Glaucienne
Diagnosed with AHP (Brazil)

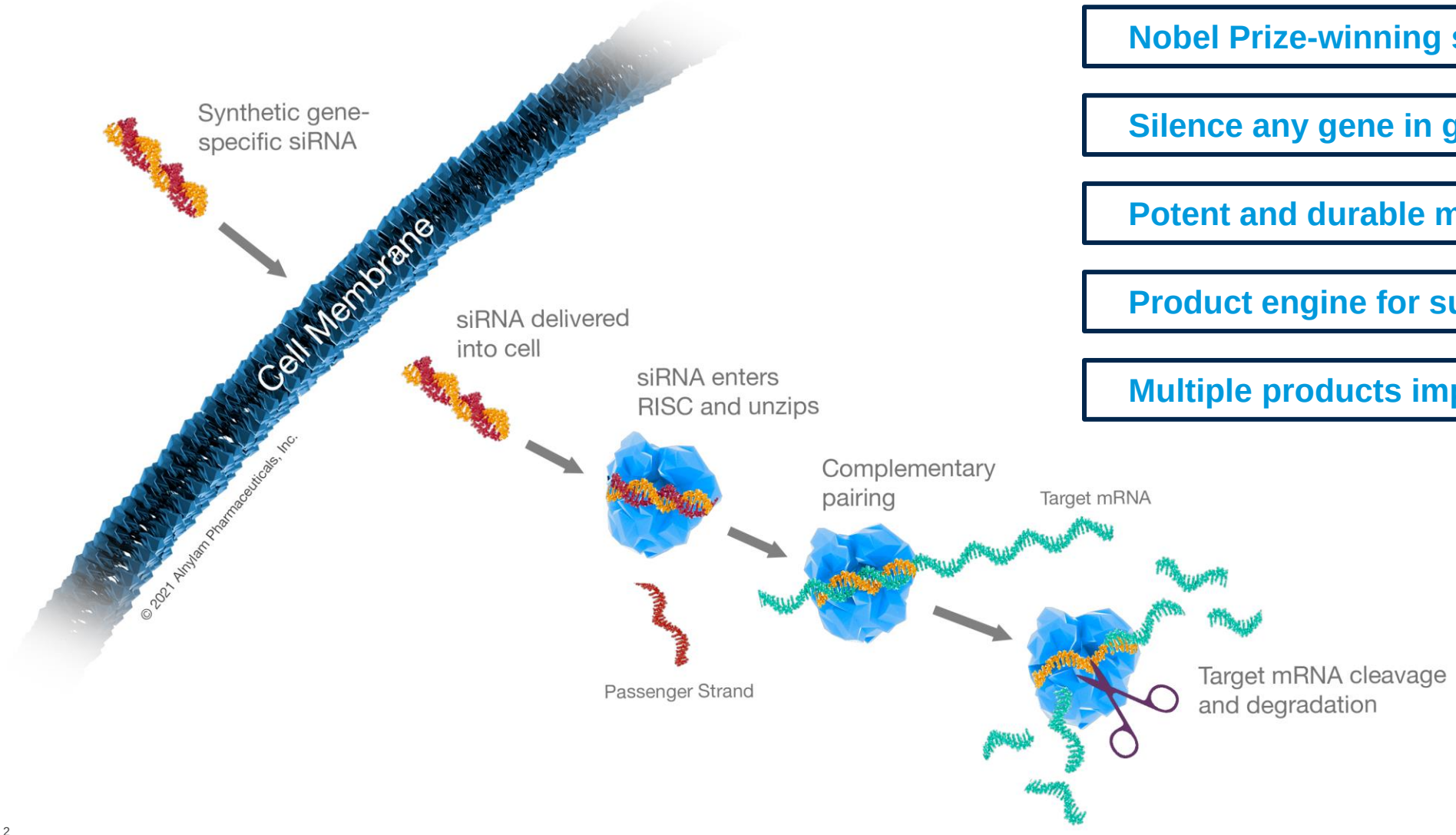
Harnessing RNAi for a New Class of Medicines

OTS
September 27, 2021

Alnylam® PHARMACEUTICALS

RNAi Therapeutics: New Class of Innovative Medicines

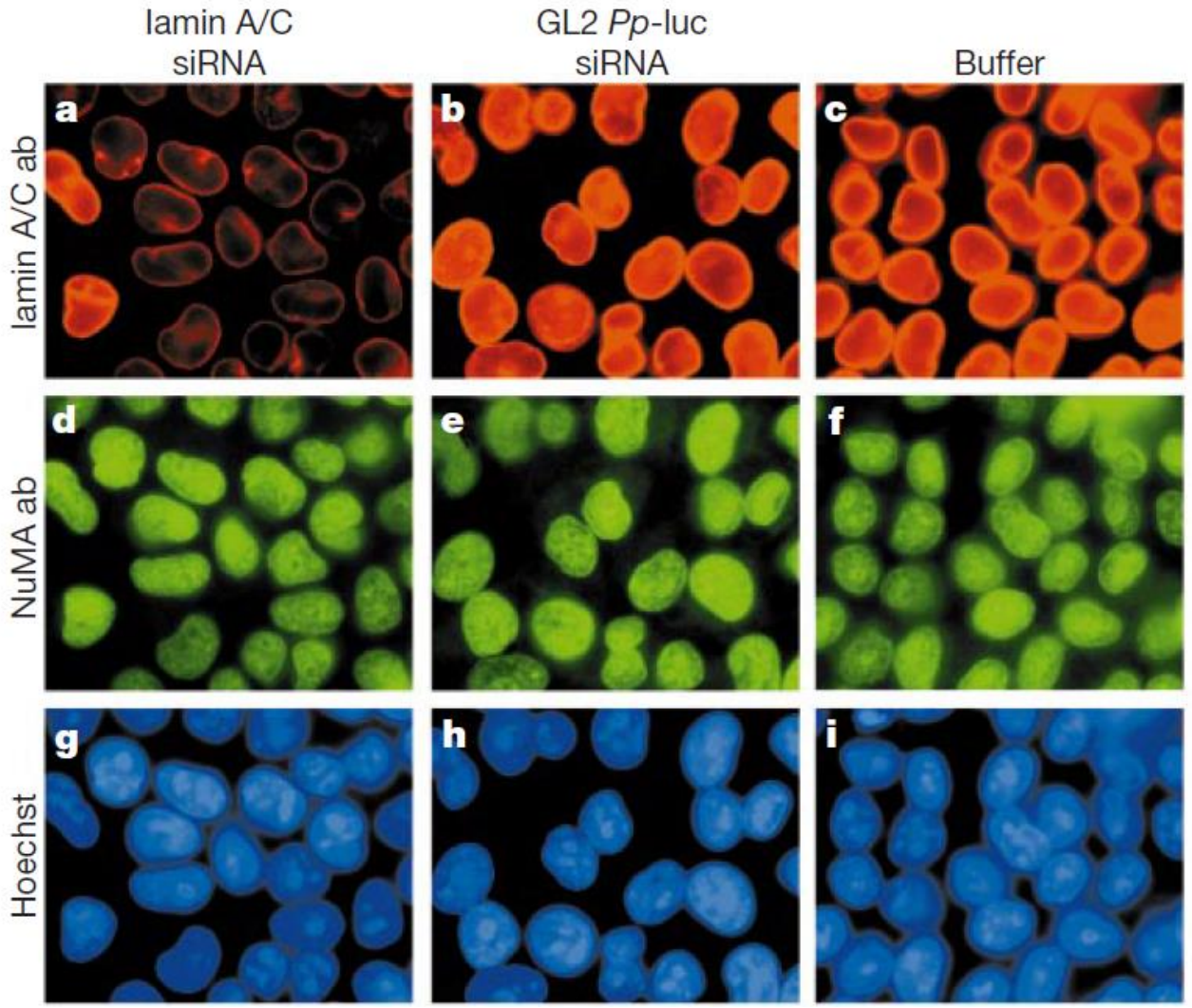
Clinically and Commercially Established Approach with Transformational Potential



- **Nobel Prize-winning science**
- **Silence any gene in genome with siRNAs**
- **Potent and durable mechanism of action**
- **Product engine for sustainable innovation**
- **Multiple products impacting patients globally**

In Vitro Data that Started Alnylam in 2002

Elbashir et al., Nature, 2001;411:494-98



Alnylam Clinical Development Pipeline

Focused in 4 Strategic Therapeutic Areas (STARs):

- Genetic Medicines
- Cardio-Metabolic Diseases
- Infectious Diseases
- CNS/Ocular Diseases

		EARLY/MID-STAGE *(IND/CTA Filed-Phase 2)*	LATE STAGE *(Phase 2-Phase 3)*	REGISTRATION/ COMMERCIAL[1] (OLE/Phase 4/IIS/registries)	COMMERCIAL RIGHTS
onpattro (patisiran)	*hATTR Amyloidosis-PN*[2]			●	Global
GIVLAARI (givosiran)	*Acute Hepatic Porphyria*[3]			●	Global
OXLUMO (lumasiran)	*Primary Hyperoxaluria Type 1*[4]			●	Global
Leqvio® (inclisiran)	*Hypercholesterolemia*			●	Milestones & up to 20% Royalties[5]
Vutrisiran*	*hATTR Amyloidosis-PN*			●	Global
Patisiran	*ATTR Amyloidosis*		●		Global
Vutrisiran*	*ATTR Amyloidosis*		●		Global
Fitusiran*	*Hemophilia*		●		15-30% Royalties
Lumasiran	*Severe PH1* *Recurrent Renal Stones*	●	●		Global
Cemdisiran*	*Complement-Mediated Diseases*	●			50-50
Cemdisiran/Pozelimab Combo[6]*	*Complement-Mediated Diseases*	●			Milestone/Royalty
Belcesiran[7]*	*Alpha-1 Liver Disease*	●			Ex-U.S. option post-Phase 3
ALN-HBV02 (VIR-2218)[8]*	*Hepatitis B Virus Infection*	●			50-50 option post-Phase 2
Zilebesiran (ALN-AGT)*	*Hypertension*	●			Global
ALN-HSD*	*NASH*	●			50-50

[1] Includes marketing application submissions; [2] Approved in the U.S. and Canada for the PN of hATTR amyloidosis in adults, and in the EU, Japan and other countries for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy; [3] Approved in the U.S., Brazil and Canada for the treatment of adults with acute hepatic porphyria (AHP), and in the EU and Japan for the treatment of AHP in adults and adolescents aged 12 years and older; [4] Approved in the U.S., EU and Brazil for the treatment of primary hyperoxaluria type 1 in all age groups; [5] Novartis has obtained global rights to develop, manufacture and commercialize inclisiran; 50% of inclisiran royalty revenue from Novartis will be payable to Blackstone by Alnylam; [6] Cemdisiran and pozelimab are each currently in Phase 2 development; Alnylam and Regeneron are evaluating potential combinations of these two investigational therapeutics; [7] Dicerna is leading and funding development of Belcesiran; [8] Vir is leading and funding development of ALN-HBV02; * Not approved for any indication and conclusions regarding the safety or efficacy of the drug have not been established.

