Alnylam Pharmaceuticals

38th Annual J.P. Morgan Healthcare Conference

January 13, 2020

Alnylam® PHARMACEUTICALS

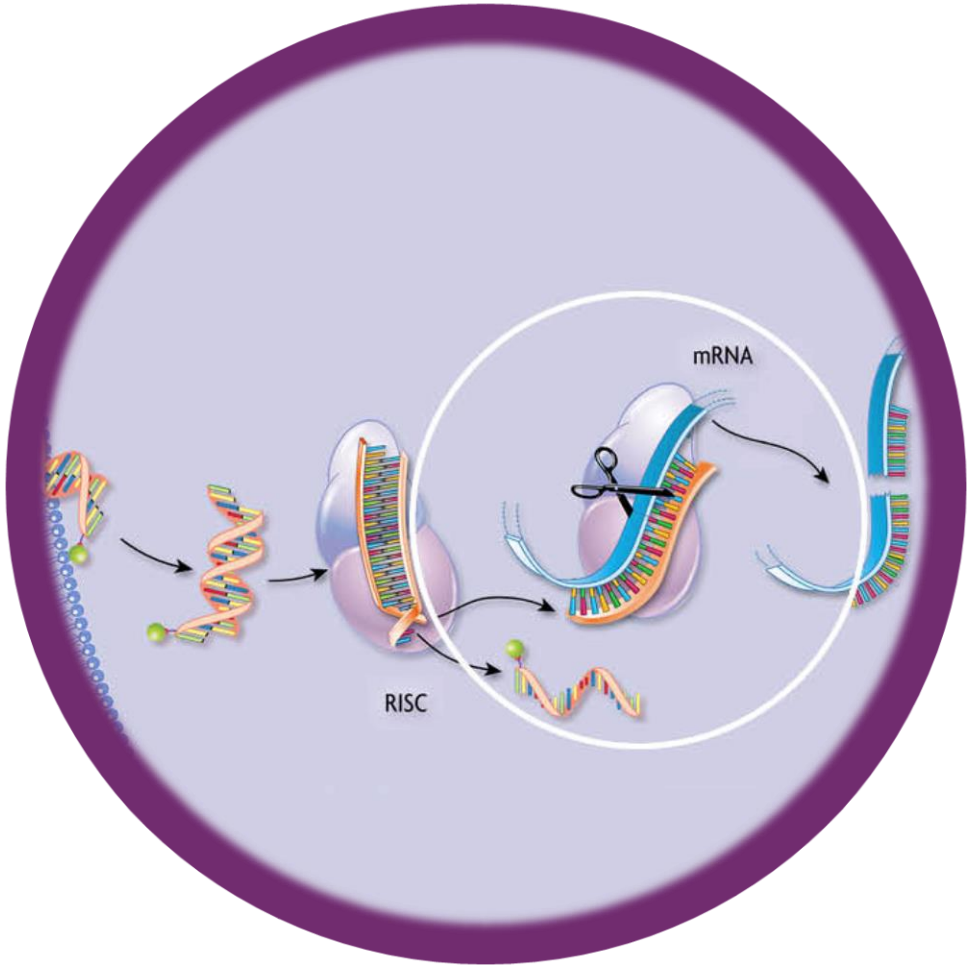
Alnylam Forward Looking Statements

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 the finalization and audit of our fourth quarter and 2019 fiscal year financial results which could potentially result in changes or adjustments to the selected preliminary financial results presented herein; 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 and our marketed products; intellectual property matters including potential patent litigation relating to our platform, products or product candidates; our ability to obtain regulatory approval for our product candidates, including lumasiran, and to maintain regulatory approval and obtain pricing and reimbursement for products, including ONPATTRO® (patisiran) and GIVLAARI™ (givosiran); our progress in continuing to establish a commercial and ex-United States infrastructure; our ability to successfully launch, market and sell our approved products globally, including ONPATTRO and GIVLAARI; our ability to successfully expand the indication for ONPATTRO in the future; competition from others using similar technology and developing products for similar uses; our ability to manage our growth and operating expenses and achieve a self-sustainable financial profile in the future; our ability to obtain additional funding to support our business activities and establish and maintain business alliances; our dependence on third parties, including Regeneron, for development, manufacture and commercialization of certain products, including eye and CNS products, and Ironwood, for assistance with the education about and promotion of GIVLAARI; the outcome of litigation; and the risk of government investigations; as well as those risks more fully discussed in our most recent quarterly 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.

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 innovation**
- **Multiple products impacting patients globally**



The first RNAi therapeutic is

APPROVED IN U.S., EU, CANADA, JAPAN & SWITZERLAND

onpattro®

(patisiran) lipid complex injection 10 mg/5 mL

onpattro®

2 mg/mL concentrate for solution for infusion patisiran

オンパットロ®

パチシランナトリウム注射液2mg/mL

Cece
Living with hATTR Amyloidosis

ATTR Amyloidosis

Rare, Progressively Debilitating, and Often 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

