Corporate Overview

May 2019

Alnylam® PHARMACEUTICALS

Alnylam Forward Looking Statements & Non-GAAP Financial Measures

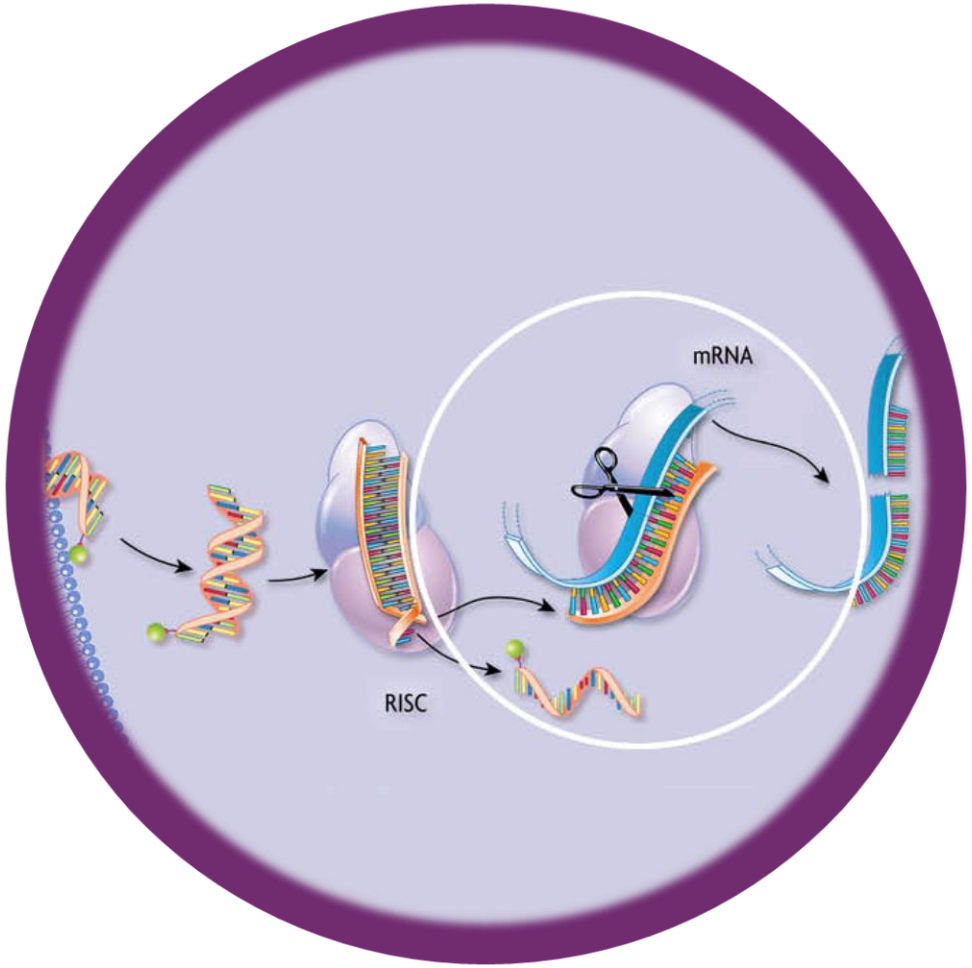
This presentation contains forward-looking statements, within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. There are a number of important factors that could cause actual results to differ materially from the results anticipated by these 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, including with respect to givosiran; 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; the timing of regulatory submissions for our product candidates and our ability to obtain and maintain regulatory approval, pricing and reimbursement for such products; our progress in establishing a commercial and ex-United States infrastructure; our ability to successfully launch, market and sell our approved products globally, including givosiran if approved for by regulatory agencies; 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 or risks 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. The safety and efficacy of givosiran were evaluated in the ENVISION Phase 3 study and have not yet been reviewed by the FDA, EMA or any other regulatory agency. 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.

This presentation contains non-GAAP financial measures, including expenses adjusted to exclude certain non-cash expenses and non-recurring gains outside the ordinary course of the Company’s business. These measures are not in accordance with, or an alternative to, GAAP, and may be difference from non-GAAP financial measures used by other companies. The items included in GAAP presentations but excluded for purposes of determining non-GAAP financial measures for the periods presented herein are stock-based compensation expense and the gain on litigation settlement. The Company has excluded the impact of stock-based compensation expense, which may fluctuate from period to period based on factors including the variability associated with performance-based grants for stock options and restricted stock units and changes in the Company’s stock price, which impacts the fair value of these awards. The Company has excluded the impact of the gain on litigation settlement because the Company believes this item is a one-time event occurring outside the ordinary course of the Company’s business.

