Glaucienne
Diagnosed with AHP (Brazil)

Second Quarter 2021 Financial Results

August 3, 2021

Alnylam® PHARMACEUTICALS

Agenda

Welcome

- Christine Lindenboom
  Senior Vice President, Investor Relations & Corporate Communications

Overview

- John Maraganore, Ph.D.
  Chief Executive Officer

Commercial Highlights

- Tolga Tanguler
  Chief Commercial Officer

Alnylam Clinical Pipeline

- Akshay Vaishnaw, M.D., Ph.D.
  President of R&D

Financial Summary and Guidance

- Jeff Poulton
  Chief Financial Officer

2021 Goals Update

- Yvonne Greenstreet, MBChB, MBA
  President and Chief Operating Officer

Q&A Session

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, including expectations regarding our aspiration to become a leading biotech company and the planned achievement of our "*Alnylam P^{5}x25*" strategy, plans for additional global regulatory filings and the continuing product launches of our approved products, the current or potential therapy options for ATTR amyloidosis, the potential expansion of the ATTR amyloidosis franchise, the evidence for investigational RNAi therapeutics in ATTR cardiomyopathy, the achievement of additional pipeline milestones and data, including relating to ongoing clinical studies of patisiran, vutrisiran, lumasiran and zilebesiran, FDA review of the vutrisiran and inclisiran NDAs, including the expected PDUFA dates, the potential market opportunity for Leqvio and fitusiran, the potential opportunity for RNAi therapeutics in prevalent diseases, expectations relating to continued revenue growth for our approved products, updates to the expected range of net product revenues for 2021, the expected range of net revenues from collaborations for 2021, the expected range of royalty revenues for 2021, and the expected range of aggregate annual GAAP and non-GAAP R&D and SG&A expenses for 2021. Actual results and future plans may differ materially from those indicated by these forward-looking statements as a result of various important risks, uncertainties and other factors, including, without limitation: the direct or indirect impact of the COVID-19 global pandemic or any future pandemic on our business, results of operations and financial condition and the effectiveness or timeliness of our efforts to mitigate the impact of the pandemic; our ability to discover and develop novel drug candidates and delivery approaches, including using our IKARIA platform, and successfully demonstrate the efficacy and safety of our product candidates; the pre-clinical and clinical results for our product candidates; actions or advice of regulatory agencies and our ability to obtain and maintain regulatory approval for our product candidates, including vutrisiran, as well as favorable pricing and reimbursement; successfully launching, marketing and selling our approved products globally; delays, interruptions or failures in the manufacture and supply of our product candidates or our marketed products; obtaining, maintaining and protecting intellectual property; our ability to successfully expand the indication for ONPATTRO (and potentially vutrisiran) in the future; our ability to manage our growth and operating expenses through disciplined investment in operations and our ability to achieve a self-sustainable financial profile in the future without the need for future equity financing; our ability to maintain strategic business collaborations; our dependence on third parties for the development and commercialization of certain products, including Novartis, Sanofi, Regeneron and Vir; the outcome of litigation; the potential impact of current and the risk of future government investigations; and unexpected expenditures; as well as those risks more fully discussed in the "Risk Factors" filed with our most recent Quarterly Report on Form 10-Q filed with the SEC and in our other SEC filings. If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance, timelines 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.

This presentation references non-GAAP financial measures. These measures are not in accordance with, or an alternative to, GAAP, and may be different 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 referenced herein are stock-based compensation expenses and costs associated with our strategic financing collaboration. We have 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 our stock price, which impacts the fair value of these awards. We have excluded the impact of the costs associated with our strategic financing collaboration because we believe these items are non-recurring transactions outside the ordinary course of our business.

John Maraganore, Ph.D.

Chief Executive Officer

Overview

TRANSFORMATIONAL MEDICINES

ROBUST & HIGH-YIELD R&D PIPELINE

ORGANIC PRODUCT ENGINE

Our New 5-Year Strategy

Patients: Over 0.5 million on Alnylam RNAi therapeutics globally

Products: 6+ marketed products in rare and prevalent diseases

Pipeline: Over 20 clinical programs, with 10+ in late stages and 4+ INDs per year

