



Agenda

Welcome

 Christine Lindenboom, Vice President, Investor Relations & Corporate Communications

Introduction and ONPATTRO (patisiran)

Eric Green, Vice President, General Manager, TTR Program

A Payer's Perspective

 Michael Sherman, M.D., M.B.A., Chief Medical Officer and Senior Vice President for Health Services, Harvard Pilgrim Health Care

ALN-TTRsc02

Rena Denoncourt, Program Leader, ALN-TTRsc02 Program

Q&A Session



Reminders

Event will run for approximately 60-75 minutes

Q&A session at end of presentation

 Questions may be submitted at any time via the 'Ask a Question' field on the webcast interface.

Replay, slides and transcript available at www.alnylam.com/capella



Alnylam Forward Looking Statements

This presentation contains forward-looking statements, within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. There are a number of important factors that could cause actual results to differ materially from the results anticipated by these forward-looking statements. These important factors include our ability to discover and develop novel drug candidates and delivery approaches and successfully demonstrate the efficacy and safety of our product candidates; pre-clinical and clinical results for our product candidates; actions or advice of regulatory agencies; delays, interruptions or failures in the manufacture and supply of our product candidates; our ability to obtain, maintain and protect intellectual property, enforce our intellectual property rights and defend our patent portfolio; our ability to obtain and maintain regulatory approval, pricing and reimbursement for products; our progress in establishing a commercial and ex-United States infrastructure; our ability to successfully launch, market and sell our approved products globally; our ability to successfully expand the indication for ONPATTRO™ (patisiran) in the future; competition from others using similar technology and developing products for similar uses; our ability to manage our growth and operating expenses, obtain additional funding to support our business activities and establish and maintain business alliances; the outcome of litigation; and the risk of government investigations; as well as those risks more fully discussed in our most recent report on Form 10-Q under the caption "Risk" Factors." If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. All forward-looking statements speak only as of the date of this presentation and, except as required by law, we undertake no obligation to update such statements.



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RNAi Therapeutics: New Class of Innovative Medicines

Clinically Proven Approach with Transformational Potential

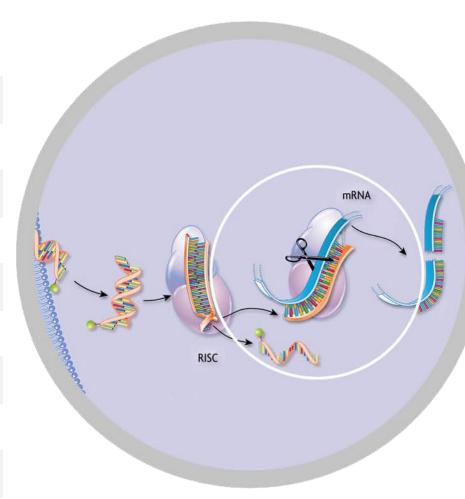
Nobel Prize-winning science

Silence any gene in genome

Potent and durable mechanism of action

Product engine for sustainable pipeline

Now commercial





Alnylam Clinical Development Pipeline

Focused in 4 Strategic Therapeutic Areas (STArs):

	Genetic Medicines
--	-------------------

	Metabolic Diseases Infectious Diseases seases	HUMAN POC1	BREAKTHROUGH DESIGNATION	EARLY STAGE (IND or CTA Filed-Phase 2)	LATE STAGE (Phase 2-Phase 3)	REGISTRATION	COMMERCIAL	COMMERCIAL RIGHTS
ONPATTRO™ (patisiran)²	hATTR Amyloidosis	2	₽.	(IND or CTA Filed-Phase 2)	(Phase 2-Phase 3)	REGIOTRATION		Global
Givosiran	Acute Hepatic Porphyrias		Q		•			Global
Fitusiran	Hemophilia and Rare Bleeding Disorders	V						15-30% Royalties
Inclisiran	Hypercholesterolemia				•			Milestones & up to 20% Royalties
ALN-TTRsc02	ATTR Amyloidosis	V		•				Global
Lumasiran	Primary Hyperoxaluria Type 1		Q	•				Global
Cemdisiran	Complement-Mediated Diseases			•				Global