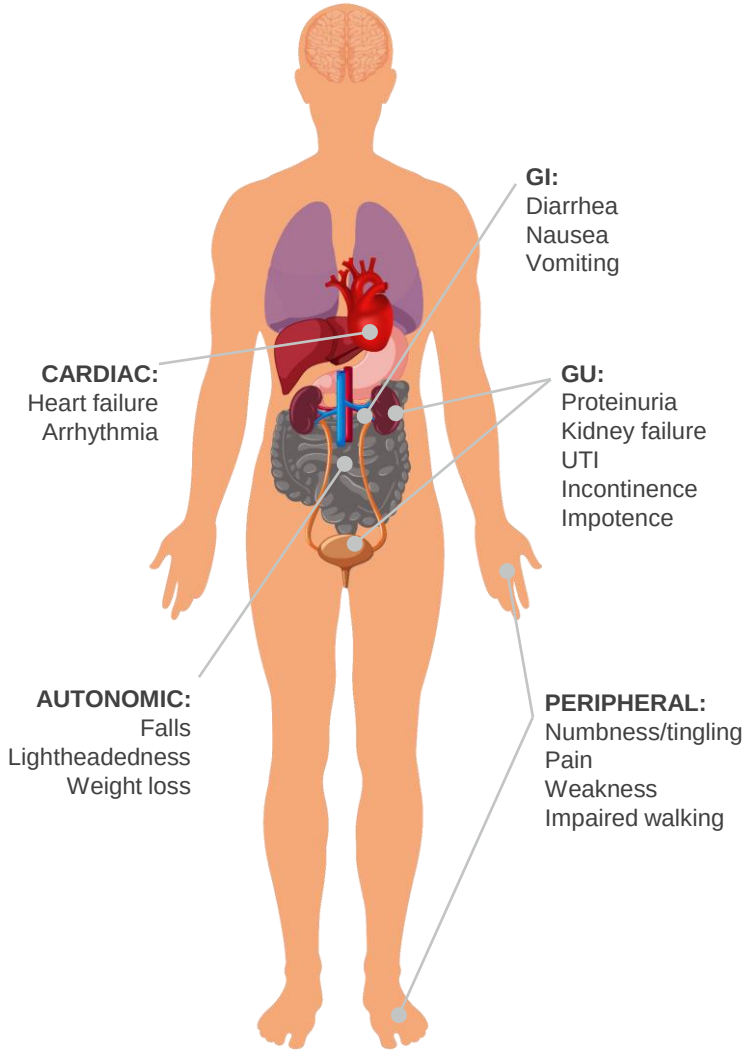
~50,000

patients worldwide*

Wild-Type ATTR (wtATTR) Amyloidosis

~200,000 – 300,000

patients worldwide



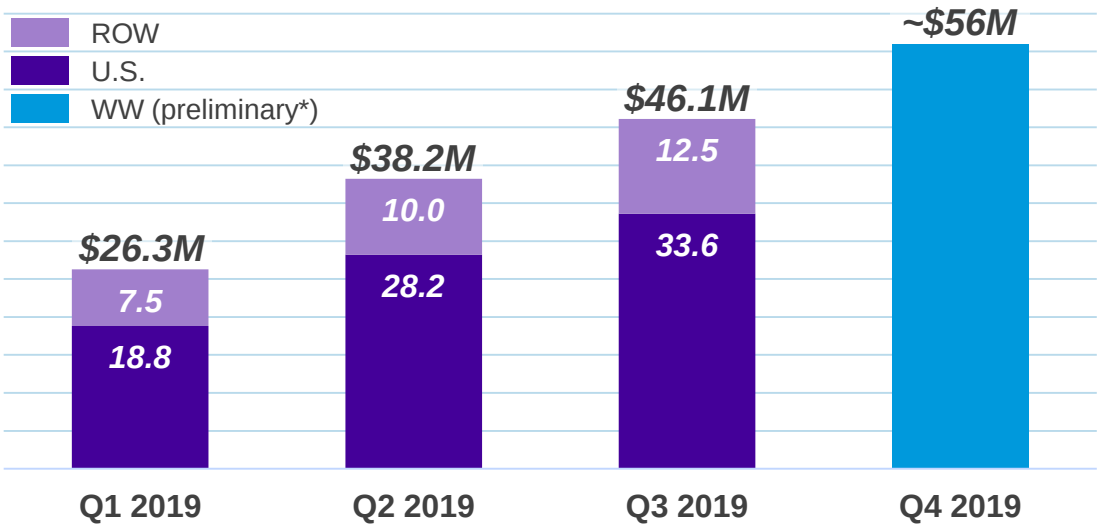
[1] Coelho T, et al. N Engl J Med. 2013;369(9):819-829
* Ando, et al. Orphanet J Rare Dis, 2013; Ruberg, et al. Circulation, 2012

ONPATTRO® Global Launch Update: Year End 2019

Strong Performance with Significant Growth Potential

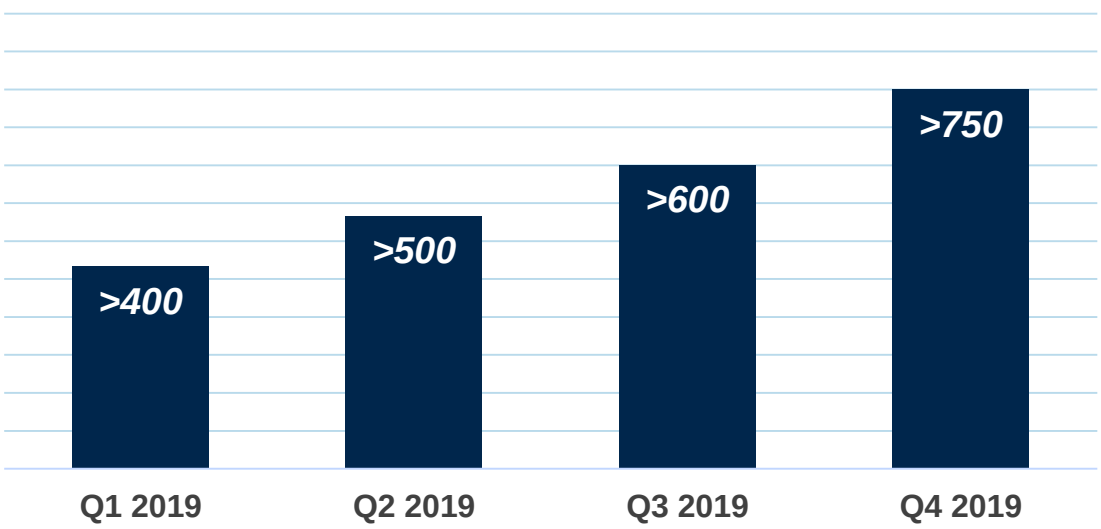
~$166M

ONPATTRO Global 2019
Net Product Revenues (Preliminary*)



>750

Patients Worldwide on Commercial
ONPATTRO at YE 2019

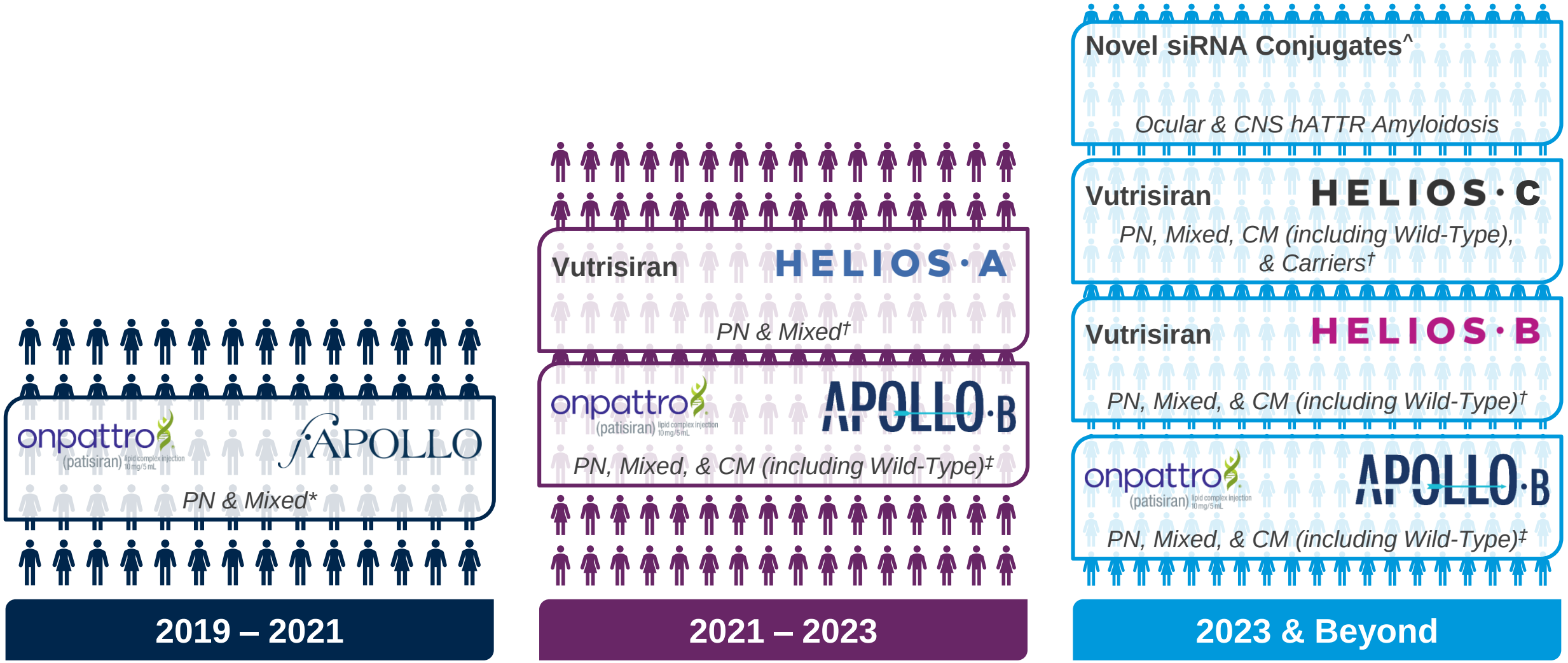


Expect steady and continued growth with new patient finding, global expansion, and evidence-generating activities

* Preliminary select financial results are unaudited, subject to adjustment, and provided as an approximation in advance of the Company's announcement of complete financial results in February 2020

Alnylam ATTR Amyloidosis Franchise

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



* ONPATTRO is approved in the U.S. and Canada for the treatment of the polyneuropathy of hATTR amyloidosis in adults, in the EU and Switzerland 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; ‡ 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; additional studies and future development possible; ^ 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

The second RNAi therapeutic is

NOW APPROVED IN THE U.S.