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**



The first RNAi therapeutic is NOW APPROVED

onpattro®

(patisiran) lipid complex injection 10 mg/5 mL

onpattro®

2 mg/mL concentrate for solution for infusion patisiran

Kipper
Living with hATTR Amyloidosis

ATTR Amyloidosis

Rare, Progressively Debilitating, and Often Fatal Disease

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

Hereditary ATTR (hATTR) Amyloidosis

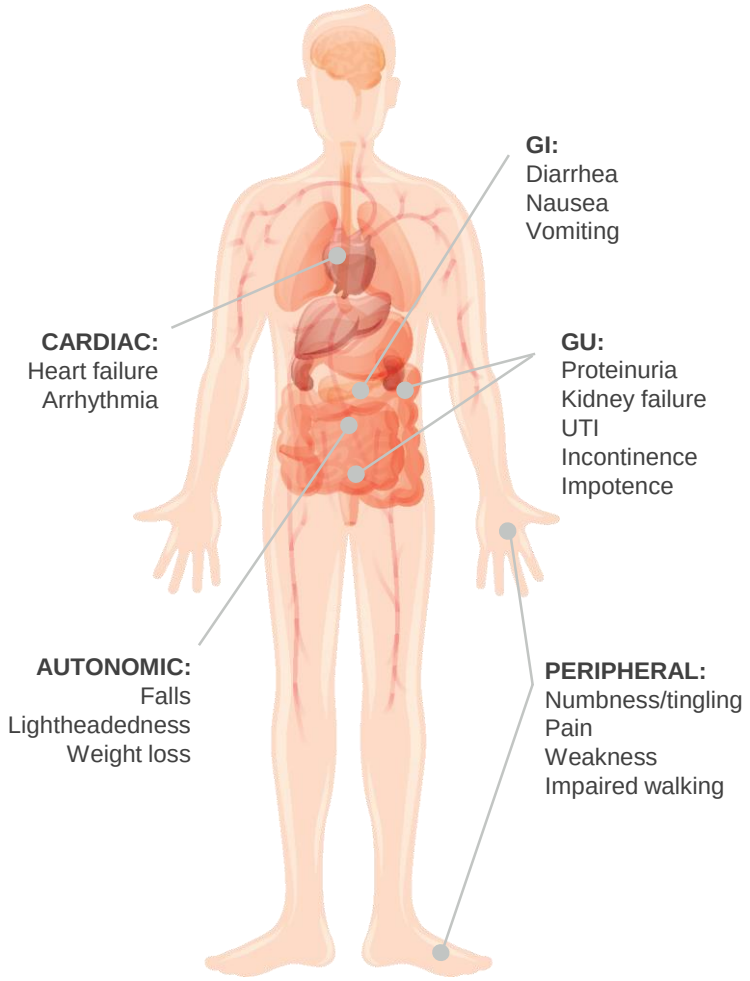
~50,000

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

hATTR Amyloidosis Market Opportunity

Estimated Disease Prevalence*†

~ 50,000 patients worldwide

NEUROLOGIC PHENOTYPE
> 50% have cardiomyopathy

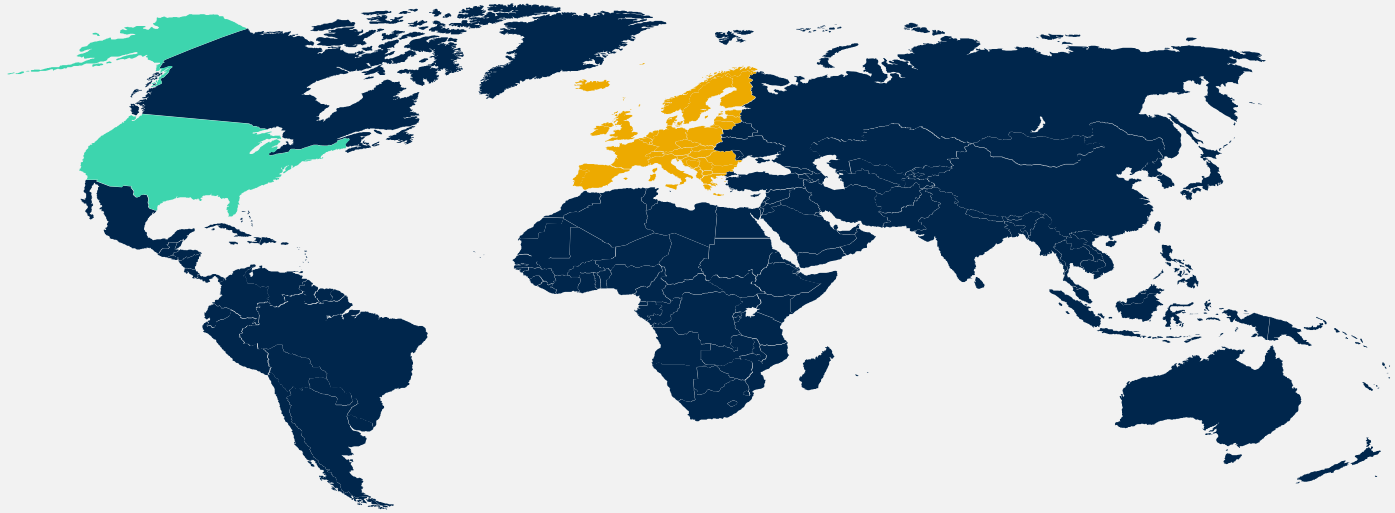
CARDIAC PHENOTYPE†
> 30% have neuropathy

WITHIN ONPATTRO LABEL†

20K to 30K worldwide
~ 10K diagnosed‡

10K to 15K in U.S.
< 3K diagnosed

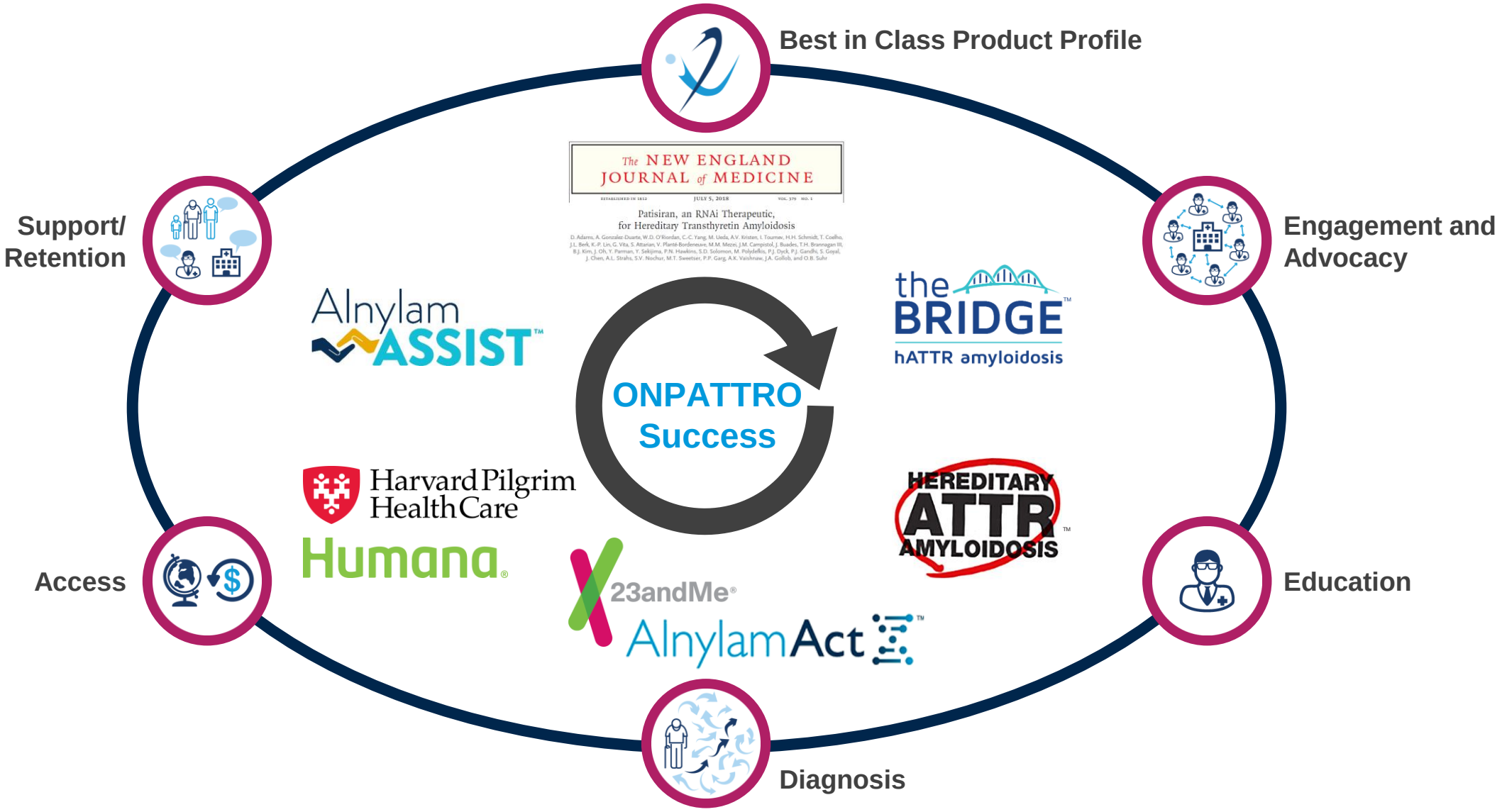
5K to 10K in EU
~ 2K diagnosed



* Based on Alnylam estimates from interviews with key opinion leaders, THAOS registry, recent clinical trials and literature
† ONPATTRO is 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
‡ Current diagnosis rates difficult to confirm and may be lower in initial launch years

Supporting ONPATTRO Success Globally

Alnylam Commitment to Medical and Commercial Excellence



ONPATTRO® (patisiran) can reverse polyneuropathy manifestations of the disease[1,2]

A novel RNAi-based approach that may transform the future for your patients[1-4]

At 18 months in a placebo-controlled study, ONPATTRO demonstrated:

- Reversal in neuropathy impairment from baseline as measured by modified Neuropathy Impairment Score + 7 (mNIS+7)[1]
- Improvement in quality of life from baseline as measured by Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) score[1]
- Improvement in autonomic symptoms from baseline as measured by Composite Autonomic Symptom Score 31 (COMPASS 31)[2]
- Improvement in gait speed from baseline as measured by 10-meter walk test (10MWT)[1]

Indication

ONPATTRO® (patisiran) is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

Important Safety Information

Infusion-Related Reactions

Infusion-related reactions (IRRs) have been observed in patients treated with ONPATTRO. 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.