¹POC, proof of concept – defined as having demonstrated target gene knockdown and/or additional evidence of activity in clinical studies

² Approved in the U.S. for the polyneuropathy of hATTR amyloidosis in adults, and in the EU for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy



Alnylam Clinical Development Pipeline

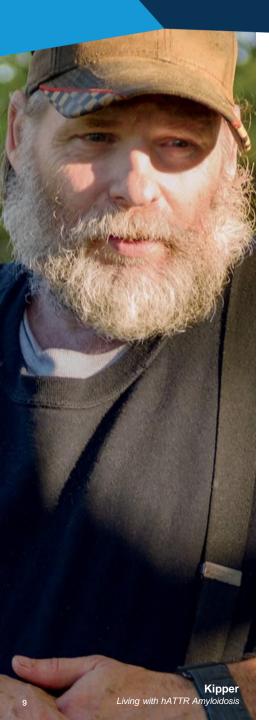
Focused in 4 Strategic Therapeutic Areas (STArs):

i ocus c u ii	14 Strategic Therape	ulic Aleas	5 (31A15).					
Genetic	Medicines							
Cardio-l	Metabolic Diseases							
	Infectious Diseases	HUMAN	BREAKTHROUGH	EARLY STAGE	LATE STAGE			COMMERCIAL
CNS Dis	seases	POC ¹	DESIGNATION	(IND or CTA Filed-Phase 2)	(Phase 2-Phase 3)	REGISTRATION	COMMERCIAL	RIGHTS
ONPATTRO™ (patisiran)²	hATTR Amyloidosis	V	S				•	Global
Givosiran	Acute Hepatic Porphyrias	2/	Q					Global
Fitusiran		2						15-30% Royalties
Inclisiran	Hypercholesterolemia	2/						Milestones & up to 20% Royalties
ALN-TTRsc02	ATTR Amyloidosis	V		•				Global
Lumasiran	Primary Hyperoxaluria Type 1	2/	Q					Global
Cemdisiran		2/						

¹ POC, proof of concept – defined as having demonstrated target gene knockdown and/or additional evidence of activity in clinical studies

² Approved in the U.S. for the polyneuropathy of hATTR amyloidosis in adults, and in the EU for the treatment of hATTR amyloidosis in adults with stage 1 or





Hereditary ATTR (hATTR) Amyloidosis

Description

Mutations in TTR gene lead to deposition of misfolded protein as amyloid, causing polyneuropathy and other multisystem disease manifestations¹

Median survival

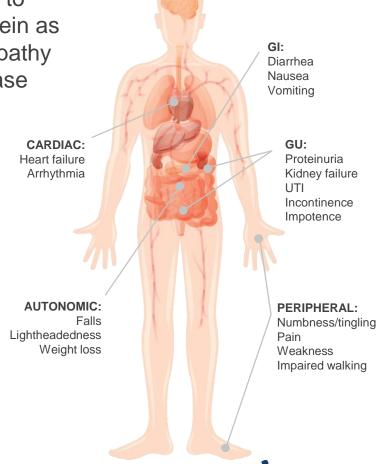
4.7

years from diagnosis

Patient Population*

~50,000

worldwide



¹ Coelho T, et al. N Engl J Med. 2013;369(9):819-829

^{*} Ando et al., Orphanet J Rare Dis, 2013; Ruberg et al., Circulation, 2012

The first RNAi therapeutic is NOW APPROVED







First and Only Therapy Approved for Patients with hATTR Amyloidosis in U.S.

Approved U.S. Indication

For the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

Data in Label Includes data from APOLLO primary and select secondary endpoints.





"This approval is part of a broader wave of advances that allow us to treat disease by actually targeting the root cause, enabling us to arrest or reverse a condition, rather than only being able to slow its progression or treat its symptoms...New technologies like RNA inhibitors, that alter the genetic drivers of a disease, have the potential to transform medicine, so we can better confront and even cure debilitating illnesses."

~ Scott Gottlieb, MD, FDA Commissioner, Press Release, 8/10/2018



ONPATTRO on Market 1st Business Day Post U.S. Approval



ONPATTRO U.S. Label Highlights

Dosing & Administration

Dosing:

- 0.3 mg/kg (patients <100 kg)
- 30 mg (patients ≥100 kg)

Premedication (day of infusion):

- · IV dexamethasone, 10 mg
- IV H1 and H2 blockers
- · Oral acetaminophen

Administration:

· Should be performed by healthcare professional.