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

Yeliz
Living with Porphyria

Acute Hepatic Porphyria (AHP)

Family of Rare Genetic Diseases with Significant Disease Burden

Description

Causes potentially life-threatening attacks and chronic manifestations that negatively impact quality of life

Predominantly

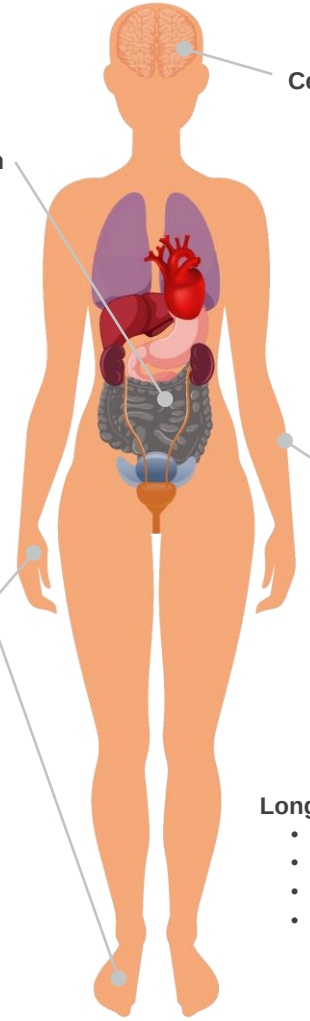
female

commonly misdiagnosed

Patient Population

~3,000

diagnosed in U.S./EU with active disease[1,2]



Central Nervous System
- Confusion
- Anxiety
- Depression
- Memory loss
- Fatigue
- Hallucinations
- Seizures

Autonomic Nervous System
- Severe abdominal pain
- Nausea/vomiting
- Hypertension
- Tachycardia
- Constipation
- Hyponatremia

Cutaneous†
- Lesions on sun-exposed skin

Peripheral Nervous System
- Neuropathic pain
- Sensory loss
- Muscle weakness
- Paralysis
- Respiratory failure

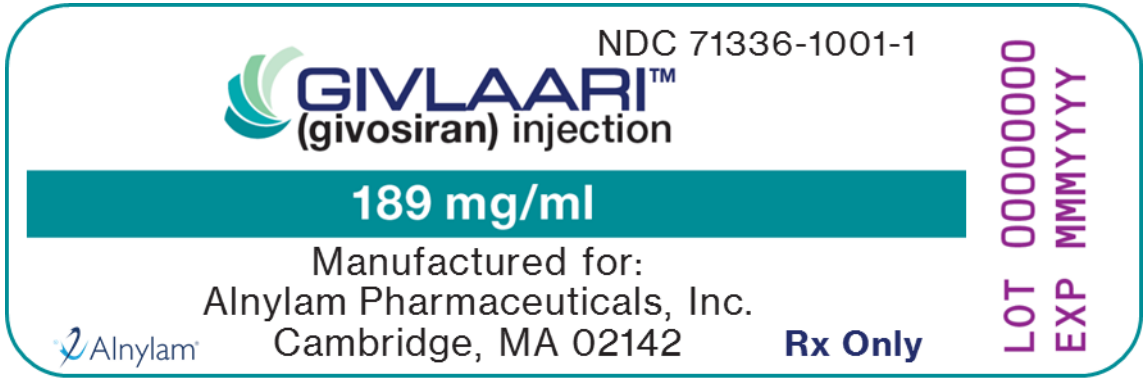
Long-term Complications
- Hepatocellular carcinoma
- Chronic kidney disease
- Hypertension
- Neuropathy

[1] Elder et al. J Inherit Metab Dis 2013;36:849–57; 2. Data on file, IBM MarketScan Commercial Claims and Medicare Supplemental Database
† Symptoms specific to hereditary coproprophyria and variegate porphyria

GIVLAARI™ (givosiran) Label

Indication

GIVLAARI is indicated for the treatment of adults with acute hepatic porphyria (AHP)



Dosing & Administration

Dosing:

- 2.5 mg/kg via subcutaneous injection once monthly

Administration:

- GIVLAARI is intended for subcutaneous use only by a healthcare professional

Safety*

Contraindications

- GIVLAARI is contraindicated in patients with known severe hypersensitivity to givosiran

