

Filed On Behalf Of:

Alnylam Pharmaceuticals, Inc.

By:

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212-218-2100

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ALNYLAM PHARMACEUTICALS, INC.,
Petitioner,
v.
SILENCE THERAPEUTICS GMBH,
Patent Owner.

Case PGR2018-00089
U.S. Patent No. 9,790,501

PETITIONER'S EXHIBIT LIST 2

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Exhibit	Description	Abbreviation
1001	U.S. Patent No. 9,790,501	'501 patent
1002	Expert Declaration of Dr. Jonathan K. Watts	
1003	Curriculum Vitae of Dr. Jonathan K. Watts	
1004	File History of U.S. Patent No. 9,790,501	'968 application
1005	U.S. Application No. 14/977,710 (continuation)	'710 application
1006	European Patent Application No. 02017601	EP1
1007	U.S. Provisional Application No. 60/402,541	'541 provisional
1008	European Patent Application No. 03008383	EP2
1009	U.S. Application No. 10/633,630 (non-provisional)	'630 application
1010	U.S. Application No. 12/200,296 (continuation)	'296 application
1011	U.S. Application No. 12/986,389 (continuation)	'389 application
1012	U.S. Application No. 13/692,178 (continuation)	'178 application
1013	U.S. Application No. 14/578,636 (continuation)	'636 application
1014	U.S. Patent Publication No. 2003/0190635	McSwiggen US
1015	U.S. Patent No. 9,695,423	'423 patent

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1016	Charles R. Allerson et al., <i>Fully 2'-Modified Oligonucleotide Duplexes with Improved In Vitro Potency and Stability Compared to Unmodified Small Interfering RNA</i> , 48 J. MED. CHEM. 901 (Jan. 20, 2005)	Allerson 2005
1017	Reserved	
1018	File History of U.S. Patent No. 7,452,987 (Excerpt 1)	
1019	Reserved	
1020	U.S. Patent No. 7,452,987	'987 patent
1021	U.S. Patent No. 7,893,245	'245 patent
1022	U.S. Patent No. 8,324,370	'370 patent
1023	U.S. Patent No. 8,933,215	'215 patent
1024	U.S. Patent No. 9,222,092	'092 patent
1025	Reserved	
1026	Reserved	
1027	Jonathan K. Watts et al., <i>Chemically Modified siRNA: Tools and Applications</i> , 13 DRUG DISCOVERY TODAY 842 (2008)	Watts 2008

Exhibit	Description	Abbreviation
1028	Frank Czauderna et al., <i>Structural Variations and Stabilising Modifications of Synthetic siRNAs in Mammalian Cells</i> , 31 NUCLEIC ACIDS RESEARCH 2705 (2003)	Czauderna 2003
1029	James C. Kaczmarek et al., <i>Advances in the Delivery of RNA Therapeutics: From Concept to Clinical Reality</i> , 9 GENOME MEDICINE 60 (2017)	
1030	Anastasia Khvorova & Jonathan K. Watts, <i>The Chemical Evolution of Oligonucleotide Therapies of Clinical Utility</i> , 35 NATURE BIOTECHNOLOGY 238 (2017)	
1031	Elie Dolgin, <i>The Greatest Hits of the Human Genome: A Tour Through the Most Studied Genes in Biology Reveals Some Surprises</i> , 551 NATURE 427 (2017)	
1032	M. Gaglione & A. Messere, <i>Recent Progress in Chemically Modified siRNAs</i> , 10 MINI-REVIEWS IN MEDICINAL CHEMISTRY 578 (2010)	Gaglione 2010

Exhibit	Description	Abbreviation
1033	Barbara Nawrot & Katarzyna Sipa, <i>Chemical and Structural Diversity of siRNA Molecules</i> , 6 CURRENT TOPICS IN MEDICINAL CHEMISTRY 913 (2006)	Nawrot 2006
1034	Susan Parrish et al., <i>Functional Anatomy of a dsRNA Trigger: Differential Requirement for the Two Trigger Strands in RNA Interference</i> , 6 MOLECULAR CELL 1077 (2000)	Parrish 2000
1035	Glen F. Deleavey et al., <i>Chemical Modification of siRNA</i> , 39 CURRENT PROTOCOLS IN NUCLEIC ACID CHEMISTRY 16.3.1 (2009)	Deleavey 2009
1036	Jesper B. Bramsen & Jørgen Kjems, <i>Development of Therapeutic-Grade Small Interfering RNAs by Chemical Engineering</i> , 3 FRONTIERS IN GENETICS 154 (2012)	Bramsen 2012
1037	Henry J. Haringsma et al., <i>mRNA Knockdown by Single Strand RNA is Improved by Chemical Modifications</i> , 40 NUCLEIC ACIDS RESEARCH 4125 (2012)	