Performance: ≥40% revenue CAGR through YE 2025

Profitability: Achieve sustainable non-GAAP profitability within period

Tolga Tanguler

Chief Commercial Officer

Commercial Highlights

ONPATTRO® (patisiran) Launch Update: Q2 2021

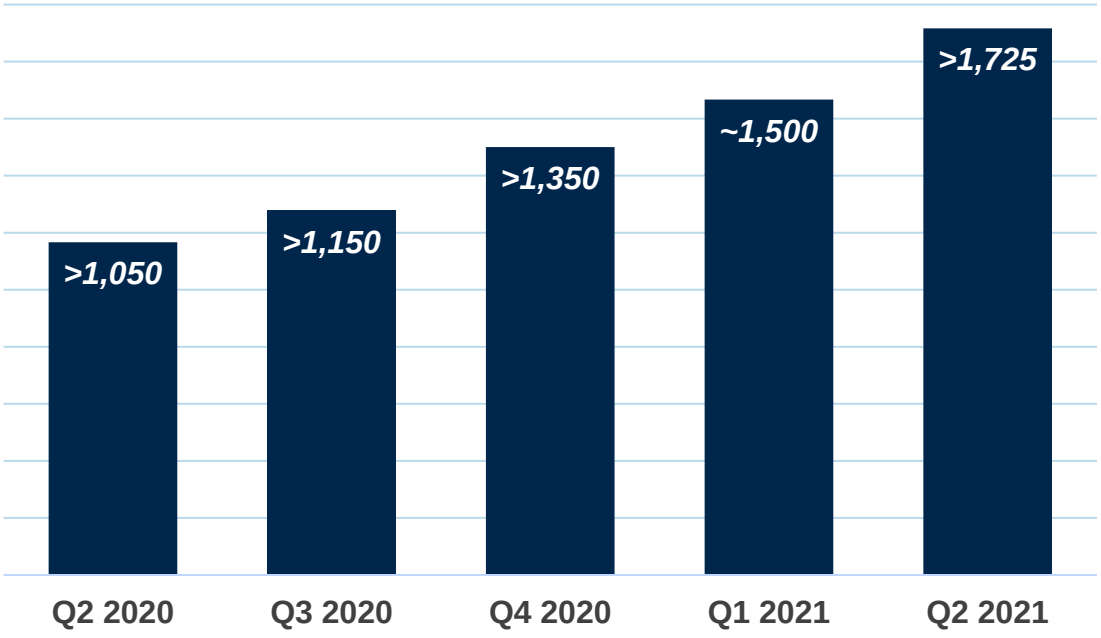
Steady and Continued Growth

$114M

ONPATTRO Global Q2 2021 Net Product Revenues

>1,725

Patients Worldwide on Commercial ONPATTRO at end of Q2 2021



Q2 U.S. Highlights

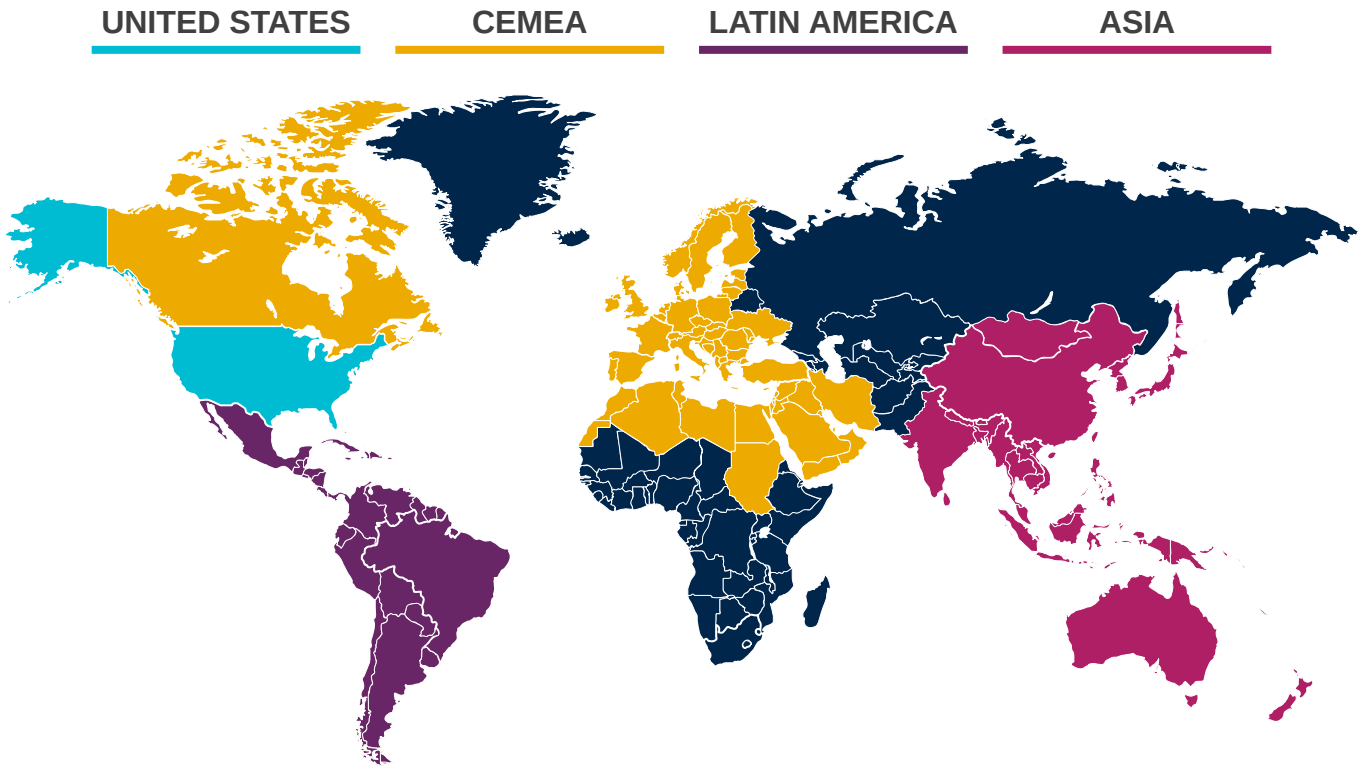
Steady, continuous patient growth; notable growth in demand and new prescribers

Increase driven by addition of new patients on therapy and continuation of >90% patient treatment compliance; highest addition of Start Forms since early 2019

ONPATTRO Global Commercialization

Increasing Access and Value Recognition

- Progress with global ONPATTRO availability
  - Over 30 countries now selling ONPATTRO through direct reimbursement, named patient sales, or reimbursed expanded access
  - Balanced use in both first-line treatment in hATTR patients with PN and switching from other products, including stabilizers



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

CEMEA: Canada, Europe, Middle East, North Africa

GIVLAARI® (givosiran) Launch Update: Q2 2021

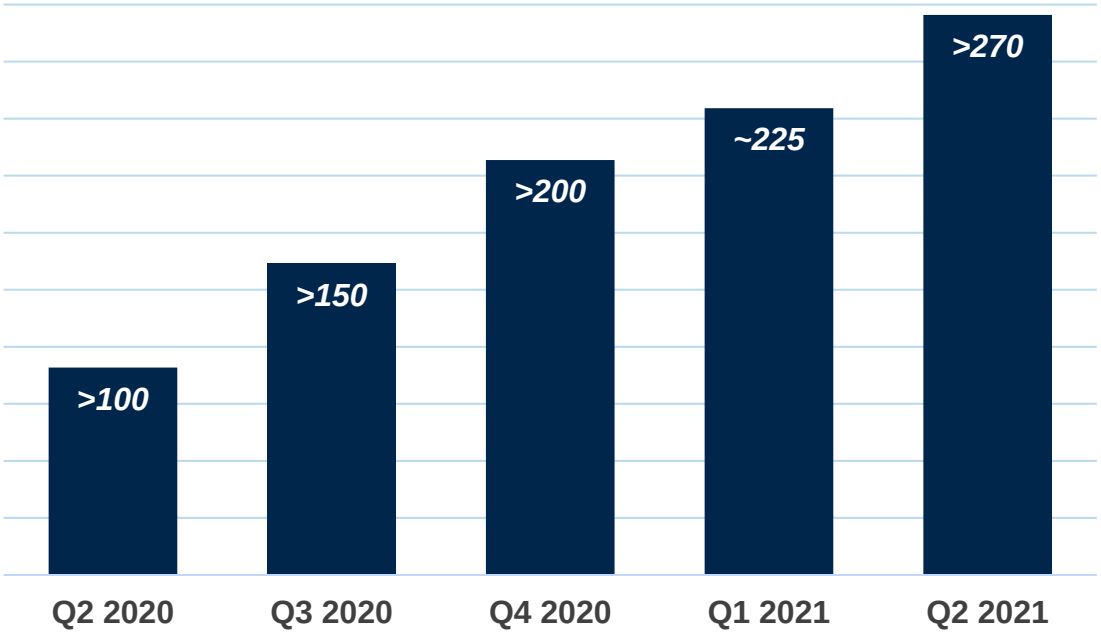
Continued Progress with Uptake and Access