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

RNA=ribonucleic acid; RNAi=RNA interference.

References: 1. ONPATTRO [U.S. package insert]. **2.** Adams D, Gonzalez-Duarte A, O'Riordan WD, et al. *N Engl J Med*. 2018;379(1):11-21 **3.** Ando Y, et al. *Orphanet J Rare Dis*. 2013;8:31. **4.** Adams D, et al. *Neurology*. 2015;85(8):675-682.

ONPATTRO® Global Launch Update: Q1 2019

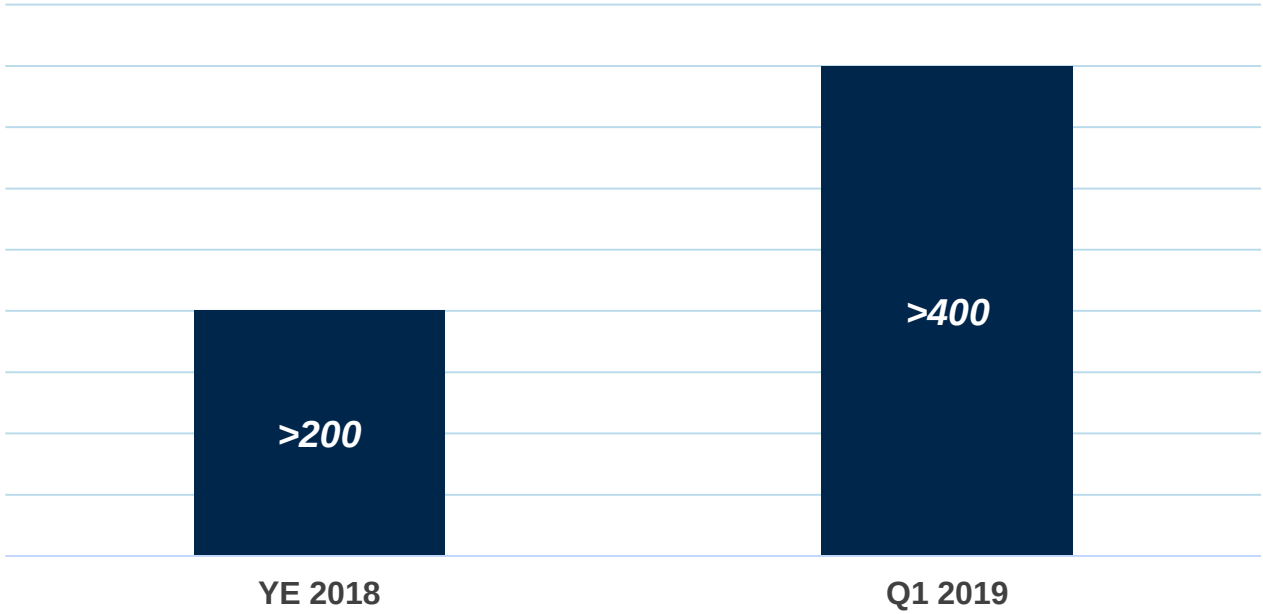
Strong Performance with Significant Growth Potential

$26.3M

ONPATTRO Global Q1
Net Product Revenues

>400

Patients Worldwide on Commercial
ONPATTRO at Q1 2019

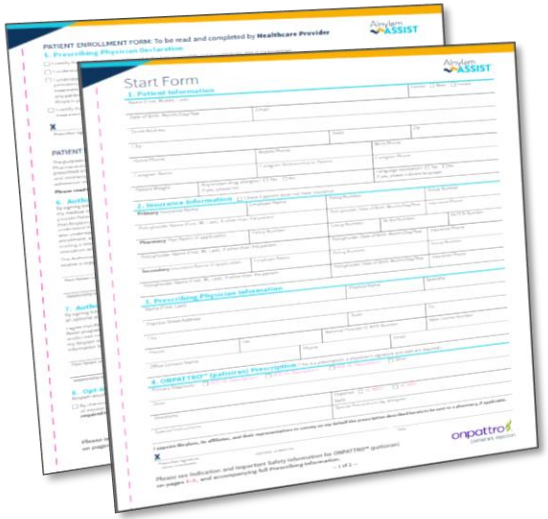


U.S. ONPATTRO Demand, Prescriber Trends, and Market Access

Q1 Metrics Based on 77 Start Forms

Patients

90% Non-EAP	10% EAP



Prescribers

55% Cardiology	35% Neurology	10% Other

>150 Physicians prescribing ONPATTRO since launch

~2 per week Average rate of new prescribers submitting Start Forms

Payers

65% Medicare	35% Other

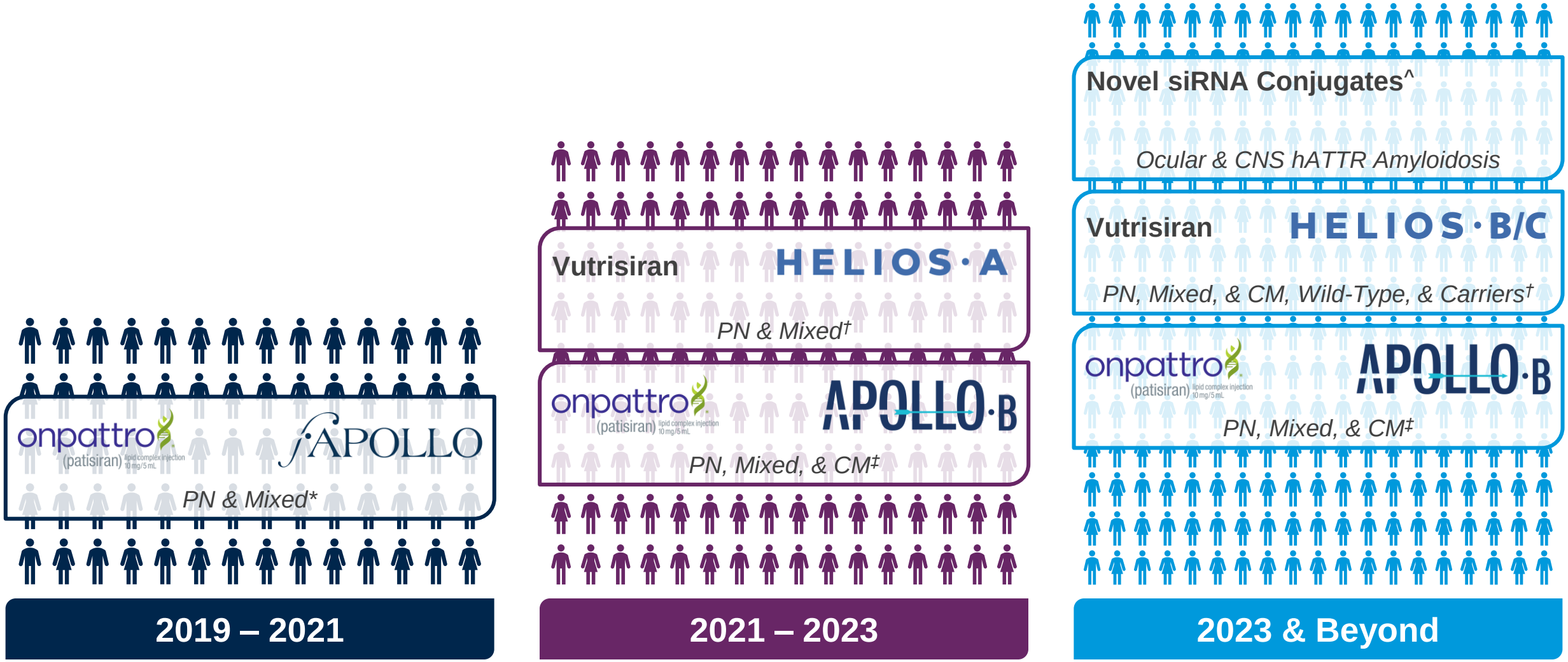
10 VBAs in place with U.S. commercial payers