As of August 2021

RNAi Therapeutics: Transformational Medicines for Rare & Prevalent Diseases

Four Global Approvals in Just Over 2 Years

onpattro® (patisiran) lipid complex injection 10 mg/5 mL

Hereditary ATTR Amyloidosis with Polyneuropathy

U.S.
EU
Canada
Japan
Switzerland
Brazil
Israel
Taiwan

2018

GIVLAARI® (givosiran) injection for subcutaneous use 189 mg/mL

Acute Hepatic Porphyria

U.S.
EU
Brazil
Canada
Switzerland
Japan

2019

OXLUMO® (lumasiran) for injection 94.5 mg/0.5 mL

Primary Hyperoxaluria Type 1

EU
U.S.
Brazil

2020

Leqvio® (inclisiran)

Hypercholesterolemia

NOVARTIS

EU, Canada, Israel, UAE, Oman, Albania, Chile, Singapore, Argentina

2020

Agenda

- RNAi Therapeutics for Rare Diseases: hATTR-PN
- RNAi Therapeutics for Common Diseases: Hypertension
- New Frontiers for RNAi Therapeutics

Cece
Living with hATTR amyloidosis (USA)

ATTR Amyloidosis

Rare, Progressively Debilitating, and Fatal Disease

Description

Caused by misfolded TTR protein that accumulates as amyloid deposits in multiple tissues including heart, nerves, and GI tract[1]

Hereditary ATTR (hATTR) Amyloidosis

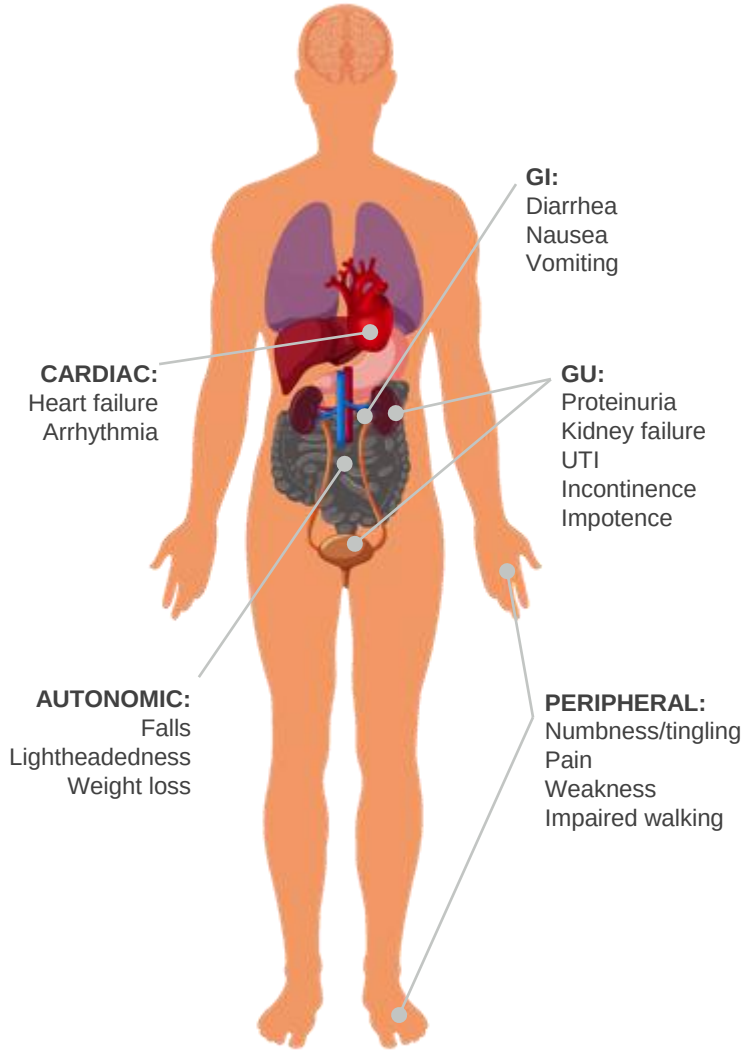
~50,000

patients worldwide*

Wild-Type ATTR (wtATTR) Amyloidosis

~200,000 – 300,000

patients worldwide



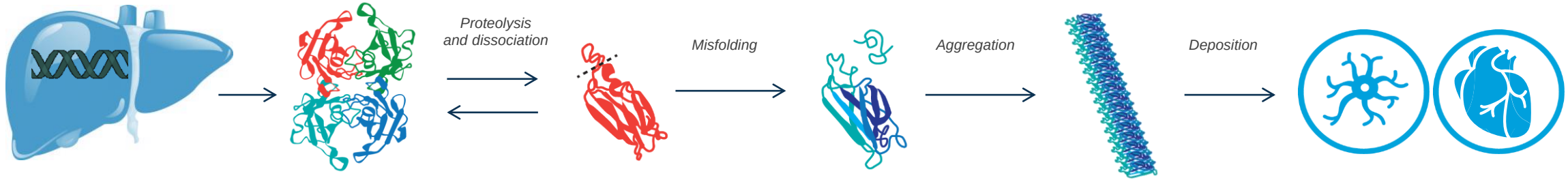
[1] Coelho T, et al. N Engl J Med. 2013;369(9):819-829

* Ando, et al. Orphanet J Rare Dis, 2013; Ruberg, et al. Circulation, 2012 (includes hATTR amyloidosis patients with polyneuropathy and cardiomyopathy)

Current or Potential Therapy Options for ATTR Amyloidosis

RNAi Therapeutics Work by Silencing the Source of Disease

ATTR Amyloidosis Disease Cascade and Current/Potential Therapies



***TTR* gene expressed in liver**

TTR tetramer

TTR fragments and full-length monomers

Misfolded, aggregation-prone monomer and fragments

Amyloid oligomers and fibril formation

Amyloidosis disease state

Eliminate production of mutant TTR:
- Orthotopic liver transplant

Suppression of TTR synthesis (gene silencing):
- **RNAi (patisiran, vutrisiran)**
- Antisense oligonucleotides
- Gene editing

Prevent dissociation of TTR tetramer:
- TTR stabilizers

Remove existing amyloid:
- Monoclonal antibodies

Alnylam's ATTR Amyloidosis Franchise

Approved Treatment Option, Investigational Clinical Programs, and a Preclinical Development Program

onpattro (patisiran) lipid complex injection 10 mg/5 mL

An Approved RNAi Therapeutic for Treatment of Polyneuropathy of hATTR Amyloidosis*

About ONPATTRO

- Favorable efficacy and safety profile in APOLLO
- APOLLO-B ongoing to evaluate patisiran in ATTR amyloidosis with cardiomyopathy ‡
- IV administration, once every 3 weeks

Vutrisiran

An Investigational RNAi Therapeutic for Potential Treatment of ATTR Amyloidosis†

About Vutrisiran

- Positive efficacy results and acceptable safety profile in HELIOS-A in hATTR amyloidosis with polyneuropathy
- HELIOS-B ongoing in ATTR amyloidosis with cardiomyopathy
- Subcutaneous administration, once every 3 months with potential for biannual dosing regimen

ALN-TTRsc04

A Preclinical RNAi Therapeutic for Potential Treatment of ATTR Amyloidosis

About ALN-TTRsc04

- IKARIA platform
- IND expected in 2022
- Subcutaneous administration with potential annual dosing regimen and >90% serum TTR reduction
- No third-party royalties; exclusivity expected to extend beyond 2040

* ONPATTRO is approved in the U.S. and Canada for the polyneuropathy of hATTR amyloidosis in adults, in the EU, Switzerland and Brazil for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy, and in Japan for the treatment of transthyretin (TTR) type familial amyloidosis with polyneuropathy; see Full Prescribing Information ‡ Patisiran has not been approved by the FDA, EMA, or any other regulatory agency for cardiac manifestations of amyloidosis. No conclusions can or should be drawn regarding its safety or effectiveness in this population;
† Vutrisiran is an investigational agent and has not been approved by the FDA, EMA, or any other regulatory agency and no conclusions can or should be drawn regarding its safety or effectiveness

Vutrisiran HELIOS·A Phase 3 Study

Randomized, Open-Label Study in Hereditary ATTR Amyloidosis Patients with Polyneuropathy

N ~ 164
Patient Population

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

3:1 RANDOMIZATION

Vutrisiran
SC q3M
25 mg

or

Reference Comparator
(patisiran)

9-Month Efficacy

- Assessment vs. APOLLO placebo arm

18-Month Efficacy

- Assessment vs. APOLLO placebo arm

Open-Label Extension

ClinicalTrials.gov Identifier: NCT03759379

HELIOS·A

Efficacy Assessments vs. APOLLO placebo arm

Primary Endpoint at 9M^

- Change in mNIS+7 from baseline

Secondary Endpoints at 9M

- Change in Norfolk QOL-DN from baseline
- 10-meter walk test (10MWT)

Secondary Endpoints at 18M Include:

- Change in mNIS+7 from baseline, change in Norfolk QOL-DN from baseline, 10MWT, mBMI, R-ODS

Exploratory Endpoints Include

- NT-proBNP
- Echo parameters
- Technetium (select sites only, change from baseline)

