylam of the particulars of the same and use Commercially Reasonable Efforts to cause the Sublicensee to comply with all the terms of the sublicense necessary for MedCo's compliance with the terms of this Agreement. In the event that (i) the Sublicensee has failed to cure a material breach of such obligations within [*] days after notice of such breach and (ii) such material breach also constitutes a breach of this Agreement, MedCo shall terminate the sublicense at the request of Alnylam; provided, however, that, if such Sublicensee disputes that it has materially breached such obligations, or disputes that it has not timely cured a breach of such obligations, MedCo shall not be obligated to terminate such sublicense until such dispute is resolved by settlement, or in a final, non-appealable decision of a court or arbitrator, finding that such Sublicensee had materially breached such sublicense and had not timely cured such material breach. Notwithstanding any sublicense, MedCo shall remain primarily liable to Alnylam for the performance of all of MedCo's obligations under, and
6.1.4 Retained Rights. Notwithstanding the license grants in Sections 6.1.1 and 6.1.2, Alnylam retains the rights under Alnylam Technology (a) to Develop and Manufacture Licensed Products in the Field in the Territory solely for the purpose and only to the extent necessary for the performance of its obligations under the Transaction Agreements, and (b) for all internal basic and preclinical research purposes, in each case including the right to collaborate with and issue sublicenses to academic collaborators and/or Third Party contractors involved in such research activities.

6.2 License Grants to Alnylam.

6.2.1 Development and Manufacturing License. Subject to the terms and conditions of this Agreement, MedCo hereby grants Alnylam a non-transferable (except as provided in Section 13.1), sublicenseable (subject to Section 6.2.3), non-exclusive, worldwide, royalty-free license, under MedCo Technology, to perform Alnylam's Development and Manufacturing obligations with respect to Licensed Products under the Transaction Agreements.

6.2.2 MedCo Improvements License. Subject to the terms and conditions of this Agreement, MedCo hereby grants Alnylam a non-transferable (except as provided in Section 13.1), sublicenseable (subject to Section 6.2.3), worldwide, non-exclusive, royalty-free license under any MedCo Improvements to research, develop, manufacture and/or commercialize products containing siRNA molecules in the Field and in the Territory. Such license is subject to the exclusive license grants to MedCo under Section 6.1 and the terms of Section 9.5.1.

6.2.3 Sublicensing Terms.

(a) Alnylam shall have the right to sublicense any of its rights under Section 6.2.1 to any of its Affiliates or to any Third Party contractor without the prior written consent of MedCo, subject to the requirements of this Section 6.2.3. Alnylam shall have the right to sublicense any of its rights under Section 6.2.2 or Section 12.3(b) to any of its Affiliates or to any Third Party without the prior written consent of MedCo, subject to the requirements of this Section 6.2.3.

(b) Each sublicense granted by Alnylam pursuant to this Section 6.2.3 shall be subject to the terms and conditions of this Agreement and shall contain terms and conditions consistent with those in this Agreement. Each such sublicense agreement shall contain the following provisions: (i) a requirement that the Sublicensee comply with confidentiality and non-use provisions that are no less stringent than Section 8.1 with respect to MedCo's Confidential Information, and (ii) subject to Section 6.4, any other provisions applicable to a Sublicensee required under any MedCo In-License or necessary to allow MedCo or its Affiliates to comply with its obligations thereunder, to the extent that Alnylam had been made aware of such provisions prior to entering into such sublicense, including any such provision regarding diligence, insurance, indemnification, confidentiality, reporting, audits, publication, data sharing or regulatory matters.

(c) If Alnylam becomes aware of a material breach of any sublicense by a Sublicensee of the rights granted to Alnylam under this Section 6.2 or Section 12.3(b), Alnylam shall promptly notify MedCo of the particulars of the same and use Commercially Reasonable Efforts to cause the Sublicensee to comply with all the terms of the sublicense necessary for Alnylam's compliance with the terms of this Agreement. In the event that (i) the Sublicensee has failed to cure a material breach of such obligations within *** days after notice of such breach and (ii) such material breach also constitutes a breach of this Agreement, Alnylam shall terminate the sublicense at the request of MedCo; provided, however, that, if such Sublicensee disputes that it has materially breached such obligations, or disputes that it has not timely cured a breach of such obligations, Alnylam shall not be obligated to terminate such sublicense until such dispute is resolved by settlement, or in a final, non-appealable decision of a court or arbitrator, finding that such Sublicensee had materially breached such sublicense and had not timely cured such material breach. Notwithstanding any sublicense, Alnylam shall remain primarily liable to MedCo for the performance of all of Alnylam's obligations under, and Alnylam's compliance with all terms and conditions of, this Agreement.

6.3 Joint Collaboration IP. Subject to the rights and licenses granted to, and the obligations of, each Party under this Agreement, including MedCo's obligations under Section 7.4 during the Term, each Party shall have the right to exploit its interest in Joint Collaboration IP without the consent of and without accounting to the other Party.

6.4 In-Licenses and Existing Alnylam Third Party Agreements.

6.4.1 Compliance with In-Licenses.

6.4.1.1 All licenses and other rights granted to MedCo under this Article 6 (including any sublicense rights) are subject to the rights and obligations of Alnylam and its Affiliates under the Alnylam In-Licenses and the Existing Alnylam Third Party Agreements. All licenses and other rights granted to Alnylam under this Article 6 and Section 12.3(b) (including any sublicense rights) are subject to the rights and obligations of MedCo and its Affiliates under the MedCo In-Licenses.
6.4.1.2 Subject to Section 6.4.1.3, (a) each Party (the “Sublicensed Party”) granted a sublicense under any of the In-Licenses of the other Party (the “Sublicensor Party”) shall comply with all applicable terms and conditions of the In-Licenses of the Sublicensor Party to the extent (i) required by the terms of such In-Licenses with respect to a sublicense under the terms of such In-License to the extent applicable to (A) the Sublicensed Party’s rights or obligations relating to the Development, Manufacture or Commercialization of Licensed Products under any of the Transaction Agreements or (B) the filing, prosecution, maintenance, extension, defense, enforcement, patent challenge or the further sublicensing of the Alnylam Technology (if Alnylam is the Sublicensor Party) or the MedCo Technology (if MedCo is the Sublicensor Party) to the extent relevant to the Sublicensed Party’s rights or obligations relating to the Development, Manufacture or Commercialization of Licensed Products under any of the Transaction Agreements, and (ii) the Sublicensed Party has been given written notice or provided a copy of such provisions on or prior to the later of (x) the Effective Date or (y) the date on which such In-License is first required to have been provided to the Sublicensed Party hereunder (provided that, with respect to an amendment thereto, such amendment is consistent with the last sentence of Section 6.4.4), and (b) each Sublicensed Party shall perform and take such actions as may be required to allow the Sublicensor Party to comply with its obligations under the Sublicensor Party’s In-Licenses, to the extent (i) applicable to (A) the Sublicensed Party’s rights or obligations relating to the Development, Manufacture or Commercialization of Licensed Products under any of the Transaction Agreements or (B) the filing, prosecution, maintenance, extension, defense, enforcement, patent challenge or the further sublicensing of the Alnylam Technology (if Alnylam is the Sublicensor Party) or the MedCo Technology (if MedCo is the Sublicensor Party) to the extent relevant to the Sublicensed Party’s rights or obligations relating to the Development, Manufacture or Commercialization of Licensed Products under any of the Transaction Agreements and (ii) that the Sublicensed Party had been given written notice or provided a copy of such provisions on or prior to the later of (x) the Effective Date or (y) the date on which such In-License is first required to have been provided to the Sublicensed Party hereunder (provided that, with respect to an amendment thereto, such amendment is consistent with the last sentence of Section 6.4.4), including any such obligations relating to sublicensing, patent matters, confidentiality, reporting, audit rights, indemnification and diligence. Without limiting the foregoing, each Sublicensed Party shall prepare and deliver to the Sublicensor Party any additional reports required under the applicable In-Licenses of the Sublicensor Party, in each case reasonably sufficiently in advance to enable the Sublicensor Party to comply with its obligations under the applicable In-Licenses, to the extent that the Sublicensed Party had been made aware of such provisions with reasonably sufficient time prior to the date on which such compliance is required in order for such Sublicensed Party, or its Related Parties, to properly prepare such reports, using Commercially Reasonable Efforts, including reasonably sufficient time to gather, analyze, format and review the relevant information (to the extent not already required to be provided to the Sublicensor Party under any Transaction Agreement other than pursuant to an In-License Agreement of the Sublicensor Party).

6.4.1.3 The Parties acknowledge that the terms of any In-License may be subject to interpretation. The Parties shall cooperate with each other in good faith to support each Sublicensed Party in complying with its obligations, in accordance with this Section 6.4, under an In-License pursuant to which such Sublicensed Party has been granted a sublicense pursuant to this Agreement. Without limitation to the foregoing, the Parties shall, from time to time, upon the reasonable request of either Party, discuss the terms of any In-License and agree upon, to the extent reasonably possible, a consistent interpretation of the terms of such In-License in order to, as fully as possible without imposing an unreasonable burden on the normal business activities of any Party, allow the Sublicensor Party and the Sublicensed Party to comply with the terms of such In-License, without imposing an unnecessarily higher burden on one Party than the other with respect to compliance with the terms of such In-License. Promptly after a Party reaches a conclusion or obtains information that such interpretation is or may be incorrect, it shall share such conclusion or information with the other Party and the Parties shall discuss such conclusion or information.

6.4.1.4 Each Sublicensor Party shall ensure that, to the fullest extent permitted under the relevant In-License, any Confidential Information of the Sublicensed Party disclosed to the relevant Third Party as required by such In-License shall be protected as confidential information of the Sublicensor Party in accordance with such In-License.

6.4.1.5 Each Sublicensor Party agrees, upon the Sublicensed Party’s request, to provide the Sublicensed Party with copies of any In-Licenses to which the Sublicensed Party is a party (other

than any amendments or side letters thereto which are not materially relevant to the rights granted to, and the obligations imposed on, the Sublicensed Party under this Agreement). Each Sublicensor Party shall promptly provide the Sublicensed Party with a copy of any amendment, including any side letter, to any In-License of the Sublicensor Party, to the extent relevant in any way to the rights or obligations of the Sublicensed Party and whether or not such amendment is consistent with the obligations of the Sublicensor Party under the last sentence of Section 6.4.4. Confidential Information of the Sublicensor Party or its counterparty may be redacted from such copies, except to the extent that such information is required in order to enable the Sublicensed Party to comply with its obligations to the Sublicensor Party under this Agreement with respect to such In-License or in order to enable the Sublicensor Party to ascertain compliance with the provisions of this Agreement.

6.4.1.6 If the Sublicensor Party receives written notice from the relevant Third Party that the Sublicensor Party is in material breach of its In-License such that it would materially adversely affect the rights of the Sublicensed Party under this Agreement, and if the Sublicensor Party determines that it cannot or chooses not to cure or otherwise resolve any such alleged breach or default, then the Sublicensor Party shall so notify the Sublicensed Party within ten (10) Business Days of such determination.

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6.4.1.7 To the extent that the Sublicensor Party receives written notice from the relevant Third Party that the Sublicensed Party is in material breach of an obligation imposed on the Sublicensed Party under an In-License of the Sublicensor Party pursuant to this Section 6.4, the Sublicensor Party shall promptly provide the Sublicensed Party with a copy of such breach notice, and any other relevant documents, received from such Third Party, but in no event more than five (5) Business Days after the Sublicensor Party’s receipt thereof.

6.4.2 New In-Licenses; Additional Alnylam In-Licenses.

6.4.2.1 Alnylam Negotiation of Future Alnylam In-Licenses. Subject to Section 6.4.2.4, in the event that Alnylam or its Affiliate determines to enter into an agreement with a Third Party after the Effective Date pursuant to which Alnylam or its Affiliate would acquire a license under Patent Right(s) that Covers the development, manufacture or commercialization of pharmaceutical products comprised of siRNA compositions (other than microRNAs, microRNA antagonists or MicroRNA Mimics) in the Field and the Territory, and if such a license with respect to Licensed Products in the Field is available, then Alnylam shall use best efforts to ensure that the terms of such license applicable to Licensed Products in the Field are not materially less favorable than the terms applicable to other pharmaceutical products containing siRNA compositions in the Field under such license agreement.

6.4.2.2 Acceptance of Future Alnylam In-Licenses. In the event that Alnylam (the “Licensing Party”) or its Affiliate enters into an agreement with a Third Party after the Effective Date that meets the criteria set forth in clause (b) of the definition of Alnylam In-License, then Alnylam shall promptly provide MedCo with notice and a copy of the applicable Third Party agreement. Within thirty (30) days following receipt of such notice, MedCo will decide, in its sole discretion, whether to accept the applicable Third Party agreement as an Alnylam In-License, and provide notice of such decision to Alnylam. In the event that MedCo declines to accept such agreement as an Alnylam In-License, any rights granted to MedCo thereunder will not be deemed to be “Controlled” by Alnylam or licensed to MedCo under this Agreement, and will not be subject to the payment provisions under this Agreement relating to In-Licenses. In the event that MedCo accepts such Third Party agreement as an Alnylam In-License, such agreement will thereafter be included within the definition of Alnylam In-License, and any rights granted to Alnylam thereunder will be deemed to be “Controlled” by Alnylam and sublicensed to MedCo pursuant to the terms of this Agreement.