$31M

GIVLAARI Global Q2 2021 Net Product Revenues

>270

Patients Worldwide on Commercial GIVLAARI at end of Q2 2021



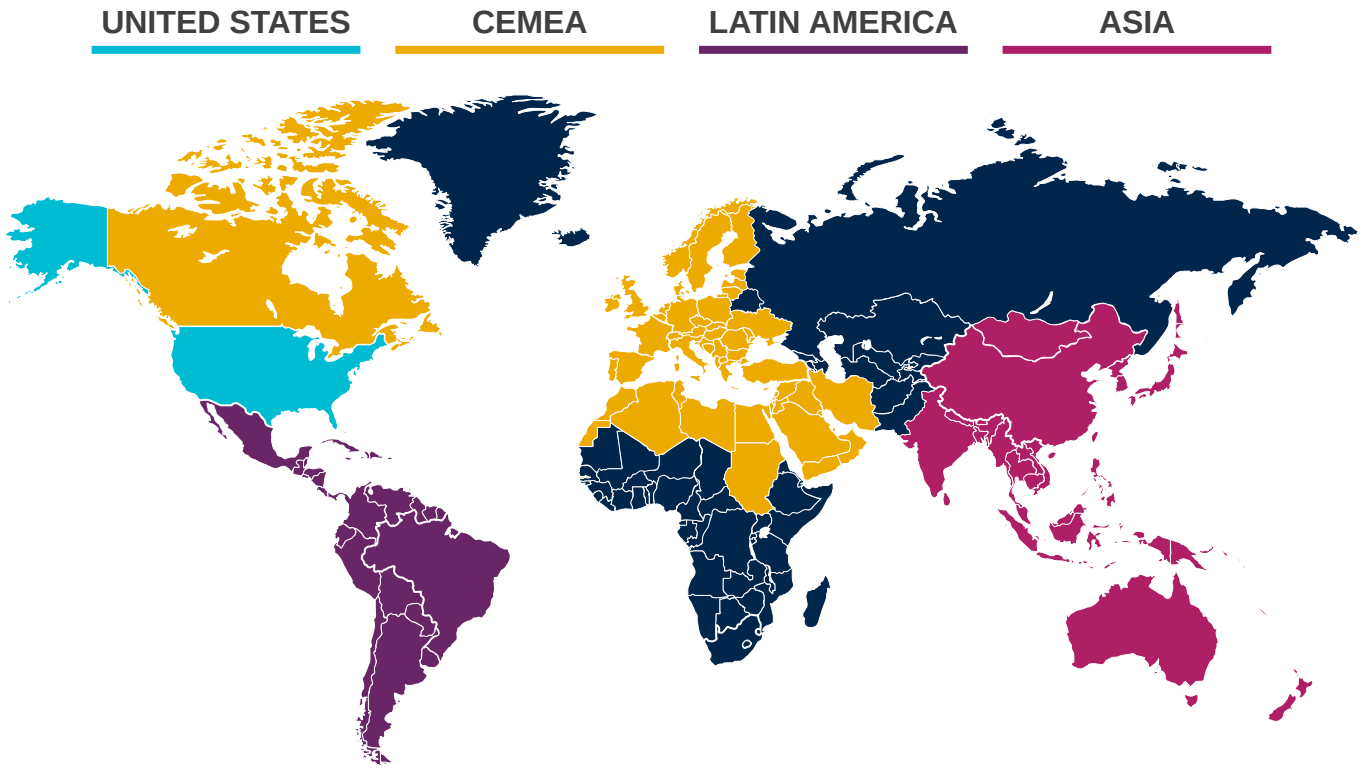
Q2 U.S. Highlights

- Significant growth driven by net new patient adds
- Continued expansion of prescriber base, including new writers, from community centers and COEs

GIVLAARI Global Commercialization

Ensuring GIVLAARI Availability Around the World

- Progress with global GIVLAARI availability
  - Recent launch in Italy
  - Ongoing launch in Germany
  - ATU supply in France
  - Approved in Japan; launch expected in September 2021



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

CEMEA: Canada, Europe, Middle East, North Africa

OXLUMO® (lumasiran) Launch Update: Q2 2021

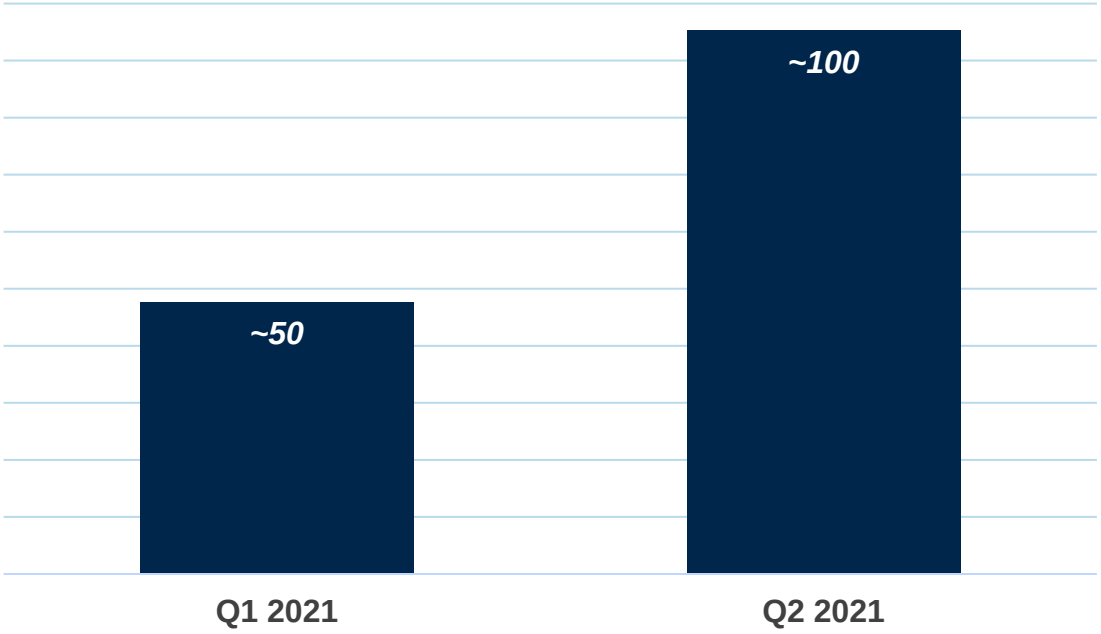
Strong Second Quarter Performance

$16M

OXLUMO Global Q2 2021 Net Product Revenues

~100

Patients Worldwide on Commercial OXLUMO at end of Q2 2021



Q2 U.S. Highlights

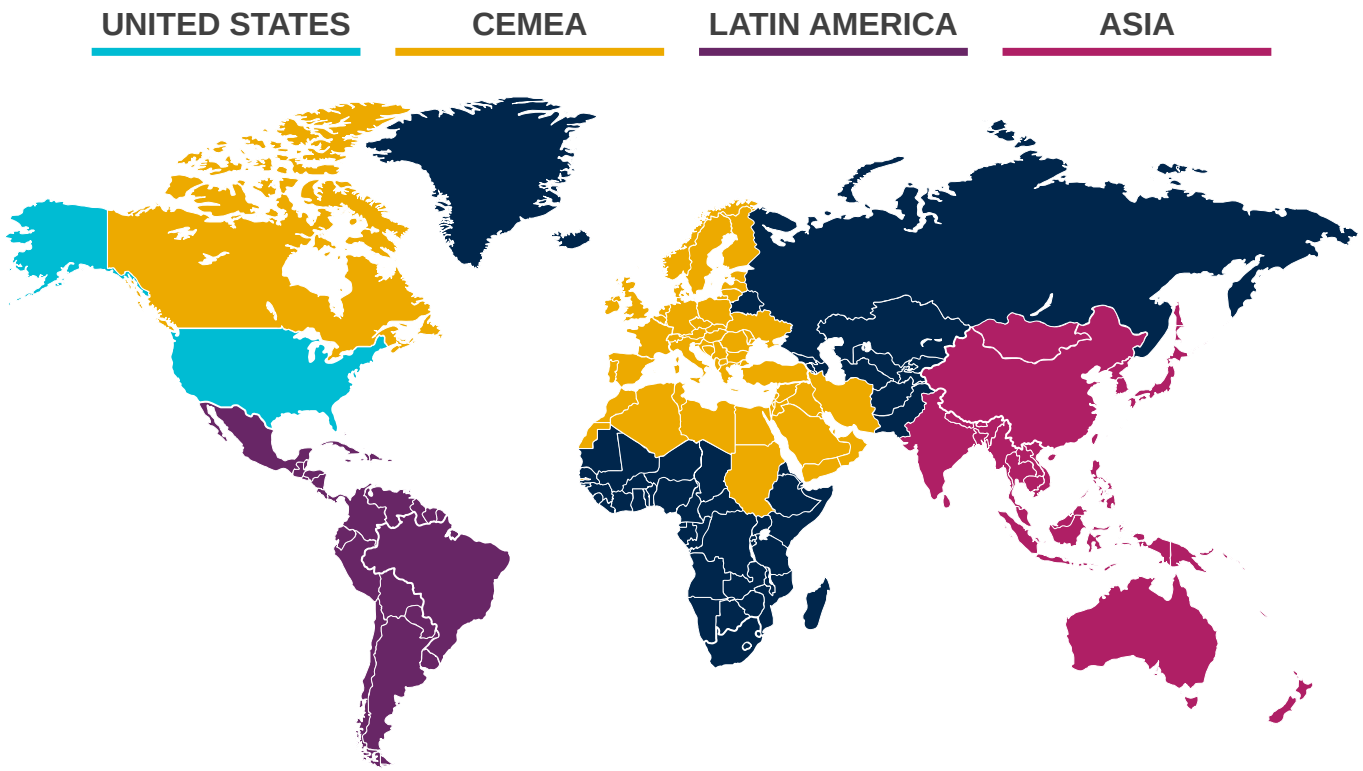
7 Value-Based Agreements (VBAs) finalized

>80% covered U.S. lives with confirmed access to OXLUMO, if prescribed

OXLUMO Global Commercialization

Ensuring OXLUMO Availability Around the World

- Progress with global OXLUMO availability
  - Recent approval in Brazil
  - Launch underway in Germany
  - ATU supply in France
  - Broad utilization across age groups and EGFR categories



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

CEMEA: Canada, Europe, Middle East, North Africa

Akshay Vaishnaw, M.D., Ph.D.