Positive results presented at **AAN (April 2021)**

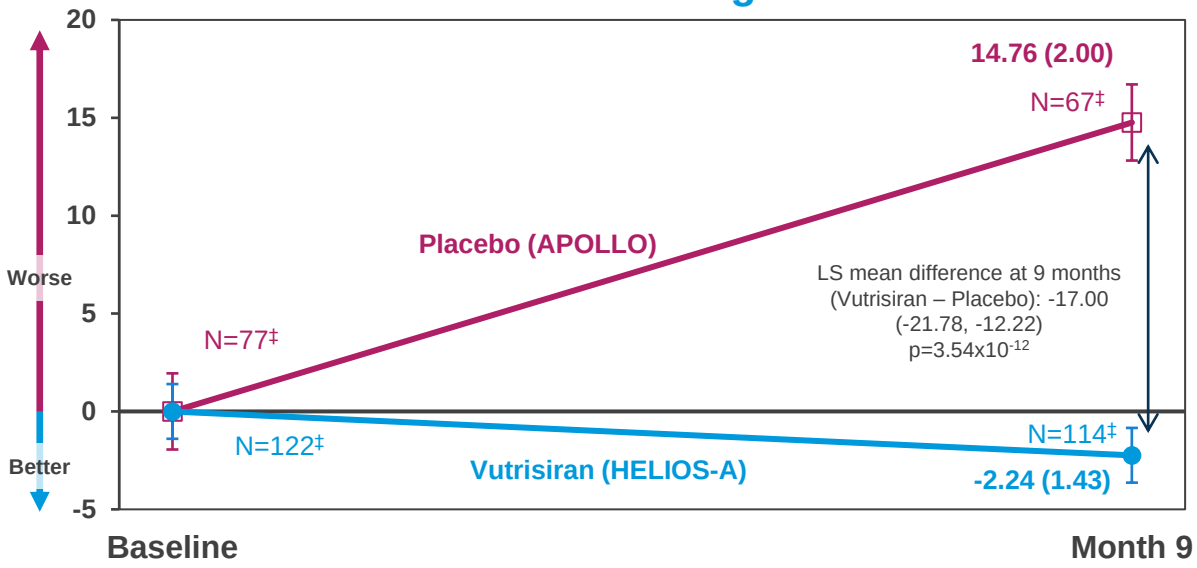
PDUFA date
April 2022

^ Primary endpoint for the study is at 9 months; in the Helios A statistical analysis plan for U.S. submissions, change in Norfolk QOL-DN from baseline will be treated as a co-primary endpoint
Vutrisiran has not been approved for any indication and conclusions regarding the safety or efficacy of the drug have not been established

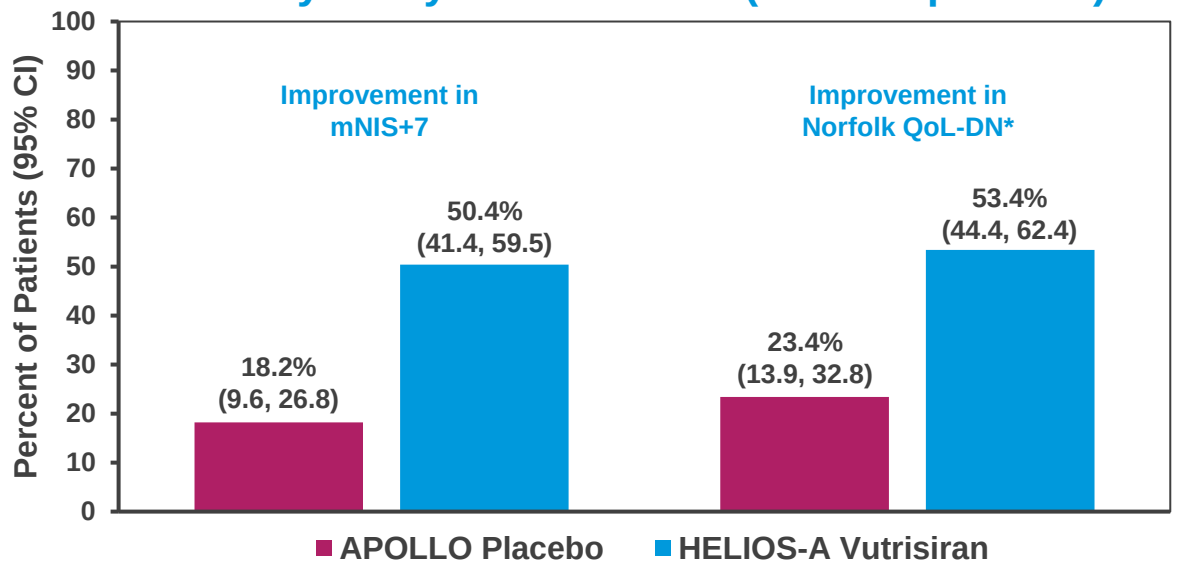
HELIOS-A 9-Month Results

Randomized, Open-Label Study in Patients with Hereditary ATTR Amyloidosis with Polyneuropathy (N=164)

mNIS+7 LS Mean Change from Baseline



Binary Analysis at Month 9 (mITT Population)



Both secondary endpoints met

- Improvement demonstrated in quality of life and 10-meter walk test

Positive exploratory cardiac endpoint result

- Improvement in NT-proBNP biomarker in cardiac subpopulation, relative to placebo (p=0.0016); additional exploratory cardiac data at Month 18 planned to be presented in Late 2021

Encouraging safety and tolerability profile

- No drug-related discontinuations or deaths; two SAEs deemed drug-related: dyslipidemia, urinary tract infection
- Treatment emergent AEs in ≥10% of vutrisiran patients all common in disease natural history and occurred at similar or lower rates than placebo comparator group
  - Include diarrhea, pain in extremity, fall and urinary tract infections
- Low incidence of injection site reactions (ISRs), all mild and transient
- No safety signals regarding liver function tests, hematology or renal function related to vutrisiran

Adams et al., *AAN*, April 2021 as to primary endpoint and safety/tolerability at Month 9; additional data presented by Alnylam in conference call held April 19, 2021

APOLLO refers to the randomized, placebo-controlled Phase 3 study of ONPATTRO (patisiran) in hATTR patients with polyneuropathy (Adams et al, NEJM, 2018). HELIOS-A compares vutrisiran treated hATTR patients with polyneuropathy to the prespecified external placebo group from APOLLO

ATTR Amyloidosis Franchise Phase 3 Program

Randomized, Double-Blind, Placebo-Controlled Studies in ATTR Amyloidosis Patients with Cardiomyopathy

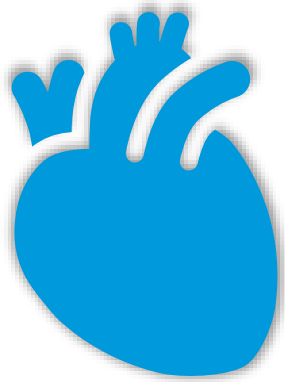
APOLLO-B

patisiran

N ~ 300
hereditary & wild-type
6-minute walk test
12 months

Enrollment **complete**

Topline results expected **mid-2022**



HELIOS-B

vutrisiran

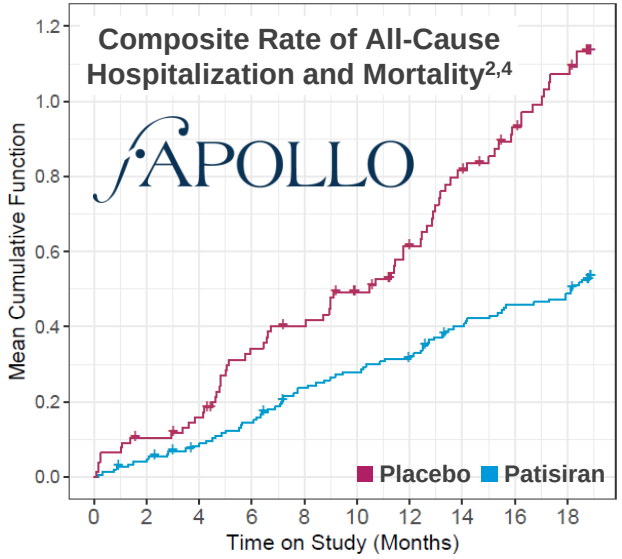
N ~ 600
hereditary & wild-type
mortality & cardiovascular events
30 months

Enrollment **complete**

Study includes planned interim analysis

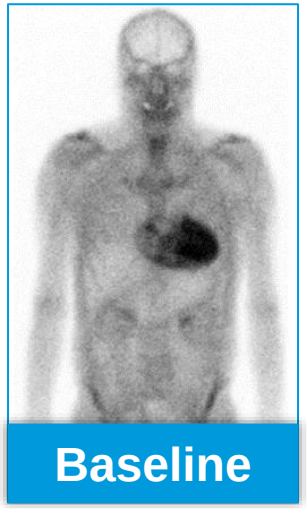
Evidence for Investigational RNAi Therapeutics in ATTR Cardiomyopathy[1]

Exploratory & Post-hoc Data from APOLLO[2]



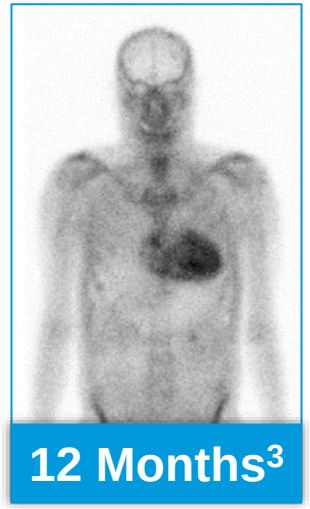
- **55%** Relative reduction in **NT-proBNP** vs. placebo[2,†]
- **0.9mm** Mean reduction in **LV wall thickness** vs. placebo[2,‡]
- **-1.4%** Improvement in **global longitudinal strain** vs. placebo[2,‡]
- **0.35m/s** Improvement in **10-MWT** vs. placebo[2,†]

Investigator-Sponsored Study from National Amyloidosis Centre, UK[3]



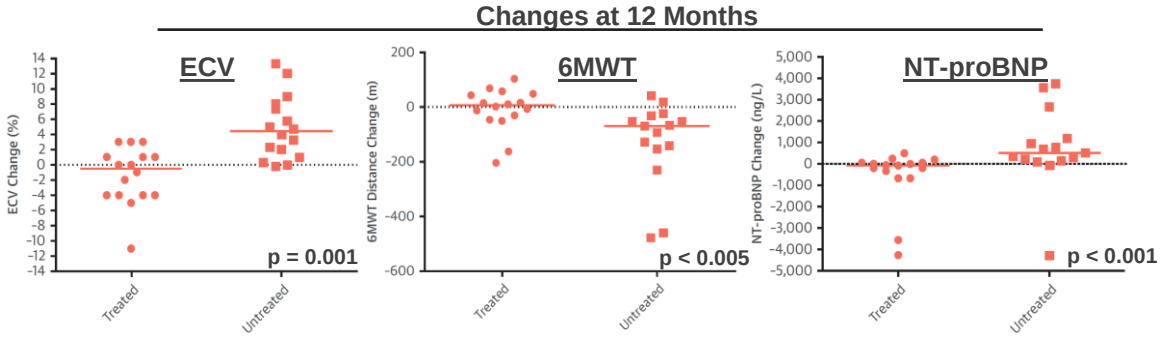
Patient with hATTR and CM, receiving patisiran and diflunisal

Example Tc-DPD Bone Scintigraphy & Image Analysis conducted as part of study, in this patient showing "unequivocal reduction in cardiac and soft tissue uptake"[3]