6.4.2.3 Additional Alnylam In-Licenses. MedCo shall have the option, exercisable during the Term upon written notice to Alnylam, and on an Additional Alnylam In-License basis, to expand the definition of Alnylam Patent Rights under this Agreement to include the Patent Rights Controlled by Alnylam under such Additional Alnylam In-License. Upon receipt of such written notice from MedCo, then such agreement will thereafter be included within the definition of Existing Alnylam In-Licenses, and all rights granted to Alnylam thereunder will be deemed to be “Controlled” by Alnylam and sublicensed to MedCo under this Agreement effective as of the date of such written notice, and Schedule D will be updated accordingly.

6.4.2.4 Product-Specific Rights. As between the Parties, MedCo and its Affiliates shall have the sole right to enter into an agreement with a Third Party after the Effective Date to acquire a license with respect to Licensed Products in the Field under any Patent Right that (a) Covers the Development, Manufacture or Commercialization of any Licensed Product and (b) if such license had been acquired by Alnylam, would be an Alnylam Product-Specific Patent Right.

6.4.3 Payments Under In-Licenses.

6.4.3.1 Alnylam shall bear [**] percent ([**]%) of any Third Party License Payments under the Alnylam In-Licenses, other than the payments described in Section 6.4.3.2, that become payable based on the licensing or sublicensing to MedCo of rights thereunder, or the exercise by MedCo of rights thereunder, with respect to Licensed Products.

6.4.3.2 Subject to Sections 6.1.3(a), and 7.4.5 (to the extent applicable), MedCo shall bear [**] percent ([**]%) of, and shall reimburse Alnylam for:

(a) [**] and, if MedCo exercises its option pursuant to Section 6.4.2.3 with respect to [**], under the [**], that become payable based on the Manufacture or Commercialization by MedCo or its Related Parties of Licensed Products; provided, however, that (i) such [**], as the case may be, shall not [**] as set forth as of the Effective Date in such [**], as applicable, and (ii) the [**] taken together shall not exceed (x) with respect to [**], (A) on or prior to [**], and (B) after [**] (as defined on Schedule D), [**] (as defined on Schedule D) and, [**], which cover [**], [**]; and (y) with respect to [**], (A) on or prior to [**], and (B) after [**], which cover [**].

(b) [**], other than the [**], that become payable based on the Manufacture or Commercialization by MedCo or its Related Parties of Licensed Products [**]; provided, however, that the [**] under each [**] shall not [**] as set forth as of the Effective Date in such [**].

(c)
provisions are without prejudice to any rights the Non-Bankrupt Party may have arising under the Bankruptcy Code or other Laws. Necessary or desirable for the Non-Bankrupt Party to exercise such rights and licenses in accordance with this Agreement. The foregoing obtaining such intellectual property and such embodiments of intellectual property in the possession or control of Third Parties as reasonably available to obtain such intellectual property and such embodiments of intellectual property in accordance with this Agreement, and agrees to assist the Non-Bankrupt Party and its Related Parties in obtaining such intellectual property and such embodiments of intellectual property in accordance with this Agreement.

6.4.4 Maintenance of In-Licenses. Each Sublicensor Party and its Affiliates shall use its Commercially Reasonable Efforts to maintain its good standing under each of its In-Licenses (including by not initiating any patent challenges which could result in the termination of any such In-License in accordance with its terms and promptly forwarding to the relevant Third Party all reports, payments and other information and material provided by the Sublicensed Party to the Sublicensor Party which, in accordance with the terms of such In-License, are to be forwarded or paid to the relevant Third Party). Without the prior written consent of the Sublicensed Party, neither Sublicensor Party nor its Affiliates shall (a) breach any of its material obligations or waive any of its rights under any of its In-Licenses, (b) amend any of its In-Licenses in any manner that would be materially adverse to the rights granted to the Sublicensed Party under this Agreement, or (c) terminate any of its In-Licenses, including by failure to satisfy any of its diligence obligations thereunder.

6.5 Bankruptcy. All rights and licenses granted under or pursuant to this Agreement by a Party to the other, including those set forth in Sections 6.1 and 6.2, are and shall otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy Code, licenses of right to “intellectual property” as defined under Section 101 of the U.S. Bankruptcy Code. The Parties agree that the Parties and their respective Related Parties, as sublicensees of such rights under this Agreement, shall retain and may fully exercise all of their rights and elections under the U.S. Bankruptcy Code and any foreign counterpart thereto. The Parties further agree that that upon commencement of a bankruptcy proceeding by or against a Party (the “Bankrupt Party”) under the Bankruptcy Code, the other Party (the “Non-Bankrupt Party”) will be entitled to a complete duplicate of, or complete access to (as the Non-Bankrupt Party deems appropriate), all such intellectual property and all embodiments of such intellectual property. Such intellectual property and all embodiments of such intellectual property will be promptly delivered to the Non-Bankrupt Party (a) upon any such commencement of a bankruptcy proceeding and upon written request by the Non-Bankrupt Party, unless the Bankrupt Party elects to continue to perform all of its obligations under this Agreement; or (b) if not delivered under (a) above, upon the rejection of this Agreement by or on behalf of the Bankrupt Party and upon written request by the Non-Bankrupt Party. The Bankrupt Party (in any capacity, including debtor-in-possession) and its successors and assigns (including any trustee) agrees not to interfere with the exercise by Non-Bankrupt Party or its Related Parties of its rights and licenses to such intellectual property and such embodiments of intellectual property in accordance with this Agreement, and agrees to assist the Non-Bankrupt Party and its Related Parties in obtaining such intellectual property and such embodiments of intellectual property in accordance with this Agreement, and agrees to assist the Non-Bankrupt Party and its Related Parties in obtaining such intellectual property and such embodiments of intellectual property in accordance with this Agreement.

6.6 No Other Rights. Except as otherwise expressly provided in this Agreement, under no circumstances shall a Party, as a result of this Agreement, obtain any ownership interest or other right in any Know-How, Patent Rights or other intellectual property rights of the other Party, including items owned, controlled or developed by the other Party, or provided by the other Party to the receiving Party at any time pursuant to this Agreement.

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6.7 No Reach Through to Acquirer IP. Notwithstanding anything in this Agreement to the contrary, following the closing of a Change of Control of a Party (the "Acquired Party"), the Parties agree that the other Party (the "Non-Acquired Party") shall not obtain rights or access to the Patent Rights or Know-How controlled by the Acquirer (as defined below) or any of the Affiliates of such Acquirer (other than the Acquired Party and its Affiliates which exist immediately prior to the closing of such Change of Control (such Affiliates, the "Pre-Existing Affiliates")); and the Acquirer and its Affiliates (other than the Acquired Party and its Pre-Existing Affiliates) shall not obtain rights or access to the Patent Rights or Know-How controlled by the Non-Acquired Party or any of its Affiliates pursuant to this Agreement, or be bound by the restrictions set forth in Section 9.5.1. For clarity but without limitation, the Non-Acquired Party's rights in all Patent Rights and Know-How Controlled by the Acquired Party or any of its Pre-Existing Affiliates, which Patent Rights and Know-How exist as of the date of the closing of such Change of Control and are then licensed hereunder to the Non-Acquired Party, shall remain licensed to such Non-Acquired Party after the date of the closing of such Change of Control in accordance with and subject to the terms and conditions of this Agreement and shall not be affected in any manner by virtue of such Change of Control. "Acquirer" means, with respect to the Acquired Party, the Third Party that acquires such Acquired Party or its direct or indirect controlling Affiliate.

7. CERTAIN FINANCIAL TERMS

7.1 Upfront Fee. As partial consideration for the licenses and other rights granted by Alnylam to MedCo under this Agreement, and to fund Alnylam's Development Costs under the Initial Development Plan up to the Development Costs Cap under this Agreement, within five (5) days after the Effective Date,

MedCo shall pay Alnylam a non-refundable, non-creditable initial payment of Twenty-Five Million U.S. Dollars ($25,000,000).

7.2 Development Milestone Fees.

(a) As partial consideration for the licenses and other rights granted in this Agreement, and to fund Alnylam's Development Costs under the Initial Development Plan up to the Development Costs Cap under this Agreement, MedCo shall make the non-refundable, non-creditable milestone payments to Alnylam set forth below no later than [**] days after the earliest date on which MedCo becomes aware that the corresponding milestone event has first been achieved with respect to a Licensed Product.

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<tr>
<th>Milestone Event</th>
<th>Milestone Payment</th>
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<td>(i) First dosing of a subject in a Phase I Study of a Licensed Product</td>
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(b) Each milestone payment by MedCo to Alnylam hereunder shall be payable only once, regardless of the number of times achieved with respect to a Licensed Product or the Licensed Products and in no event shall the total milestone payments under this Section 7.2 exceed eighty million dollars ($80,000,000).

(d) MedCo shall provide Alnylam with written notice of the achievement by MedCo or any of its Related Parties of any milestone event set forth in Section 7.2(a)(iii)-(v) within [**] days after MedCo becomes aware of such event; provided, however, that, except as required by Law, MedCo shall inform Alnylam of such event prior to any public disclosure of such event by MedCo.

(e) Alnylam shall provide MedCo with written notice of the achievement by Alnylam or any of its Related Parties of any milestone event set forth in Section 7.2(a)(i) within [**] after Alnylam becomes aware of such event; provided, however, that, except as required by Law, Alnylam shall inform MedCo of such event prior to any public disclosure of such event by Alnylam.
7.3 Sales Milestone Fees. As partial consideration for the licenses and other rights granted in this Agreement, MedCo shall make the non-refundable, non-creditable milestone payments to Alnylam set forth below no later than [*] after the end of the Calendar Year in which the corresponding milestone event (a “Sales Milestone”) has first been achieved with respect to the Licensed Products.

Aggregate Calendar Year Net Sales of the Licensed Products in the Territory Equals or Exceeds (in U.S. Dollars):

Milestone Payment

[*]

[*]

[*]

[*]

[*]

[*]

[*]

32

With respect to the foregoing Sales Milestones, payment shall be made only once for each milestone regardless of the number of times aggregate Calendar Year Net Sales for Licensed Products in the Territory reach a particular dollar threshold and in no event shall the total milestone payments under this Section 7.3 exceed one hundred million dollars ($100,000,000). If Licensed Products achieve a higher Sales Milestone in a Calendar Year without having first achieved a lower Sales Milestone in any previous Calendar Year, then the milestone payment(s) for the lower Sales Milestone(s) shall be due and payable to Alnylam concurrently with the milestone payment for the higher Sales Milestone that has been achieved. For example, if aggregate Net Sales of the Licensed Products in the Territory are [*] in the first Calendar Year, and then [*] in the next Calendar Year, then MedCo will owe Alnylam a milestone payment of [*] with respect to the second Calendar Year ([$**] for the [*] milestone and [*] for the [*] milestone).

7.4 Royalties.

7.4.1 Royalties Payable on Licensed Products. Subject to the terms and conditions of this Agreement, as partial consideration for the licenses and other rights granted in this Agreement MedCo shall pay to Alnylam royalties on aggregate Net Sales by MedCo and its Related Parties of all Licensed Products in the Territory, as follows:

Aggregate Calendar Year

Net Sales of all Licensed Products in the Territory

Royalty

(as a percentage of Net Sales)

[*]

[*]

[*]

[*]

[*]

[*]

[*]

[*]

[*]

[*]

[*]

[*]

Royalties on aggregate Net Sales shall be paid at the rate applicable to the portion of such aggregate Net Sales within each of the Net Sales levels above during such Calendar Year.

7.4.2 Royalty Term. The period during which the royalties set forth in Section 7.4.1 shall be payable, on a Licensed Product-by-Licensed Product and country-by-country basis, shall commence with the First Commercial Sale of such Licensed Product in such country and continue until the latest of (a) the expiration of the last Valid Claim of any Patent Right that is (i) included in Alnylam Technology or MedCo Improvements, and (ii)
determined.

7.4.3 Royalty Adjustment for Generic Competition. Subject to Section 7.4.6, the royalties to be paid by MedCo to Alnylam pursuant to this Section 7.4 shall be reduced by 

\[ **\% \times (\text{Net Sales in a country} \times \text{Generic Market Share}) \]


with respect to Net Sales in a country of any Licensed Product as to which Generic Competition exists. “Generic Competition” means, with respect to aLicensed Product in any country in the Territory in a given Calendar Quarter, that, during such Calendar Quarter, one or more Generic Products are commercially available in such country and such Generic Products have a combined market share (calculated on the basis of the number of units sold) of at least 

\[ **\% \]


of the aggregate market share of Licensed Products and Generic Products (based on data provided by IMS International, or if such data is not available, such other reliable data source as reasonably agreed by the Parties).

7.4.4 Royalty Adjustment for Necessary Third Party IP. Subject to Section 7.4.6, (a) if MedCo or any of its Related Parties is required to obtain a license or similar right from any Third Party under any Patent Rights that would be infringed by the practice of the Alnylam Patent Rights with respect to Licensed Products in the Field, and if MedCo or any of its Related Parties is required to pay to such Third Party a royalty, license fees or milestone payments to obtain such license or similar right with respect to the Development, Manufacture or Commercialization of Licensed Products in the Field, then the royalties to be paid by MedCo to Alnylam on Net Sales of a Licensed Product pursuant to this Section 7.4 in a Calendar Quarter shall be reduced by 

\[ **\% \times (\text{Royalty or milestone payments made to Third Party}) \]


attributable to the Development, Manufacture or Commercialization of such Licensed Product and actually paid to such Third Party to the extent MedCo, directly or indirectly, bears the cost of such payment in such Calendar Quarter, and (b) the royalties to be paid by MedCo to Alnylam on Net Sales of a Licensed Product pursuant to this Section 7.4 in a Calendar Quarter shall be reduced by 

\[ **\% \times (\text{any payments made by MedCo to any Alnylam pursuant to Section 6.4)} \]


reasonably attributable to the Development, Manufacture or Commercialization of such Licensed Product and actually paid to such Third Party to the extent MedCo, directly or indirectly, bears the cost of such payment in such Calendar Quarter.