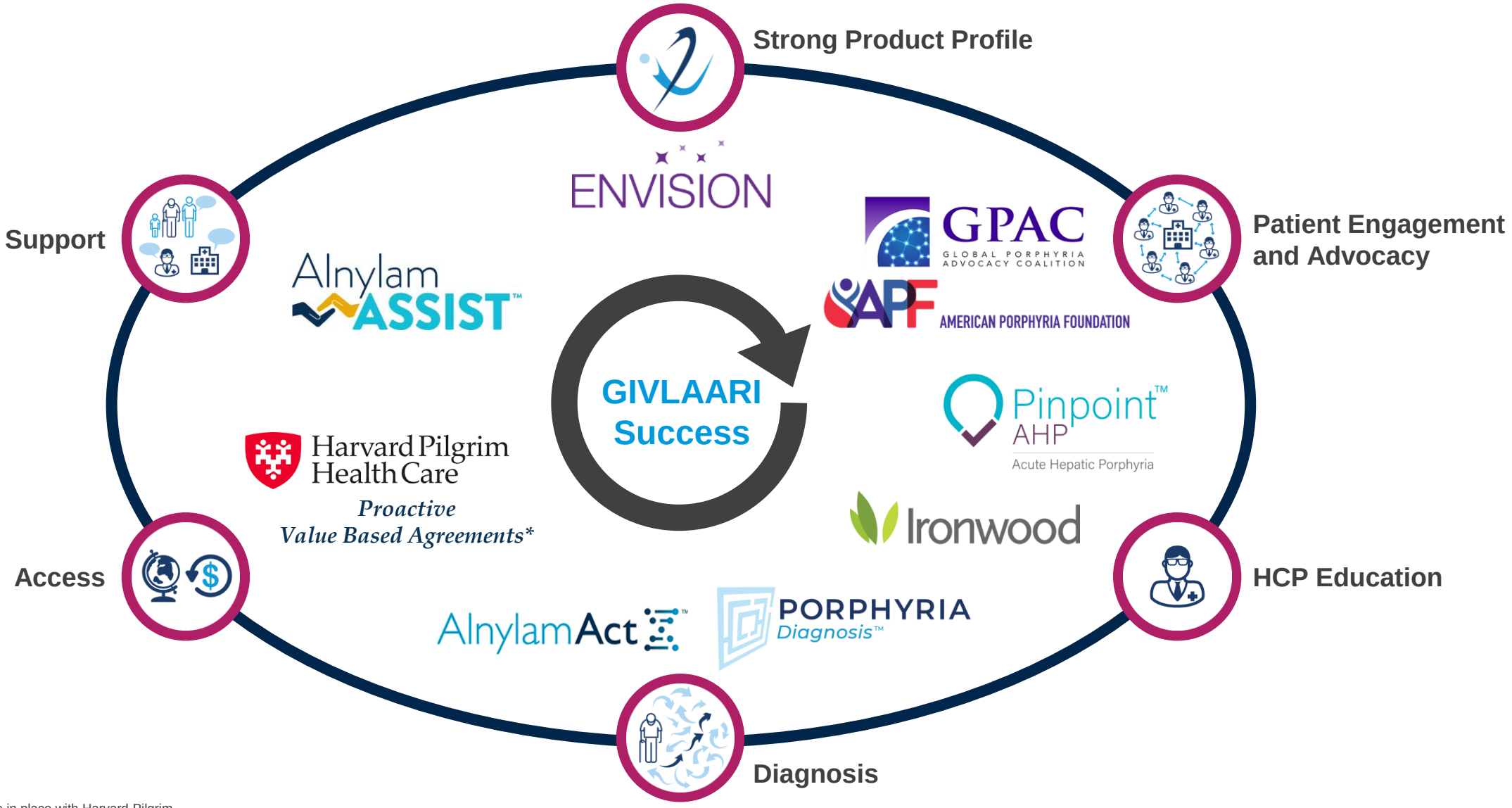
Warnings and Precautions

- Anaphylactic Reaction: Ensure that medical support is available to appropriately manage anaphylactic reactions when administering GIVLAARI. Monitor for signs and symptoms. If anaphylaxis occurs, discontinue GIVLAARI and administer appropriate medical treatment.
- Hepatic Toxicity: Measure liver function at baseline and periodically during treatment with GIVLAARI. Interrupt or discontinue treatment with GIVLAARI for severe or clinically significant transaminase elevations.
- Renal Toxicity: Monitor renal function during treatment with GIVLAARI as clinically indicated.
- Injection Site Reactions: May occur, including recall reactions. Monitor for reactions and manage clinically as needed.

* For additional Important Safety Information on GIVLAARI, see full Prescribing Information

Launching GIVLAARI Globally

Building on ONPATTRO Capabilities and Playbook



* Agreement in principle in place with Harvard Pilgrim

GIVLAARI™ (givosiran) Market Opportunity

Ultra-Rare Orphan Disease with Significant Disease Burden and Limited Treatment Options

PREVALENCE	DIAGNOSIS	DISEASE BURDEN	COST BURDEN
~3,000	**~20-50%**	**65%**	**$400–650K**
patients in U.S./EU, diagnosed with active disease[1,2]	currently diagnosed; delays up to 15 years	recurrent attack patients with chronic symptoms[3]	average annual expenditure, recurrent attack patients[4]

GIVLAARI | ACUTE HEPATIC PORPHYRIA

>$500M potential market opportunity

[1] Elder et al. J Inherit Metab Dis 2013;36:849–57
[2] Data on file, IBM MarketScan Commercial Claims and Medicare Supplemental Database
[3] Gouya, et al. EASL 2018
[4] 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.

Multiple Launches Planned in Next 12-24 Months

2018	2019	2020	2021	Partnered programs*: 2020-2021	
onpattro® (patisiran) lipid complex injection 10 mg/5 mL	GIVLAARI™ (givosiran) injection for subcutaneous use 189 mg/mL	**Lumasiran**	**Vutrisiran**	**Inclisiran**	**Fitusiran**
ONPATTRO is indicated in the U.S. for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults^	GIVLAARI is indicated in the U.S. for the treatment of adults with acute hepatic porphyria†	Primary hyperoxaluria type 1 **Ph3** ✓	ATTR amyloidosis	Hypercholesterolemia **Ph3** ✓	Hemophilia
		Rolling NDA initiated	*Phase 3 enrolling*	*NDA filed*	*Phase 3 enrolling*

Robust pipeline fuels sustainable product launches ***beyond 2021***, leveraging global commercial infrastructure

* Novartis is leading and funding development of inclisiran and will commercialize inclisiran, assuming regulatory approvals; Sanofi Genzyme is leading and funding development of fitusiran and will commercialize fitusiran, if successful

^ ONPATTRO is approved in Canada for the polyneuropathy of hATTR amyloidosis in adults, the EU and Switzerland for the treatment of hATTR amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy, and Japan for the treatment of transthyretin (TTR) type familial amyloidosis with polyneuropathy; For additional information on ONPATTRO, see Full Prescribing Information

† Alnylam has filed for marketing authorization for givosiran in Europe and Brazil and plans to file in Japan and other countries in 2020; For additional information on GIVLAARI, see Full Prescribing Information

Anticipated dates of launch based on current development timelines for investigational therapeutics and assuming positive pivotal study data and regulatory approval.

Alnylam Commercial Products and Late Stage Clinical Development Pipeline

Focused in 4 Strategic Therapeutic Areas (STArs):

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

		BREAKTHROUGH DESIGNATION	LATE STAGE *(Phase 2-Phase 3)*	REGISTRATION	COMMERCIAL	COMMERCIAL RIGHTS
onpattro (patisiran) lipid complex injection 10 mg/5 mL	*hATTR Amyloidosis*[1]	●			●	Global
GIVLAARI™ (givosiran) injection for subcutaneous use 189 mg/mL	*Acute Hepatic Porphyria*[2]	●			●	Global
Lumasiran	*Primary Hyperoxaluria Type 1*	●		●		Global
Inclisiran	*Hypercholesterolemia*			●		Milestones & up to 20% Royalties **(Novartis)**
Patisiran	*ATTR Amyloidosis Label Expansion*		●			Global
Fitusiran	*Hemophilia and Rare Bleeding Disorders*		●			15-30% Royalties **(Sanofi)**
Vutrisiran	*ATTR Amyloidosis*		●			Global

[1] Approved in the U.S. and Canada for the polyneuropathy of hATTR amyloidosis in adults, in the EU and Switzerland 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

[2] Approved in the U.S. for the treatment of adults with acute hepatic porphyria

As of January 2020

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-MWT at 12 months

Key Secondary Endpoints

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

12-Month Treatment Extension

APOLLO-B

Study initiated
September 2019

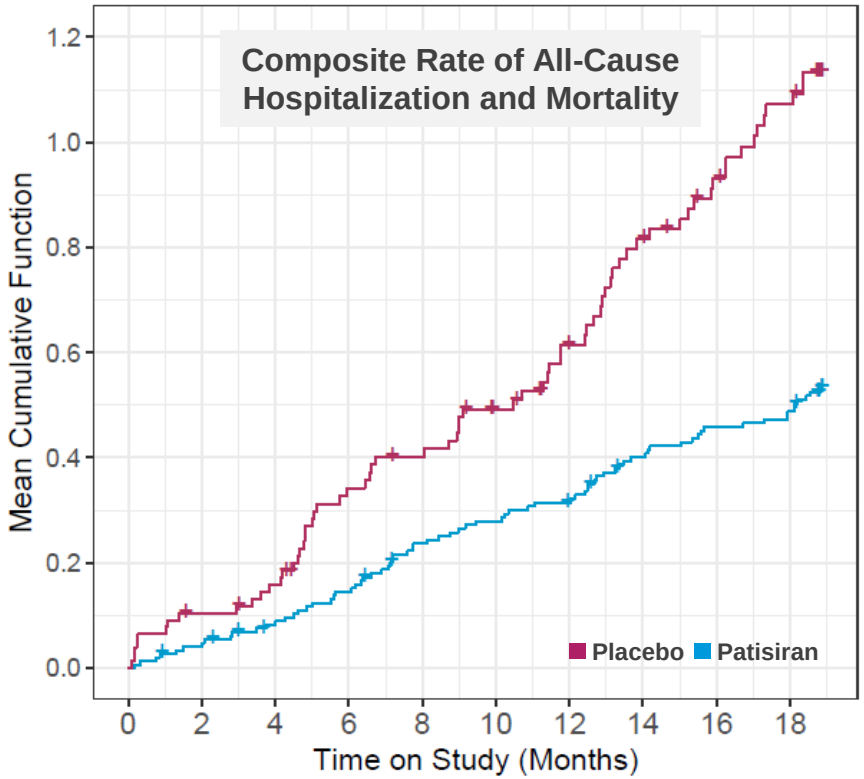
Topline results expected
2021

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-MWT: 6-Minute Walk Test

APOLLO Phase 3 Study Results

Encouraging Evidence for Patisiran's Potential in ATTR Cardiomyopathy[1]