Cardiac Safety Data in Entire APOLLO Study Population:

	Placebo[5] (n=77)	Patisiran[5] (n=148)
Rates of Death/Hospitalization, per 100 py (95% CI)		
Death	6.2 (2.5 – 12.7)	3.2 (1.4 – 6.2)
All-cause hospitalization	69.7 (54.3 – 87.7)	32.9 (25.9 – 41.1)
Cardiac hospitalization	15.6 (9.0 – 24.9)	8.2 (5.0 – 12.6)
Hospitalization and/or death	71.8 (56.1 – 90.1)	34.7 (27.5 – 43.1)
Cardiac hospitalization and/or death	18.7 (11.4 – 28.8)	10.1 (6.4 – 14.9)



[1] Patisiran has not been approved by the FDA, EMA, or any other regulatory agency for treatment of cardiac amyloidosis. No conclusions can or should be drawn regarding its safety or effectiveness in treating CM in this population; [2] Solomon S, et al. Circulation 2018;
[3] Fontana, et al. J Am Coll Cardiol Cardiovasc Imaging. Oct 28, 2020. Epublished DOI:10.1016/j.jcmg.2020.07.043; [4] Analysis of hospitalization/death data was conducted post-hoc based on data collected from AE CRFs; hospitalization/death events caused by SAEs within 28 days of last dose of study drug were included; hospitalization events caused by SAEs within SOC of cardiac disorder were classified as cardiac hospitalization; [5] For any hospitalization/death analysis: negative binomial regression rate ratio (RR) 0.49 [0.30, 0.79]; Anderson-Gill hazard ratio (HR) 0.48 [0.34, 0.69]; † nominal p<0.01; ‡ nominal p<0.05

Agenda

- RNAi Therapeutics for Rare Diseases
- RNAi Therapeutics for Common Diseases
- New Frontiers for RNAi Therapeutics

RNAi Therapeutics Profile Supports Potential Expansion to Prevalent Diseases

- Durability
- Clamped pharmacology
- Safety profile evaluated in clinical trials
- Improved access

RARE

ONPATTRO: hATTR-PN[1]
GIVLAARI
OXLUMO
Vutrisiran: hATTR-PN[3]
Fitusiran
Belcesiran
ALN-APP
ALN-HTT

SPECIALTY

Patisiran: ATTR-CM[2]
Vutrisiran: ATTR-CM[3]
Cemdisiran

PREVALENT

Leqvio® (inclisiran)[4]
ALN-HBV02 (VIR-2218)
Zilebesiran (ALN-AGT)
ALN-HSD
ALN-XDH
ALN-KHK

[1] ONPATTRO is approved in the U.S. and Canada for the treatment of the PN of hATTR amyloidosis in adults, and in the EU, Japan and other countries for the treatment of hATTR amyloidosis in adults with stage 1 or 2 PN; [2] Patisiran has not been approved by the FDA, EMA, or any other regulatory agency for cardiac manifestations of amyloidosis. No conclusions can or should be drawn regarding its safety or effectiveness in this population; [3] Vutrisiran is an investigational agent and has not been approved by the FDA, EMA, or any other regulatory agency and no conclusions can or should be drawn regarding its safety or effectiveness; NDA accepted seeking approval of vutrisiran for the treatment of the polyneuropathy of hATTR amyloidosis in adults based on positive 9-Month results in HELIOS-A study; HELIOS-B study of vutrisiran in ATTR patients with cardiomyopathy is ongoing; [4] Leqvio is approved in the EU for the treatment of adults with hypocholesterolemia or mixed dyslipidemia; in the U.S., NDA for inclisiran resubmitted in response to Complete Response Letter.

RNAi Therapeutics Could Potentially Reimagine Treatment of Hypertension

Opportunity for Tonic Blood Pressure Control

Disease Overview

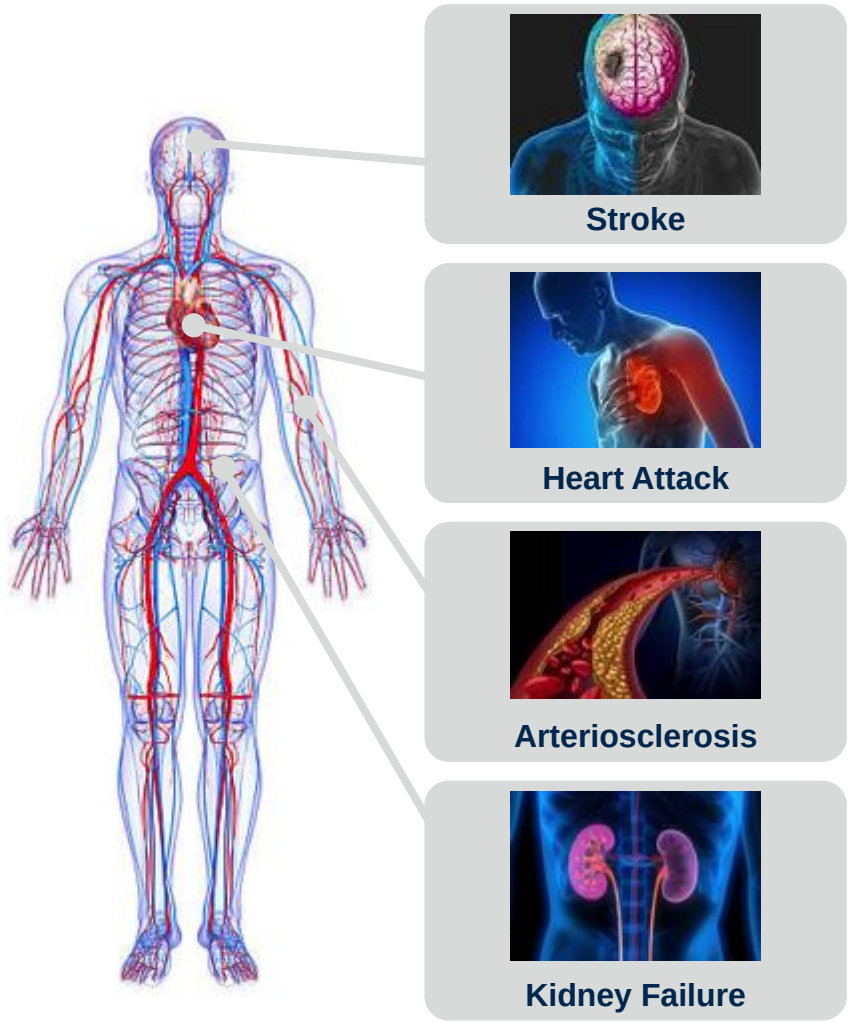
Primary Hypertension[1]	Hypertension at high CV risk[2]
~108 Million in U.S.	**~38 Million** in U.S.

>71% of patients have uncontrolled hypertension (>130/80 despite treatment)[3]

Hypertension risk further exacerbated by variability in BP **control**, lack of nighttime **dipping**, and poor medication **adherence**

Together, contribute to substantial risk of CV morbidity and mortality

Potential Complications of Uncontrolled Hypertension



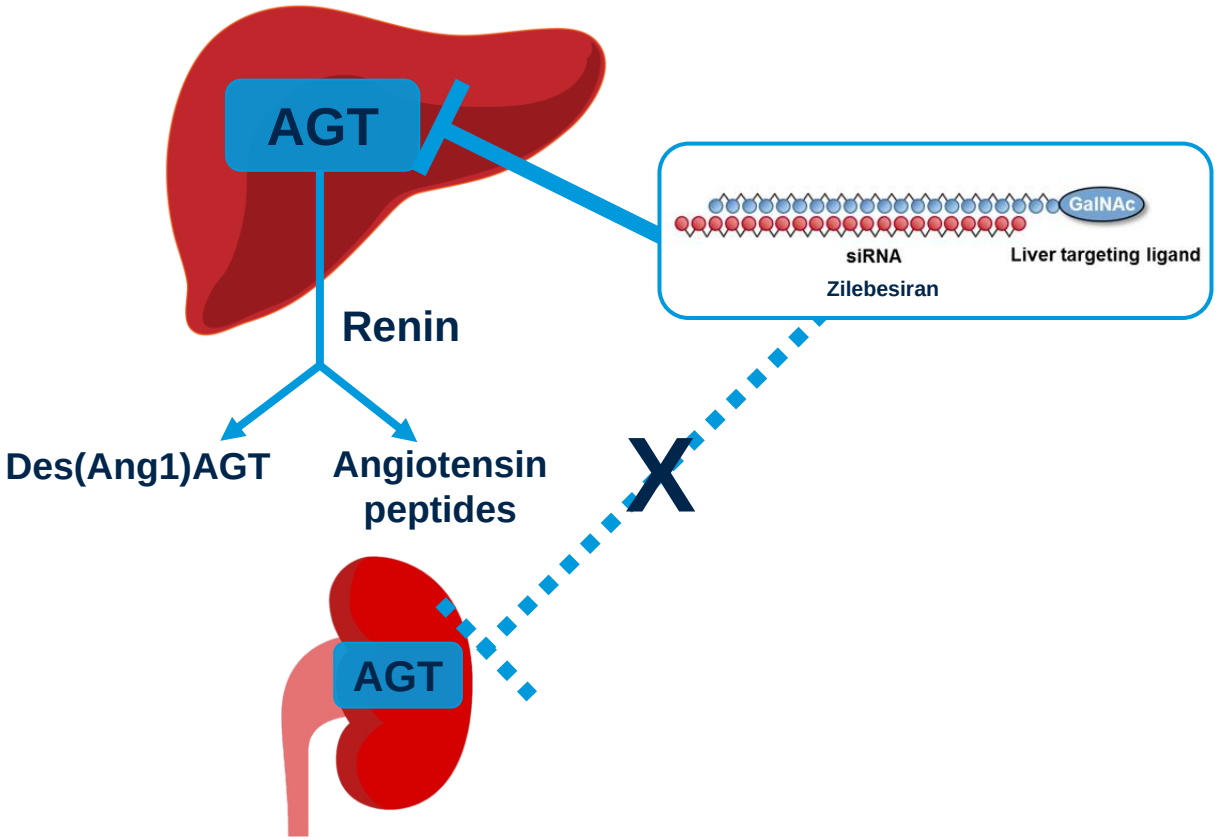
[1] Centers for Disease Control and Prevention (CDC). Hypertension Cascade: Hypertension Prevalence, Treatment and Control Estimates Among US Adults Aged 18 Years and Older Applying the Criteria From the American College of Cardiology and American Heart Association's 2017 Hypertension Guideline—NHANES 2013–2016. Atlanta, GA: US Department of Health and Human Services; 2019.