7.4.5 Royalty Floor. Notwithstanding the foregoing provisions of this Section 7.4, in no event during the applicable Royalty Term for a Licensed Product in a country of the Territory shall the royalties payable to Alnylam hereunder for such Licensed Product in such country for any Calendar Quarter be reduced pursuant to Sections 7.4.3, 7.4.4, and 7.4.5 to less than 

\[ **\% \]


percent of the royalties payable pursuant to Section 7.4.1 as to such Licensed Product in such country for such Calendar Quarter.

7.4.6 Reports; Payment of Royalty. During the Term, following the First Commercial Sale of the Licensed Product in the Territory, MedCo shall furnish to Alnylam a written report within [**] days after the end of each Calendar Quarter showing, on a Licensed Product-by-Licensed Product and country-by-country basis, the gross sales of each Licensed Product in each country of the Territory, deductions from gross sales (itemized by deduction category) for each Licensed Product in each country of the Territory included in the calculation of Net Sales, the Net Sales in each country of the Territory of Licensed Product during the reporting period, a calculation of royalty adjustments pursuant to Section 7.4 if any, for such period and the royalties payable under this Agreement. Quarterly reports shall be due no later than the [**] day following the end of each Calendar Quarter. In addition, to the extent required under Sections 6.1.3(b) or 6.4.1, MedCo shall prepare and deliver to Alnylam any additional reports as required under the Alnylam In-Licenses and to determine any payments due under Section 6.4. Royalties shown to have accrued by each royalty report shall be due and payable on the date such royalty report is due. Along with the last report for a Calendar Year provided hereunder, MedCo will provide a final report for such entire Calendar Year that includes a calculation ofroyalty adjustments [**] (if any) for such period, and a statement on whether any reconciling payments must be made at such time to effect the intent of Section 7.4.4. Within [**] days after such statement is provided, the Party that owes any amounts to the other Party to effect such reconciliation will pay the relevant amount to the other Party. MedCo and its Related Parties shall keep complete and accurate records in sufficient detail to enable the royalties and other payments payable hereunder, and, to the extent required under Sections 6.1.3(b) or 6.4.1, by Alnylam to Third Parties under the Alnylam In-Licenses, to be determined.

7.4.7 Blended Royalty Rates. The Parties acknowledge and agree that the Patent Rights and Know-How licensed pursuant to this Agreement justify royalty rates of differing amounts with respect to the sales of Licensed Products, which rates could be applied separately to Licensed Products involving the exercise of such Licensed Patents and/or the incorporation of such Know-How, and that, if such royalties were calculated separately, royalties relating to Patent-Rights and royalties relating to Know-How would last for different terms. Notwithstanding the foregoing, the Parties have determined, for reasons of convenience, that blended royalty rates for the Patent Rights and the Know-How licensed hereunder, as set forth above, will apply during a single Royalty Term.

7.5 Audits.

7.5.1 Upon the written request of a Party and not more than [**], the other Party and its Related Parties shall permit an independent certified public accounting firm of internationally-recognized standing selected by the requesting Party and reasonably acceptable to the other Party, at
the Payee intends to take actions that will reduce, or obviate the need for, such withholding, in which case the Paying Party shall make such payment until the earliest to occur of: (a) such Business Day period has expired; (b) the Payee instructs the Paying Party that...

7.5.2If such accounting firm identifies a discrepancy made during such period, the appropriate Party shall pay the other Party the amount of the discrepancy, together with late-payment interest in accordance with Section 7.7, within [**] days after the date the requesting Party delivers to the other Party such accounting firm's written report so concluding, or as otherwise agreed by the Parties in writing. The fees charged by such accounting firm shall be paid by the requesting Party, unless such discrepancy results from a reporting error by the other Party and represents an underpayment by such other Party of at least five percent (5%) of the total amounts due from such other Party hereunder, or represents an overpayment to such other Party of at least five percent (5%) of the total amounts due to such other Party hereunder, in a Calendar Year, in which case such fees, to the extent reasonable, shall be paid by the other Party.

7.5.3To the extent required under Sections 6.1.3(b) or 6.4.1, and subject to Section 6.4, MedCo shall comply with all applicable audit requirements in the Alnylam In-Licenses and shall include in each sublicense granted by it pursuant to this Agreement a provision requiring its Sublicensees to make reports to Alnylam, to keep and maintain records of sales made pursuant to such sublicense and to grant access to such records by the independent accountants of the Person(s) that are also party to such Alnylam In-Licenses to the same extent required of MedCo under this Agreement.

7.5.4Unless an audit for a Calendar Year has been commenced prior to the [**] anniversary of the end of such Calendar Year, the calculation of royalties, Cost reimbursement and other payments payable with respect to such Calendar Year shall be binding and conclusive upon both Parties, and each Party and its Related Parties shall be released from any further liability or accountability with respect to such royalties or expense reimbursement for such Calendar Year, upon such [**] anniversary. If an audit for a Calendar Year has been commenced prior to the [**] anniversary of the end of such Calendar Year, the calculation of royalties, Cost reimbursement and other payments payable with respect to such Calendar Year shall be binding and conclusive upon both Parties, and each Party and its Related Parties shall be released from any further liability or accountability with respect to such royalties or expense reimbursement for such Calendar Year, following the conclusion of such audit.

7.5.5Each Party shall treat all financial information subject to review under this Section 7.5 or under any sublicense agreement as the audited Party's Confidential Information in accordance with the confidentiality and non-use provisions of this Agreement, and shall cause its accounting firm to enter into an acceptable confidentiality agreement with the audited Party and/or its Related Parties obligating it to retain all such information in confidence pursuant to such confidentiality agreement.

7.6Payment Exchange Rate. All payments to be made under this Agreement shall be made in United States dollars and shall be paid by bank wire transfer in immediately available funds to such bank account in the United States as may be designated in writing by the receiving Party from time to time. In the case of Net Sales made or expenses incurred by a Party and its Related Parties in currencies other than United States dollars, the rate of exchange to be used in computing the amount of United States dollars due shall be the rate of exchange utilized by such Party in its worldwide accounting system and calculated in accordance with generally accepted accounting principles in the United States consistently applied, prevailing on the last day of each Calendar Quarter for royalty payments.

7.7Late Payments. Any amount owed by a Party to the other Party under this Agreement that is not paid on or before the date such payment is due shall bear interest at a rate per annum equal to the lesser of (a) the then current one (1) month London Inter-Bank Offering Rate for US Dollars, as quoted on the British Banker's Association's website currently located at www.bba.org.uk (or such other source as may be mutually agreed by the Parties), plus [**] percentage points, per annum or (b) the highest rate permitted by Law, calculated on the number of days such payments are paid after such payments are due and compounded monthly.

7.8Blocked Payments. If, by reason of Laws in any jurisdiction in the Territory, it becomes impossible or illegal for a Party to transfer milestone payments, royalties or other payments under this Agreement to the other Party, the payor shall promptly notify the payee. During any such period described above, the payor shall deposit such payments in local currency in the relevant jurisdiction to the credit of the payee in a recognized banking institution designated by the payee or, if none is designated by the payee within a period of [**] days, in a recognized banking institution selected by the payor and identified in a written notice given to the payee.

7.9Taxes.

7.9.1The Parties acknowledge and agree that, as of the Effective Date, no deduction for any tax withholding shall be required with respect to the payments due under this Agreement. Each Party (the "Paying Party") shall use reasonable efforts to minimize tax withholding on payments made to the other Party (the "Payee"). Notwithstanding such efforts, if the Paying Party concludes that tax withholdings under the Laws of any country are required with respect to payments to the Payee, the Paying Party shall promptly notify the Payee and allow the Payee [**] Business Days to determine whether there are actions the Payee can lawfully undertake to avoid such withholding. The Paying Party shall refrain from making such payment until the earliest to occur of: (a) such [**] Business Day period has expired; (b) the Payee instructs the Paying Party that the Payee intends to take actions that will reduce, or obviate the need for, such withholding, in which case the Paying Party shall make such
payment (and future payments subject to the same or similar treatment), subject to no or such reduced withholding of tax, only after (i) it is instructed to do so by the Payee and (ii) it has received written advice from the Payee's counsel, in form and substance reasonably satisfactory to the Paying Party, that such actions have been taken, are lawful and are effective to so reduce or eliminate such withholding; or (c) the Payee instructs the Paying Party to make such payment and withhold the required amount of tax and pay it to the appropriate Governmental Authority in accordance with applicable Laws, in which case, the Paying Party shall take such actions and shall promptly thereafter provide the Payee with copies of receipts or other evidence of such withheld amount and such payment, including to the extent reasonably available to the Paying Party, such evidence as is reasonably required and sufficient to allow the Payee to document such tax withholdings adequately for purposes of claiming foreign tax credits and similar benefits. The Parties will cooperate reasonably in completing and filing documents required under the provisions of any applicable tax Laws or under any other applicable Law, in connection with the making of any required tax withholding payment, or in connection with any claim to a refund of, or credit for, any such payment. Each Party will reasonably cooperate with the other Party (at such other Party's expense and request) to minimize such taxes imposed on such other Party in accordance with applicable Laws.

7.9.2 Notwithstanding the foregoing, if, as a result of (a) the assignment of this Agreement by the Paying Party to an Affiliate or a Third Party outside of the United States or (b) the exercise by the Paying Party of its rights under this Agreement through an Affiliate or Third Party outside of the United States, foreign withholding tax in excess of the foreign withholding tax amount that would have been payable in the absence of such assignment or exercise of rights becomes payable with respect to amounts due to the Payee hereunder, such amount due to the Payee will be increased so that the amount actually paid to the Payee (after withholding of the excess withholding tax) equals the amount that would have been payable to the Payee in the absence of such excess withholding.

7.9.3 For clarity, the provisions of Sections 7.9.1 and 7.9.2 shall not apply to taxes imposed on a Party's net income.

7.10 Invoices. To the extent necessary for the Paying Party to comply with applicable Law or GAAP, the Paying Party may require the other Party to issue an invoice to the Paying Party for any amount due by the Paying Party hereunder prior to the Paying Party paying such amount.

7.11 Good Faith Disputes Over Payment Obligations. With respect to any payment due or purported to be due hereunder, the portion of any such payment which is disputed in good faith shall not be owed until the dispute is resolved, and the Parties shall use good faith efforts to promptly resolve such dispute; provided, however, that any such amount finally determined to be due shall be paid with interest pursuant to Section 7.7 from the date originally due (without regard to this Section 7.11).

8. CONFIDENTIALITY AND PUBLICATION

8.1 Nondisclosure Obligation.

(a) All Confidential Information disclosed by one Party to the other Party hereunder shall be maintained in confidence by the receiving Party and shall not be disclosed to a Third Party or used for any purpose except as set forth herein without the prior written consent of the disclosing Party, except that no information or data shall be considered Confidential Information to the extent that such information or data:

(i) is known by the receiving Party at the time of its receipt, and not through a prior disclosure by the disclosing Party, as documented by the receiving Party's business records;

(ii) is in the public domain or publicly known by use and/or publication before its receipt from the disclosing Party (or, with respect to Joint Collaboration IP, before its development hereunder), or thereafter enters the public domain or becomes publicly known through no fault of the receiving Party;

(iii) is subsequently disclosed to the receiving Party by a Third Party who may lawfully do so and is not under an obligation of confidentiality to the disclosing Party; or

(iv) is developed by the receiving Party independently of Confidential Information received from the disclosing Party (including any Joint Collaboration IP), as documented by the receiving Party's business records.
(b) Notwithstanding the obligations of confidentiality and non-use set forth above and in Section 8.2 below, a receiving Party may provide Confidential Information disclosed to it, and disclose the existence and terms of this Agreement, as may be reasonably required in order to perform its obligations and to exploit its rights under this Agreement, to (i) Related Parties, and their employees, directors, agents, consultants, advisors and/or other Third Parties for the performance of its obligations hereunder (or for such entities to determine their interest in performing such activities) in accordance with this Agreement, in each case who are obligated to keep such Confidential Information confidential on terms no less stringent than those in this Section 8.1; (ii) Governmental Authorities or other Regulatory Authorities in order to obtain patents in accordance with this Agreement, or otherwise perform its obligations or exploit its rights under this Agreement; provided, that such Confidential Information shall be disclosed only to the extent reasonably necessary to do so; (iii) the extent required by Law, including by the rules or regulations of the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States or of any stock exchange or listing entity; (iv) any bona fide actual or prospective underwriters, investors, lenders, other financing sources, acquirers, permitted sublicensees, collaborators or strategic partners and to consultants and advisors of such Party, in each case who are obligated to keep such Confidential Information confidential on terms no less stringent than those in this Section 8.1; and (v) Third Parties to the extent a Party is required to do so pursuant to the terms of an In-License.

If a Party is required by Law to disclose Confidential Information that is subject to the non-disclosure provisions of this Section 8.1 or Section 8.2, such Party shall, to the extent permitted by Law, promptly inform the other Party of the disclosure that is being sought in order to provide the other Party an opportunity to challenge or limit the disclosure obligations. Confidential Information that is required to be disclosed by Law shall remain otherwise subject to the confidentiality and non-use provisions of this Section 8.1 and Section 8.2. If either Party concludes that a copy of this Agreement must be filed with the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States, such Party will provide the other Party with a copy of this Agreement showing any provisions hereof as to which the Party proposes to request confidential treatment, will provide the other Party with an opportunity to comment on any such proposed redactions and to suggest additional redactions, and will take such Party's reasonable and timely comments into consideration before filing the Agreement.