President of R&D

Alnylam Clinical Pipeline

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

ClinicalTrials.gov Identifier: NCT03997383

APOLLO-B

Enrollment **complete**

Topline results expected **mid-2022**

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

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

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
  - With or without TTR stabilizer use
- Confirmed cardiomyopathy and medical history of symptomatic heart failure
- NYHA ≤ III; minimum walk and NT-proBNP limits at baseline

ClinicalTrials.gov Identifier: NCT04153149

1:1 RANDOMIZATION

Vutrisiran
SC q3M
25 mg

or

Placebo
SC q3M

Primary Endpoint

- Composite outcome of all-cause mortality and recurrent CV events (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 and HF events
- All-cause mortality
- Recurrent CV events
- NT-proBNP

HELIOS·B

HELIOS-B Phase 3 study planned enrollment completion in **August 2021**

Study includes optional interim analysis

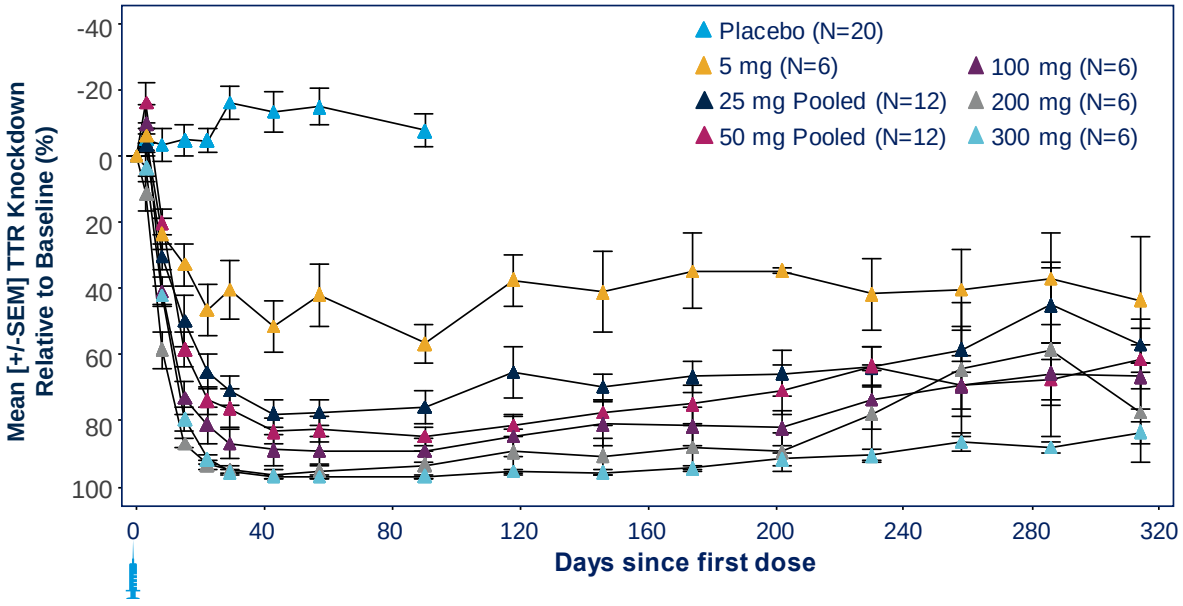
Potential Opportunity for Biannual Vutrisiran Dosing Regimen

q6M Regimen in Development to Strengthen Leadership Prospects for Future

- Plan to generate TTR reduction and safety data in patients receiving 50mg q6M to support potential sNDA to add biannual dosing regimen aligned with FDA input
- q6M dosing study initiated **early 2021**

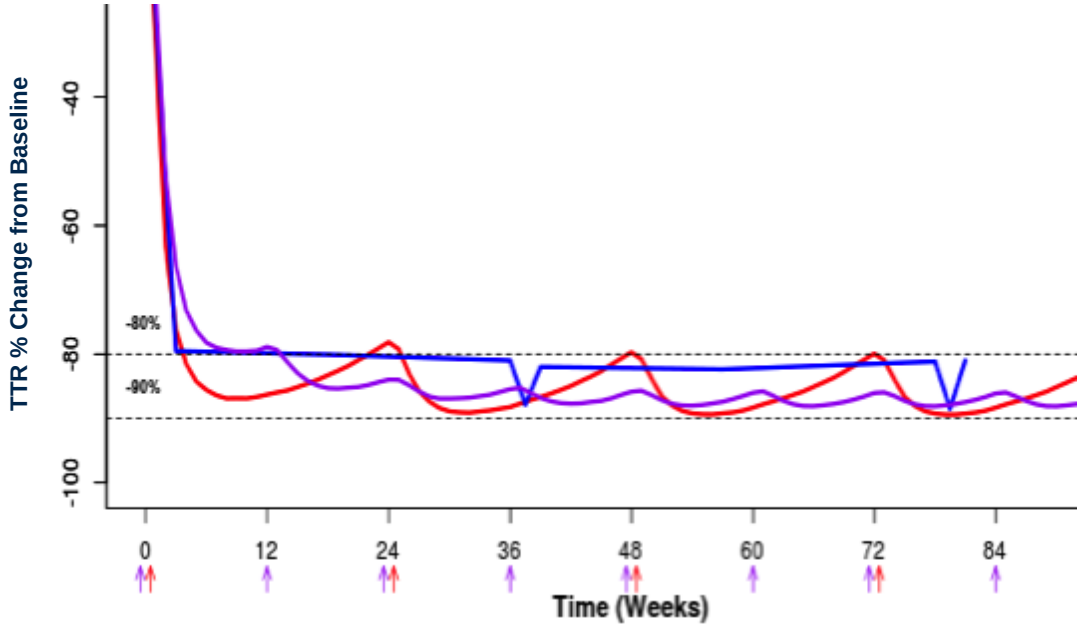
Phase 1 Study – Healthy Volunteers

- Mean max TTR reduction of >80% after single dose of either 25mg or 50mg†



Pharmacodynamic Modeling

- After repeat dosing, ~90% peak TTR reduction predicted with both 25mg q3M and 50mg q6M vutrisiran regimens