[2] Estimated from multiple sources and internal estimates: Dorans. JAHA. 2018; Al Kibria. Hypertens Res. 2019; CDC Hypertension Cascade. 2019; High CV risk: ASCVD risk score ≥20% and/or history of CVD

[3] U.S. Department of Health and Human Services. The Surgeon General's Call to Action to Control Hypertension. Washington, DC: U.S. Department of Health and Human Services, Office of the Surgeon General; 2020.

Zilebesiran Therapeutic Hypothesis

Liver-specific AGT Knockdown



Potential Mechanistic Advantages

- **Liver-specific silencing of AGT**
- **Prolonged duration of action**
  - Consistent and durable BP response
  - Infrequent dose administration
  - Potential for improved adherence

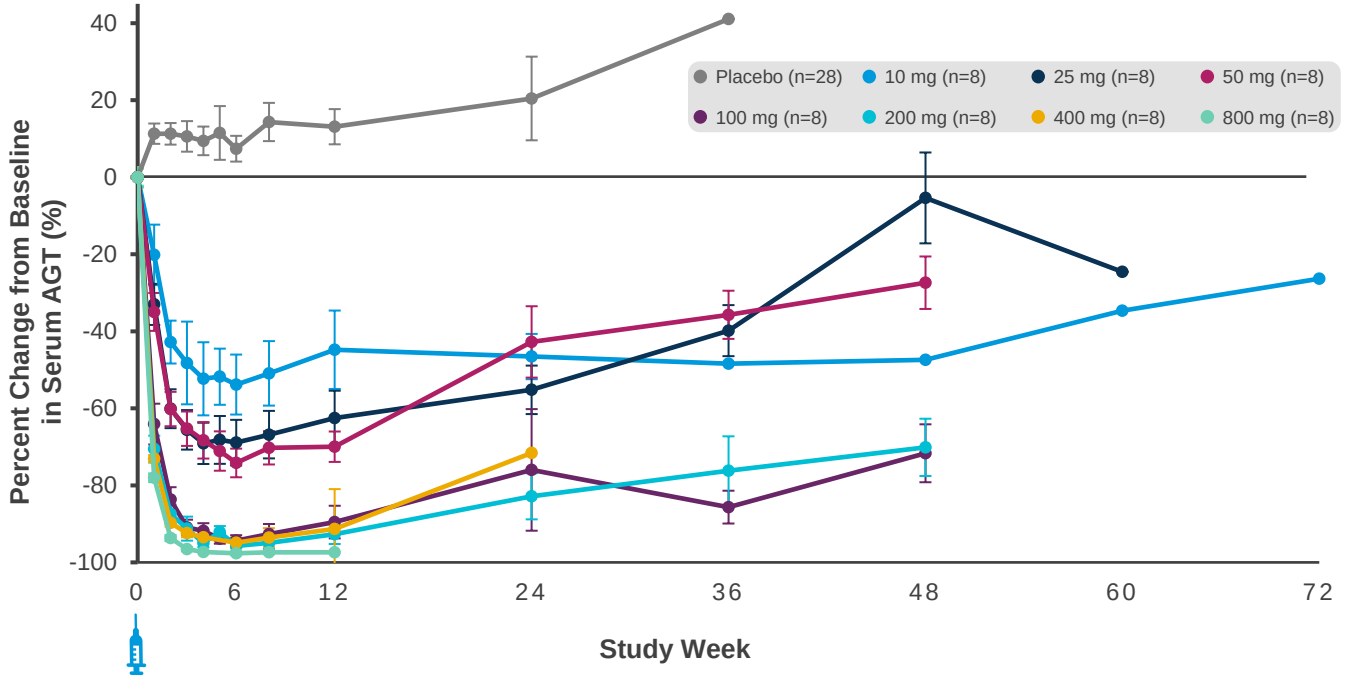
AGT, angiotensinogen; BP, blood pressure; GalNAc, N-acetylgalactosamine; siRNA, small interfering ribonucleic acid

Zilebesiran (ALN-AGT) Interim Phase 1 Results

Results for Investigational Therapy Presented at ESH-ISH Meeting

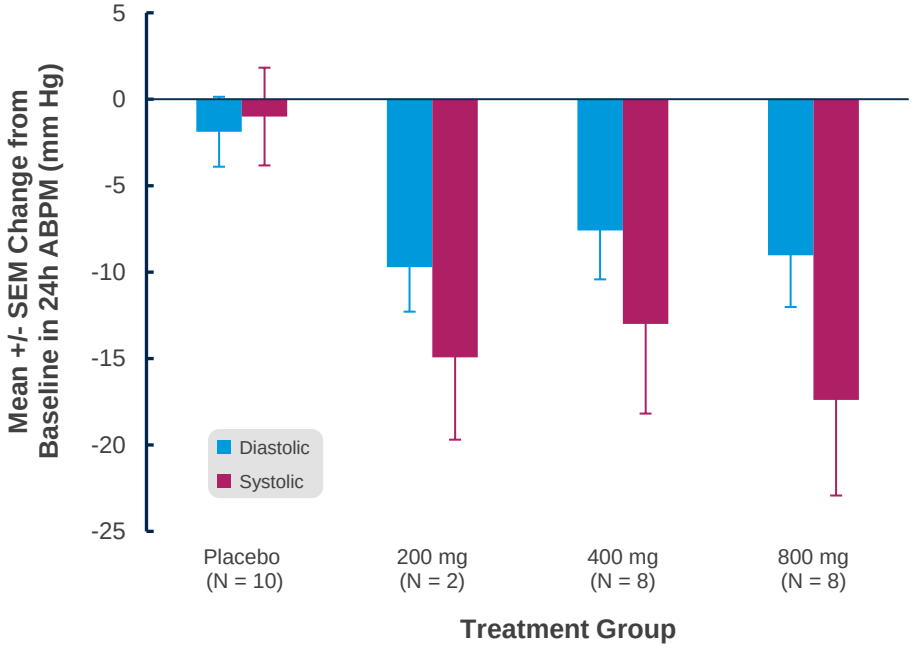
Durable Reduction of Serum AGT >90% Sustained for 12 Weeks After Single Doses of ALN-AGT ≥100 mg

Serum AGT reduced 96-98% at Week 12 in all patients given single dose of 800 mg



Dose-Dependent Reductions in SBP and DBP[2]

Mean 24h blood pressure reduction of 17 mmHg / 9 mmHg at Week 12 in patients given single dose of 800 mg



Encouraging safety and tolerability profile

- Most AEs mild or moderate in severity
- ISRs in 5 of 56 patients (8.9%) were all mild and transient
- No treatment-related SAEs

KARDIA-1 Phase 2 Study initiated **June 2021**

KARDIA-2 initiation expected in **late 2021**

[1] Desai et al, *ESH-ISH*, April 2021; Data cutoff date: 25 Feb 2021

[2] SBP: systolic blood pressure; DBP: diastolic blood pressure

Phase 2 Clinical Development Plan

KARDIA$_1$

Monotherapy Phase 2 Study (N ~400)

- IND opened May 2021
- Evaluate efficacy and safety of zilebesiran as a monotherapy in patients with mild-to-moderate hypertension
- Exploring both quarterly and biannual dosing regimens
- Study initiated June 2021

KARDIA$_2$

Add-On Phase 2 Study (N ~800)

- Evaluate efficacy and safety of zilebesiran as add-on therapy in patients with hypertension despite treatment with a potent RAAS inhibitor, a calcium channel blocker, or a diuretic
- Targeting study initiation in late 2021

Agenda

- RNAi Therapeutics for Rare Diseases
- RNAi Therapeutics for Common Diseases
- New Frontiers for RNAi Therapeutics

Alnylam Platform Expands Opportunities for Novel RNAi Therapeutics

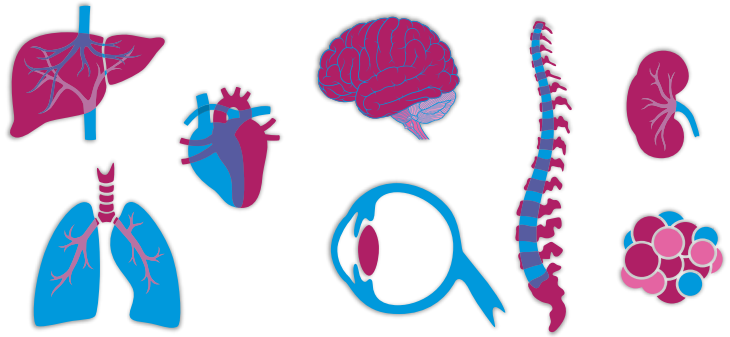
Human Genetics

UCLA

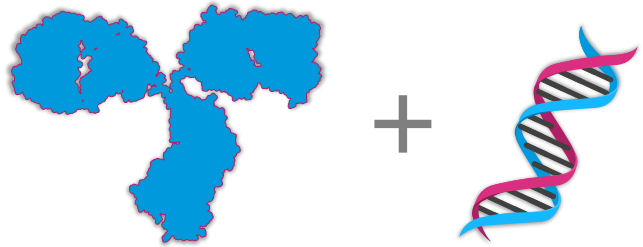
biobank uk

REGENERON

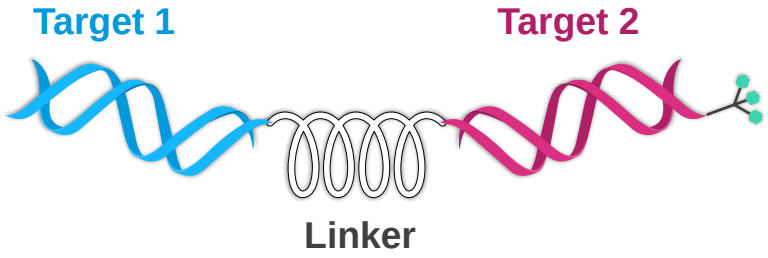
New Tissues



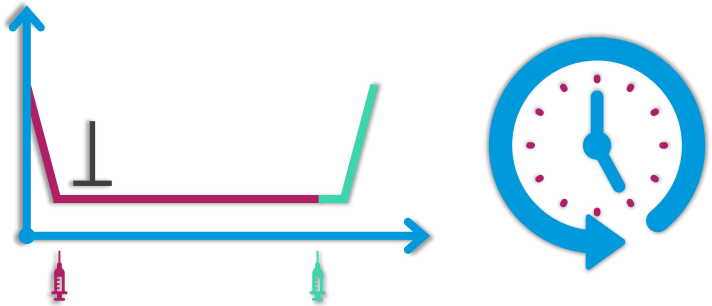
Novel mAb Combos



Bis-RNAi™



Reversir™



Novel Administration

RNAi Therapeutics for CNS and Ocular Diseases

Expand Alnylam Opportunities Beyond Liver

Devastating diseases with enormous burden and unmet need

- Alzheimer's disease
- Amyotrophic lateral sclerosis (ALS)
- Cerebral amyloid angiopathy
- Frontotemporal dementia
- Huntington's disease
- Multi-system atrophy
- Parkinson's disease
- Spinocerebellar ataxia