Safety

No contraindications Warnings and Precautions

- <u>Infusion-related reactions</u>: Monitor for signs and symptoms during infusion. Slow or interrupt the infusion if clinically indicated. Discontinue the infusion if a serious or life-threatening infusion-related reaction occurs.
- Reduced serum vitamin A levels and recommended supplementation:
 Supplement with the recommended daily allowance of vitamin A. Refer to an ophthalmologist if ocular symptoms suggestive of vitamin A deficiency occur.

Common adverse reactions are upper respiratory tract infections and infusion-related reactions

No required laboratory monitoring

For additional information about ONPATTRO, please see the full Prescribing Information.



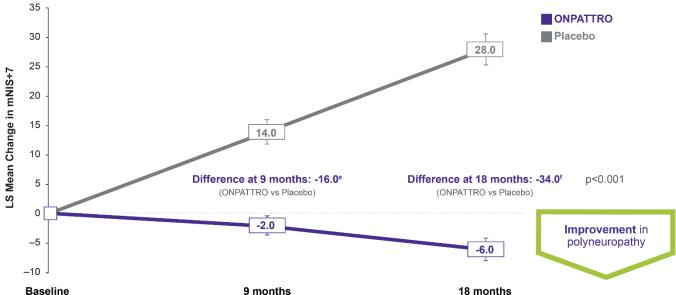
Change From Baseline in mNIS+7¹

Primary Endpoint: Change from baseline in mNIS+7, a specialized assessment of polyneuropathy in hATTR amyloidosis^{a-d}

• The mean change from baseline in mNIS+7 at 18 months was -6.0 points (improvement) for ONPATTRO-treated patients versus 28.0 points (worsening) for patients who received placebo, a difference of -34 points

• In a binary analysis of the primary endpoint, 56% of ONPATTRO-treated patients experienced reversal in neuropathy impairment, defined as a change in mNIS+7 of <0 from baseline at 18 months, compared with 4% of placebo-treated





^aPossible total score ranges from 0 to 304.

hATTR=hereditary transthyretin-mediated LS=least squares mNIS=modified Neuropathy Impairment Score



bImprovement defined as a decrease in mNIS+7 compared to placebo.

^cBars represent SEM (standard error of the mean).

dMean mNIS+7 at baseline was 80.9 with ONPATTRO and 74.6 with placebo.

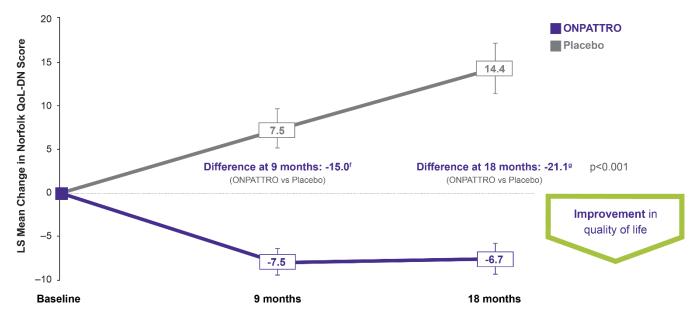
e95% CI: -20.7, -11.3.

f95% CI: -39.9, -28.1.

Change From Baseline in Norfolk QoL-DN Score¹

Significant improvement in quality of life vs placebo, as measured by Norfolk QoL-DNa-d

- For ONPATTRO-treated patients, the mean change from baseline in Norfolk QoL-DN at 18 months was -6.7 points (improvement) versus 14.4 points (worsening) for patients who received placebo, a difference of -21.1 points
- At 18 months, 51% of ONPATTRO-treated patients experienced improvement from baseline in QoL compared with 10% of placebo-treated patients²



^aPossible total score ranges from -4 to 136.

f95% CI: -27.2, -15.0.

LS=least squares

Norfolk QoL-DN=Norfolk Quality of Life-Diabetic Neuropathy



bImprovement defined as Norfolk QoL-DN change from baseline <0 points.