8.2 Publication and Publicity.

8.2.1 Publication. MedCo and Alnylam each acknowledge the other Party's interest in publishing the results of the Collaboration. Each Party also recognizes the mutual interest in obtaining valid patent protection and in protecting trade secret information. Consequently, except for disclosures permitted pursuant to Section 8.1, 8.2.2(b) or 8.2.2(c), either Party wishing to make a publication or public presentation of Development results that contains the Confidential Information of the other Party shall deliver to the other Party a copy of the proposed written publication or presentation at least [***] days prior to submission for publication or presentation. The reviewing Party shall have the right (a) to propose modifications to the publication or presentation for patent reasons, trade secret reasons or business reasons, which proposals the publishing Party may accept or reject in its discretion, and (b) to request a reasonable delay in publication or presentation in order to protect patentable information in accordance with Article 11. If the reviewing Party requests a delay pursuant to clause (b), the publishing Party shall delay submission or presentation for a period of an additional [***] days to enable the non-publishing Party to file patent applications protecting such Party's rights in such information in accordance with Article 11. With respect to any proposed publications or disclosures by clinical investigators or academic or non-profit collaborators, such materials shall be subject to review under this Section 8.2 to the extent that MedCo or Alnylam, as the case may be, has the right and ability (after using Commercially Reasonable Efforts to obtain such right and ability) to do so.

8.2.2 Publicity.

(a) Except as set forth in Section 8.1 above and clause (b) below, the terms of this Agreement may not be disclosed by either Party, and no Party shall use the name, trademark, trade name or logo of the other Party or its employees in any publicity, news release or disclosure relating to this Agreement or its subject matter, without the prior express written permission of the other Party, except as may be required by Law or expressly permitted by the terms of the Transaction Agreements.

(b) Following the execution of this Agreement, the Parties shall issue a joint press release agreed to by the Parties and substantially in the form set forth in Schedule F. After such initial press release, except as provided in Sections 8.1, 8.2.2(a), or 8.2.2(c), neither Party shall issue a press release or public announcement relating to this Agreement without the prior written approval of the other Party, which approval shall not be unreasonably withheld, conditioned or delayed, except that a Party may (i) once a press release or public statement is approved in writing by both Parties, make subsequent public disclosure of the information contained in such press release or other written statement without the further approval of the other Party, and (ii) issue a press release or public announcement as required, in the reasonable judgment of such Party, by Law, including by the rules or regulations of the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States or of any stock exchange or listing entity.

(c) Either Party may issue a press release or make a public disclosure relating to this Agreement or the Parties' activities under this Agreement to the extent that such disclosure describes the commencement and/or "top-line" results of Clinical Trials of a Licensed Product conducted by such Party, the achievement by such Party of any material Development events with respect to a Licensed Product or the filing for or receipt of Regulatory Approval with respect to the Licensed Product by such Party or its Related Parties in the Territory, or amounts paid to either Party in respect of the achievement of any milestone events. Prior to making any such disclosure, the Party making the disclosure shall provide the other Party with a draft of such proposed disclosure at least five (5) Business Days (or, to the extent faster timely disclosure of a material event is
required by Law or stock exchange or stock market rules, such shorter period of time sufficiently in advance of the disclosure so that the other Party will have the opportunity to comment upon the disclosure and the disclosing Party will be able to comply with its obligations) prior to making any such disclosure, for the other Party’s review and comment, which shall be considered in good faith by the disclosing Party.

(d) Subject to Sections 8.2.1 and 8.2.2(c), MedCo and its Related Parties may make public announcements or disclosures reasonably necessary or useful to Develop or Commercialize the Licensed Products in the Field in the Territory, including disclosures necessary to recruit subjects to clinical trials and disclosures to advertise, promote and otherwise Commercialize the Licensed Products.

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9.REPRESENTATIONS, WARRANTIES AND COVENANTS; INDEMNIFICATION

9.1Mutual Representations and Warranties. Each Party represents and warrants to the other Party that as of the Effective Date:

9.1.1It is duly organized and validly existing under the laws of its jurisdiction of incorporation or formation, and has full corporate or other power and authority to enter into this Agreement, and to carry out the provisions hereof.

9.1.2It is duly authorized to execute and deliver this Agreement, and to perform its obligations hereunder, and the person or persons executing this Agreement on its behalf has been duly authorized to do so by all requisite corporate action.

9.1.3This Agreement is legally binding upon it and enforceable in accordance with its terms. The execution, delivery and performance of this Agreement by it does not conflict with any agreement, instrument or understanding, oral or written, to which it is a party and by which it may be bound, or with its charter or by-laws.

9.1.4It has not granted, and will not grant, during the Term, any right to any Affiliate or Third Party that would conflict with the rights granted to the other Party hereunder.

9.1.5Neither it nor any of its Affiliates has been debarred or is subject to debarment.

9.2Representations and Warranties of Alnylam. Except as provided in Schedule G, Alnylam represents and warrants to MedCo that as of the Effective Date:

9.2.1(a) Alnylam is the sole and exclusive owner of, or otherwise has the right to license to MedCo as set forth in this Agreement, pursuant to an Alnylam In-License (or will Control pursuant to an Additional Alnylam In-License at such time that such Additional Alnylam In-License is included as an Alnylam In-License pursuant to Section 6.4.2.3), the Alnylam Technology. (b) All of the Alnylam Technology licensed to MedCo hereunder in the Territory that is solely and exclusively owned by Alnylam or its Affiliates is free and clear of liens, charges or encumbrances, other than licenses granted to Third Parties that are not inconsistent with the rights and licenses granted to MedCo under this Agreement. (c) The Alnylam Technology and the Patent Rights licensed by Alnylam pursuant to the Additional Alnylam In-Licenses constitute all the intellectual property that Alnylam or its Affiliates own or have rights under that are or may reasonably be necessary or useful for the Development, Manufacturing and Commercialization of the Licensed Products.

9.2.2Alnylam has sufficient legal and/or beneficial title and ownership of, or sufficient license rights under, the Alnylam Patent Rights listed in Schedule C to grant the licenses to such Alnylam Patent Rights granted to MedCo pursuant to this Agreement.

9.2.3(a) To Alnylam’s knowledge, Schedule C-1 sets forth a complete and accurate list of the Alnylam Core Technology Patent Rights. (b) To Alnylam’s knowledge, Schedule C-2 sets forth a complete and accurate list of the Alnylam Product-Specific Patent Rights. (c) Schedules C-1 and C-2 collectively set forth a complete and accurate list of the Alnylam Patent Rights owned, either solely or jointly, by Alnylam or its Affiliates. (d) To Alnylam’s knowledge, Schedules C-1 and C-2 collectively set forth a complete and accurate list of the Alnylam Patent Rights licensed, either exclusively or nonexclusively, to Alnylam or its Affiliates. (e) To Alnylam’s knowledge, each issued Alnylam Patent Right remains in full force and effect. (f) Alnylam or its Affiliates have timely paid all filing and renewal fees payable with respect to such Alnylam Patent Rights for which Alnylam controls prosecution and maintenance. (g) Schedules C-1 and C-2 indicate whether each Alnylam Patent Right is owned exclusively by Alnylam or its Affiliates, is owned jointly by Alnylam and one or more Affiliates or Third Parties, or is licensed to Alnylam or its Affiliates. (h) For each Alnylam Patent Right that is owned, but not owned exclusively, by Alnylam or its Affiliates, or that is licensed to Alnylam or its Affiliates, Schedules C-1 and C-2 indicate the Third Party owner(s) and, if applicable, the Alnylam In-License pursuant to which Alnylam Controls such Alnylam Patent Right. (i) For each Alnylam Product-Specific Patent Right that is licensed, but not exclusively licensed, to Alnylam or its Affiliates, Schedule C-2 indicates the non-exclusive nature of the license. (j) For each Alnylam Core Technology Patent Right family (other than Patent Rights licensed from Isis Pharmaceuticals, Inc.) that is licensed, but not exclusively licensed, to Alnylam or its Affiliates, Schedule C-1 indicates the non-exclusive nature of the license. (k) Alnylam or its Affiliates is/are the sole and exclusive owner(s) of all Patent Rights controlled by Alnylam or its Affiliates. (l) Alnylam or its Affiliates is/are the sole and exclusive owner(s) of all Patent Rights licensed to Alnylam or its Affiliates. (m) Alnylam or its Affiliates is/are the sole and exclusive owner(s) of all Patent Rights owned by Alnylam or its Affiliates.

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9.2.4(a) To Alnylam's knowledge, the Alnylam Product-Specific Patent Rights, are, or, upon issuance, will be, valid and enforceable patents and no Third Party has challenged or threatened to challenge the scope, validity or enforceability of any Alnylam Product-Specific Patent Right (including, by way of example, through opposition or the institution or written threat of institution of interference, nullity or similar invalidity proceedings before the United States Patent and Trademark Office or any analogous foreign Governmental Authority). (b) Alnylam has complied with all applicable Laws, including any duties of candor to applicable patent offices, in connection with its filing, prosecution and maintenance of the Alnylam Patent Rights for which Alnylam controls filing, prosecution and maintenance.

9.2.5 (a) Section A and Section C of Schedule D sets forth a complete and accurate list of all agreements between Alnylam or any of its Affiliates, on the one hand, and a Third Party(ies), on the other hand, entered into on or prior to the Effective Date and pursuant to which Alnylam or any of its Affiliates licenses or acquires any intellectual property rights owned or controlled by Alnylam or its Affiliates which are reasonably necessary or useful to Develop, Manufacture or Commercialize Licensed Products in the Field. (b) Alnylam and its Affiliates have not granted any Third Party, and are not under any obligation to grant any Third Party, any right to Develop, Manufacture or Commercialize Licensed Products in the Field. except for the non-exclusive licenses granted to the Third Parties pursuant to the Existing Alnylam Third Party Agreements. (c) Alnylam Controls all Know-How and Patent Rights licensed to Alnylam under the Existing Alnylam In-Licenses that are necessary or useful for MedCo to Develop, Manufacture and/or Commercialize Licensed Products in the Field. (d) Without limiting the generality of the foregoing, (i) Alnylam has obtained all necessary consents (if any) and fulfilled all necessary conditions (if any) to sublicense MedCo under this Agreement, such Know-How and Patent Rights licensed to Alnylam or its Affiliates under the Existing Alnylam In-Licenses, and (ii) Alnylam has obtained all necessary consents (if any) under the Existing Alnylam Third Party Agreements to grant the licenses to MedCo to Alnylam Technology that are purported to be granted to MedCo pursuant to this Agreement. (e) At such time that an Additional Alnylam In-License is included as an Alnylam In-License pursuant to Section 6.4.2.3, Alnylam will Control all Know-How, if any, and Patent Rights licensed to Alnylam or its Affiliates under such Additional Alnylam In-License that is necessary or useful for MedCo to Develop, Manufacture and/or Commercialize Licensed Products in the Field.

9.2.6 To Alnylam's knowledge, neither Alnylam nor its Affiliates are in breach or default under any Existing Alnylam In-License or Additional Alnylam In-License, and neither Alnylam nor its Affiliates have received any written notice of breach or default with respect to any Existing Alnylam In-License or Additional Alnylam In-License.

9.2.7 Alnylam has provided MedCo with true and complete copies of all Existing Alnylam In-Licenses, Additional Alnylam In-Licenses and Existing Alnylam Third Party Agreements; provided, however, that, (a) to the extent that the terms of any such agreements require Alnylam to redact any provisions thereof before providing such agreements, or relevant portion thereof, to MedCo, Alnylam has provided MedCo with copies of such agreements, which are true and complete to the fullest extent possible under such agreements and that any provisions or portions which have not been provided to MedCo either (i) are not relevant to any obligations owed by MedCo, or rights granted to MedCo, under such agreement or any Transaction Agreement or (ii) have been summarized by Alnylam to MedCo in writing, and such summary is true and complete in all material respects; and (b) Alnylam is not required by this Section 9.2.7 to provide to MedCo copies of any amendment or side letter to any Existing Alnylam In-License, Additional Alnylam In-License or Existing Alnylam Third Party Agreement which is not materially relevant to the rights granted to, and the obligations imposed on, MedCo under this Agreement.

9.2.8 To Alnylam's knowledge, the use, Development, Manufacture or Commercialization by Alnylam or MedCo (or their respective Related Parties) of any Licensed Product as formulated and manufactured as of the Effective Date, or as intended to be formulated and manufactured as of the Effective Date, (a) does not and will not infringe any issued, valid and enforceable patent of any Third Party or (b) will not infringe the claims of any published Third Party patent application when and if such claims were to issue in scope that was valid and enforceable.

9.2.9 There is no (a) claim, demand, suit, proceeding, arbitration, inquiry, investigation or other legal action of any nature, civil, criminal, regulatory or otherwise, pending or, to Alnylam's knowledge, threatened against Alnylam or any of its Affiliates or (b) judgment or settlement against or owed by Alnylam or any of its Affiliates, in each case in connection with the Alnylam Technology or any Licensed Product.

9.2.10 To Alnylam's knowledge, the Development of Licensed Product in the Territory to date has been conducted by Alnylam and its Affiliates and its subcontractors, in compliance (in all material respects) with all applicable Laws.

9.3 [Intentionally Omitted].