- AMD, dry
- AMD, wet
- Birdshot chorioretinopathy
- Dominant retinitis pigmentosa 4
- Fuch's dystrophy
- hATTR amyloidosis
- Hereditary and sporadic glaucoma
- Stargardt's disease

Investigational RNAi therapeutics demonstrate potent, widely distributed, and highly durable effects

ALN-APP

Targeting amyloid precursor protein (APP) for hereditary cerebral amyloid angiopathy (hCAA)

- hCAA caused by APP mutations leading to arteriolar Aβ deposition with microbleeds and intracranial hemorrhages
- Multiple CSF and radiologic biomarkers for early readout
- Study of hCAA potential gateway to larger indications (e.g., sporadic CAA, EOFAD, AD)

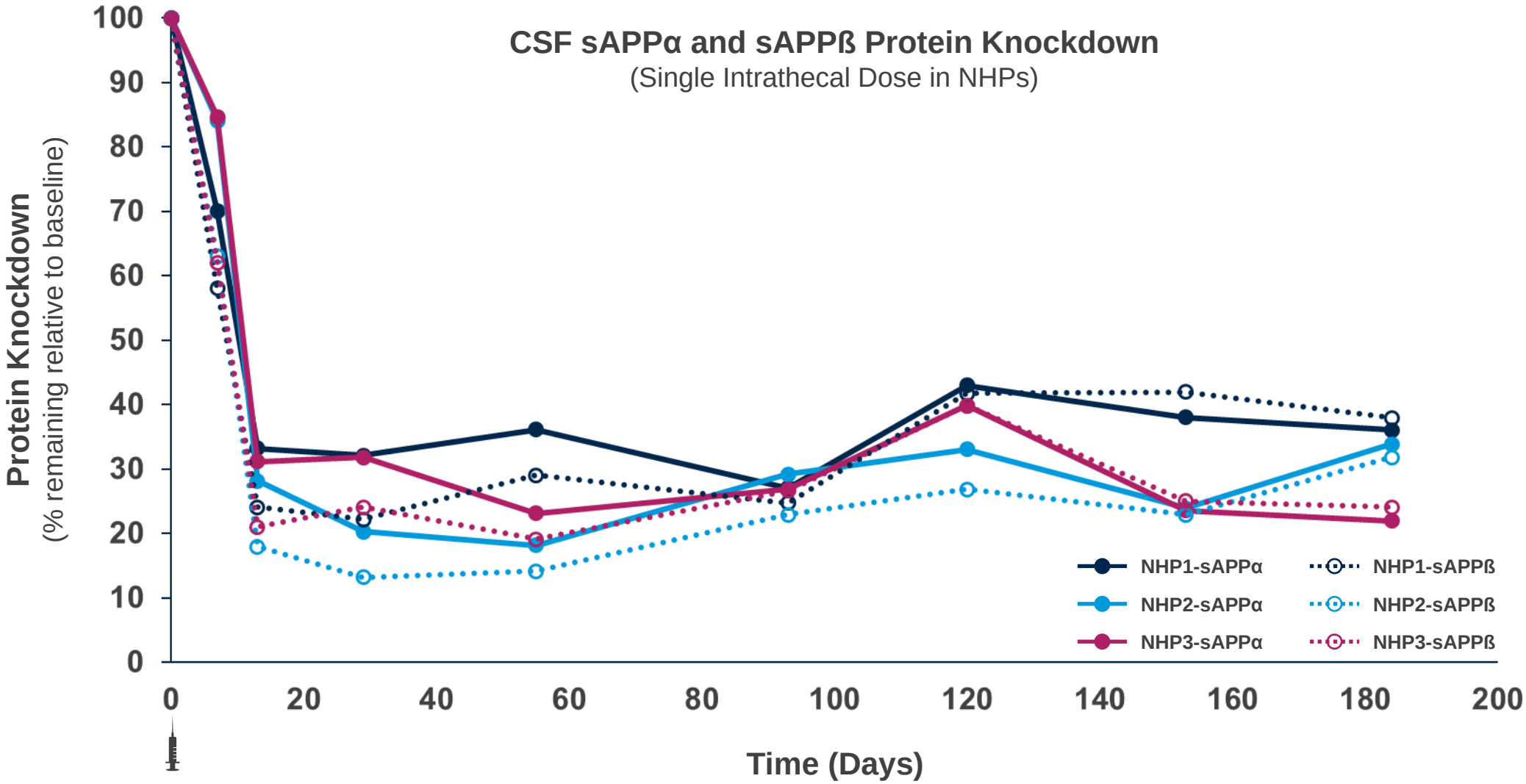
ALN-HTT

Targeting huntingtin gene (HTT) for early manifest Huntington's disease

- Autosomal dominant, gain-of-function genetic disease with 100% age-related penetrance
- Patients present with progressive motor, cognitive and psychiatric decline
- Affects ~30,000 in U.S. with disease duration of 15-20 years

Highly Durable Amyloid Precursor Protein (APP) Knockdown in NHP

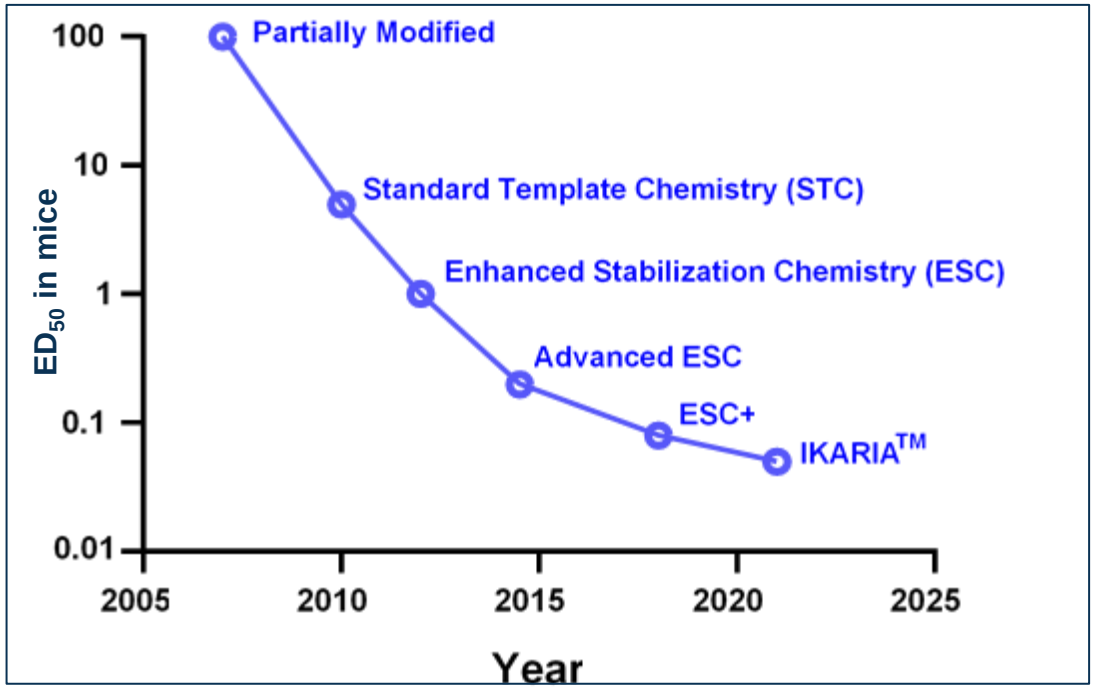
Single Intrathecal Dose of ALN-APP Supports Bi-Annual or Less Frequent Regimen