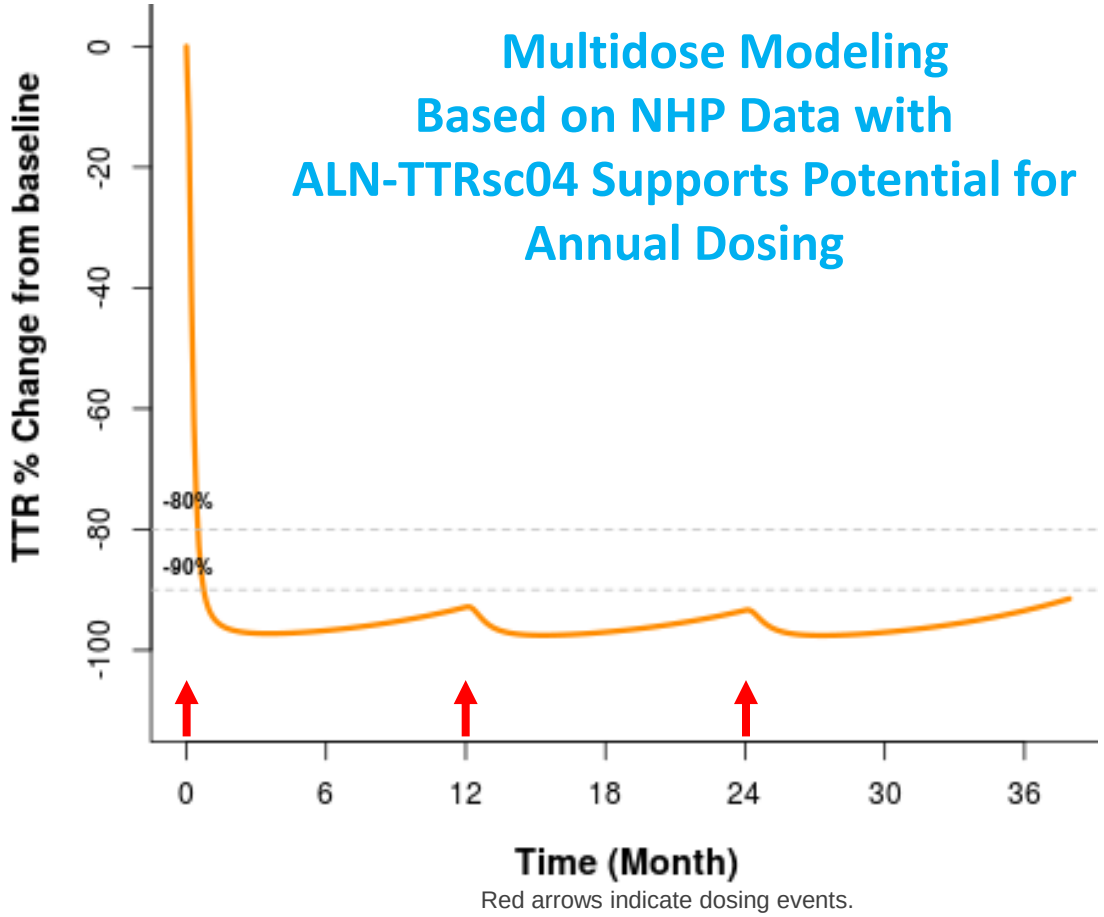
† Taubel J, et al. Phase 1 Study of ALN-TTRsc02, a Subcutaneously Administered Investigational RNAi Therapeutic for the Treatment of Transthyretin-Mediated Amyloidosis. ISA 2018: XVIIth International Symposium of Amyloidosis; Kumamoto, Japan; March 2018 (poster)

q3M – dosing every three months
q6M – dosing every six months

IKARIA™ Platform and Preclinical ALN-TTRsc04

- Continued innovation in RNAi therapeutics
- Extended duration platform with potential for once annual dosing – long-acting and reversible
- Potential for highly potent knockdown (>90%) of target
- Lead IKARIA program: preclinical development with ALN-TTRsc04
- Data to be presented at scientific meeting in mid-'21

Multidose Modeling Based on NHP Data with ALN-TTRsc04 Supports Potential for Annual Dosing



Modeling suggests potential rapid and sustained TTR reduction >90% with annual dosing

ILLUMINATE-C Phase 3 Results

Single Arm, Open-Label Study in PH1 Patients with Impaired Renal Function, Including Advanced Disease (N=21)

Lumasiran achieved substantial reductions in plasma oxalate relative to baseline

- Both in dialysis-independent and -dependent patients

Lumasiran demonstrated an encouraging safety and tolerability profile

- No deaths or drug related SAEs
- Most common AEs were ISRs in 5 patients (23.8%), all of which were mild
- Two discontinuations due to AEs, both occurring during extension period and neither related to study drug

Supplemental regulatory filings expected to be submitted to FDA and EMA in late 2021

ILLUMINATE•C

Driving Innovation Through Late-Stage Partnered Programs

Leqvio® (inclisiran)

NOVARTIS

Blackstone

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]

Approved in EU
NDA resubmitted to FDA to address CRL
PDUFA date January 1, 2022

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 frequent dosing, SC)[2]
<10%	Emicizumab patients on monthly dosing[3]
~90%	Emicizumab patients experienced acute bleeds[2]

Data from Phase 3 ATLAS program expected as early as beginning of 2022, with potential regulatory submission later in 2022

[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

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

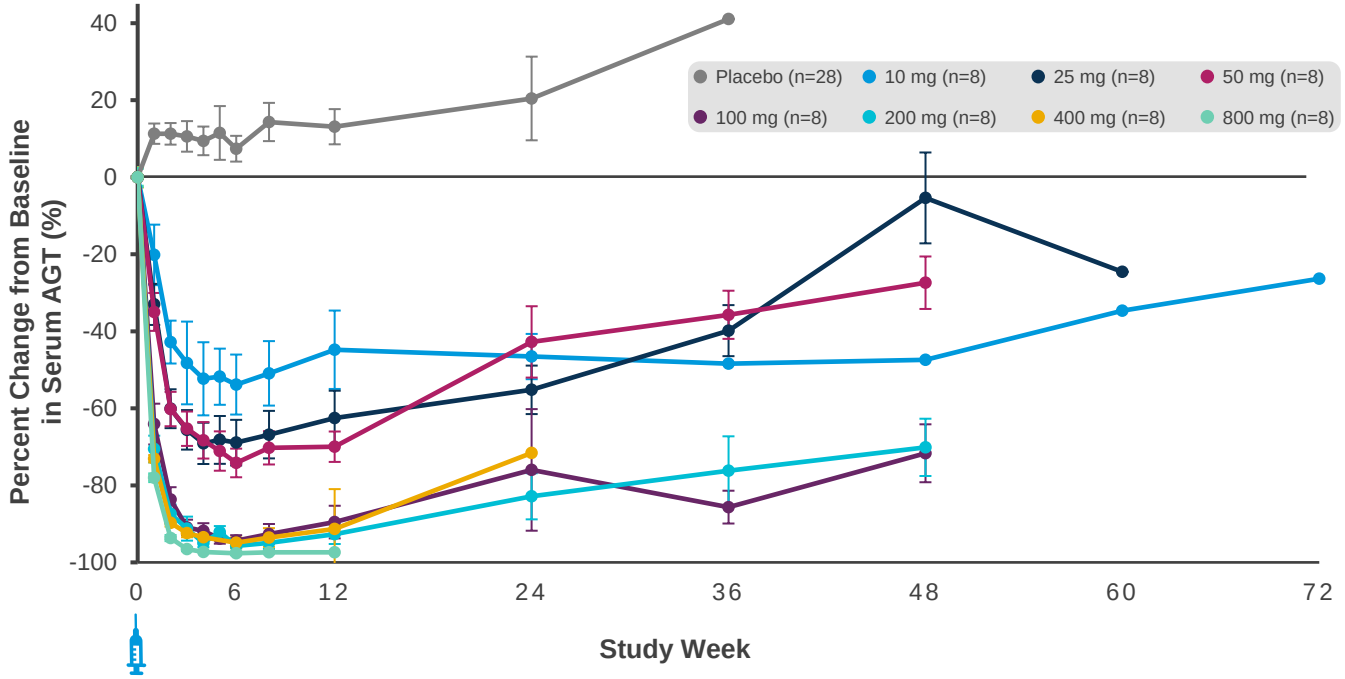
[1] ONPATTRO is approved in the U.S. and Canada for the treatment of the PN of hATTR amyloidosis in adults, and in the EU, Japan and other countries for the treatment of hATTR amyloidosis in adults with stage 1 or 2 PN; [2] Patisiran has not been approved by the FDA, EMA, or any other regulatory agency 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.