^cBars represent SEM (standard error of the mean).

^dNorfolk QoL-DN scores at baseline were 59.6 with ONPATTRO and 55.5 with placebo.

e95% CI: -19.8, -10.2.

Full Results of APOLLO Study Published July 2018

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JULY 5, 2018

VOL. 379 NO. 1

Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis

D. Adams, A. Gonzalez-Duarte, W.D. O'Riordan, C.-C. Yang, M. Ueda, A.V. Kristen, I. Tournev, H.H. Schmidt, T. Coelho, J.L. Berk, K.-P. Lin, G. Vita, S. Attarian, V. Planté-Bordeneuve, M.M. Mezei, J.M. Campistol, J. Buades, T.H. Brannagan III, B.J. Kim, J. Oh, Y. Parman, Y. Sekijima, P.N. Hawkins, S.D. Solomon, M. Polydefkis, P.J. Dyck, P.J. Gandhi, S. Goyal, J. Chen, A.L. Strahs, S.V. Nochur, M.T. Sweetser, P.P. Garg, A.K. Vaishnaw, J.A. Gollob, and O.B. Suhr

ABSTRACT

Patisiran, an investigational RNA interference therapeutic agent, specifically inhibits
The authors' full names, academic dehepatic synthesis of transthyretin.

In this phase 3 trial, we randomly assigned patients with hereditary transthyretin amyloidosis with polyneuropathy, in a 2:1 ratio, to receive intravenous patisiran (0.3 mg per kilogram of body weight) or placebo once every 3 weeks. The primary end point was the change from baseline in the modified Neuropathy Impairment Score+7 (mNIS+7; range, 0 to 304, with higher scores indicating more impairment) Copyright © 2018 Massachusens Medical Society. at 18 months. Other assessments included the Norfolk Quality of Life-Diabetic Neuropathy (Norfolk QOL-DN) questionnaire (range, -4 to 136, with higher scores indicating worse quality of life), 10-m walk test (with gait speed measured in meters per second), and modified body-mass index (modified BMI, defined as [weight in kilograms divided by square of height in meters] xalbumin level in grams per liter; lower values indicated worse nutritional status).

A total of 225 patients underwent randomization (148 to the patisiran group and 77 to the placebo group). The mean (±SD) mNIS+7 at baseline was 80.9±41.5 in the patisiran group and 74.6±37.0 in the placebo group; the least-squares mean (±SE) change from baseline was -6.0±1.7 versus 28.0±2.6 (difference, -34.0 points; P<0.001) at 18 months. The mean (±SD) baseline Norfolk QOL-DN score was 59.6±28.2 in the patisiran group and 55.5±24.3 in the placebo group; the least-squares mean (±SE) change from baseline was -6.7±1.8 versus 14.4±2.7 (difference, -21.1 points; P<0.001) at 18 months. Patisiran also showed an effect on gait speed and modified BMI. At 18 months, the least-squares mean change from baseline in gait speed was 0.08±0.02 m per second with patisiran versus -0.24±0.04 m per second with placebo (difference, 0.31 m per second; P<0.001), and the least-squares mean change from baseline in the modified BMI was -3.7±9.6 versus -119.4±14.5 (difference, 115.7; P<0.001). Approximately 20% of the patients who received patisiran and 10% of those who received placebo had mild or moderate infusion-related reactions; the overall incidence and types of adverse events were similar in the two groups.

In this trial, patisiran improved multiple clinical manifestations of hereditary transthyretin amyloidosis. (Funded by Alnylam Pharmaceuticals; APOLLO ClinicalTrials .gov number, NCT01960348.)

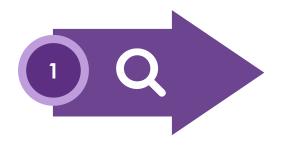
N ENGL | MED 379:1 NEIM.ORG | JULY 5, 2018

The New England Journal of Medicine

grees, and affiliations are listed in the Apendix. Address reprint requests to Dr. Adams at the Department of Neurology, CHU Bicêtre, 78 rue du Général Leclerc, 94275 Le Kremlin-Bicêtre CEDEX, France, or at david.adams@aphp.fr.