Evolution of Conjugate Chemistry Over Nearly Two Decades

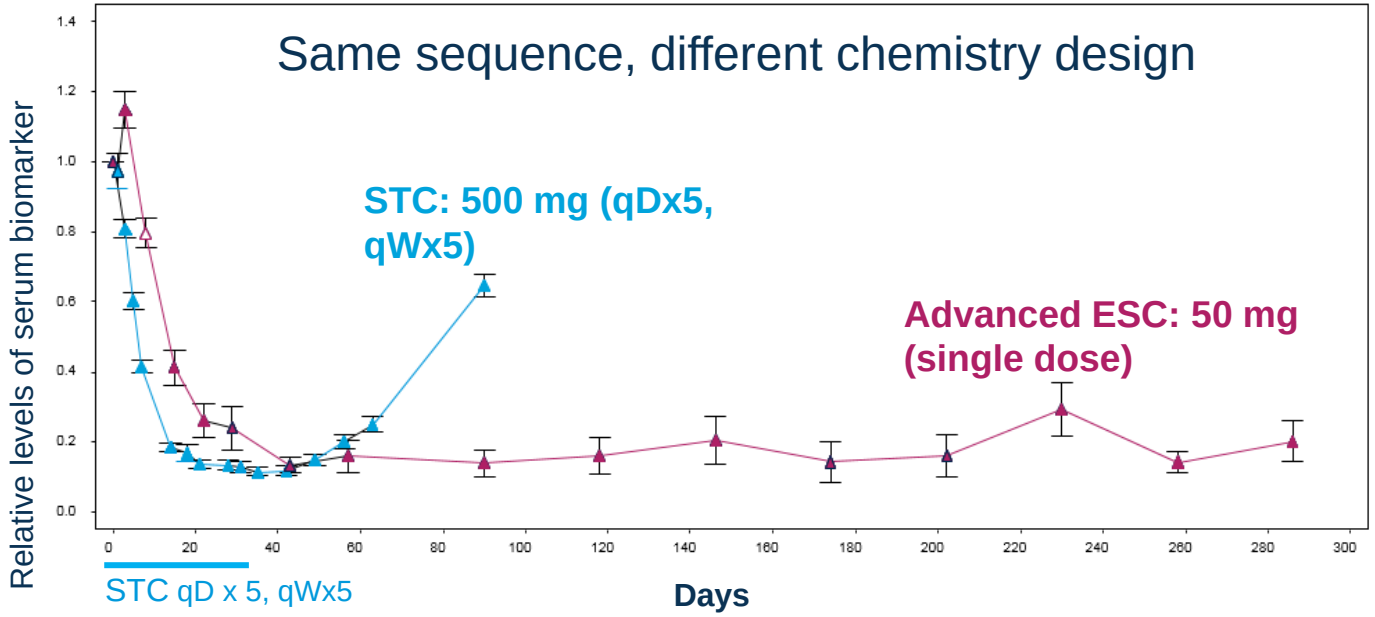
Potency and specificity

ED_{50} Dose in mice for various designs



Durability

Human PD* of two siRNAs

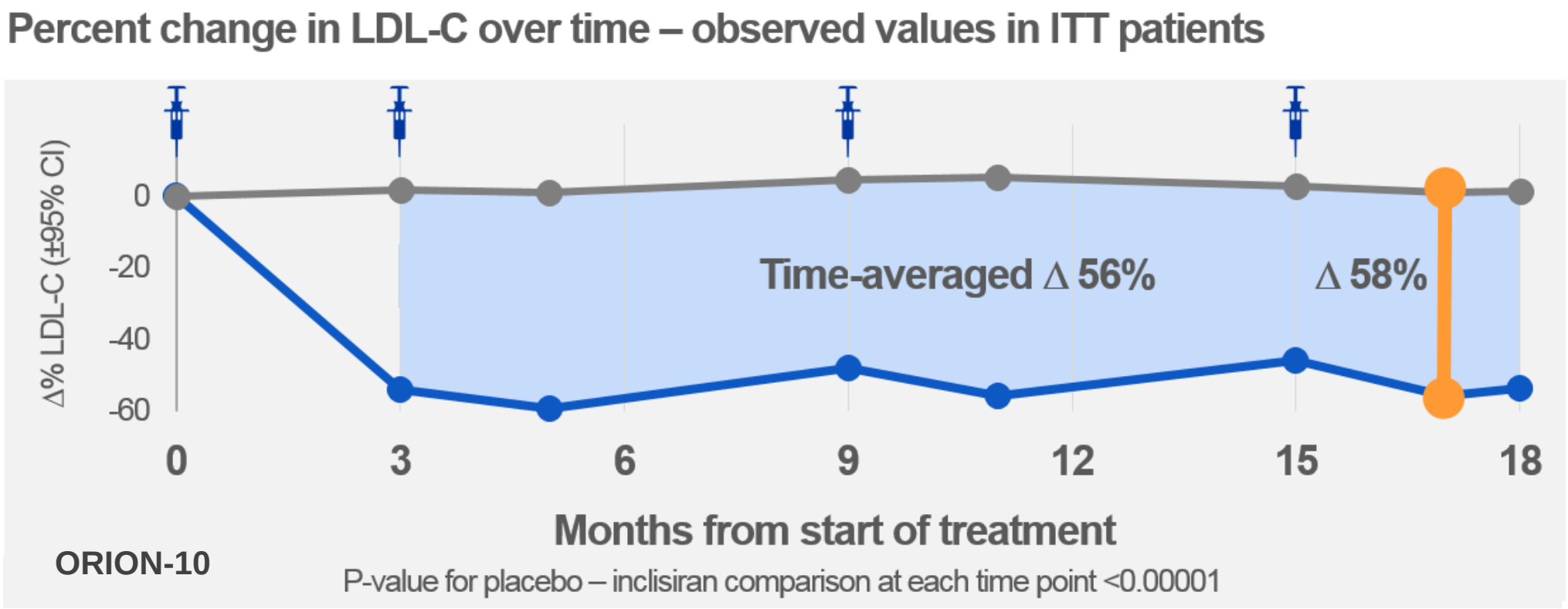


*Phase 1 data in healthy volunteers from separate studies

Zimmermann et al *Nature* 2006; Nair et al. *JACS* 2014; Foster et al. *Mol. Ther.* 2018; Janas et al. *Nature Comm*. 2018

Inclisiran ORION-10+11 Results

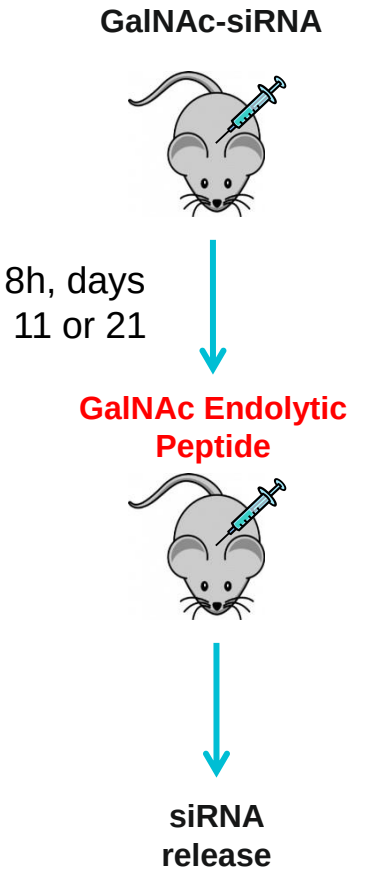
Durable, Potent, and Consistent LDL-C Lowering Over 18 Months

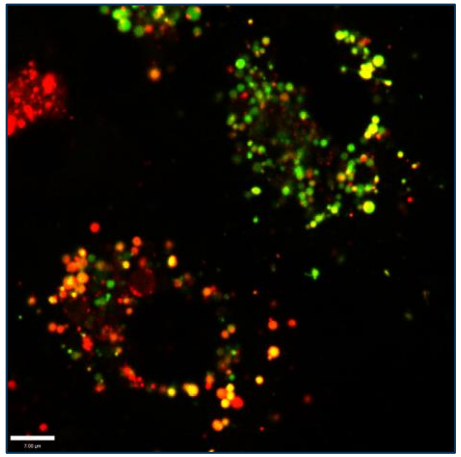


- Inclisiran safety profile similar to placebo, with no adverse changes in laboratory markers
- Injection site events 2.6-4.7% - predominantly mild and none persistent
- ORION-10+11: Numerically fewer CV events reported for inclisiran than placebo (exploratory endpoint)

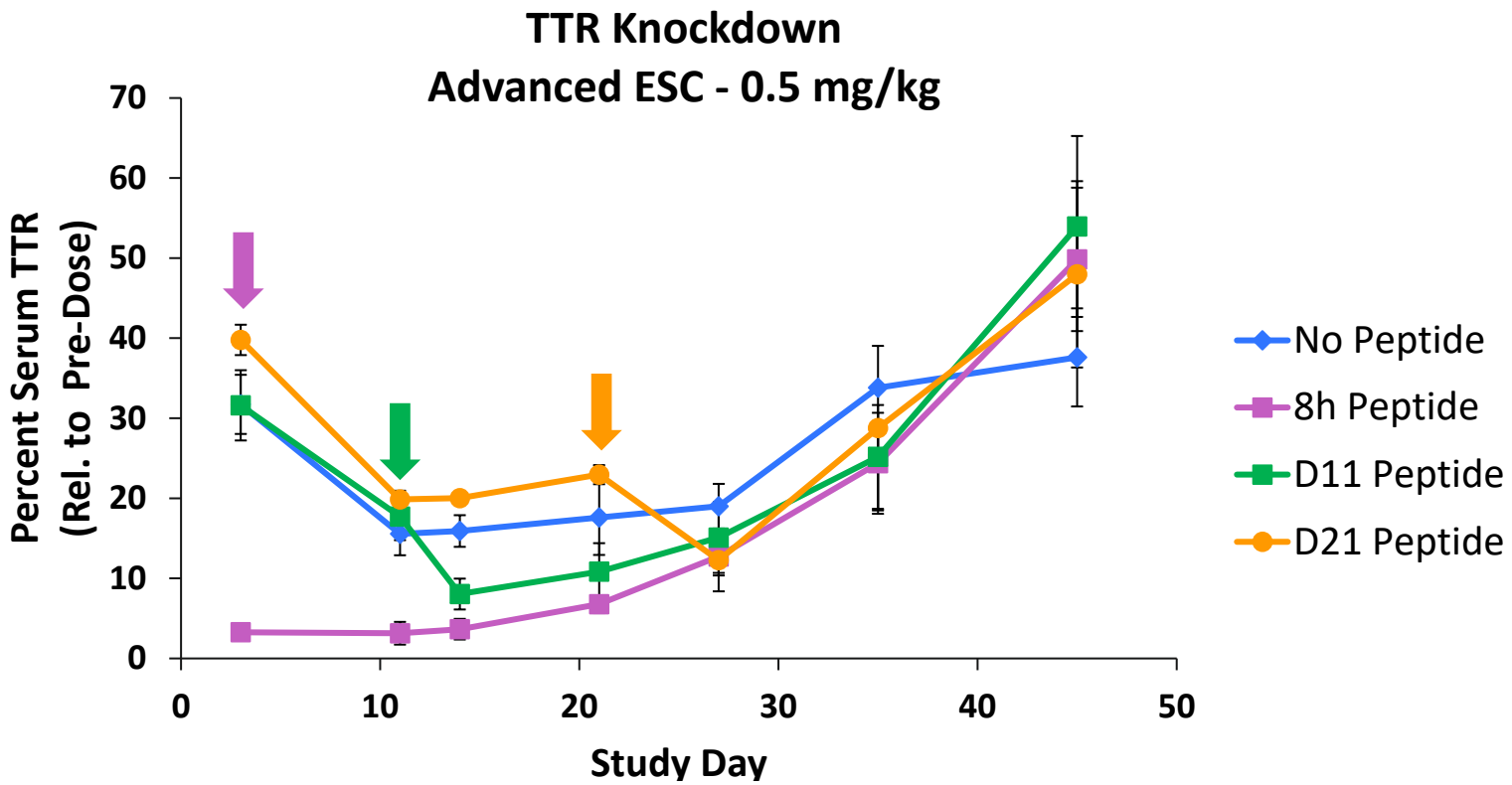
Wright et al., AHA 2019; Ray et al., ESC Congress 2019
All 95% confidence intervals are less than ±2% and therefore are not visible outside data points

Intracellular Depot Drives Durability of Conjugates





siRNA
Lysopainter



NAR Breakthrough Article

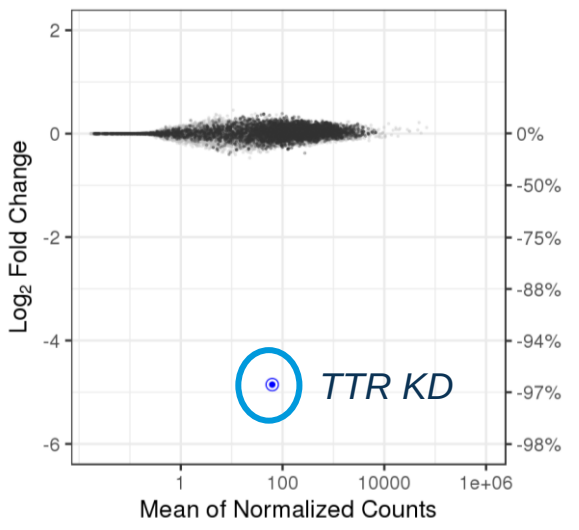
Investigating the pharmacodynamic durability of GalNAc–siRNA conjugates