>90% U.S. lives with confirmed access to ONPATTRO*

Start Forms are an incomplete picture of U.S. demand (U.S. vial demand of 20-25% outside Alnylam Assist Channel); * DKP PayerScope® August 1, 2018 through March 31, 2019
EAP: Expanded Access Program; VBA: Value-Based Agreement

Alnylam ATTR Amyloidosis Franchise

Potential to Expand Value to Patients Globally for Many Years to Come



* ONPATTRO is approved in the U.S. for the treatment of 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; ‡ ONPATTRO 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; ^ Novel siRNA conjugate development candidates for ocular or CNS hATTR amyloidosis not yet selected.

Intended to be illustrative and not intended to represent specific estimates of patient numbers

Beyond ONPATTRO: Multiple Launches Planned in Next 2-3 Years

2018	2019-2021			Partnered programs*: 2020-2021	
onpattro (patisiran) lipid complex injection 10 mg/5 mL	Givosiran	Lumasiran	Vutrisiran	Fitusiran	Inclisiran
ONPATTRO is indicated in the U.S. for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults^	Acute hepatic porphyria	Primary hyperoxaluria type 1	ATTR amyloidosis	Hemophilia	Hypercholesterolemia

Robust pipeline and global commercial infrastructure support sustainable product launches ***beyond 2021***

* Sanofi Genzyme is leading and funding development of fitusiran and will commercialize program, if successful;
The Medicines Company is leading and funding development of inclisiran and will commercialize program, if successful
^ ONPATTRO is approved in the EU for the treatment of hATTR amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy
Anticipated dates of launch based on current development timelines for investigational therapeutics and assuming positive pivotal study data and regulatory approval

Alnylam Clinical Development Pipeline

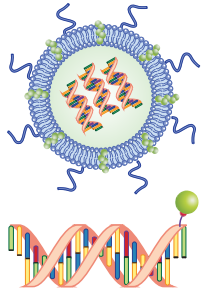
Focused in 4 Strategic Therapeutic Areas (STArs):

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

		HUMAN POC[1]	BREAKTHROUGH DESIGNATION	EARLY STAGE *(IND or CTA Filed-Phase 2)*	LATE STAGE *(Phase 2-Phase 4)*	REGISTRATION/ COMMERCIAL[3]	COMMERCIAL RIGHTS
onpattro (patisiran) lipid complex injection 10 mg/5 mL	*hATTR Amyloidosis*[2]	✓	✓			●	Global
Givosiran	*Acute Hepatic Porphyria*	✓	✓			●	Global
Patisiran	*ATTR Amyloidosis Label Expansion*	✓			●		Global
Fitusiran	*Hemophilia and Rare Bleeding Disorders*	✓			●		15-30% royalties
Inclisiran	*Hypercholesterolemia*	✓			●		Milestones & up to 20% royalties
Lumasiran	*Primary Hyperoxaluria Type 1*	✓	✓		●		Global
Vutrisiran	*ATTR Amyloidosis*	✓			●		Global
Cemdisiran	*Complement-Mediated Diseases*	✓		●			50-50
Cemdisiran/Pozelimab Combo[4]	*Complement-Mediated Diseases*			●			Milestone/Royalty
ALN-AAT02	*Alpha-1 Liver Disease*			●			Global
ALN-HBV02 (VIR-2218)	*Hepatitis B Virus Infection*			●			50-50 option rights post-Phase 2
ALN-AGT	*Hypertension*			●			Global

[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 stage 2 polyneuropathy
[3] Includes marketing application submissions
[4] Cemdisiran is currently in Phase 2 development and pozelimab is currently in Phase 1 development; Alnylam and Regeneron are evaluating potential combinations of these two investigational therapeutics
As of May 2019

RNAi Therapeutics Target Cause of ATTR Amyloidosis



Production of mutant and wild type TTR

Unstable circulating TTR tetramers ***reduced***

Organ deposition of monomers, amyloid (β-pleated) fibril ***prevented***, ***clearance promoted***

Disease manifestation ***stabilization or improvement***

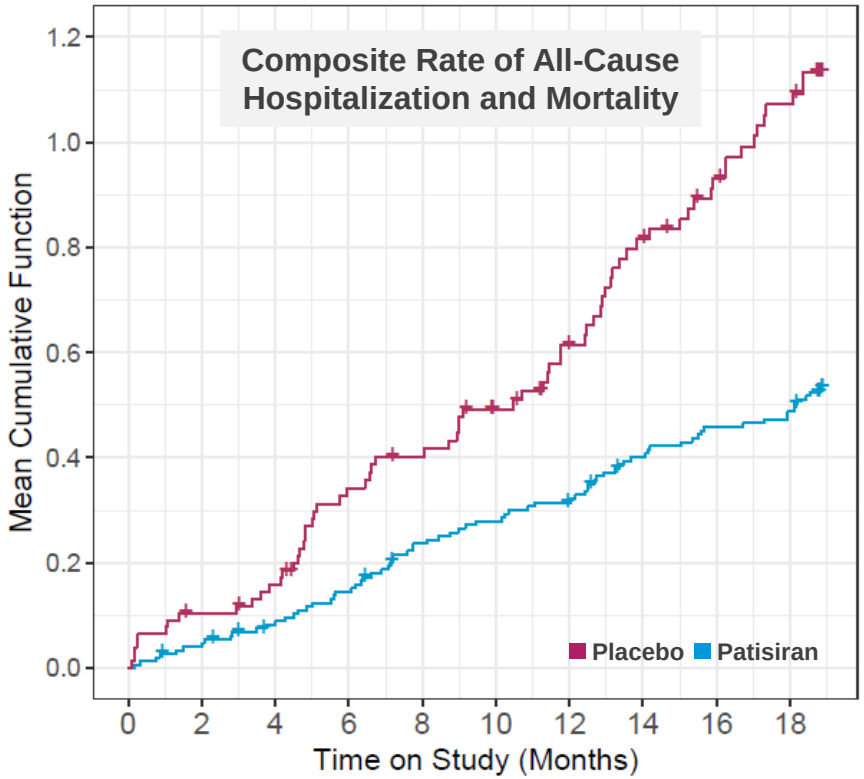
RNAi Therapeutic Hypothesis

Patisiran and vutrisiran act to silence both mutant and wild type TTR

APOLLO Phase 3 Study Results

Encouraging Evidence for Patisiran's Potential in ATTR Cardiomyopathy

~50% **Reduction in all-cause hospitalization and mortality in post-hoc analysis***



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

55%
- Relative reduction in **NT-proBNP** vs. placebo†
  - Effect noted as early as 9 months

0.9mm
- Mean reduction in **LV wall thickness** vs. placebo‡

-1.4%
- Improvement in **global longitudinal strain** vs. placebo‡

0.35m/s
- Improvement in **10-MWT** vs. placebo†

Cardiac Safety Data in Entire APOLLO Study Population:

	Placebo* (n=77)	Patisiran* (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)

* 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; Solomon S, et al. Circulation 2018

Patisiran APOLLO-B Phase 3 Study*

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

N ~ 300
Patient Population

- ATTR amyloidosis; wild-type or any TTR mutation
  - TTR stabilizer naïve and/or TTR stabilizer progressor
- Confirmed cardiomyopathy and medical history of symptomatic heart failure
- NYHA ≤III; minimum walk and NT-proBNP limits at baseline

1:1 RANDOMIZATION

Patisiran
IV q3w†
0.3 mg/kg

or

Placebo
IV q3w†

Primary Endpoint

- Change in 6-MWD at 12 months

Key Secondary Endpoints

- Cardiomyopathy symptoms and health status
- Death and hospitalization outcomes
- Cardiac biomarkers

12-Month Treatment Extension

APOLLO-B

Expected to initiate in **mid-2019**

* Subject to protocol finalization; concomitant use of local standard of care allowed during study, including TTR stabilizer

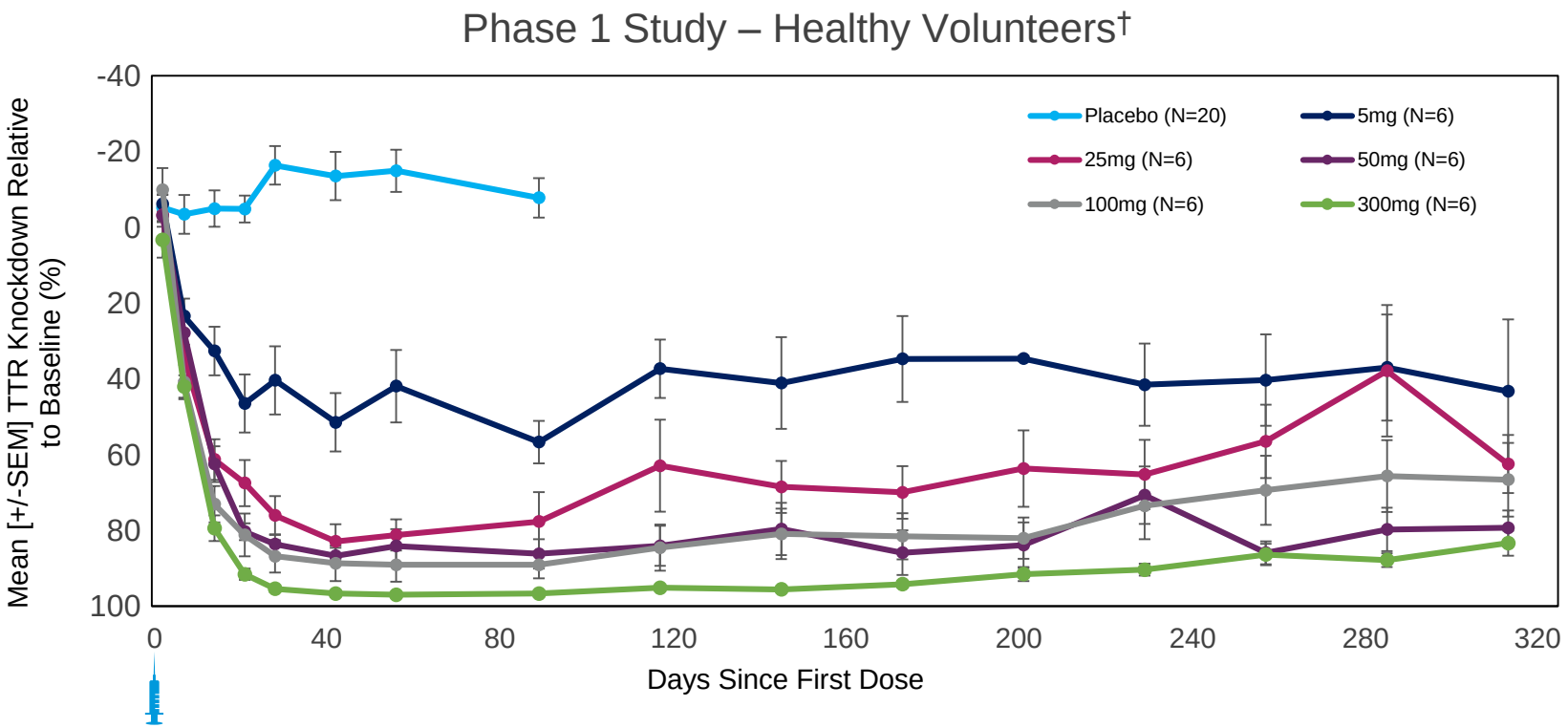
† To reduce likelihood of infusion-related reactions, patients receive following premedication or equivalent at least 60 min. before each study drug infusion: 10 mg (low dose) dexamethasone; oral acetaminophen; H1 and H2 blockers

NYHA: New York Heart Association; NT-proBNP: N-terminal pro b-type natriuretic peptide; 6-MWD: 6-Minute Walk Distance

Vutrisiran Opportunity

Advancing Continued Innovation to Patients with ATTR Amyloidosis

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



Vutrisiran

4 **DOSES PER YEAR**

~90% peak TTR KD predicted after repeat dosing

Safety (N=80):

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

* 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)

† As of data cutoff on May 31, 2017

Vutrisiran HELIOS·A Phase 3 Study

Randomized, Open-Label Study in Hereditary ATTR Amyloidosis Patients

HELIOS·A

Efficacy Assessments vs. APOLLO placebo arm

Co-Primary Endpoints
- Change in mNIS+7 from baseline
- Change in Norfolk QOL-DN from baseline

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

HELIOS-A Phase 3 study **now initiated**

HELIOS-B Phase 3 outcomes study for ATTR* cardiomyopathy expected to initiate in **late 2019**

^ Primary endpoint for the study is at 9 months

* ATTR amyloidosis – wild-type or any TTR mutation

Acute Hepatic Porphyria

Givosiran

Description

Family of ultra-rare orphan diseases causing incapacitating and potentially fatal attacks, leading to frequent hospitalizations and chronic pain