Zilebesiran (ALN-AGT) Interim Phase 1 Results

Results for Investigational Therapy Presented at ESH-ISH Meeting

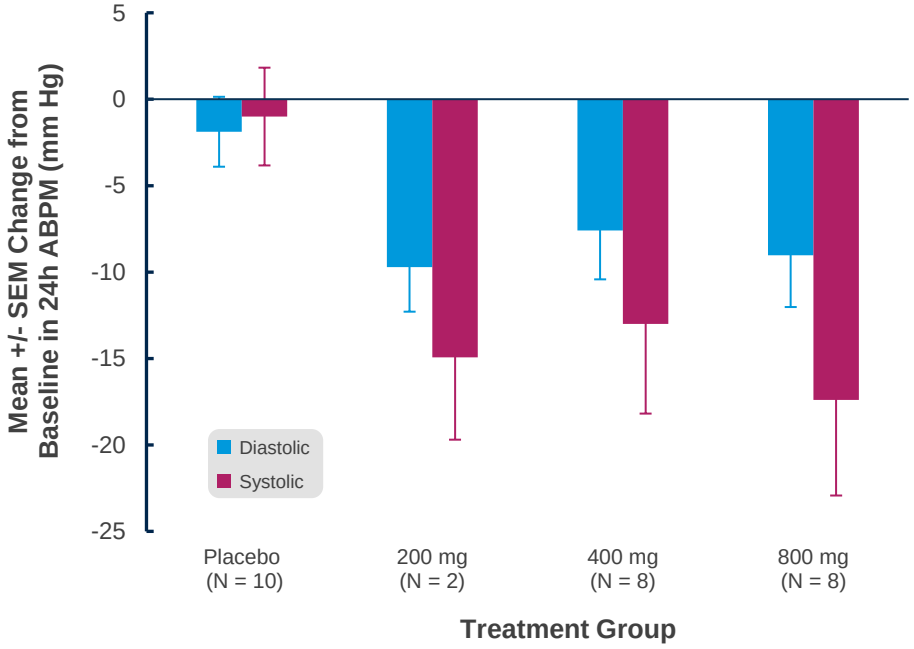
Durable Reduction of Serum AGT >90% Sustained for 12 Weeks After Single Doses of ALN-AGT ≥100 mg

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

Zilebesiran Phase 2 Clinical Development Plan

KARDIA$_1$

Monotherapy Phase 2 Study (N ~375)

- 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**

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

Over 25 Preclinical Programs in Four Tissues Feeding Sustainable Innovation

Alnylam
- ALN-XDH
- ALN-KHK
- ALN-LEC
- ALN-CC3
- ALN-F12
- Many others

Alnylam/Regeneron
- ALN-PNP
- ALN-REGN-L2
- ALN-REGN-L4
- ALN-REGN-L5

Alnylam/Regeneron
- ALN-APP
- ALN-HTT
- ALN-REGN-C3
- ALN-REGN-C4
- ALN-REGN-C5
- ALN-REGN-C6
- ALN-REGN-C7
- ALN-REGN-C8
- ALN-REGN-C9

Alnylam
- ALN-TTRoc

Alnylam/Regeneron
- ALN-REGN-E1
- ALN-REGN-E2
- ALN-REGN-E3
- ALN-REGN-E4

Alnylam/Vir
- ALN-COV
  - *discontinued*
- ALN-VIR2 (ACE2)
- ALN-VIR3 (TMPRSS2)

2-4 *INDs planned per year from organic product engine (4+ planned by end-'25)*

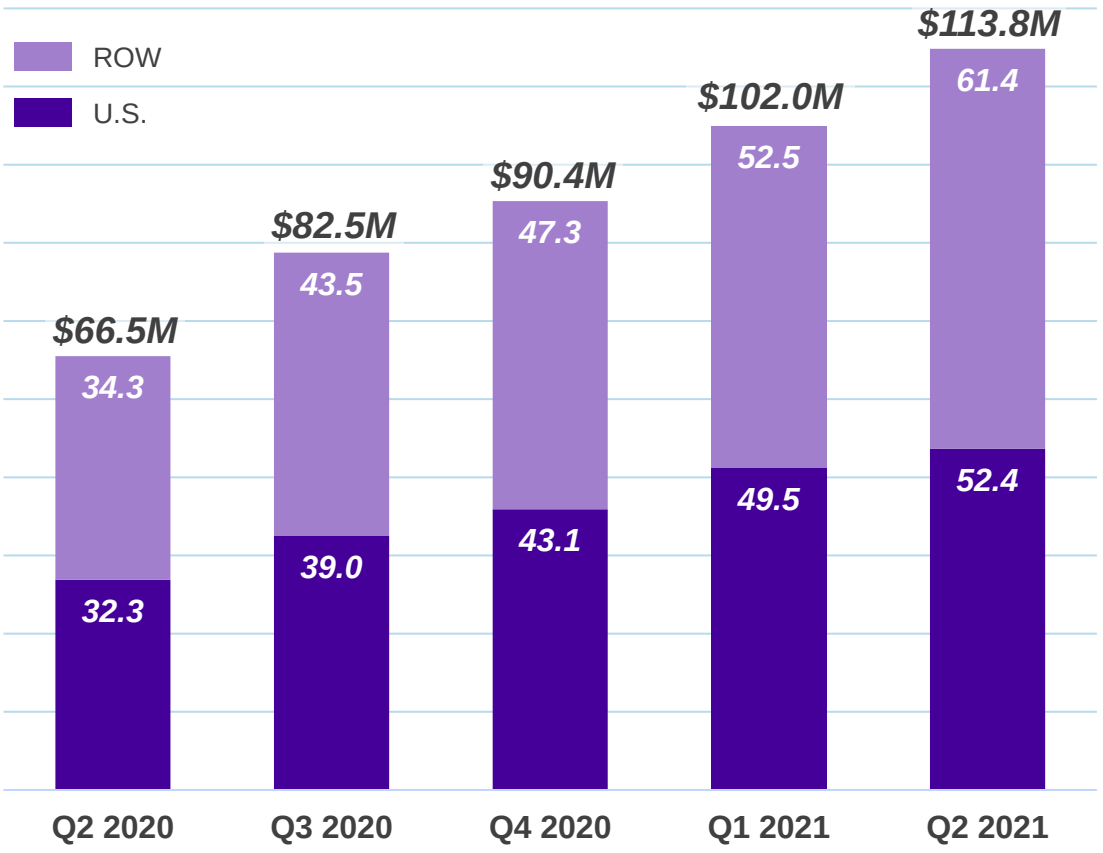
Jeff Poulton

Chief Financial Officer

Financial Summary and Guidance

Global ONPATTRO Q2 2021 Performance

Revenue ($M)