9.4 Warranty Disclaimer. EXCEPT AS OTHERWISE EXPRESSLY PROVIDED IN THIS AGREEMENT, NEITHER PARTY MAKES ANY REPRESENTATION OR EXTENDS ANY WARRANTY OF ANY KIND, EITHER EXPRESS OR IMPLIED, TO THE OTHER PARTY WITH RESPECT TO ANY TECHNOLOGY, LICENSED PRODUCT, GOODS, SERVICES, RIGHTS OR OTHER SUBJECT MATTER OF THIS AGREEMENT AND HEREBY DISCLAIMS ALL IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE AND NON-INFRINGEMENT WITH RESPECT TO ANY AND ALL OF THE FOREGOING. EACH PARTY HEREBY DISCLAIMS ANY REPRESENTATION OR WARRANTY THAT THE DEVELOPMENT, MANUFACTURE OR COMMERCIALIZATION OF THE LICENSED PRODUCTS PURSUANT TO THIS AGREEMENT WILL BE SUCCESSFUL OR THAT ANY PARTICULAR SALES LEVEL WITH RESPECT TO THE LICENSED PRODUCTS WILL BE ACHIEVED.

9.5 Certain Covenants.

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9.5.1. Exclusivity. During the Term but subject to this Agreement including Sections 6.1.4 and 6.7, neither Party or its Affiliates will, without the prior written agreement of the other Party, alone or with or for an Affiliate or Third Party, or grant any Third Party a license to, research, develop, manufacture or commercialize in any country any product directed to the human PCSK9 gene, other than a Licensed Product pursuant to this Agreement. For purposes of this Section 9.5.1, “directed to” means, with respect to a compound, molecule or siRNA and a target, that such compound, molecule or siRNA modulates the expression or activity of such target, influences the expression or activity of such target or otherwise antagonizes or inhibits the expression or activity of such target, and with respect to a product and a target, that such product contains a compound, molecule or siRNA that modulates the expression or activity of such target, influences the expression or activity of such target or otherwise antagonizes or inhibits the expression or activity of such target.

9.5.2. Compliance. Each Party and its Related Parties shall conduct the Collaboration and the Development, Manufacture and Commercialization of the Licensed Product in material accordance with all Laws and industry standards, including current governmental regulations concerning good laboratory practices, good clinical practices and good manufacturing practices.

9.5.3. Debarment. Neither Party nor any of its Affiliates will use in any capacity, in connection with the Collaboration or the performance of its obligations under this Agreement, any person or entity that has been debarred pursuant to Section 306 of the United States Federal Food, Drug, and Cosmetic Act, as amended, or that is the subject of a conviction described in such section. Each Party agrees to inform the other Party in writing immediately if it learns that (a) it or any person or entity that is performing activities in the Collaboration or under this Agreement, is debarred or is subject to debarment or is the subject of a conviction described in Section 306, or (b) any action, suit, claim, investigation or legal or administrative proceeding is pending or, to the notifying Party's knowledge, is threatened, relating to the debarment or conviction of the notifying Party or any person or entity used in any capacity by such Party or any of its Affiliates in connection with the Collaboration or the performance of its other obligations under this Agreement.

10. INDEMNIFICATION; LIMITATION OF LIABILITY; INSURANCE

10.1. General Indemnification by MedCo. MedCo shall indemnify, hold harmless, and defend Alnylam, its Related Parties, and their respective directors, officers, employees and agents (“Alnylam Indemnitees”) from and against any and all Third Party claims, suits, losses, liabilities, damages, costs, fees and expenses (including reasonable attorneys' fees) (collectively, “Losses”) to the extent such Losses arise out of or result from, directly or indirectly, (a) any breach of, or inaccuracy in, any representation or warranty made by MedCo in the Transaction Agreements or any breach or violation of any covenant or agreement of MedCo in the Transaction Agreements, (b) the negligence or willful misconduct by or of MedCo and its Related Parties, and their respective directors, officers, employees and agents, in the performance of MedCo's obligations under the Transaction Agreements, (c) the Development, Manufacture or Commercialization of Licensed Products by MedCo or its Related Parties. MedCo shall have no obligation to indemnify the Alnylam Indemnitees to the extent that the Losses arise out of or result from, directly or indirectly, any breach of, or inaccuracy in, any representation or warranty made by Alnylam in the Transaction Agreements, or any breach or violation of any covenant or agreement of Alnylam in the Transaction Agreements, or the negligence or willful misconduct by or of any of the Alnylam Indemnitees.

10.2. General Indemnification by Alnylam. Alnylam shall indemnify, hold harmless, and defend MedCo, its Related Parties and their respective directors, officers, employees and agents (“MedCo Indemnitees”) from and against any and all Losses to the extent such Losses arise out of or result from, directly or indirectly, (a) any breach of, or inaccuracy in, any representation or warranty made by Alnylam in the Transaction Agreements or any breach or violation of any covenant or agreement of Alnylam in the Transaction Agreements, (b) the negligence or willful misconduct by or of Alnylam and its Related Parties, and their respective directors, officers, employees and agents, in the performance of Alnylam's obligations under the Transaction Agreements, (c) the Development, Manufacture or Commercialization of Licensed Products by Alnylam or its Related Parties pursuant to the Initial Development Plan, the Development Supply Agreement or Section 12.3, or (d) the exercise by Alnylam or its Related Parties of its rights in Section 6.2.2. Alnylam shall have no obligation to indemnify the MedCo Indemnitees to the extent that the Losses arise out of or result from, directly or indirectly, any breach of, or inaccuracy in, any representation or warranty made by MedCo in the Transaction Agreements, or any breach or violation of any covenant or agreement of MedCo in the Transaction Agreements, or the negligence or willful misconduct by or of any of the MedCo Indemnitees.

10.3. Indemnification Procedure. In the event of any such claim against any MedCo Indemnitee or Alnylam Indemnitee (individually, an “Indemnitee”), the indemnified Party shall promptly notify the other Party in writing of the claim once the indemnified Party learns of it, and the indemnifying Party shall manage and control, at its sole expense, the defense of the claim and its settlement. The Indemnitee shall cooperate with the indemnifying Party, at the indemnifying Party's reasonable request and expense, and may, at its option and expense, be represented in any such action or proceeding. The indemnifying Party shall not be liable for any settlements, litigation costs or expenses incurred by any Indemnitee without the indemnifying Party's written authorization. The indemnifying Party shall not settle any such claim without the Indemnitee's consent, unless such settlement requires only payments by the indemnifying Party. Notwithstanding the foregoing, if the indemnifying Party believes that any of the exceptions to its obligation of indemnification of the Indemnitees set forth in Sections 10.1 or 10.2 may apply, the indemnifying Party shall promptly notify the Indemnitees, which shall then have the right to be represented in any such action or proceeding by separate counsel at their expense; provided, that the indemnifying Party shall be responsible for payment of such expenses if the Indemnitees are ultimately determined to be entitled to indemnification from the indemnifying Party for the matters to which the indemnifying Party notified the Indemnitees that such exception(s) may apply. To the extent that an indemnification obligation hereunder results in payments to a Third Party
which are described in Section 6.4.3, the provisions of Sections 10.1 through 10.3 shall be subject to the provisions of Section 6.4.3 to the extent Section 6.4.3 is applicable.

10.4 Limitation of Liability. NEITHER PARTY HERETO WILL BE LIABLE FOR SPECIAL, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE DAMAGES ARISING OUT OF THIS AGREEMENT OR THE EXERCISE OF ITS RIGHTS HEREUNDER, INCLUDING LOST PROFITS ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF SUCH DAMAGES, EXCEPT AS A RESULT OF A PARTY’S WILLFUL MISCONDUCT, A MATERIAL BREACH OF THE CONFIDENTIALITY AND NON-USE OBLIGATIONS IN ARTICLE 8, OR A BREACH OF THE EXCLUSIVITY PROVISION IN SECTION 9.5.1. NOTHING IN THIS SECTION 10.4 IS INTENDED TO LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF EITHER PARTY.

10.5 Insurance. Each Party shall maintain insurance during the Term and for a period of at least [**] years after the last commercial sale of any Licensed Product under this Agreement by such Party or its Related Parties, with a reputable, solvent insurer in an amount appropriate for its business and products of the type that are the subject of this Agreement, and for its obligations under this Agreement. Specifically, each Party shall maintain product liability insurance of at least [**] U.S. Dollars ($[**]) per occurrence. Upon reasonable request, each Party shall provide the other Party with evidence of the existence and maintenance of such insurance coverage.

10.6 Obligations with Respect to IP Representations, Warranties and Covenants. In the event that Alnylam has materially breached any of its representations, warranties or covenants under Sections 9.2 or 6.4.4 and such breach has a material adverse effect on the rights of MedCo under this Agreement, then Alnylam shall use Commercially Reasonable Efforts to remedy such breach and obtain the right from the relevant Affiliate or Third Party in order to Control the relevant intellectual property such that it is considered Alnylam Technology and licensed or sublicensed to MedCo hereunder, and Alnylam shall bear any additional incremental payments that may be owed to such Affiliate or Third Party with respect to such remedy and such rights, license and sublicense, including any costs and expenses that might otherwise reasonably be imposed on MedCo or its Related Parties with respect to such consent or such rights, license or sublicense, other than the payment of royalties in accordance with Section 6.4.3 as set forth as of the Effective Date under any Existing Alnylam In-License (or any Additional Alnylam In-License, as the case may be) with respect to sales of Licensed Products by MedCo or its Related Parties. For clarity, the foregoing shall not be deemed to be MedCo's sole remedy with respect to such breach.

11. INTELLECTUAL PROPERTY OWNERSHIP, PROTECTION AND RELATED MATTERS

11.1 Inventorship. Inventorship for patentable inventions conceived or reduced to practice during the course of the performance of activities pursuant to this Agreement shall be determined in accordance with United States patent laws for determining inventorship.

11.2 Ownership. Alnylam shall own the entire right, title and interest in and to all inventions and discoveries (and Patent Rights claiming patentable inventions therein) first conceived or reduced to practice or, with respect to inventions and discoveries other than patentable inventions, otherwise identified, developed, made or discovered, solely by employees or consultants of Alnylam or acquired solely by Alnylam in the course of conducting the Collaboration. MedCo shall own the entire right, title and interest in and to all inventions and discoveries (and Patent Rights claiming patentable inventions therein) first conceived or reduced to practice or, with respect to inventions and discoveries other than patentable inventions, otherwise identified, developed, made or discovered, solely by employees or consultants of MedCo or acquired solely by MedCo in the course of conducting the Collaboration. The Parties shall jointly own any inventions and discoveries (and Patent Rights claiming patentable inventions therein) first conceived or reduced to practice or, with respect to inventions and discoveries other than patentable inventions, otherwise identified, developed, made or discovered, jointly in the course of conducting the Collaboration.

11.3 Prosecution and Maintenance of Patent Rights.

11.3.1 MedCo Technology and Product-Specific Technology. MedCo has the sole right and responsibility to, at MedCo's discretion, file, conduct prosecution, and maintain (including the defense of any interference, opposition or any other pre- or post-grant proceedings or challenges), all Patent Rights comprising MedCo Technology (other than Joint Collaboration IP), in MedCo's name.

11.3.2 Alnylam Technology.

(a) Subject to Sections 11.3.2(b) and 11.3.2(c), Alnylam has the sole right and responsibility to, at Alnylam’s discretion, file, conduct prosecution, and maintain (including the defense of any interference, opposition or any other pre- or post-grant proceedings or challenges), all Patent Rights comprising Alnylam Technology (other than Joint Collaboration IP), in Alnylam's name. Alnylam agrees to use Commercially Reasonable Efforts to prosecute and maintain such Alnylam Patent Rights in the

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Major Market Countries, and to prosecute and maintain Alnylam Product-Specific Patent Rights in all other countries reasonably requested by MedCo.

(b) Alnylam shall provide MedCo, sufficiently in advance for MedCo to comment, with copies of all patent applications and other material submissions and correspondence intended to be filed with any patent counsel or patent authorities pertaining to Patent Rights comprising Alnylam Product-Specific Patent Rights, and Alnylam shall consider in good faith MedCo's reasonable and promptly provided comments and

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advice with respect to the prosecution or maintenance strategy with respect to such Patent Rights; provided, however, that if Alnylam determines that MedCo's comments or advice are not reasonable, Alnylam shall promptly notify MedCo thereof and the Parties shall promptly discuss such determination. If the Parties cannot promptly reach agreement with respect to such issue, the Parties shall hire an outside patent attorney, mutually agreeable to the Parties, to determine which Party's approach is more likely to obtain the broadest enforceable patent coverage for the Licensed Products in the Field, and the Parties shall implement such approach. In the event that MedCo fails to provide any such comments or advice reasonably in advance of a patent office deadline, Alnylam shall in good faith file a response designed to obtain the broadest enforceable patent coverage for the Licensed Products in the Field. Alnylam shall promptly provide MedCo with copies of all material correspondence received from any patent counsel or patent authorities pertaining to Patent Rights comprising Alnylam Product-Specific Patent Rights.

(c) In the event that Alnylam elects not to seek or continue to seek or maintain patent protection on any Alnylam Product-Specific Patent Rights, subject to the terms and conditions of any applicable Alnylam In-License or Existing Alnylam Third Party Agreement, Alnylam shall notify MedCo of such decision in sufficient time so as to permit MedCo to decide whether to seek, prosecute and maintain such Patent Right and to take any necessary actions without losing patent protection, and MedCo shall have the right (but not the obligation), at its expense, to seek, prosecute and maintain in any country patent protection on such Alnylam Product-Specific Patent Rights in the name of Alnylam. Alnylam shall use Commercially Reasonable Efforts to make available to MedCo its documentation, and its authorized attorneys, agents or representatives, and such of its employees, as are reasonably necessary to assist MedCo in obtaining and maintaining the patent protection described under this Section 11.3.3(c). Alnylam shall sign or use Commercially Reasonable Efforts to have signed all legal documents necessary to file and prosecute such patent applications or to obtain or maintain such patents.