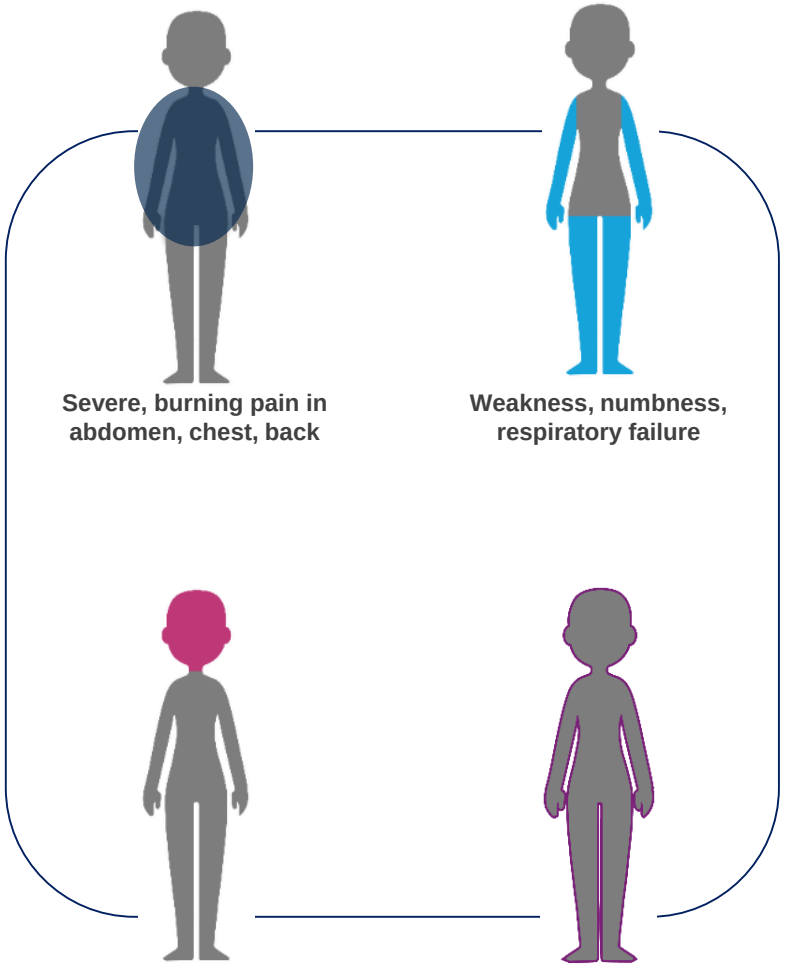
Predominantly

female

commonly misdiagnosed

Patient Population*

~5,000	~1,000
with **sporadic attacks** in U.S./EU	with **recurrent attacks** in U.S./EU



* ORPHANET; The Porphyria Consortium

† Symptoms specific to hereditary coproprophyria and variegate porphyria

Givosiran ENVISION Phase 3 Study

Randomized, Double-Blind, Placebo-Controlled Study in Acute Hepatic Porphyria (AHP) Patients

94 patients enrolled at 36 sites in 18 countries

Patient Population (N = 94)

- Age ≥12 years
- Diagnosis of AHP
- ≥2 attacks within prior 6 months

1:1 RANDOMIZATION

Givosiran
SC qM
2.5 mg/kg

or

Placebo
SC qM

Primary Endpoint

- Composite annualized attacks in AIP over 6 months†

Secondary Endpoints*

- ALA and PBG
- Hemin doses
- Composite annualized attacks in AHP over 6 months†
- Pain
- Fatigue
- Nausea
- PCS of SF-12

Open-Label Extension

FDA Breakthrough and EMA PRIME Designations

Complete NDA and MAA filings expected in **mid-2019**

† Attacks requiring hospitalization, urgent healthcare visit, or IV hemin administration at home

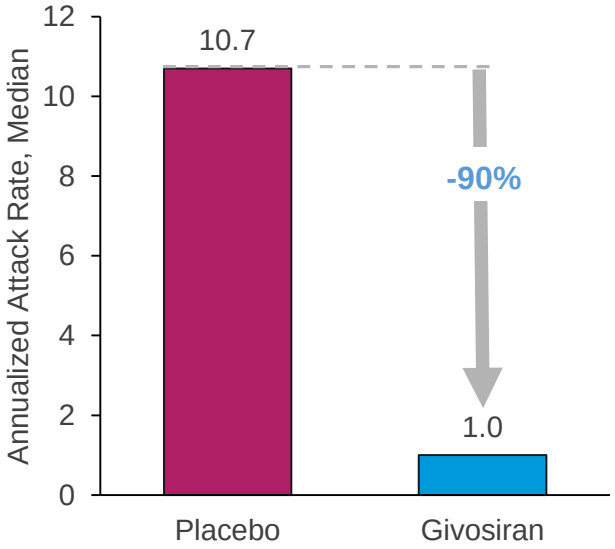
* Endpoints evaluated in AIP patients, unless otherwise noted

Givosiran ENVISION Phase 3 Study

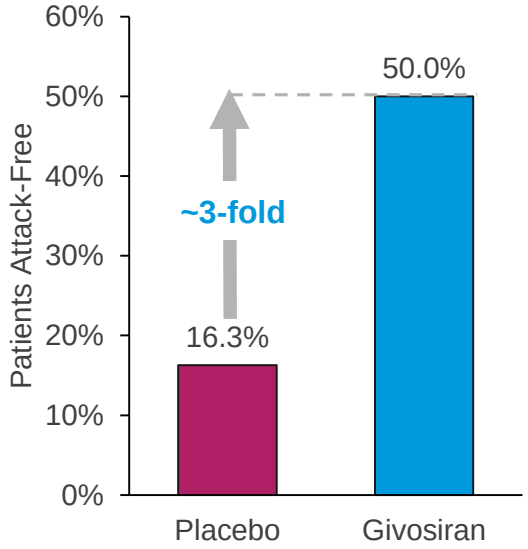
Givosiran Meets Primary Endpoint with Encouraging Profile in High Unmet Need Disease

Primary Endpoint*	Givosiran (N=46)	Placebo (N=43)	Rate Ratio	P-Value
Composite† Annualized Attack Rate, Mean	3.2	12.5	0.26	6.04×10^{-9}

Reduction in median composite attack rate



Increase in patients attack-free



Adverse Event, n of patients (%)	Placebo (N = 46)	Givosiran (N = 48)
Adverse Event (AE)	37 (80.4%)	43 (89.6%)
Serious Adverse Event (SAE)	4 (8.7%)	10 (20.8%)
Deaths	0 (0.0%)	0 (0.0%)
Discontinuations Due to AEs	0 (0.0%)	1 (2.1%)

- Three SAEs in givosiran patients reported as study drug related
  - 1 pyrexia, 1 abnormal liver function test, and 1 chronic kidney disease
- Common AEs (>10% in either arm)
  - More common in givosiran than placebo: nausea, injection site reaction, chronic kidney disease, fatigue
  - More common in placebo than givosiran: headache, vomiting, urinary tract infection, pyrexia
- ALT elevations >3x ULN occurred in 7 givosiran patients compared to 1 placebo
  - Majority of ALT elevations mild to moderate in severity; occurred after the first 3 to 5 doses of givosiran
  - One givosiran-treated patient discontinued due to ALT >8x ULN, a protocol-defined stopping rule; the elevation subsequently resolved; in remaining 6 patients, all events resolved with continued dosing (n=5) or after a brief pause in dosing (n=1)
- Mild and mostly reversible increases in serum creatinine and decreases in eGFR were seen more commonly in givosiran than placebo; none led to discontinuation
- 93/94 (99%) patients enrolled into Open Label Extension (OLE) study

Completed primary analysis as of April 13, 2019; see Balwani, et al., EASL Meeting, April 13, 2019 for full ENVISION study results

* Efficacy endpoints evaluated in AIP patients, unless otherwise noted

† Attacks requiring hospitalization, urgent healthcare visit, or IV hemin administration at home

Givosiran Market Opportunity

Ultra-Rare Orphan Disease with Significant Disease Burden and Essentially No Competition

PREVALENCE

~1,000 *recurrent attacks*

~5,000 *sporadic attacks*

patients in U.S./EU[1]

DIAGNOSIS

~20%

currently diagnosed;
delays up to 15 years

DISEASE BURDEN

65%

recurrent attack patients
with chronic symptoms[2]

COST BURDEN

$400–650K

average annual expenditure,
recurrent attack patients[3]

GIVOSIRAN | ACUTE HEPATIC PORPHYRIA

>$500M potential market opportunity

[1] ORPHANET; The Porphyrias Consortium
[2] Gouya, et al. EASL 2018
[3] EXPLORE Natural History Study (includes patients with ≥ 3 attacks per year). Annual expenditure per patient; based on both hospitalization charges (amount billed) and costs (amount paid) from published data sources in U.S.