Q2 Highlights

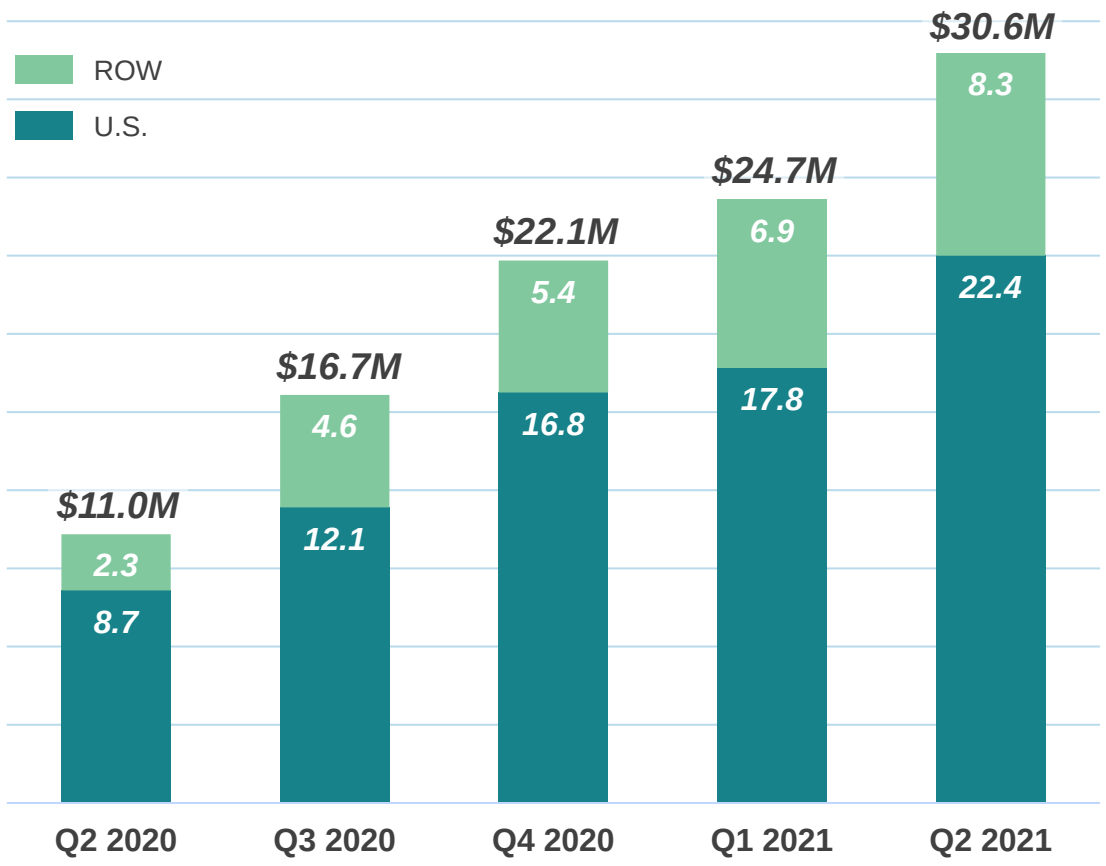
	YoY % Growth	QoQ % Growth
U.S.	62%	6%
ROW	79%	17%
Global	71%	12%

- Steady and continuous patient growth continues across key markets (>1,725 commercial patients at end of Q2)
- 4th consecutive quarter of double-digit quarter on quarter global growth
- U.S. demand growth +12% due to an increase in patients on therapy and >90% patient treatment compliance
- U.S. demand growth offset by higher gross to net deductions and less inventory stocking than Q1

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

Global GIVLAARI Q2 2021 Performance

Revenue ($M)



Q2 Highlights

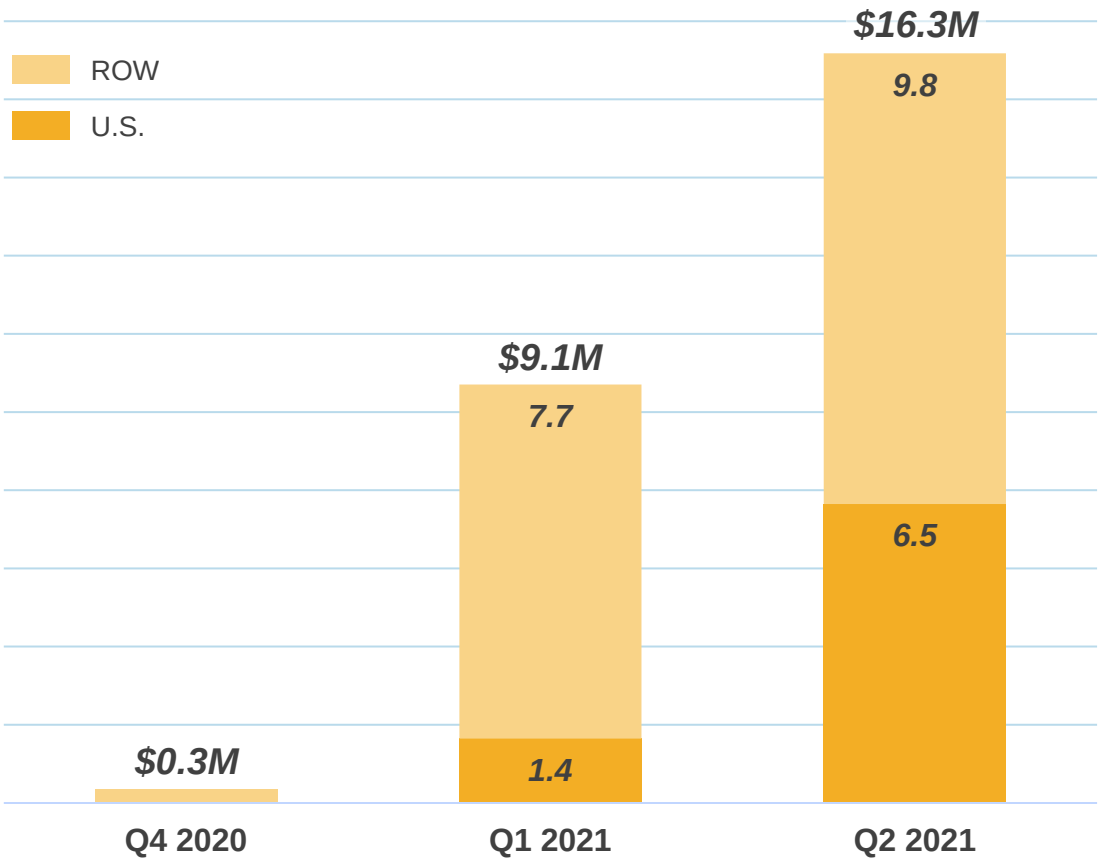
	YoY % Growth	QoQ % Growth
U.S.	158%	26%
ROW	254%	20%
Global	179%	24%

- >270 global patients on therapy since launch
- U.S. growth primarily driven by an increase in patients on therapy and patient treatment compliance >90%
- Received JNDA approval in Japan; anticipate first commercial sales in Q3

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

Global OXLUMO Q2 2021 Performance

Revenue ($M)



Q2 Highlights

	QoQ % Growth
U.S.	363%
ROW	27%
Global	79%

- ~100 patients on commercial treatment in U.S. and Europe since launch
- Continued strong sales in Europe primarily driven by launch in Germany and ATU sales in France
- Encouraging initial broad utilization across age groups and EGFR categories

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

Q2 2021 Financial Summary

Financial Results ($ millions)	Q2 2021	Q2 2020	YoY % Change
Net Product Revenues	$160.8	$77.5	107%
Net Revenues from Collaborations	$59.4	$26.4	125%
Royalty Revenues	$0.3	-	-
Total Revenues	$220.6	$104.0	112%
Cost of Goods Sold and Cost of Collaborations and Royalties	$38.8	$19.9	94%
Gross Margin	$181.8	$84.0	116%
GM as % of Total Revenues[1]	*82.4%*	*80.8%*	-
Non-GAAP R&D Expenses[2]	$169.5	$139.2	22%
Non-GAAP SG&A Expenses[2]	$126.3	$109.6	15%
Non-GAAP Operating Loss [2]	($114.1)	($164.8)	(31%)

Financial Results ($ millions)	Jun 30, 2021	Dec 31, 2020
Cash & Investments[3]	$1,900.1	$1,874.4

[1] GM as a % of Total Net Product Revenues for Q2 2021 is 81.2% and Q2 2020 is 76.4% (Q2 2021 and 2020 exclude $8.5M and $1.7M Cost of Collaborations and Royalties associated with Net Revenues from Collaborations, respectively).
[2] Non-GAAP R&D expenses, non-GAAP SG&A expenses, and non-GAAP operating loss primarily excludes costs related to stock-based compensation expense.
[3] Cash, cash equivalents and marketable securities
See Appendix for a reconciliation between GAAP and non-GAAP measures

Updated Full Year 2021 Guidance

	Prior FY 2021 Guidance	Updated FY 2021 Guidance[1]
Net Product Revenue (ONPATTRO, GIVLAARI, OXLUMO)	$610M - $660M	$640M - $665M
Net Revenue from Collaborations & Royalties	$150M - $200M	No Change
Non-GAAP Combined R&D and SG&A Expenses[2]	$1,175M - $1,275M	No Change