Christopher R. Brown[1], Swati Gupta[1], June Qin[1], Timothy Racie[1], Guo He[1], Scott Lentini[1], Ryan Malone[1], Mikyung Yu[1], Shigeo Matsuda[1], Svetlana Shulga-Morskaya[1], Anil V. Nair[2], Christopher S. Theile[1], Karyn Schmidt[1], Azar Shahraz[1], Varun Goel[1], Rubina G. Parmar[1], Ivan Zlatev[1], Mark K. Schlegel[1], Jayaprakash K. Nair[1], Muthusamy Jayaraman[1], Muthiah Manoharan[1], Dennis Brown[2], Martin A. Maier[1] and Vasant Jadhav[1,*]

IKARIA™ Platform: Proprietary siRNA Design with Novel Chemistry

Super-specific siRNAs Enable Higher Doses to Achieve Annual Dosing

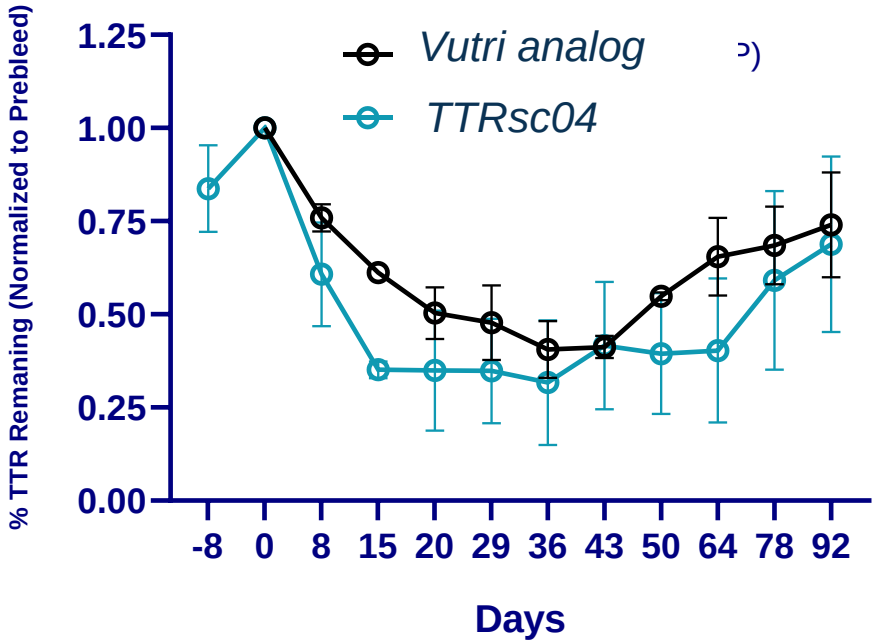
Exquisite specificity



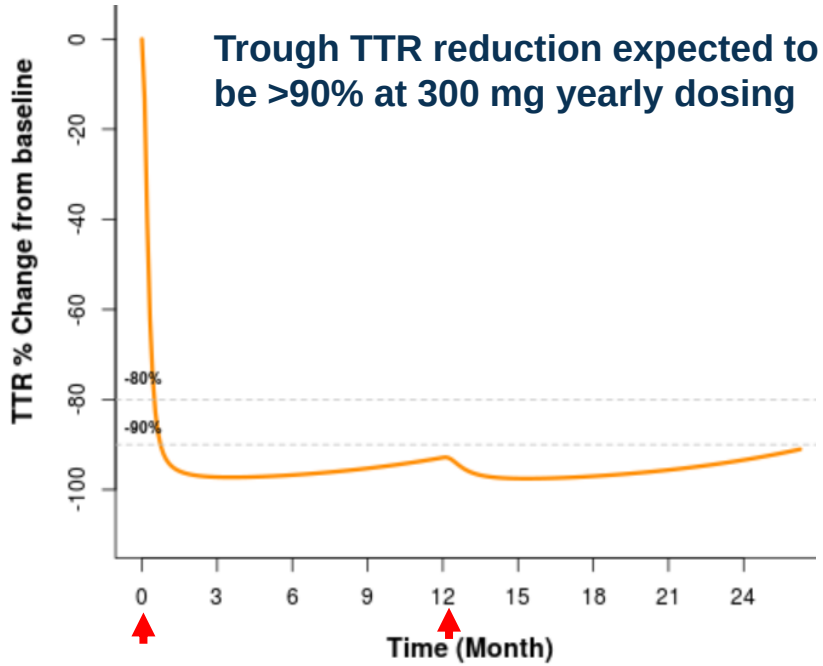
RNAseq analysis

High potency in NHP

0.5 mg/kg single sc dose



Human dose projection



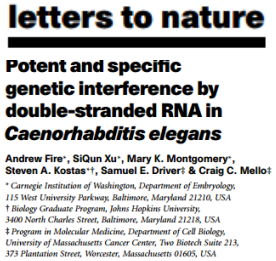
Potential for once-a-year dosing in humans with Vutri-like therapeutic benefit

RNAi Therapeutics: A Timeline

From Observation to Nobel Prize to Innovative Medicines in ~3 Decades

First scientific report of RNAi phenomenon in which Napoli and Jorgensen report that violet petunias turned white instead of a deeper violet[1]

1990



letters to nature

Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*

Andrew Fire*, SiQun Xu*, Mary K. Montgomery*, Steven A. Kostas*†, Samuel E. Driver‡ & Craig C. Mello‡

* Carnegie Institution of Washington, Department of Embryology, 115 West University Parkway, Baltimore, Maryland 21210, USA
† Biology Graduate Program, Johns Hopkins University, 3400 North Charles Street, Baltimore, Maryland 21218, USA
‡ Program in Molecular Medicine, Department of Cell Biology, University of Massachusetts Cancer Center, Two Biotech Suite 213, 373 Plantation Street, Worcester, Massachusetts 01605, USA

Fire and Mello published a paper that reported a potent gene silencing effect in worms and coined the term RNA interference[2]

1998

Alnylam founded with a core focus on developing RNAi therapeutics

2002

Fire and Mello awarded the 2006 Nobel Prize in Physiology or Medicine

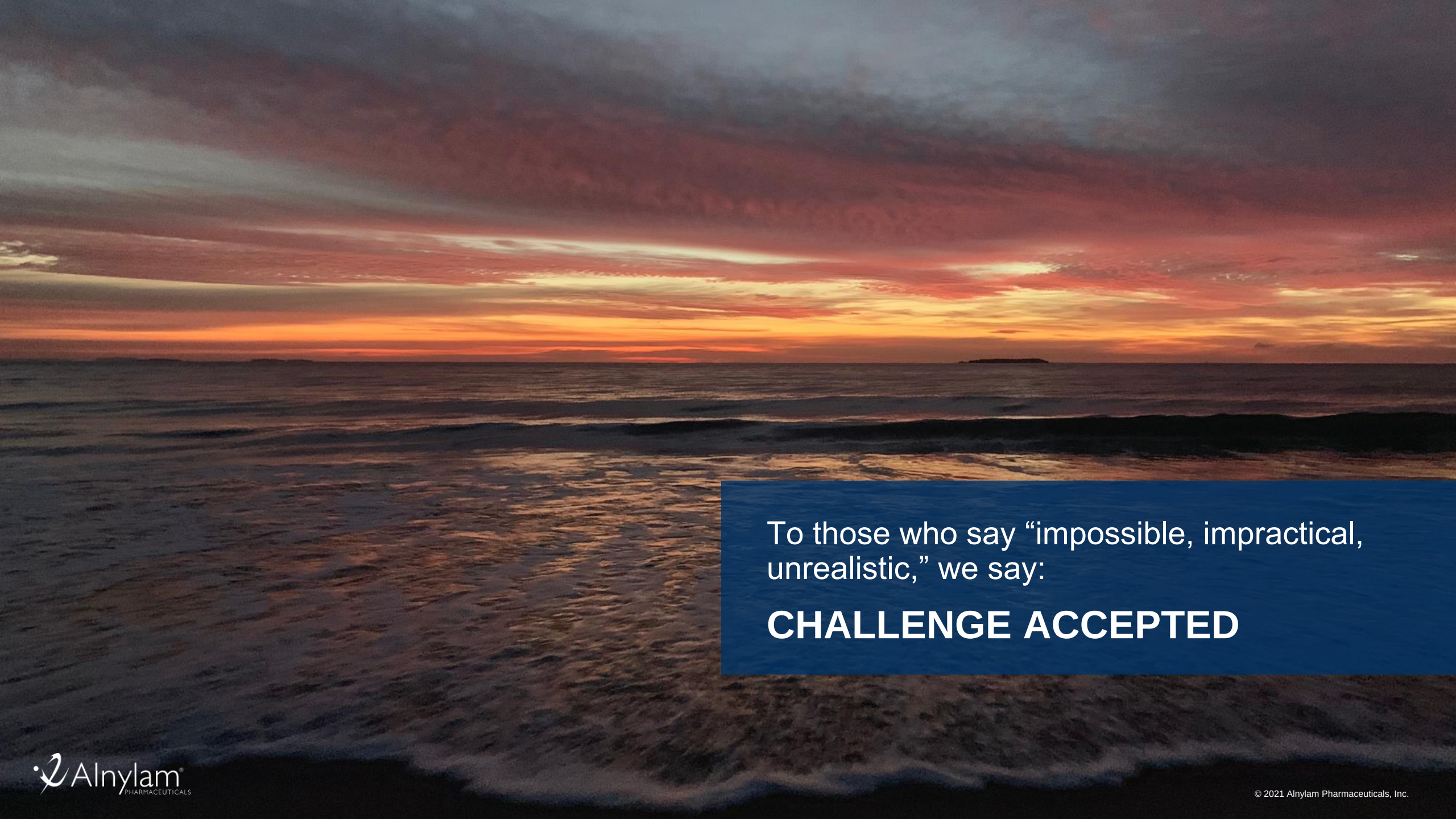
2006

onpattro™ (patisiran) injection

APOLLO, first Phase 3 trial for a RNAi therapeutic, meets primary and all secondary endpoints; APPROVED in U.S. and EU

2018

1. Napoli C et al. Plant Cell. 1990;2(4):279-289; 2. Fire A et al. Nature. 1998;391(6669):806-811



Alnylam PHARMACEUTICALS