Primary Hyperoxaluria Type 1

Lumasiran

Description

Rare autosomal recessive disorder of increased oxalate synthesis resulting in kidney stones and renal failure, with subsequent oxalate accumulation in extra-renal tissues

Onset generally

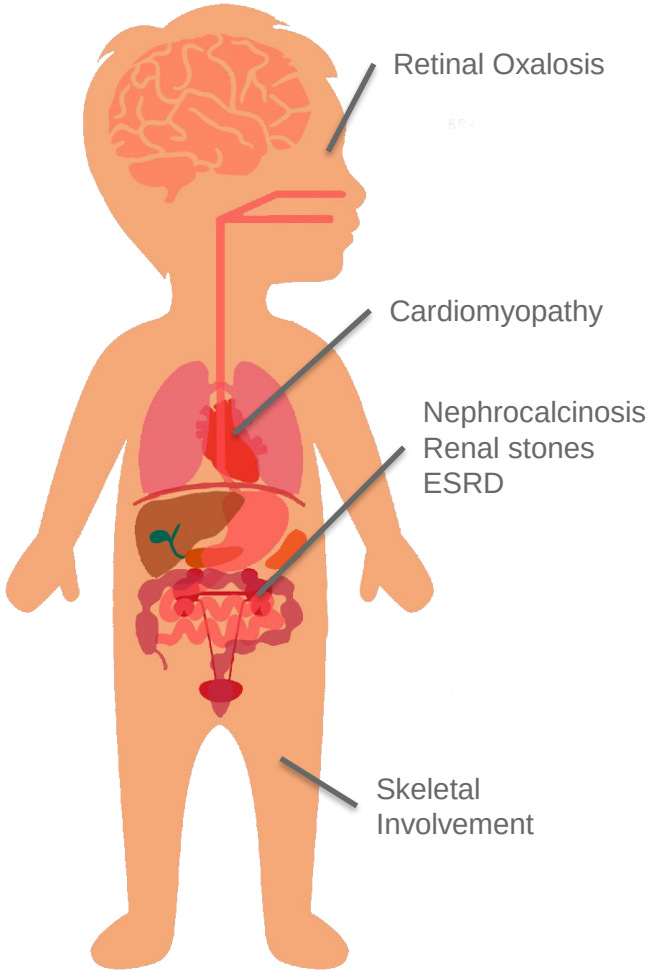
pediatric

very limited treatment options

Patient Population

~3,000 – 5,000

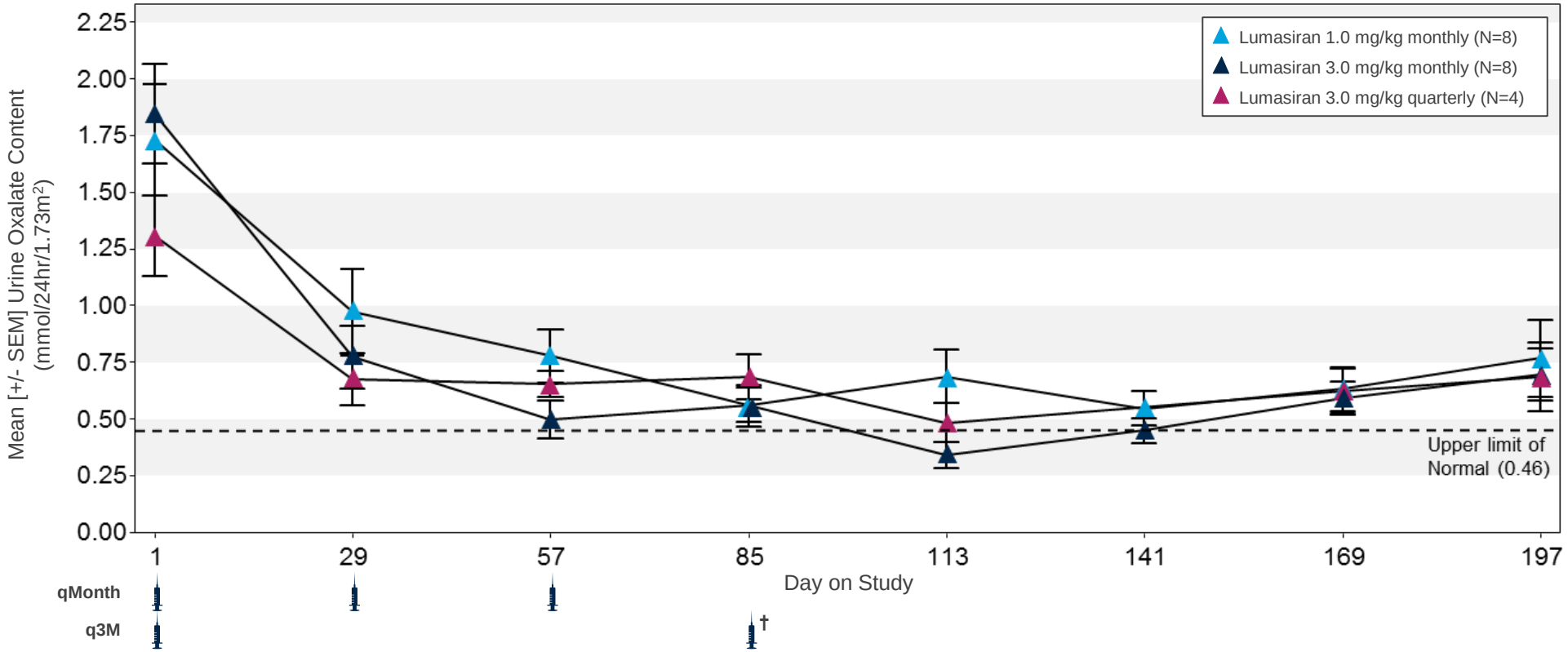
U.S./EU



Lumasiran Phase 1/2 Study Updated Results*

75% Mean Maximal Reduction in Urinary Oxalate

All patients (N=20) achieved reductions in urinary oxalate to <1.5ULN



Part B Safety (N=20):

- No discontinuations from study treatment
- Majority of AEs mild or moderate, unrelated to study drug
  - AEs reported in >3 lumasiran patients: vomiting, pyrexia, cough (N=6); abdominal pain, headache (N=5); rhinitis (N=4)
- No drug-related SAEs (most common: kidney stones (N=2 on lumasiran, 1 on placebo))

* Part B data as of August 15, 2018; only data points with at least 3 contributing patients are represented; placebo data not shown due to limited valid collections

† Patients randomized (3:1 drug:placebo) to placebo received subsequent dosing of lumasiran and are included in the lumasiran dosing cohort in which they were randomized; Day 1 relative to first lumasiran dose; patient randomized to placebo 3 mg/kg quarterly received single dose of lumasiran on Day 1

Lumasiran ILLUMINATE•A Phase 3 Study

Randomized, Double-Blind Study in Primary Hyperoxaluria Type 1 Patients

N = 30
Patient Population

- Adults & children ≥6 years
- Urinary oxalate excretion ≥0.7 mmol/24hr/1.73m^2
- Confirmed alanine glyoxalate aminotransferase (*AGXT*) mutations
- eGFR >45 mL/min/1.73m^2