11.3.3 Joint Collaboration IP.

(a) Alnylam shall have the first right to, at Alnylam's discretion, file, prosecute and maintain (including the defense of any interference, opposition or any other pre- or post-grant proceedings or challenges), all Patent Rights comprising Joint Collaboration IP, in the names of both Alnylam and MedCo. Alnylam shall provide MedCo, sufficiently in advance for MedCo to comment, with copies of all patent applications and other material submissions and correspondence intended to be filed with any patent counsel or patent authorities pertaining to Patent Rights comprising Joint Collaboration IP, and Alnylam shall consider in good faith MedCo's reasonable and promptly provided comments and advice with respect to the prosecution or maintenance strategy with respect to such Patent Rights; provided, however, that if Alnylam determines that MedCo's comments or advice are not reasonable, Alnylam shall promptly notify MedCo thereof and the Parties shall promptly discuss such determination. If the Parties cannot promptly reach agreement with respect to such issue, the Parties shall hire an outside patent attorney, mutually agreeable to the Parties, to determine which Party's approach is more likely to obtain the broadest enforceable patent coverage for the Licensed Products in the Field, and the Parties shall implement such approach. In the event that MedCo fails to provide any such comments or advice reasonably in advance of a patent office deadline, Alnylam shall in good faith file a response designed to obtain the broadest enforceable patent coverage for the Licensed Products in the Field. Alnylam shall promptly provide MedCo with copies of all material correspondence received from any patent counsel or patent authorities pertaining to Patent Rights comprising Joint Collaboration IP. Each Party shall sign, or use Commercially Reasonable Efforts to have signed, all legal documents necessary to file and prosecute patent applications or to obtain or maintain patents in respect of such Joint Collaboration IP, at its own cost.

(b) In the event that Alnylam elects not to file or continue to prosecute or maintain patent protection on any Joint Collaboration IP in the Territory, Alnylam shall notify MedCo of such decision in sufficient time so as to permit MedCo to decide whether to seek, prosecute and maintain such Patent Right and to take any necessary actions without losing patent protection, and MedCo shall have the right (but not the obligation), at its own cost, to file, prosecute and maintain in any country Patent Rights comprising Joint Collaboration IP in the names of both Alnylam and MedCo. Alnylam shall use Commercially Reasonable Efforts to make available to MedCo its documentation, and its authorized attorneys, agents or representatives, and such of its employees, as are reasonably necessary to assist MedCo in obtaining and maintaining the patent protection described under this Section 11.3.3(b). Alnylam shall sign or use Commercially Reasonable Efforts to have signed all legal documents necessary to file and prosecute such patent applications or to obtain or maintain such patents.

11.3.4 Cooperation. With respect to the rights granted to a Party under Sections 11.3.2 or 11.3.3, each Party hereby agrees: (a) to make its employees, agents and consultants reasonably available to the other Party (or to the other Party's authorized attorneys, agents or representatives), to the extent reasonably necessary to enable such Party to undertake patent prosecution; (b) to provide the other Party with copies of all material correspondence pertaining to prosecution with the patent offices; (c) to cooperate, if necessary and appropriate, with the other Party in gaining patent term extensions wherever applicable to Patent Rights licensed under this Agreement; and (d) to endeavor in good faith to coordinate its efforts with the other Party to minimize or avoid interference with the prosecution and maintenance of the other Party's patent applications.

11.3.5 Patent Expenses. Except as provided below with respect to Alnylam Product-Specific Patent Rights and Patent Rights comprising Joint Collaboration IP in the Territory, the patent filing, prosecution and maintenance expenses incurred after the Effective Date with respect to Patent Rights comprised of Alnylam Technology and MedCo Technology shall be borne by each Party having the right to file, prosecute and maintain such Patent Rights under this Section 11.3. MedCo shall reimburse Alnylam on a Calendar Quarter basis (and within thirty (30) days after receipt of an invoice) with respect to the out-of-pocket patent filing, prosecution and maintenance expenses incurred by Alnylam after the Effective Date with respect to the Alnylam Product-Specific Patent Rights in the Territory, up to “[**] [$[*]]” of such expenses per Calendar Year. The Parties shall share equally the out-of-pocket patent filing, prosecution and maintenance expenses incurred with respect to Patent Rights comprising
Joint Collaboration IP. Each Party shall keep complete and accurate records with respect to such amount required to be paid by the other Party, and such other Party shall have the right to audit such records in accordance with Section 7.5.

11.3.6 Patent Term Extension. MedCo will determine, in its sole discretion, a strategy of seeking available patent term extension, restorations and supplementary protection certificates ("SPC") and other extensions from among Alnylam Product-Specific Patent Rights, MedCo Patent Rights and Patent Rights comprising Joint Collaboration IP, to the extent applicable, that will be designed to maximize patent protection and commercial value for the Licensed Products in the Field in the Territory, and the Parties, subject to the provisions of any In-License, will seek patent term extensions, restorations, SPCs and other extensions in all relevant countries in the Territory for such Patent Rights as selected by MedCo in accordance with that strategy. If MedCo determines not to so file for any extension, restoration or SPC

for any of such Patent Rights in any relevant country of the Territory, it will give notice of such determination to Alnylam at least [**] days prior to the date on which such a filing must be made or the right to do so is lost, and Alnylam will have the right to make such filing. Where required under national law, Alnylam will make the filings for such extensions, restorations and SPCs for Alnylam Product-Specific Patents and, as applicable, will make, or cooperate with MedCo to make, the filing for Patent Rights comprising Joint Collaboration IP in the Territory, in each case as directed by MedCo. Each Party will execute such authorizations and other documents and take such other actions as may be reasonably requested by the other Party to obtain any such extensions, restorations and SPCs in the Territory.

11.4 Third Party Infringement.

11.4.1 Notices. Each Party shall promptly report in writing to the other Party any (a) known or suspected infringement of any Alnylam Technology, MedCo Technology or Joint Collaboration IP or (b) unauthorized use or misappropriation of any Confidential Information or Know-How of a Party by a Third Party of which it becomes aware, in each case to the extent such infringing, unauthorized or misappropriating activities involve, as to a Licensed Product, a Generic Product or competing product in the Field ("Competitive Infringement"), and shall provide the other Party with all available evidence of such infringement, unauthorized use or misappropriation.

11.4.2 Rights to Enforce.

(a) MedCo Technology. Subject to the provisions of any In-License, MedCo shall have the sole and exclusive right to initiate an infringement or other appropriate suit anywhere in the world against any Third Party as to any infringement, or suspected infringement of, any Patent Rights, or of any use or suspected use without proper authorization of any Know-How, comprising MedCo Patent Rights, MedCo Know-How (other than MedCo's interest in Joint Collaboration IP), or MedCo Collaboration IP. MedCo will consider in good faith any request from Alnylam to initiate an infringement or other appropriate suit against any Third Party with respect to a Competitive Infringement in the Territory of MedCo Patent Rights, MedCo Know-How (other than MedCo's interest in Joint Collaboration IP) or MedCo Collaboration IP; provided, however, that MedCo shall not be required to initiate any such suit or permit Alnylam to initiate any such suit.

(b) Alnylam Technology and Joint Collaboration IP. Subject to the provisions of any In-License or Existing Alnylam Third Party Agreement, MedCo shall have the first right to initiate an infringement or other appropriate suit or action anywhere in the world against any Third Party with respect to any Competitive Infringement in the Territory of any Alnylam Product-Specific Patent Rights, Joint Collaboration IP (with respect to which MedCo shall consider Alnylam's input in good faith), or, with Alnylam's prior written consent, Alnylam Core Technology Patent Right or Alnylam Know-How (other than Alnylam's interest in Joint Collaboration IP). Alnylam will consider in good faith any request from MedCo to initiate an infringement or other appropriate suit against any Third Party with respect to a Competitive Infringement in the Territory of any Alnylam Core Technology Patent Right or such Alnylam Know-How (other than Alnylam's interest in Joint Collaboration IP); provided, however, that Alnylam shall not be required to initiate any such suit or permit MedCo to initiate any such suit.

(c) Step-In Right. If within [**] days after MedCo's receipt of a notice of a Competitive Infringement with respect to any Alnylam Product-Specific Patent Right or Joint Collaboration IP (or at least ten (10) days before the loss of the right to take an action as described in Section 11.4.2(b) and permitted hereunder with respect to such Competitive Infringement, except if MedCo has notified Alnylam in writing that it intends to, and actually does, take action as described in Section 11.4.2(b) and permitted hereunder

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against such Competitive Infringement), MedCo does not take any action as described in Section 11.4.2(b) and permitted hereunder against such Competitive Infringement in the relevant country in the Territory, Alnylam may in its sole discretion, bring and control any legal action in connection therewith at its sole expense.

11.4.3 Procedures; Expenses and Recoveries. The Party having the right to initiate any infringement suit under Section 11.4.2 above shall have the sole and exclusive right to select counsel for any such suit and shall pay all expenses of the suit, including attorneys' fees and court costs and reimbursement of the other Party's reasonable out-of-pocket expense in rendering assistance requested by the initiating Party. If required under applicable Law in order for the initiating Party to initiate and/or maintain such suit, or if either Party is unable to initiate or prosecute such suit solely in its own name or it is otherwise advisable to obtain an effective legal remedy, in each case, the other Party shall join as a party to the suit and will execute and cause its Affiliates to execute all documents, and take all actions, reasonably necessary for the initiating Party to initiate litigation and maintain such action. In addition, at the initiating Party's request, the other Party shall provide other reasonable assistance to the initiating Party in connection with an infringement suit at no charge to the initiating Party except for reimbursement by the initiating Party of
reasonable out-of-pocket expenses incurred in rendering such assistance. The non-initiating Party shall have the right to participate and be represented in any such suit under Section 11.4.2(b) or 11.4.2(c) by its own counsel at its own expense. If the Parties obtain from a Third Party, in connection with any such suit under Section 11.4.2(b) or 11.4.2(c), any damages, license fees, royalties or other compensation (including any amount received in settlement of such litigation), such amounts shall be allocated in all cases as follows:

(i)

first, to reimburse each Party for all out-of-pocket expenses of the suit incurred by the Parties, including attorneys' fees and disbursements, court costs and other litigation expenses and, to the extent that such recovery is insufficient to fully reimburse each Party, each Party will be reimbursed pro rata in accordance with each Party’s out-of-pocket expenses; and

(ii)

second, the balance shall be paid as follows: (A) damages designated by the relevant court as multiple or punitive damages shall be paid [**] percent ([**]%)) to the Party initiating the suit and [**] percent ([**]%)) to the other Party; and (B) any other amounts shall be paid to MedCo, but, to the extent that MedCo would otherwise owe a royalty to Alnylam if MedCo or its Related Parties had sold the relevant Licensed Product subject to the Competitive Infringement in the Field in the relevant country in the Territory, such balance shall be considered “Net Sales” for purposes of determining royalties owed to Alnylam hereunder.

11.5 Trademarks. MedCo and its Related Parties have the sole right to use any trademark it owns or controls for Licensed Products in the Territory at its sole discretion, and each Party and its Related Parties shall retain all right, title and interest in and to its and their respective corporate names and logos. MedCo will develop one or more Product Trademark(s) for use by MedCo and its Related Parties in the Territory to Commercialize Licensed Products which have received Regulatory Approval in the Field in the Territory. MedCo (or its Related Parties, as appropriate) shall own all rights to such Product Trademarks and all goodwill associated therewith, throughout the Territory, and the rights to any Internet domain names incorporating the applicable Product Trademarks or any variation or part of such Product Trademarks used as its URL address or any part of such address. For the avoidance of doubt, neither Party shall have any right to use the other Party’s or the other Party’s Related Parties’ corporate names or logos in connection with Commercialization of Licensed Products without the prior written consent of the other Party.

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12. TERM AND TERMINATION

12.1 Term. This Agreement shall be effective as of the Effective Date and, unless terminated earlier pursuant to Section 12.2, this Agreement shall continue in effect on a Licensed Product-by-Licensed Product and country-by-country basis until expiration of the last Royalty Term to expire under this Agreement (“Term”). Upon expiration of the Term, all licenses of MedCo granted by Alnylam under Article 6 shall become fully paid-up, irrevocable, perpetual, non-exclusive, sublicenseable licenses.

12.2 Termination Rights.

12.2.1 Termination for Convenience. MedCo shall have the right to terminate this Agreement at any time after the Effective Date on four (4) months prior written notice to Alnylam.

12.2.2 Termination for Cause. This Agreement may be terminated at any time during the Term upon written notice by either Party (the “Non-Breaching Party”) if the other Party (the “Breaching Party”) is in material breach of its obligations hereunder and has not cured such breach within ten (10) days in the case of a payment breach, or within sixty (60) days in the case of all other breaches, after notice requesting cure of the breach, or, if cure of such breach other than non-payment cannot reasonably be effected within such sixty (60) day period, to deliver to the Non-Breaching Party a plan reasonably calculated to cure such breach within a timeframe that is reasonably prompt in light of the circumstances then prevailing, but in no event more than [**]. Following delivery of such a plan, the Breaching Party will carry out the plan and cure the breach. If the Breaching Party fails to cure a material breach of this Agreement as provided above, then the Non-Breaching Party may terminate this Agreement upon written notice to the Breaching Party.