~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†

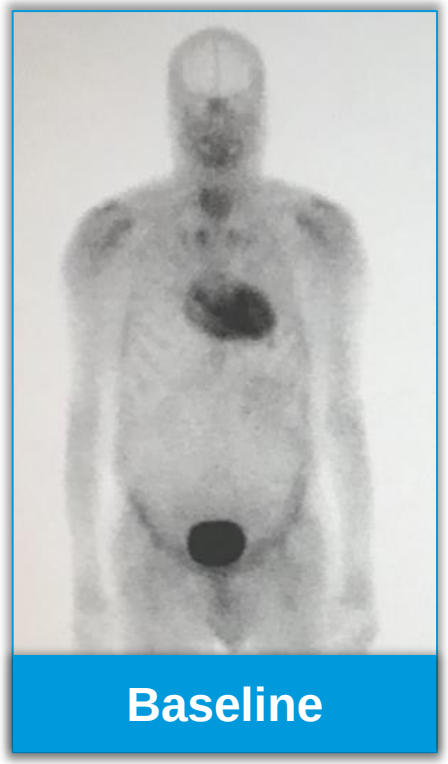
Cardiac Safety Data in Entire APOLLO Study Population:

	Placebo[2] (n=77)	Patisiran[2] (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 cardiac manifestations of amyloidosis. No conclusions can or should be drawn regarding its safety or effectiveness in this population
[2] 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 Treatment of hATTR Amyloidosis

Evidence for Potential Cardiac Amyloid Regression[1]

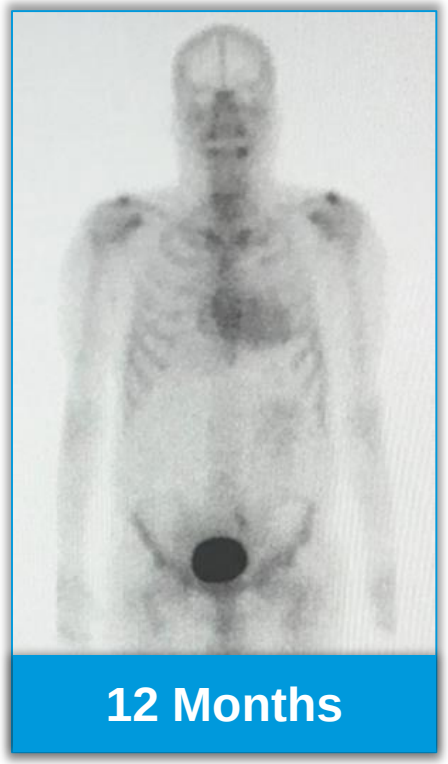


Baseline

~60 y.o. man with V30M mutation enrolled in EAP

Mixed phenotype: polyneuropathy predominant

Initiated patisiran (on top of diflunisal)
due to disease progression



12 Months

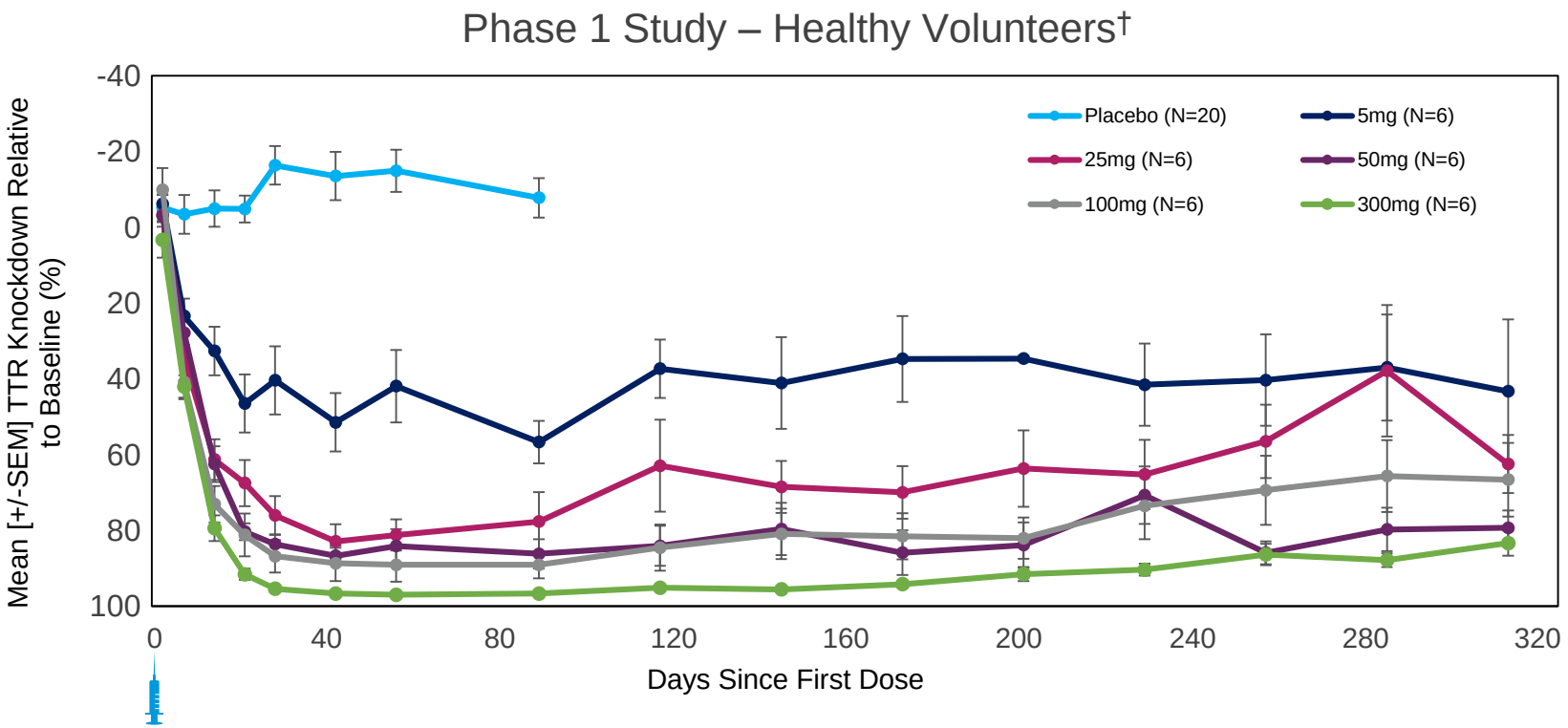
- Recent uncontrolled case series[2]
- Recently published similar findings by Nienhaus *et al*.[3]
- Patisiran treatment may be associated with cardiac remodeling and/or amyloid regression
- Cardiac effects to be further assessed in randomized, controlled trials

[1] 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
[2] Gilmore, OTS Munich 2019
[3] Mayo Clinic Proceedings, 2019

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 enrolling

Topline results expected
Early 2021

^ Primary endpoint for the study is at 9 months
* ATTR amyloidosis – wild-type or any TTR mutation

Vutrisiran HELIOS·B Phase 3 Study

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

N ~ 600
Patient Population

- ATTR amyloidosis; wild-type or any TTR mutation
  - ≤ 30% tafamidis use at baseline
- Confirmed cardiomyopathy and medical history of symptomatic heart failure
- NYHA ≤ III; minimum walk and NT-proBNP limits at baseline