N Engl J Med 2018;379:11-21.

U.S. Commercialization Underway











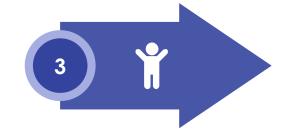




Brand Choice







Treatment Experience and Access





Unified Commercial, Market Access, & Medical Affairs teams driving disease education, diagnosis, optimized patient experience, and access to care

Alnylam Act :: No-charge, Third-party Genetic Testing and Counseling Program

Developed to reduce barriers to genetic testing and counseling to help people make more informed decisions about their health

Alnylam provides financial support for the program, but **the tests and services are performed by independent third parties** for individuals who may carry gene mutations known to be associated with hATTR amyloidosis

Genetic counselors provide information and support for people who have, or may be at risk for, genetic conditions

Genetic testing service available in U.S. and Canada. Genetic counseling service available in U.S.

Healthcare professionals who use this program **have no obligation** to recommend, purchase, order, prescribe, promote, administer, use or support any Alnylam product

More information regarding this program available at: www.alnylamact.com



Ongoing Support from Alnylam Assist™

Alnylam Assist is a comprehensive program dedicated to helping guide patients through treatment with ONPATTRO



A dedicated Case Manager

Alnylam Assist will connect patients with a dedicated Alnylam Case Manager who can provide personalized support throughout the treatment process.



Benefit verification

Coverage for ONPATTRO will vary by plan and by patient. Alnylam Assist can help determine patient-specific coverage requirements.



Financial assistance for patients

Eligible patients may qualify for the Alnylam Assist Quick Start Program, Patient Assistance Program (PAP), or Commercial Copay Program.



Treatment coverage

Alnylam Assist can explain the requirements and processes for prior authorizations, claims, and appeals.



Coding and billing

A Field Reimbursement Director can provide education about billing, coding, and the reimbursement process for ONPATTRO.



Disease and product education

Patient Education Liaisons are available to help patients gain a better understanding of the disease.



Ordering assistance

Alnylam Assist will help with ordering and facilitation of delivery via specialty distributor or specialty pharmacy.





First-Ever RNAi Therapeutic Approved in the EU

Approved EU Indication

For the treatment of hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) in adults with stage 1 or stage 2 polyneuropathy

Data in Label

Includes data from APOLLO primary and secondary endpoints, as well as exploratory cardiac endpoints



August 29, 2018



"The safety and efficacy of Onpattro was evaluated in a pivotal trial involving 225 patients with hATTR amyloidosis and symptomatic polyneuropathy. The study showed clinically-relevant improvements in the neurological manifestations of the disease and on patients' quality of life, as well as a positive impact on cardiac parameters."

~ CHMP Opinion Press Release, 7/27/2018

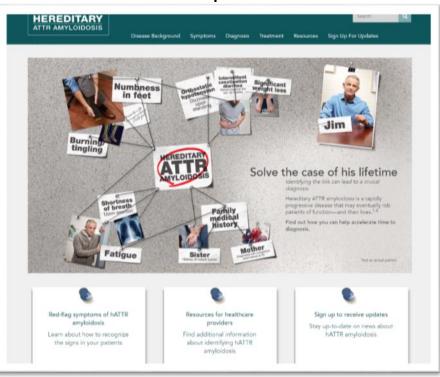


For additional information about ONPATTRO, please see the Summary of Product Characteristics (<u>SmPC</u>).



Global Disease Education Resources

Health care professionals



Patients and their families



www.hattramyloidosis.de www.hattramyloidosis.fr www.hattramyloidosis.it www.hattramyloidosis.es www.hattramyloidosis.pt www.hattramyloidosis.co.uk www.hATTRbridge.de
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Global Progress of ONPATTRO



 Provide patisiran to eligible adults in UK with hATTR amyloidosis through MHRA Early Access to Medicines Scheme (EAMS)





- Additional regulatory submissions by year end
 - Continued infrastructure build out for global commercialization in 2019 and beyond



Japan

- Increasing presence in Japan
 - Head of Asia and seasoned leadership team on board
- On track for JNDA filing with Japanese Pharmaceuticals and Medical Devices Agency (PMDA) in mid-2018
 - PMDA decision for approval anticipated June 2019