2:1 RANDOMIZATION

Lumasiran
3xqM loading dose, then q3M
3.0 mg/kg SC†

or

Placebo
3xqM loading dose, then q3M SC

Primary Endpoint

- Percent change in 24-hour urinary oxalate excretion at 6 months

Open-Label Extension

ILLUMINATE•A

FDA Breakthrough and EMA PRIME Designations

Topline ILLUMINATE-A results expected in **late 2019**

ILLUMINATE-C expected to initiate in **mid-2019**

NDA submission planned in **early 2020** (assuming positive results)

Topline ILLUMINATE-B results expected in **mid-2020**

† 3.0 mg/kg once monthly for 3 consecutive months (loading dose phase) followed by 3.0 mg/kg once every 3 months (maintenance phase) starting 1 month after last loading dose
ILLUMINATE-B: global Phase 3 pediatric study in patients under six years of age; ILLUMINATE-C: single-arm, open-label study in patients with impaired renal function

Lumasiran Market Opportunity

Ultra-Rare Orphan Disease with Potential First-in-Class/Best-in-Class Medicine

PREVALENCE	DIAGNOSIS	DISEASE BURDEN	COST BURDEN
~3–5K	**~50%**	**30–65%**	**$1M+**
patients in U.S./EU[1]	currently diagnosed[2]; mean time to diagnosis ~6 years[3]	reach end-stage renal disease before diagnosis[3]	average cost (transplant & lifelong immunosuppression)

LUMASIRAN | PRIMARY HYPEROXALURIA TYPE 1

>$500M potential market opportunity

[1] Cochat P, et al. N Engl J Med. 2013;369:649-658
[2] Hopp R, et al. J Am Soc Nephrol. 2015;26:2559-2570
[3] Harambat J, et al. Kidney Int. 2010;77(5):443-449

Other Programs to Watch

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Other Clinical and Late Pre-Clinical Programs

Large Number of Additional Programs Across Orphan and Prevalent Diseases

PROGRAM	INDICATION	PREVALENCE	STAGE	EXPECTED MILESTONE	PARTNER
Inclisiran	*Hypercholesterolemia*	**~31 million** in U.S. with LDL-C levels >240 mg/dl	**Phase 3**	**2019** topline results	The Medicines Company
Fitusiran	*Hemophilia and Rare Bleeding Disorders*	**~200,000** worldwide	**Phase 3**	**2019** support Sanofi	SANOFI
Cemdisiran	*Complement-Mediated Diseases*	**>100,000** total complement-mediated diseases	**Phase 2**	**2019** advance Phase 2 IgA nephropathy study	REGENERON
Cemdisiran/ Pozelimab Combo	*Complement-Mediated Diseases*	**>100,000** total complement-mediated diseases	**Phase 1 planned**	**2019** advance combo studies	REGENERON
ALN-AAT02	*Alpha-1 Liver Disease*	**~12,000** worldwide	**Phase 1/2**	**Late 2019** initial Phase 1/2 data	Alnylam PHARMACEUTICALS
ALN-HBV02 (VIR-2218)	*Hepatitis B Virus Infection*	**~400 million** worldwide with chronic disease	**Phase 1/2**	**Late 2019** initial Phase 1/2 data	VIR
ALN-AGT	*Hypertension*	**~9.1 million** in U.S. with resistant Hypertension	**Phase 1**	**Late 2019** initial Phase 1 data	Alnylam PHARMACEUTICALS

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

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)

1st IND expected in **early 2020**

1-2 INDs/year planned starting in **2020**

Alnylam-Regeneron Alliance*

Landmark Alliance Focused on CNS & Ocular RNAi Therapeutics

- Partnership of two leading biopharmaceutical companies committed to innovation
  - Alnylam R&D expertise and scientific excellence in RNAi therapeutics with emerging global commercial presence
  - Regeneron scientific excellence, world-leading capabilities in human genetics, and industry-leading commercial presence in ophthalmology and other large markets
- Broad, multi-product alliance across CNS, ocular, and select liver targets
  - Both companies fully participate in value creation with 50-50 structure in CNS and select liver programs
  - Milestone/royalty structure for ocular disease programs
- Accelerates Alnylam CNS and ocular programs, driving significant pipeline expansion
  - Robust, highly durable, and widely distributed RNAi knockdown of key targets in CNS/ocular pre-clinical models
  - Adds 1-2 new planned INDs/year toward CNS or ocular targets to previously planned 1-2 new INDs/year in liver beginning in 2020
- Significantly bolsters Alnylam balance sheet to >$2B *pro forma* for increased pipeline investment and future growth

* Alliance and equity agreements with Regeneron expected to close during Q2 2019

Guidance and Goals


Alnylam®
PHARMACEUTICALS
2020
3 STArs
3 Marketed Products
10 Clinical Programs
4 Late Stage Programs

Alnylam 2019 Goals

*Early is Q1-Q2, Mid is Q2-Q3, and Late is Q3-Q4

		2019*		
		Early	Mid	Late
onpattro (patisiran) lipid complex injection 10 mg/5 mL (ATTR Amyloidosis)	Commercial Execution	✓	●	●
	Japan Launch			●
	Additional Country Launches	✓	●	●
	Start APOLLO-B Cardiomyopathy Phase 3		●	
VUTRISIRAN (ATTR Amyloidosis)	HELIOS-A Polyneuropathy Phase 3 Enrollment	✓	●	●
	Start HELIOS-B Cardiomyopathy Phase 3			●
GIVOSIRAN (Acute Hepatic Porphyria)	ENVISION Phase 3 Topline Results	✓		
	File NDA		●	
	File MAA		●	
LUMASIRAN (Primary Hyperoxaluria Type 1)	Complete ILLUMINATE-A Phase 3 Enrollment		●	
	ILLUMINATE-A Phase 3 Topline Results			●
	Start ILLUMINATE-B & C Phase 3 Studies	✓	●	
ADDITIONAL CLINICAL PROGRAMS	Continue to advance early/mid-stage pipeline; File new INDs; Present clinical data	✓	●	●
PARTNERED PROGRAMS				
INCLISIRAN (Hypercholesterolemia)	ORION-9, 10, & 11 Phase 3 Topline Results		●	●
	File NDA			●
FITUSIRAN (Hemophilia and RBD)	Support Sanofi on ATLAS Phase 3	✓	●	●

Financial Summary and Guidance

Financial Results	Q1 2019	Q1 2018
ONPATTRO Net Product Revenues	$26.3M	*n/a*
Total Revenues	$33.3M	$21.9M
Total GAAP Operating Costs and Expenses	$222.1M	$169.3M
• *R&D Expenses*	*$129.1M*	*$96.9M*
• *SG&A Expenses*	*$89.6M*	*$72.4M*
• *Cost of Goods Sold*	*$3.3M*	*n/a*
Non-GAAP Expenses		
• *Non-GAAP R&D Expenses**	*$113.0M*	*$86.7M*
• *Non-GAAP SG&A Expenses**	*$73.7M*	*$63.0M*
GAAP Net Loss	$181.9M	$141.2M
Non-GAAP Net Loss**	$149.9M	$121.6M

First Quarter 2019 Cash & Shares

- Cash $1.29B
  - Includes $44.8M in restricted investments
  - >$2B *pro-forma* cash upon Regeneron closing
- Shares Outstanding 106.4M

2019 Financial Guidance

- Annual Non-GAAP Operating Expenses:
  - Non-GAAP R&D Expenses* in the range of $550M to $590M
  - Non-GAAP SG&A Expenses* in the range of $390M to $410M
- Current cash, cash equivalents, and marketable debt securities expected to support company operations for multiple years based on current operating plan

* Non-GAAP operating expenses exclude stock-based compensation expenses.
** Non-GAAP net loss excludes stock-based compensation expenses.

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