1:1 RANDOMIZATION

Vutrisiran
SC q3M
25 mg

or

Placebo
SC q3M

Primary Endpoint

- Composite outcome of all-cause mortality and recurrent CV hospitalizations (when last patient reaches Month 30)

Select Secondary Endpoints

- 6-MWT distance
- Kansas City Cardiomyopathy Questionnaire (KCCQ OS) score
- Echocardiographic parameters
- All-cause mortality and recurrent all-cause hospitalizations
- All-cause mortality
- Recurrent CV hospitalizations
- NT-proBNP

HELIOS·B

HELIOS-B Phase 3 study
now enrolling

Study includes optional interim analysis

Benson
Living with Primary Hyperoxaluria Type 1

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

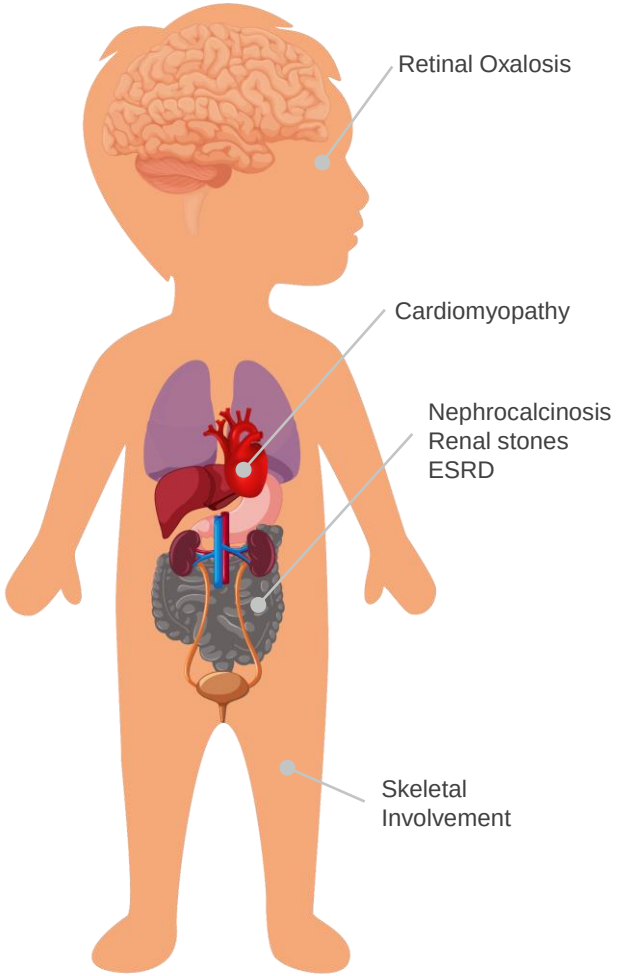
pediatric

very limited treatment options

Patient Population

~3,000 – 5,000

U.S./EU



Lumasiran Registrational Program

Robust Registrational Program to Evaluate Lumasiran Across all Ages and Full PH1 Disease Spectrum

ILLUMINATE

ILLUMINATE•A

Double-blind, placebo-controlled trial in PH1 patients at least 6 years old with preserved renal function

Detailed results in
March 2020 (OxalEurope)

ILLUMINATE•B

Single arm, open-label study in PH1 patients less than 6 years old with preserved renal function

Topline results expected in
mid-2020

ILLUMINATE•C

Single arm, open-label study in PH1 patients with impaired renal function, including advanced disease

Topline results expected in
2021

Expanded Access Protocol (EAP) for PH1 patients at least 6 years old with preserved renal function recently initiated in U.S.

Lumasiran ILLUMINATE•A Phase 3 Study

Topline Results

Primary Endpoint	p-value
Percent change from baseline in 24-hour urinary oxalate excretion, averaged across months 3 to 6 relative to placebo	1.69×10^{-14}

Secondary Endpoints	p-value
Absolute change from baseline in 24-hour urinary oxalate corrected for body surface area (BSA), averaged across months 3 to 6	1.23×10^{-11}
Percent change from baseline in 24-hour urinary oxalate:creatinine ratio, averaged across months 3 to 6	5.03×10^{-10}
Percent change from baseline in plasma oxalate, averaged across months 3 to 6	2.86×10^{-8}
Proportion of patients with 24-hour urinary oxalate level ≤ 1.5x ULN at month 6	8.34×10^{-7}
Proportion of patients with 24-hour urinary oxalate level ≤ ULN at month 6	0.001
Absolute change from baseline in plasma oxalate, averaged across months 3 to 6	3.89×10^{-7}

Safety

- No serious or severe adverse events
- Lumasiran generally well tolerated
- Most common adverse events were injection site reactions
  - All mild and transient
- Overall profile generally consistent with previously reported results from lumasiran Phase 1/2 and OLE studies

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

Late Stage Partnered Program Opportunities

INCLISIRAN

NOVARTIS

Hypercholesterolemia

40%	Adults WW with high LDL-C; ASCVD leading cause of death WW
>50M	Patients in key markets with ASCVD or FH on current SOC not at goal
7%	Treated patients statin intolerant
>60%	Patients treated with statins +/- ezetimibe do not meet goal[1]

NDA filed

FITUSIRAN

SANOFI

Hemophilia A or B, with and without inhibitors

~200K	Patients WW with hemophilia A or B, with and without inhibitors
~75%	Patients switched to emicizumab due to convenience (less freq. dosing, SC)[2]
<10%	Emicizumab patients on monthly dosing[3]
~90%	Emicizumab patients experienced acute bleeds[2]

>70% patients enrolled in ATLAS Phase 3 trials

[1] Boekholdt et al. Very Low LDL-C levels and CVD Risk JACC VOL 64.No5 2014:485-94

[2] Consumer Awareness, Trial, and Usage study among patients conducted over 359 Adult patients and caregivers surveyed online in April 2019, of which 131 were Adult Hemophilia A patients and 78 were Hemophilia A caregivers. Patients who switched to emicizumab answered questions specific to their treatment experience

[3] 2019 Specialty Pharmacy data obtained through Specialty Pharmacy Distributors, Hemophilia Alliance HTCs and Direct HTCs

Late Stage Partnered Program Opportunities

INCLISIRAN

NOVARTIS

Hypercholesterolemia

Royalties up to 20%

NDA filed

FITUSIRAN

SANOFI

Hemophilia A or B, with and without inhibitors

Royalties 15% to 30%

>70% patients enrolled in ATLAS Phase 3 trials

[1] Boekholdt et al. Very Low LDL-C levels and CVD Risk JACC VOL 64.No5 2014:485-94

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[3] 2019 Specialty Pharmacy data obtained through Specialty Pharmacy Distributors, Hemophilia Alliance HTCs and Direct HTCs

Alnylam Early Stage Clinical Development and 2020 IND Pipeline

Focused in 4 Strategic Therapeutic Areas (STArs):

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

		HUMAN POC[1]	BREAKTHROUGH DESIGNATION	2020 IND CANDIDATES	EARLY STAGE *(Phase 1-Phase 2)*	COMMERCIAL RIGHTS
Cemdisiran	*Complement-Mediated Diseases*	✓			●	50-50 **(Regeneron)**
Cemdisiran/Pozelimab Combo[2]	*Complement-Mediated Diseases*				●	Milestone/Royalty **(Regeneron)**
ALN-AAT02	*Alpha-1 Liver Disease*	✓			●	Global
ALN-HBV02 (VIR-2218)	*Hepatitis B Virus Infection*	✓			●	50-50 option post-Phase 2 **(Vir)**
ALN-AGT	*Hypertension*				●	Global
ALN-HSD	*NASH*			○		Milestone/Royalty **(Regeneron)**
ALN-LEC	*ALECT2 Amyloidosis*			○		Global