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Q&A Session



A Payer's Perspective





Michael Sherman, M.D., M.B.A Chief Medical Officer and Senior Vice President for Health Services Harvard Pilgrim Health Care

In his role as Senior Vice President & Chief Medical Officer at Harvard Pilgrim Health Care, Dr. Sherman is responsible for Harvard Pilgrim's medical trend management, network medical management, medical informatics, wellness and health promotion initiatives, care and disease management services, pharmacy services, NCQA accreditation and quality and utilization management programs. He also serves as chair of the board of managers of the Harvard Pilgrim Health Care Institute, which includes the Department of Population Medicine at Harvard Medical School. A leader in driving adoption of outcomes-based provider and pharmaceutical contracts. Dr. Sherman has overseen the execution of over a dozen outcomes-based contracts with major pharmaceutical companies that go beyond the current "pay per pill" paradigm.

Dr. Sherman serves as chair of the Board of Managers of the Harvard Pilgrim Health Care Institute, which encompasses the Department of Population Medicine at Harvard Medical School and on the Advisory Board of the Institute for Clinical and Economic Review (ICER). He also is the current chair for AHIP's CMO Leadership Council, comprising chief medical officers from health plans throughout the United States, and serves on the board of directors for the Personalized Medicine Coalition.

Prior to joining Harvard Pilgrim, Dr. Sherman held leadership roles at Humana, UnitedHealth Group, and Thomson Medstat (now IBM Truven). He holds a B.A. and an M.S. in biomedical anthropology from the University of Pennsylvania and received his M.D. from Yale and M.B.A. from the Harvard Business School.



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ALN-TTRsc02

Rena Denoncourt, Program Leader, ALN-TTRsc02 Program

Q&A Session



Alnylam's Commitment to ATTR Amyloidosis Patients

Continued Innovation in ATTR with Investigational ALN-TTRsc02

Development Status for ALN-TTRsc02

- Completed Phase 1 study in healthy volunteers
- Granted Orphan Drug Designation (ODD) in US and Europe for Treatment of Transthyretin-Mediated Amyloidosis (ATTR amyloidosis)
 - Covers both the hereditary and wild-type forms of the disease
- Proactively engaging with regulatory agencies, physicians, and payers to establish a clinical development plan addressing heterogeneous needs of the broad patient population

Potential Product Attributes for ALN-TTRsc02



POTENT AND SUSTAINED TTR KNOCKDOWN



INFREQUENT, QUARTERLY SUBCUTANEOUS DOSING



SIMPLE, FIXED DOSE, SELF-ADMINISTRATION VIA PRE-FILLED SYRINGE

Expect to initiate a
Phase 3 pivotal study in
hATTR amyloidosis in Late 2018

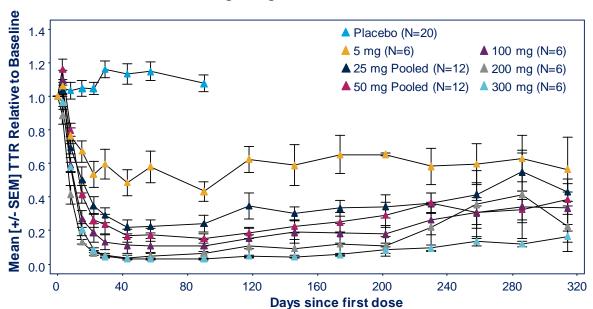


ALN-TTRsc02 Phase 1 Study*

Phase 1 Study Design



TTR Reduction Following Single Dose ALN-TTRsc02 Administration



ALN-TTRsc02 Achieves Robust and Durable Serum TTR Knockdown (KD)

Mean max TTR KD of 83% after single 25 mg dose

Safety (N=80):

- No SAEs and no discontinuations due to AEs
- All AEs mild or moderate in severity

~90% peak TTR KD predicted after repeat dosing



^{*} Taubel J, et al. Phase 1 Study of ALN-TTRsc02, a Subcutaneously Administered Investigational RNAi Therapeutic for the Treatment of Transthyretin-Mediated Amyloidosis. ISA 2018: XVIIth International Symposium of Amyloidosis; Kumamoto, Japan; March 2018 (poster)

ALN-TTRsc02 Phase 3 HELIOS · A Study

Planned Initiation Late 2018





Alignment reached on pivotal trial design

Endpoints

mNIS+7 & Norfolk-QOL (co-primary) certain cardiac parameters

~120 patients with hATTR amyloidosis

VS.