12.2.3 Termination for Failure to Designate a Lead Product. Alnylam shall have the right to terminate this Agreement upon thirty (30) days prior written notice to MedCo in the event that a Lead Product has not been designated by the JSC (or by the Chief Executive Officer of MedCo pursuant to Section 4.4.3) prior to the earlier of: (a) thirty (30) days after Alnylam reaches the Development Costs Cap described in Section 2.3.1(a) and provides notice thereof to MedCo pursuant to Section 2.3.3, unless MedCo has agreed to pay or has paid the relevant Extra Early Development Costs; and (b) on or prior to June 30, 2015.

12.2.4 Challenges of Patent Rights. In the event that a Party (the “Challenging Party”) or any of its Related Parties (a) commences or participates in any action or proceeding (including any patent opposition, re-examination or any other pre- or post-grant challenge or proceeding), or otherwise asserts any claim, challenging or denying the validity or enforceability (such an action or proceeding, a “Challenge”) of any of the Patent Rights licensed to such Challenging Party by the other Party (the “Licensor Party”) under this Agreement or any claim thereof or (b) actively assists any other person or entity in bringing or prosecuting any action or proceeding (including any patent opposition, re-examination or any other pre- or post-grant challenge or proceeding) challenging or denying the validity or enforceability of any of such Patent Rights or any claim thereof, then (i) such Challenging Party shall give notice thereof to such Licensor Party within [**] days of taking such action or of learning
that its Related Party has taken such action, and (ii) such Licensor Party will have the right, in its sole discretion, to give notice to such Challenging Party that this Agreement will terminate thirty (30) days following such notice (or such longer period as such Licensor Party may designate in such notice), and, unless, with respect to a challenge brought by such Challenging Party, such Challenging Party withdraws, or, with respect to a challenge brought by

its Affiliates, causes, or, with respect to a challenge brought by its Sublicensee, uses Commercially Reasonable Efforts to cause, to be withdrawn, all such challenge(s) within such thirty (30)-day (or longer) period, this Agreement will so terminate. Notwithstanding the foregoing, in such event, MedCo, as the Licensor Party under this Agreement, may only terminate the licenses it has granted under this Agreement to Alnylam as the Challenging Party with respect to the Patent Rights that are the subject of the Challenge. In the event that such Licensor Party is not permitted under Law to terminate this Agreement such that the licenses with respect to all the Patent Rights under this Agreement are terminated, then the Parties agree to construe this provision to permit such Licensor Party to terminate only the licenses to that portion of such Patent Rights with respect to which such Licensor Party may terminate consistent with Law.

12.3 Effect of Termination. Without limiting any other legal or equitable remedies that either Party may have, if this Agreement is terminated by Alnylam, or by MedCo in accordance with Section 12.2.1, then:

(a) If this Agreement is terminated by MedCo pursuant to Section 12.2.1, then MedCo’s obligation under Section 9.5.1 shall survive for a period of eight (8) months after the effective date of termination, and if this Agreement is terminated by Alnylam pursuant to Sections 12.2.2 or 12.2.4, then MedCo’s obligations under Section 9.5.1 shall survive for a period of twelve (12) months after the effective date of termination.

(b) Subject to the terms and conditions of this Agreement (including Sections 6.4.1 and 6.4.4 with respect to the MedCo In-Licenses (if any) applicable to the rights granted to Alnylam pursuant to this Section 12.3(b)), MedCo shall and hereby does grant Alnylam a non-transferable (except as provided in Section 13.1), sublicenseable (subject to Section 6.2.3), worldwide, non-exclusive, royalty-bearing license, under any MedCo Technology that is produced, generated, conceived and/or reduced to practice as a result of the Development, Manufacturing or Commercialization activities of MedCo under this Agreement to Develop, Manufacture and Commercialize Licensed Products in the Field in the Territory. The Parties shall negotiate in good faith the royalty to be paid to MedCo by Alnylam in exchange for, and reflecting the then net present value of, the foregoing license, and, in the event that the Parties cannot mutually agree upon such amount within [*] days following the effective date of termination, the Parties will, as soon as reasonably practicable and in no event later than [*] days following the expiration of such [*]-day period, mutually decide upon an independent Third Party valuation firm with substantial experience in valuing licenses of intellectual property rights for the commercialization of pharmaceutical and biotechnology products, which shall make a final and binding determination of the net value of such license and both Parties shall promptly provide all reasonable materials and information requested by such valuation firm and shall share equally in the expenses of such valuation firm.

(c) MedCo shall use Commercially Reasonable Efforts to as promptly as practicable transfer to Alnylam or Alnylam’s designee (i) possession and ownership of all governmental or regulatory correspondence, conversation logs, filings and approvals (including all Regulatory Approvals and pricing and reimbursement approvals) in MedCo’s or its Affiliates’ possession and Control relating to the Development, Manufacture or Commercialization of the Licensed Products and all Product Trademarks, (ii) copies of all data, reports, records and materials, and other sales and marketing related information in MedCo’s or its Affiliates’ possession and Control to the extent that such data, reports, records, materials or other information relate to the Development, Manufacture or Commercialization of Licensed Products, including all non-clinical and clinical data relating to Licensed Products, and

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customer lists and customer contact information and all adverse event data in MedCo’s possession and Control, and (iii) all records and materials in MedCo’s possession and Control containing Confidential Information of Alnylam. MedCo shall further appoint Alnylam as MedCo’s and/or MedCo’s Affiliates’ agent for all Licensed Product-related matters involving Regulatory Authorities in the Territory until all such Regulatory Approvals and other regulatory filings have been transferred to Alnylam or its designee,

(d) if the effective date of termination is after First Commercial Sale, then MedCo shall appoint Alnylam as its exclusive distributor of the Licensed Product in the Territory and grant Alnylam the right to appoint sub-distributors, until such time as all such Regulatory Approvals in the Territory have been transferred to Alnylam or its designee,
if MedCo or its Affiliates are Manufacturing Licensed Product, then at Alnylam's option, MedCo shall supply the Licensed Product to Alnylam in the Territory on commercially reasonable terms to be negotiated in good faith by the Parties, until such time as all such Regulatory Approvals in the Territory have been transferred to Alnylam or its designee, Alnylam has obtained all necessary manufacturing approvals or Alnylam has procured or developed its own source(s) of Licensed Product supply.

(f)

if Alnylam so requests, MedCo shall use Commercially Reasonable Efforts to assign to Alnylam any Third Party agreements solely relating to the Development, Manufacture or Commercialization of the Licensed Product to which MedCo is a party, subject to any required consents of such Third Party, which MedCo shall use Commercially Reasonable Efforts to obtain promptly,

(g)

MedCo shall promptly transfer and assign to Alnylam all of MedCo's and its Affiliates' rights, title and interests in and to the Product Trademark(s) owned by MedCo or its Affiliates and used for the Licensed Products in the Field in the Territory,

(h)

MedCo shall transfer to Alnylam any inventory of Licensed Products Controlled by MedCo or its Affiliates as of the termination date, on commercially reasonable terms to be negotiated in good faith by the Parties,

(i)

MedCo shall use Commercially Reasonable Efforts to provide, at Alnylam's reasonable expense, any other assistance reasonably requested by Alnylam for the purpose of allowing Alnylam or its designee to proceed expeditiously with the Development, Manufacture and Commercialization of Licensed Products in the Territory, and

(j)

MedCo shall execute all documents and take all such further actions as may be reasonably requested by Alnylam in order to give effect to the foregoing clauses.

12.4 Effect of Expiration or Termination; Survival. Expiration or termination of this Agreement shall not relieve the Parties of any obligation accruing prior to such expiration or termination. Any expiration or termination of this Agreement shall be without prejudice to the rights of either Party against the other accrued or accruing under this Agreement prior to expiration or termination, including the obligation to pay royalties for the Licensed Product sold prior to such expiration or termination. The provisions of Articles 10 (other than Section 10.6) and 13, Sections 6.1.4(b), 6.3, 6.5, 6.6, 6.7, 8.1, 8.2.2, 9.4, 11.1, 11.2, 11.3.3, 11.3.4 (with respect to the rights granted to each Party under Section 11.3.3), 11.3.5 (with respect to Joint Collaboration IP), 12.3 (if applicable) and 12.4, Section 7.4.7 (with respect to any royalty report for the last Calendar Quarter), Sections 7.5 through 7.11 (with respect to amounts owed prior to expiration or termination of this Agreement or amounts due thereafter pursuant to Section 12.4), and the last sentences of Sections 6.1.1, 6.1.2 or 12.1 (with respect to the licenses which have converted as set forth therein on or before the expiration or termination of this Agreement) shall survive any expiration or termination of this Agreement. Except as set forth in this Article 12, upon termination or expiration of this Agreement all other rights and obligations of the Parties under this Agreement cease.

13. MISCELLANEOUS

13.1 Assignment. Except as provided in this Section 13.1, this Agreement may not be assigned or otherwise transferred, nor may any right or obligation hereunder be assigned or transferred, by either Party without the written consent of the other Party. However, either Party may, without the other Party's written consent, assign this Agreement and its rights and obligations hereunder in whole or in part to an Affiliate or to a Person that acquires, by merger, sale of assets or otherwise, all or substantially all of the business of the assigning Party to which the subject matter of this Agreement relates. The Parties acknowledge that MedCo is considering the potential assignment of all or a significant portion of its obligations under this Agreement to a Third Party joint venture in which MedCo may hold a non-controlling equity interest, and Alnylam agrees to discuss in good faith with MedCo such an assignment together with appropriate financial and other protections for Alnylam; provided, however, that nothing in the foregoing sentence shall be construed to require Alnylam to agree to such an assignment. The assigning Party shall remain responsible for the performance by its assignee of this Agreement or any obligations hereunder so assigned. Any assignment of the rights or obligations of this Agreement not in accordance with the foregoing shall be void.

13.2 Governing Law. This Agreement shall be construed and the respective rights of the Parties determined in accordance with the substantive laws of the State of New York, notwithstanding any provisions of New York law governing conflicts of laws to the contrary, and the patent laws of the relevant jurisdiction without reference to any rules of conflict of laws.
13.3 Entire Agreement; Amendments. This Agreement and, when executed, the other Transaction Agreements, contain the entire understanding of the Parties with respect to the subject matter hereof, and supersedes all previous arrangements with respect to the subject matter hereof, whether written or oral, including the Mutual Confidential Disclosure Agreement made as of January 16, 2012 by the Parties. This Agreement (including the Schedules hereto) may be amended, or any term hereof modified, only by a written instrument duly-executed by authorized representatives of both Parties.

13.4 Severability. If any provision hereof should be held invalid, illegal or unenforceable in any respect in any jurisdiction, the Parties shall substitute, by mutual consent, valid provisions for such invalid, illegal or unenforceable provisions, which valid provisions in their economic effect are sufficiently similar to the invalid, illegal or unenforceable provisions that it can be reasonably assumed that the Parties would have entered into this Agreement with such valid provisions. In case such valid provisions cannot be agreed upon, the invalid, illegal or unenforceable of one or several provisions of this Agreement shall not affect the validity of this Agreement as a whole, unless the invalid, illegal or unenforceable provisions are of such essential importance to this Agreement that it is to be reasonably assumed that the Parties would not have entered into this Agreement without the invalid, illegal or unenforceable provisions.

13.5 Headings. The captions to the Articles and Sections hereof are not a part of this Agreement, but are merely for convenience to assist in locating and reading the several Articles and Sections hereof.

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13.6 Interpretation. Whenever the context may require, any pronoun shall include the corresponding masculine, feminine and neuter forms and any noun shall include the corresponding singular and plural forms. The words "include", "includes" and "including" shall be deemed to be followed by the phrase "but not limited to." The word "will" shall be construed to have the same meaning and effect as the word "shall." "$" or "(D)(d)ollar" means U.S. Dollars. With respect to any license grant, "exclusive" means exclusive as between the licensor Party and the licensed Party to the fullest extent possible, in light of any rights already granted by the licensor Party to Third Parties prior to the date on which such license is first granted and in light of any limitations on the rights granted to the licensor Party by its licensors. Unless the context requires otherwise, (a) any definition of or reference to any agreement, instrument or other document herein shall be construed as referring to such agreement, instrument or other document as from time to time amended, supplemented or otherwise modified (subject to any restrictions on such amendments, supplements or modifications set forth herein or therein), (b) any reference to any Laws herein shall be construed as referring to such Laws as from time to time enacted, repealed or amended, (c) any reference herein to any Person shall be construed to include the Person's successors and permitted assigns, (d) the words "herein", "hereof" and "hereunder", and words of similar import, shall be construed to refer to this Agreement in its entirety and not to any particular provision hereof, (e) all references herein to Articles, Sections or Schedules shall be construed to refer to Articles, Sections and Schedules of this Agreement, (f) the word "or" shall be construed to have the same meaning and effect as "and/or", and (g) a term not defined herein but reflecting a different part of speech than a term which is defined herein shall be interpreted in a correlative manner.

13.7 Waiver of Rule of Construction. Each Party has had the opportunity to consult with counsel in connection with the review, drafting and negotiation of this Agreement. Accordingly, the rule of construction that any ambiguity in this Agreement shall be construed against the drafting Party shall not apply.

13.8 No Implied Waivers; Rights Cumulative. No failure on the part of Alnylam or MedCo to exercise, and no delay in exercising, any right, power, remedy or privilege under this Agreement, or provided by statute or at law or in equity or otherwise, shall impair, prejudice or constitute a waiver of any such right, power, remedy or privilege or be construed as a waiver of any breach of this Agreement or as an acquiescence therein, nor shall any single or partial exercise of any such right, power, remedy or privilege preclude any other or further exercise thereof or the exercise of any other right, power, remedy or privilege. Except as expressly provided in this Agreement, no right or remedy herein conferred upon or reserved to either Party is intended to be exclusive of any other right or remedy.