2-4 *INDs per year planned from organic product engine*

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

[2] 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 January 2020

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)

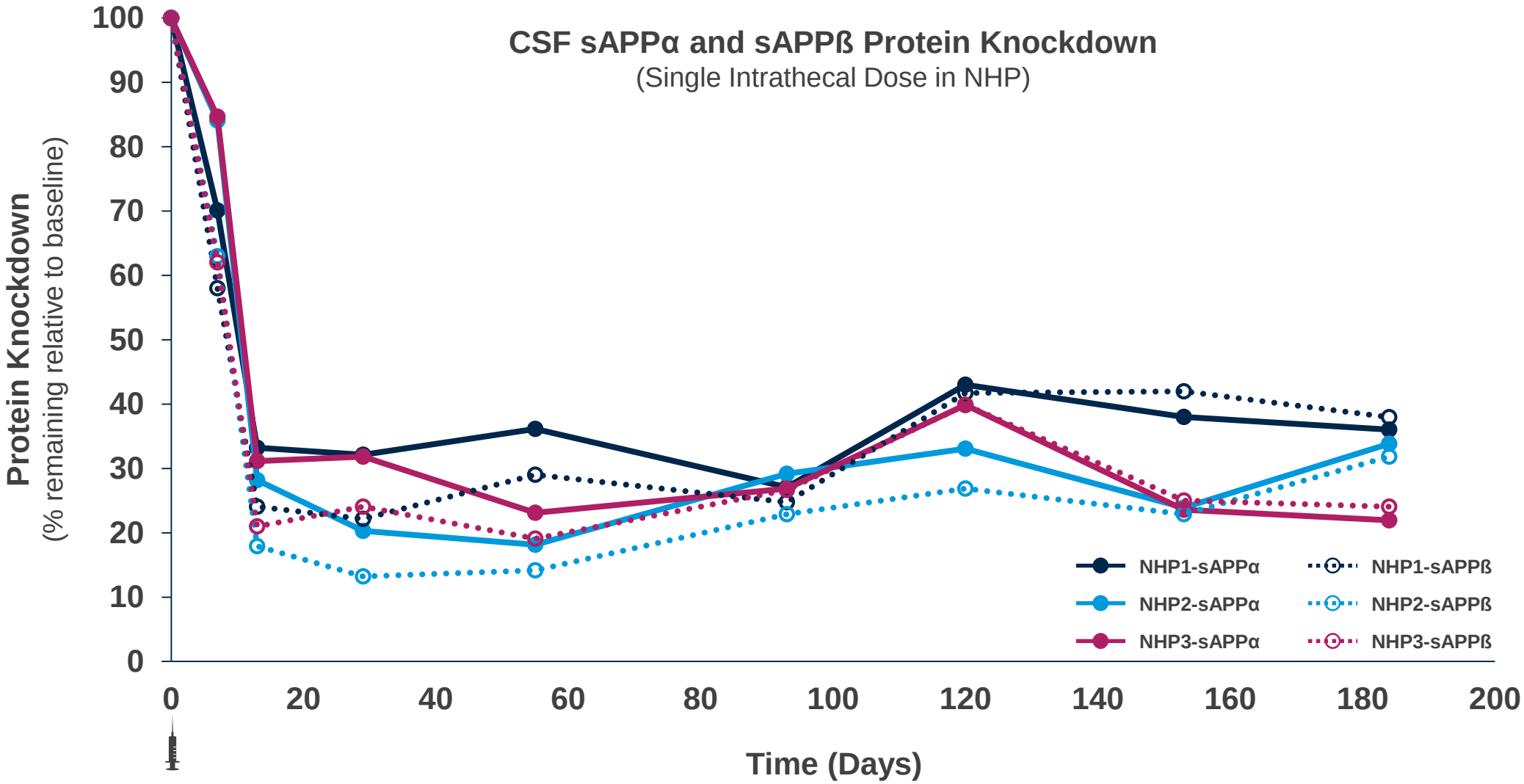
ALN-HTT

Targeting huntingtin gene (HTT) for early manfiest 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



Guidance, Goals, & Perspective

Alnylam PHARMACEUTICALS


Alnylam®
PHARMACEUTICALS
2020
3 STArs 4
3 Marketed Products 4
10 Clinical Programs 14
4 Late Stage Programs 6

Alnylam 2020 Goals

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

		2020*		
		Early	Mid	Late
onpattro® (patisiran) lipid complex injection (ATTR Amyloidosis)	Global Commercial Execution	●	●	●
	Brazil Approval		●	
	Additional Country Launches	●	●	●
	Complete APOLLO-B Enrollment			●
GIVLAARI™ (givosiran) injection for subcutaneous use 189 mg/mL (Acute Hepatic Porphyria)	EMA Approval	●		
	Global Commercial Execution	●	●	●
	Additional ENVISION Results		●	
	Additional Country Filings and Approvals	●	●	●
VUTRISIRAN (ATTR Amyloidosis)	Complete HELIOS-A Enrollment	●		
	HELIOS-B Enrollment	●	●	●
LUMASIRAN (Primary Hyperoxaluria Type 1)	File MAA	●		
	FDA/EMA Approval			●
	ILLUMINATE-B Phase 3 Topline		●	
ADDITIONAL CLINICAL PROGRAMS	Continue to advance early/mid-stage pipeline; File 3 new INDs; Present clinical data	●	●	●
PARTNERED PROGRAMS				
INCLISIRAN (Hypercholesterolemia)	FDA Approval			●
	MAA Filing	●		
	ORION-4 CVOT Phase 3 Enrollment	●	●	●
FITUSIRAN (Hemophilia)	Support Sanofi on ATLAS Phase 3	●	●	●