Exhibit	Description	Abbreviation
1038	Michael A. Collingwood et al., <i>Chemical Modification Patterns Compatible with High Potency Dicer-Substrate Small Interfering RNAs</i> , 18 OLIGONUCLEOTIDES 187 (2008)	
1039	Mark A. Behlke, <i>Chemical Modification of siRNAs for In Vivo Use</i> , 18 OLIGONUCLEOTIDES 305 (2008)	Behlke 2008
1040	Yi Pei & Thomas Tuschl, <i>On the Art of Identifying Effective and Specific siRNAs</i> , 3 NATURE METHODS 670 (2006)	Pei and Tuschl 2006
1041	Jens Kurreck, <i>Antisense Technologies: Improvement Through Novel Chemical Modifications</i> , 270 EUR. J. BIOCHEM. 1628 (2003)	
1042	Sayda M. Elbashir et al., <i>Duplexes of 21-nucleotide RNAs Mediate RNA Interference in Cultured Mammalian Cells</i> , 411 NATURE 494 (2001)	Elbashir 2001
1043	Mohammed Amarzguioui et al., <i>Tolerance for Mutations and Chemical Modifications in a siRNA</i> , 31 NUCLEIC ACIDS RESEARCH 589 (2003)	Amarzguioui 2003

Exhibit	Description	Abbreviation
1044	Ya-Lin Chiu & Tariq M. Rana, <i>siRNA Function in RNAi: A Chemical Modification Analysis</i> , 9 RNA 1034 (2003)	Chiu and Rana 2003
1045	Agnieszka Patkaniowska & Thomas Tuschl, <i>Chapter 4, Gene Silencing by Synthetic siRNA Duplexes in Mammalian Cell Culture</i> , in RNA INTERFERENCE (RNAi) NUTS & BOLTS OF RNAi TECHNOLOGY 71 (David R. Engelke ed., 2003).	Patkaniowska 2003
1046	Muthiah Manoharan, <i>RNA Interference and Chemically Modified Small Interfering RNAs</i> , 8 CURRENT OPINION IN CHEMICAL BIOLOGY 570 (2004)	
1047	Ji-Joon Song et al., <i>Crystal Structure of Argonaute and its Implication for RISC Slicer Activity</i> , 305 SCIENCE 1434 (2004)	Song 2004
1048	Jidong Liu et al., <i>Argonaute2 is the Catalytic Engine of Mammalian RNAi</i> , 305 SCIENCE 1437 (2004)	

Exhibit	Description	Abbreviation
1049	Gunter Meister, <i>Argonaute Proteins: Functional Insights and Emerging Roles</i> , 14 NATURE REVIEWS GENETICS 447 (2013)	
1050	Antonin R. de Fougérolles & John M. Maraganore, <i>Chapter 16 Discovery and Development of RNAi Therapeutics</i> , in ANTISENSE DRUG TECHNOLOGY: PRINCIPLES, STRATEGIES AND APPLICATIONS 465 (Stanley T. Crooke 2d ed. 2008)	de Fougérolles 2008
1051	Reserved	
1052	<i>First Version of Human Genome Reference Sequence Debuts on DNA's 50th</i> , NCBI NEWS (Spring 2003)	
1053	Phillip A. Sharp, <i>RNA Interference-2001</i> , 15 GENES & DEVELOPMENT 485 (2001)	
1054	Peter M. Waterhouse et al., <i>Gene Silencing as an Adaptive Defence Against Viruses</i> , 411 NATURE 834 (2001)	

Exhibit	Description	Abbreviation
1055	Thomas Tuschl & Arndt Borkhardt, <i>Small Interfering RNAs: A Revolutionary Tool for the Analysis of Gene Function and Gene Therapy</i> , 2 MOL. INTERVENTIONS 158 (2002)	
1056	Jochen W. Klingelhoefer et al., <i>Approximate Bayesian Feature Selection on a Large Meta-Dataset Offers Novel Insights on Factors that Affect siRNA Potency</i> , 25 BIOINFORMATICS 1594 (2009)	
1057	Jens Harborth et al., <i>Identification of Essential Genes in Cultured Mammalian Cells Using Small Interfering RNAs</i> , 114 J. CELL SCI. 4557 (2001)	
1058	Andrew Fire et al., <i>Potent and Specific Genetic Interference by Double-Stranded RNA in <i>Caenorhabditis elegans</i></i> , 391 NATURE 806 (1998)	
1059	Harvey Lodish et al., <i>Chapter 4, Nucleic Acids, the Genetic Code and the Synthesis of Macromolecules</i> , in MOLECULAR CELL BIOLOGY 100 (4th ed. 2000)	