13.9 Notices. All notices which are required or permitted hereunder shall be in writing and sufficient if delivered personally, sent by facsimile (and promptly confirmed by personal delivery, registered or certified mail or overnight courier), sent by nationally-recognized overnight courier or sent by registered or certified mail, postage prepaid, return receipt requested, addressed as follows:

If to Alnylam, to: Alnylam Pharmaceuticals, Inc.
300 Third Street
Cambridge, MA 02142
Attention: Legal Department
Facsimile No.: (617) 551-8101

If to MedCo, to: MedCo
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With a copy to: Faber Daeufer Itrato & Cabot PC
950 Winter Street

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13.10 Compliance with Export Regulations. Neither Party shall export any technology licensed to it by the other Party under this Agreement except in compliance with U.S. export laws and regulations.

13.11 Force Majeure. Neither Party shall be held liable to the other Party nor be deemed to have defaulted under or breached this Agreement for failure or delay in performing any obligation under this Agreement to the extent that such failure or delay is caused by or results from causes beyond the reasonable control of the affected Party, potentially including embargoes, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts or other labor disturbances, fire, floods, or other acts of God, or acts, omissions or delays in acting by any Governmental Authority or the other Party. The affected Party shall notify the other Party of such force majeure circumstances as soon as reasonably practical, and shall promptly undertake all reasonable efforts necessary to cure such force majeure circumstances.

13.12 Dispute Resolution. In the event that the Parties do not resolve any dispute, controversy or claim arising from, or related to, this Agreement or to the breach hereof (collectively, “Dispute”) and neither Party has final decision-making authority as to such Dispute pursuant to Section 4.4, and a Party wishes to pursue the matter, such Party may file suit to have such Dispute adjudicated in a court of competent jurisdiction.

13.13 Independent Contractors. It is expressly agreed that Alnylam and MedCo shall be independent contractors and that the relationship between Alnylam and MedCo shall not constitute a partnership, joint venture or agency. Alnylam shall not have the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on MedCo, without the prior written consent of MedCo, and MedCo shall not have the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on Alnylam without the prior written consent of Alnylam.

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13.14 Counterparts. The Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Facsimile signatures and signatures transmitted via PDF shall be treated as original signatures.

13.15 Performance by Affiliates. Each Party shall have the right to have any of its obligations hereunder performed by, any of its Affiliates and the performance of such obligations by any such Affiliate(s) shall be deemed to be performance by such Party; provided, however, that such Affiliate shall be bound by the corresponding obligations of such Party and such Party shall be responsible for ensuring the performance of its obligations under this Agreement and that any failure of any Affiliate performing obligations of such Party hereunder shall be deemed to be a failure by such Party to perform such obligations.
13.16 Binding Effect; No Third Party Beneficiaries. As of the Effective Date, this Agreement shall be binding upon and inure to the benefit of the Parties and their respective successors and permitted assigns. Except as expressly set forth in this Agreement, no person or entity other than the Parties and their respective permitted assignees hereunder shall be deemed an intended beneficiary hereunder or have any right to enforce any obligation of this Agreement.

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IN WITNESS WHEREOF, the Parties have executed this Agreement as of the Effective Date.

THE MEDICINES COMPANY

ALNYLAMPHARMACEUTICALS, INC.

BY:/s/ Glenn Sblendorio BY:/s/ John M. Maraganore

NAME: Glenn Sblendorio NAME: John M. Maraganore, Ph.D.

TITLE: President and CFO TITLE: Chief Executive Officer

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SCHEDULE A

ALN-PCS02

ALN-PCS02 is an investigational ribonucleic acid interference (RNAi) therapeutic agent that is comprised of active pharmaceutical ingredient [**] (see sequence & diagram below), a synthetic small interfering RNA (siRNA) that is Targeted to the PCS messenger RNA (mRNA) in a [**] lipid nanoparticle formulation (see description below).

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 5 pages were omitted. [**]

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SCHEDULE B

ALN-PCSsc

ALN-PCSsc is an investigational ribonucleic acid interference (RNAi) therapeutic agent that is comprised of an active pharmaceutical ingredient which is a synthetic small interfering RNA (siRNA) that is Targeted to the PCS messenger RNA (mRNA) and covalently linked on the 3’ end of the sense strand to a triantennary N-acetylgalactosamine (GalNAc3) ligand (see diagram below). The active pharmaceutical ingredient may be [**] (see sequence & diagram below).

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 2 pages were omitted. [**]

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SCHEDULE C

Alnylam PATENT RIGHTS

SCHEDULE C-1

ALNYLAM CORE TECHNOLOGY PATENT RIGHTS

See attached.

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 183 pages were omitted. [**]

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SCHEDULE C-2

ALNYLAM PRODUCT-SPECIFIC PATENT RIGHTS

See attached.

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SCHEDULE C-3

PATENT RIGHTS IN ADDITIONAL ALNYLAM IN-LICENSES

See attached.

SCHEDULE D

EXISTING Alnylam IN-LICENSES,

EXISTING ALNYLAM THIRD PARTY AGREEMENTS AND ADDITIONAL ALNYLAM IN-LICENSES

A. As of the Effective Date, Existing Alnylam In-Licenses are the following Third Party agreements:

1. Co-Exclusive License Agreement between Max Planck Innovation GmbH (formerly Garching Innovation GmbH) and Alnylam Pharmaceuticals, Inc., dated December 20, 2002, as amended by Amendment dated July 2, 2003, the Requirements Amendment effective June 15, 2005, the Waiver Amendment effective August 9, 2007 and the Amendment to the Alnylam Co-Exclusive License Agreement dated as of March 14, 2011, by and between Alnylam Pharmaceuticals, Inc., on the one hand, and Whitehead Institute for Biomedical Research, Massachusetts Institute of Technology and Max-Planck-Innovation GmbH, on the other hand; and Co-Exclusive License Agreement between Max Planck Innovation GmbH (formerly Garching Innovation GmbH) and Alnylam Europe AG (formerly Ribopharma AG), dated July 30, 2003 (collectively, the “Garching Agreements”)


4. Supplemental Agreement among Tekmira Pharmaceuticals Corporation (“Tekmira”), Protiva Biotherapeutics Inc. (“Protiva”), UBC and AlCana

5. Sublicense Agreement dated January 8, 2007 between Alnylam and Tekmira (as successor in interest to Inex Pharmaceuticals Corporation)


B. As of the Effective Date, Existing Alnylam Third Party Agreements are the following Third Party agreements:


C. As of the Effective Date, the Additional Alnylam In-Licenses are the following Third Party agreements:

[**]

SCHEDULE E

INITIAL DEVELOPMENT PLAN

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 5 pages were omitted. [**]

SCHEDULE F
The Medicines Company and Alnylam Form Strategic Alliance to
Develop and Commercialize RNAi Therapeutics Targeting PCSK9 for the
Treatment of Hypercholesterolemia

The Medicines Company Obtains Exclusive Global License to Advance ALN-PCS
RNAi Therapeutic Program

Alnylam to Receive $25 Million in Upfront Payment in Addition to Milestone Payments and Royalties on Product Sales

Companies to Host Conference Call Today at 8:30 a.m. ET to Discuss Collaboration

Parsippany, N.J. and Cambridge, Mass., February 4, 2013 - The Medicines Company (Nasdaq: MDCO) and Alnylam Pharmaceuticals, Inc. (Nasdaq: 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 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-PCSc a subcutaneously administered RNAi therapeutic currently in pre-clinical development. Alnylam will continue the program while funded by The Medicines Company for an estimated one to two years to complete certain pre-clinical and Phase I clinical studies. The Medicines Company will then lead and fund development from Phase II forward and commercialize 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-PCSc 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.

Conference Call Information

The Medicines Company and Alnylam will host a conference call today at 8:30 a.m. ET to discuss this new collaboration. To access the call, please dial 877-312-7507 (domestic) or 631-813-4828 (international) five minutes prior to the start time and refer to conference ID 96998933. A replay of the call will be available beginning at 11:30 a.m. ET. To access the replay, please dial 855-859-2056 (domestic) or 404-537-3406 (international) and refer to conference ID 96998933. A live audio webcast of the presentation will be available on The Medicines Company website at www.themedicinescompany.com, and on the News & Investors section of the Alnylam's website, www.alnylam.com

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

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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 bloodstream. 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 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 medicines. 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 (Nasdaq: 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.

The Medicines Company Forward-Looking Statement

Statements contained in this press release about The Medicines Company that are not purely historical, and all other statements that are not purely historical, may be deemed to be forward-looking statements for purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Without limiting the foregoing, the words "believes," "anticipates" and "expects" and similar expressions are intended to identify forward-looking statements. These forward-looking statements involve known and unknown risks and uncertainties that may cause the Company's actual results, levels of activity, performance or achievements to be materially different from those expressed or implied by these forward-looking statements. Important factors that may cause or contribute to such differences include whether the Company's products will advance in the clinical trials process on a timely basis or at all, whether the Company will make regulatory submissions for product candidates on a timely basis, whether its regulatory submissions will receive approvals from regulatory agencies on a timely basis or at all, whether physicians, patients and other key decision makers will accept clinical trial results, and such other factors as are set forth in the risk factors detailed from time to time in the Company's periodic reports and registration statements filed with the Securities and Exchange Commission including, without limitation, the risk factors detailed in the Company's Quarterly Report on Form 10-Q filed on November 9, 2012, which are incorporated herein by reference. The Company specifically disclaims any obligation to update these forward-looking statements.

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 and rare bleeding disorders (RBD), ALN-AS1 for the treatment of acute intermittent porphyria (AIP), ALN-PCS for the treatment of hypercholesterolemia, and ALN-TMP for the treatment of hemoglobinopathies. As part of its "Alnylam 5x15TM" 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-RSOV1 for the treatment of respiratory syncytial virus (RSV) infection and ALN-VSP for the treatment of liver cancers. 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, Asclelis, Monsanto, Genzyme, and The Medicines Company. In addition, Alnylam holds a significant equity position in Regulus Therapeutics Inc., a company focused on discovery, development, and commercialization of microRNA therapeutics. 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 VasiRNA™ 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.

About "Alnylam 5x15TM"

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The “Alnylam 5x15” strategy, launched in January 2011, establishes a path for development and commercialization of novel RNAi therapeutics directed toward genetically defined targets for diseases with high unmet medical need. Products arising from this initiative share several key characteristics including: a genetically defined target and disease; the potential to have a major impact in a high unmet need population; the ability to leverage the existing Alnylam RNAi delivery platform; the opportunity to monitor an early biomarker in Phase I clinical trials for human proof of concept; and the existence of clinically relevant endpoints for the filing of a new drug application (NDA) with a focused patient database and possible accelerated paths for commercialization. By the end of 2015, the company expects to have five such RNAi therapeutic programs in clinical development, including programs in advanced stages, on its own or with a partner. The “Alnylam 5x15” programs include ALN-TTR for the treatment of transthyretin-mediated amyloidosis (ATTR), ALN-AT3 for the treatment of hemophilia and rare bleeding disorders (RBD), ALN-AS1 for the treatment of acute intermittent porphyria (AIP), ALN-PCS for the treatment of hypercholesterolemia, ALN-TMP for the treatment of hemoglobinopathies, and other programs. Alnylam intends to focus on developing and commercializing certain programs from this product strategy itself in North and South America, Europe, and other parts of the world; these include ALN-TTR, ALN-AT3, and ALN-AS1; the company will seek global development and commercial alliances for other programs.

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 the potential for the ALN-PCS program, including ALN-PCS02 and ALN-PCSsc, its expectations regarding the receipt of upfront and potential development and commercialization milestones and royalty payments on worldwide net sales, if any, under The Medicines Company agreement, 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 successfully demonstrate the efficacy and safety of its drug candidates and the pre-clinical and clinical results for these product candidates, including ALN-PCS02 and ALN-PCSsc, which may not support further development of such product candidates, both our and The Medicines Company's ability to successfully advance ALN-PCS02 and/or ALN-PCSsc resulting in the potential payment of milestones and royalties to us, 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, including its collaboration with The Medicines Company, and new business initiatives, as well as those risks more fully discussed in the “Risk Factors” filed with Alnylam's current report on Form 8-K filed with the Securities and Exchange Commission (SEC) on January 14, 2013 and in other filings that Alnylam makes with the SEC. 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.

SCHEDULE G

DISCLOSURE SCHEDULE

Section 9.2.1(a):
- Reference is made to certain claims alleged by the plaintiffs in the action entitled:

[**]

Section 9.2.2:
- Reference is made to certain claims alleged by the plaintiff in the [**] Litigation.

Section 9.2.5(c):
- Reference is made to certain claims alleged by the plaintiff in the [**] Litigation.

Section 9.2.8:
- [**]

Section 9.2.9(a):
- Reference is made to certain claims alleged by the plaintiff in the [**] Litigation.

Section 9.2.9(b):
SCHEDULE H
EXAMPLE FOR SECTION 6.4.3.3

If, with respect to a particular Alnylam In-License, royalties are payable with respect to aggregate net sales of all products covered by such Alnylam In-License, and are not determined on a product-by-product basis, according to the following tiered royalty rates:

Aggregate Calendar Year

net sales by Alnylam, its Affiliates or any of its sublicensees of all products

Royalty
(as a percentage of such net sales)

[**]
[**]
[**]
[**]
[**]
[**]
[**]

And if sales are made during each of the four Calendar Quarters of the relevant Calendar Year as shown in the table below, then royalties owed by MedCo pursuant to such Alnylam In-License shall be as shown in such table:

Sales By
Calendar Quarter 1
Calendar Quarter 2
Calendar Quarter 3
Calendar Quarter 4

[**]
[**]
[**]
[**]
[**]
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