Alnylam 2020 Goals

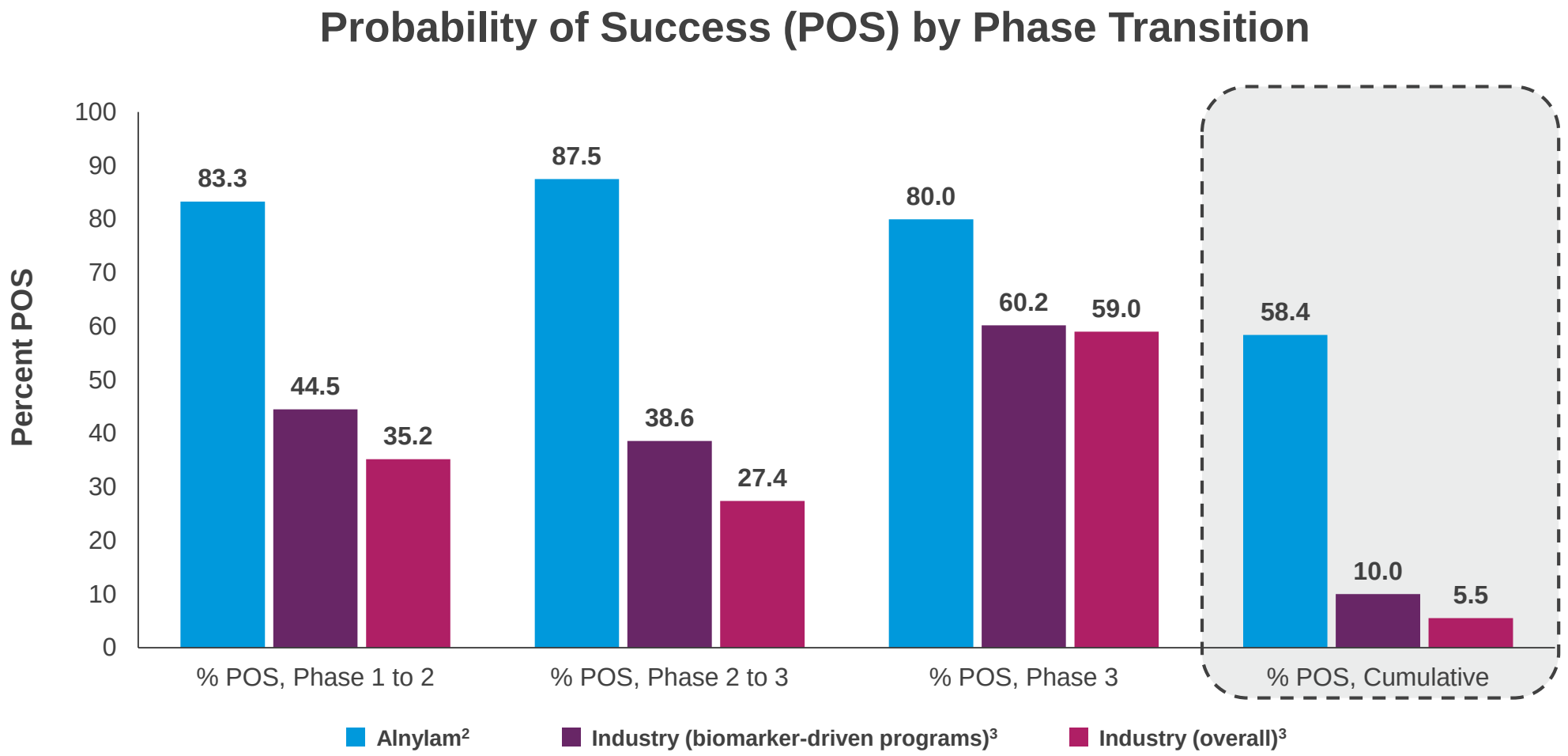
*Early is Q1-Q2, Mid is Q2-Q3, and Late is Q3-Q4

		2020*		
		Early	Mid	Late
onpattro (patisiran) lipid complex injection (AT	Global Commercial Execution	●	●	●
	Brazil Approval		●	
	Additional Country Launches	●	●	●
				●
G (giv (Acute				
				●
(AT				
				●
(Primary				
				●
ADDI PROGRAMS	File 3 new INDs; Present clinical data			●
PARTNERED PROGRAMS				
INCLISIRAN (Hypercholesterolemia)	FDA Approval			●
	MAA Filing	●		
	ORION-4 CVOT Phase 3 Enrollment	●	●	●
FITUSIRAN (Hemophilia)	Support Sanofi on ATLAS Phase 3	●	●	●

- Global commercial execution: ONPATTRO & GIVLAARI
- 2 regulatory approvals: lumasiran & inclisiran
- 1 Phase 3 readout: ILLUMINATE-B (lumasiran)
- 6 late-stage programs in 9 separate Phase 3 trials
- 2-4 new INDs

Productivity of Alnylam RNAi Therapeutic Platform

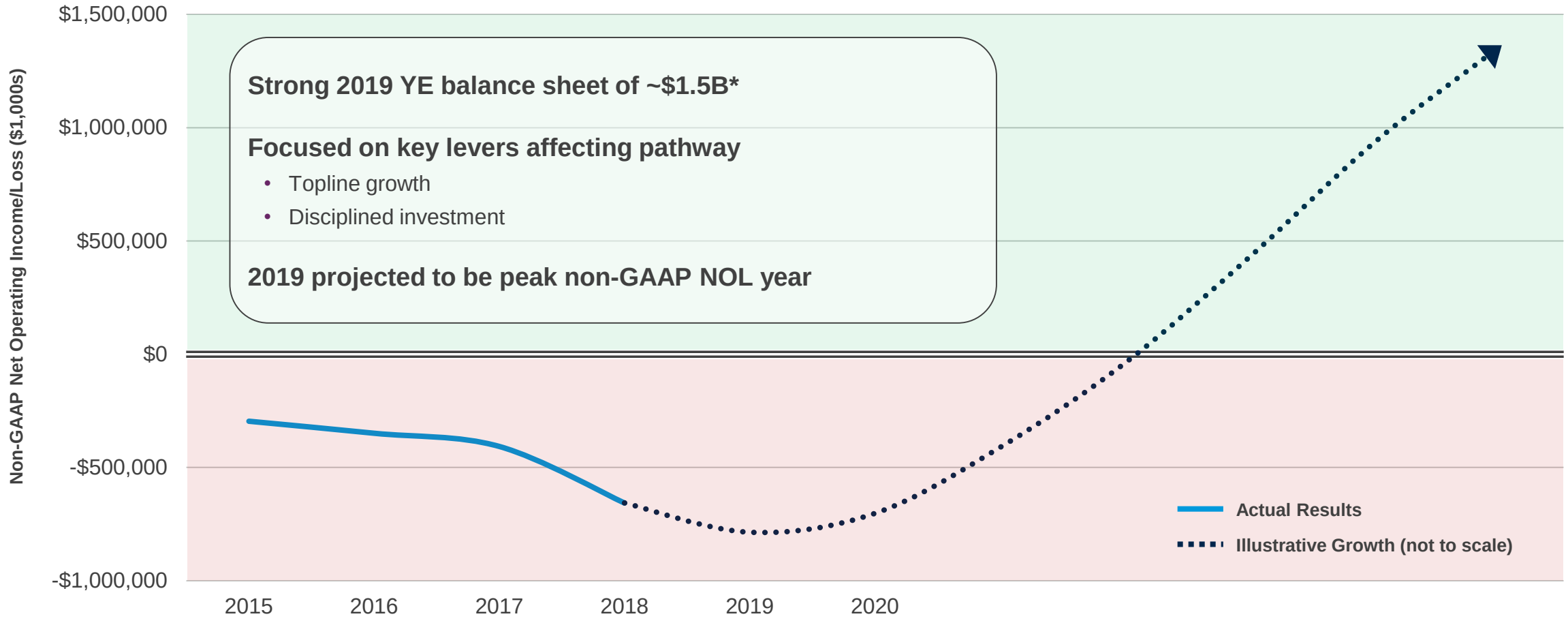
Comparison of Historical Industry Metrics to Alnylam Portfolio[1]



[1] Past rates of Alnylam and industry respectively may not be predictive of the future
[2] Alnylam programs biomarker-driven at all stages of development (100%)
[3] Wong et al., Biostatistics (2019) 20, 2, pp. 273–286

Path to Self-Sustainability

A Top Priority for Alnylam



	2015	2016	2017	2018	2019	2020
# Late Stage Programs:	2	1	4	6	6	6
# Commercial Products:	0	0	0	1	2	4

* Preliminary selected 2019 financial results are unaudited, subject to adjustment, and are provided as an approximation in advance of the Company's announcement of complete financial results for Q4 and FY 2019 in Feb. 2020

Building a Top-Tier Biotech

Potential for Significant Transformation of Alnylam over Next 6 Years

Today

2	Approved Products
6	Late Stage Programs
4	STArs
	10+ Markets
~1K	Employees
	CMOs

2025

8+	Approved Products
10+	Late Stage Programs
4+	STArs
	Global
~2.5K	Employees
	Norton + CMOs

Top 5 independent, global biopharma company admired for its dedication to **patients**, corporate **culture**, scientific **innovation**, social **responsibility**, and commercial **excellence** with numerous RNAi products across orphan and large disease areas

Alnylam PHARMACEUTICALS