Details

open label nine months

APOLLO placebo arm results

Reference arm of ~30 patients on patisiran to be included. No formal comparisons between patisiran and ALN-TTRsc02 planned.

Additional Phase 3 studies, including in wild-type ATTR amyloidosis, planned for 2019



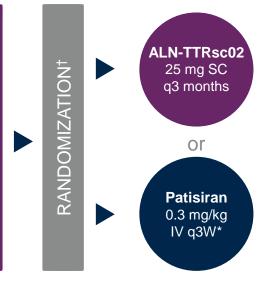
ALN-TTRsc02 Phase 3 HELIOS · A Study

Randomized, Open-label Study in Hereditary ATTR Amyloidosis Patients



Patient Population N=~150

- hATTR amyloidosis; any TTR mutation
- Neuropathy Impairment Score (NIS) of 5-130
- Prior tetramer stabilizer use permitted





- * Patisiran-treated patients will receive premedication prior to patisiran infusion: 10 mg (low dose) dexamethasone; oral acetaminophen; H1 and H2 blockers. After relevant efficacy assessments have been completed, patients will transition to q3m ALN-TTRsc02 for the remainder of the study
- ^ Primary efficacy endpoint at 9 months; total treatment period is 18 months. Full set of assessments conducted at 9 and 18 months. Additionally, at 18 months, all-cause death and hospitalization will be assessed.

Trial design is not final and is subject to further diligence and health authority feedback



Efficacy Assessments[^]

Co-Primary Endpoints (vs APOLLO placebo)

- Change in mNIS+7 from baseline
- · Change in Norfolk QOL-DN from baseline

Secondary Endpoints

- 10-meter walk test (10-MWT)
- mBMI
- Activities of daily living (R-ODS)
- TTR reduction
- · All-cause death and hospitalization (mITT)
- All-cause death and hospitalization (patients with cardiac involvement)

Exploratory Endpoints Include

- NT-proBNP
- Echo parameters

ALN-TTRsc02 Phase 3 HELIOS · A Study

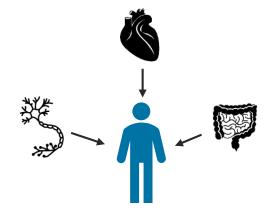
Key Study Design Elements





Global Footprint

Enrollment with various hATTR amyloidosis mutation types



Similar inclusion and exclusion criteria to APOLLO

Patients with multi-systemic disease manifestations and a range of disease severity



Assessments leveraging wellestablished tools for thorough evaluations of various aspects of disease burden

Harnessing RNAi with ALN-TTRsc02, the HELIOS-A study will evaluate a 25mg dose administered subcutaneously once every three months



A Transformative and Historic Year for Alnylam and the TTR Programs

- First-ever approval of a RNAi therapeutic in the U.S. and EU in August
- · Commercialization ongoing in U.S. and gearing up in EU
- Continued global expansion with regulatory filings in Japan, Canada and Switzerland planned this year
- Continued commitment to ATTR amyloidosis patients with ALN-TTRsc02 entering Late Stage Development later this year

			2018*		
*Early is Q1-Q2, Mid is Q2-Q3, and Late is Q3-Q4		Early	Mid	Late	
ONPATTRO (patisiran)	Additional APOLLO Phase 3 data	Ø	Ø		
	FDA approval		Ø		
	U.S. launch		Ø		
(hATTR Amyloidosis with	J-NDA submission				
polyneuropathy ¹)	EMA approval			Ø	
	EU launch				
	Additional ROW submissions				
ALN-TTRsc02 ² (ATTR Amyloidosis)	Start Phase 3			•	

¹ Approved in the U.S. for the polyneuropathy of hATTR amyloidosis in adults, and in the EU for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy; ² ALN-TTRsc02 is an investigational RNAi therapeutic



2040*

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Q&A Session