Exhibit	Description	Abbreviation
1060	Bryan A. Kraynack & Brenda F. Baker, <i>Small Interfering RNAs Containing Full 2'-O-Methylribonucleotide-Modified Sense Strands Display Argonaute2/eIF2C2-Dependent Activity</i> , 12 RNA 163 (2006)	Kraynack 2006
1061	Feb. 8, 2008 Declaration of Dr. Jörg Kaufmann ('987 File History Excerpt)	
1062	European Patent No. EP 0 586 520	
1063	European Patent No. EP 0 618 925	
1064	International Publication No. WO 03/070918	McSwiggen PCT
1065	David V. Morrissey et al., <i>Activity of Stabilized Short Interfering RNA in a Mouse Model of Hepatitis B Virus Replication</i> , 41 HEPATOLOGY 1349 (2005)	Morrissey 2005
1066	Reserved	
1067	Reserved	

Exhibit	Description	Abbreviation
1068	<i>Glossary of Class Names of Organic Compounds and Reactive Intermediates Based on Structure (IUPAC Recommendations 1995), 67 Pure and Applied Chemistry 1307 (1995) (Excerpt)</i>	
1069	Reserved	
1070	Reserved	
1071	Reserved	
1072	Sorim Choung, et al., <i>Chemical Modification of siRNAs to Improve Serum Stability without Loss of Efficacy</i> , 342 BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS 919 (2006)	Choung
1073	Reserved	
1074	Reserved	
1075	Reserved	
1076	David Bumcrot, et al., <i>RNAi Therapeutics: A Potential New Class of Pharmaceutical Drugs</i> , 2 NATURE CHEMICAL BIOLOGY 12 (December 2006)	Bumcrot 2006
1077	Reserved	

Exhibit	Description	Abbreviation
1078	Reserved	
1079	Reserved	
1080	Reserved	
1081	Reserved	
1082	Peter Podbevsek, <i>et al.</i> , <i>Solution-State Structure of a Fully Alternately 2'-F/2'-OMe modified 42-nt dimeric siRNA Construct</i> , 38 NUCLEIC ACIDS RESEARCH 20 (2010)	
1083	International Publication No. WO 2005/089224 by de Fougerolles A. <i>et al.</i>	
1084	Walter R. Strapps, <i>et al.</i> , <i>The siRNA Sequence and Guide Strand Overhangs are Determinants of In Vivo Duration of Silencing</i> , 38 NUCLEIC ACIDS RESEARCH 14 (2010)	
1085	Dong-Ho Kim, <i>et al.</i> , <i>Synthetic dsRNA Dicer Substrates Enhance RNAi Potency and Efficacy</i> , 23 NATURE BIOTECHNOLOGY 2 (2005)	

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1086	Scott D. Rose, <i>et al.</i> , <i>Functional Polarity is Introduced by Dicer Processing of Short Substrate RNAs</i> , 33 NUCLEIC ACIDS RESEARCH 13 (2005)	
1087	NCBI Nucleotide Blast Results for the 2'-F/2'-OMe siRNA	
1088	Chan Il Chang, <i>et al.</i> , A Structural-Activity Relationship Study of siRNAs with Structural Variations, 359 BIOCHEM. BIOPHYS. RES. COMMUN. 4 (2007)	
1089	Reserved	
1090	Chan Il Chang, <i>et al.</i> , <i>Structural Diversity Repertoire of Gene Silencing Small Interfering RNAs</i> , 21 NUCLEIC ACID THERAPEUTICS 3 (2011)	
1091	November 20, 2018 Declaration in Support of Petitioner's Motion for Pro Hac Vice Admission of Ha Kung Wong	

Exhibit	Description	Abbreviation
1092	November 20, 2018 Declaration in Support of Petitioner's Motion for Pro Hac Vice Admission of Robert S. Schwartz	
1093	November 20, 2018 Declaration in Support of Petitioner's Motion for Pro Hac Vice Admission of Melinda R. Roberts	

Dated: December 5, 2018

Respectfully submitted,

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CERTIFICATE OF SERVICE

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