[1] As of August 3, 2021

[2] 2021 Non-GAAP Combined R&D and SG&A Expenses guidance excludes stock-based compensation expense estimated at $160M - $180M

Yvonne Greenstreet, MBChB, MBA

President and Chief Operating Officer

2021 Goals Update

PeptiDream Collaboration

Strategic collaboration to discover and develop peptide-siRNA conjugates for targeted delivery of RNAi therapeutics to broader range of extrahepatic tissues

- Combines PeptiDream's peptide discovery platform to identify high affinity peptide ligands with Alnylam's expertise in siRNA-conjugate based delivery and in developing and commercializing RNAi therapeutics

- Potential to yield multiple treatment opportunities by targeting disease causing mRNA transcripts in wide variety of tissue types

PeptiDream

Alnylam 2021 Goals

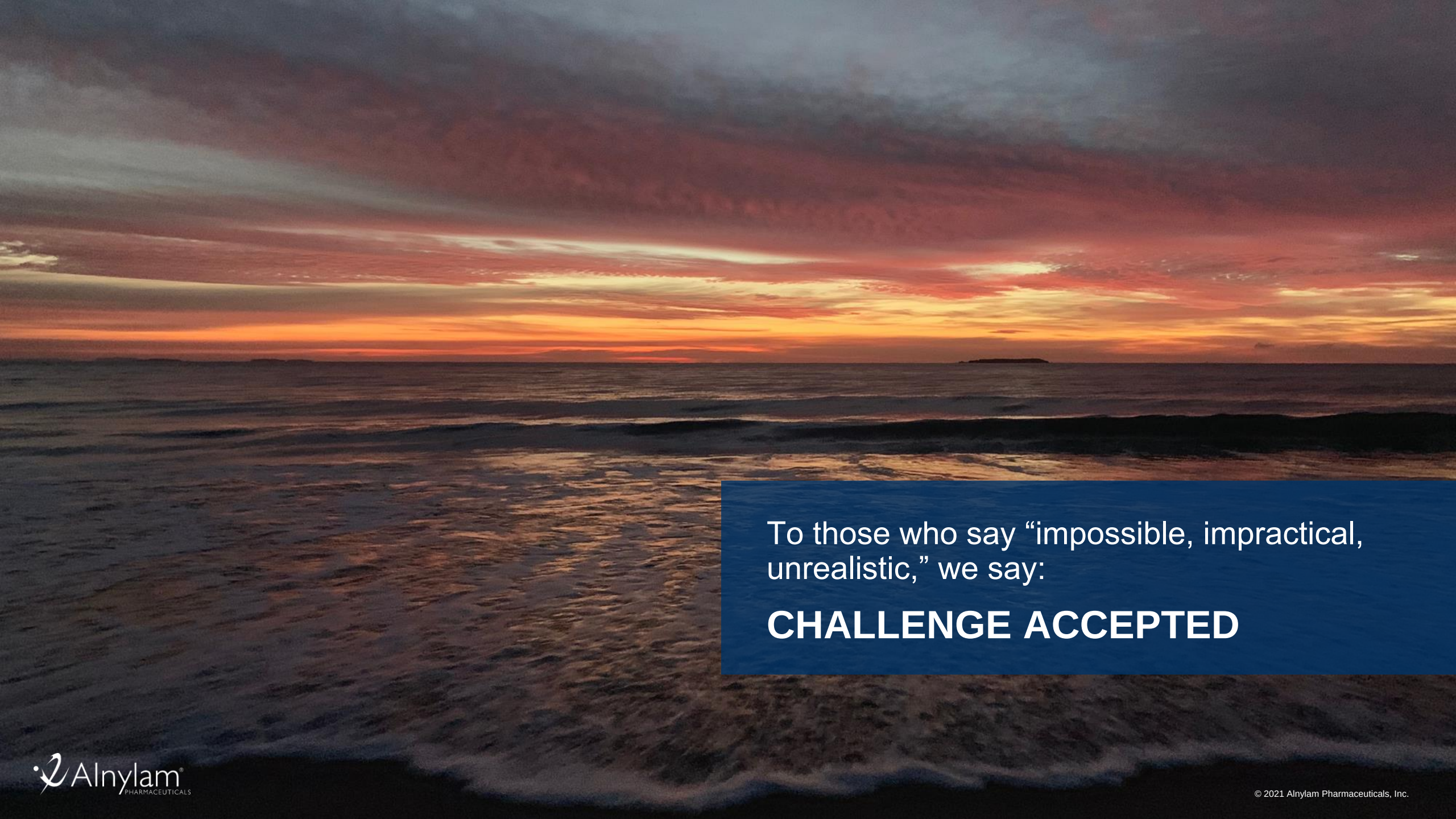
		Early	Mid	Late
onpattro® (patisiran) lipid complex injection 10 mg/5 mL (hATTR/ATTR Amyloidosis)	Global Commercial Execution	✓	●	●
	Complete APOLLO-B Phase 3 Enrollment	✓		
GIVLAARI® (givosiran) injection for subcutaneous use 189 mg/mL (Acute Hepatic Porphyria)	Global Commercial Execution	✓	●	●
	Japan Approval		✓	
OXLUMO® (lumasiran) for injection 94.5 mg/0.5 mL (Primary Hyperoxaluria Type 1)	Global Commercial Execution	✓	●	●
	Brazil Approval	✓		
	ILLUMINATE-C Phase 3 Topline		✓	
VUTRISIRAN* (hATTR/ATTR Amyloidosis)	HELIOS-A Phase 3 Topline – 9 Month Endpoints	✓		
	File NDA for hATTR-PN	✓		
	Initiate q6M Dose Regimen Study	✓		
	HELIOS-A Phase 3 Topline – 18 Month Endpoints (incl. exploratory cardiac)			●
	Complete HELIOS-B Phase 3 Enrollment			●
ZILEBESIRAN (ALN-AGT)* (Uncontrolled Hypertension)	Initiate KARDIA Phase 2 Program		✓	
ADDITIONAL CLINICAL PROGRAMS	Continue to advance early/mid-stage pipeline; File 2-4 new INDs; Present clinical data	✓	✓	●
PARTNERED PROGRAMS				
Leqvio® (inclisiran) (Hypercholesterolemia)	FDA Approval (1/1/22 PDUFA)			●
	Support, as Needed, Novartis on Global Commercial Execution	✓	●	●
	Support, as Needed, Novartis on ORION-4 CVOT Phase 3 Enrollment	✓	●	●
FITUSIRAN* (Hemophilia)	Support, as Needed, Sanofi on ATLAS Phase 3 Studies	✓	●	●

* Not approved for any indication and conclusions regarding the safety or effectiveness of these drugs have not been established

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

Q2 2021 Financial Results

Q&A Session



Alnylam PHARMACEUTICALS

Q2 2021 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

Reconciliation of Selected GAAP Measures to Non-GAAP Measures
(In thousands)

	Three Months Ended		Six Months Ended	
	June 30, 2021	June 30, 2020	June 30, 2021	June 30, 2020
Reconciliation of GAAP to Non-GAAP research and development:				
GAAP Research and development	$ 182,635	$ 154,996	368,534	324,567
Less: Stock-based compensation expenses	(13,086)	(15,790)	(37,461)	(31,839)
Non-GAAP Research and development	$ 169,549	$ 139,206	331,073	292,728
Reconciliation of GAAP to Non-GAAP selling, general and administrative:				
GAAP Selling, general and administrative	$ 145,323	$ 127,896	292,182	254,657
Less: Stock-based compensation expenses	(18,992)	(17,965)	(50,307)	(36,494)
Less: Costs associated with the strategic financing collaboration	—	(320)	—	(320)
Non-GAAP Selling, general and administrative	$ 126,331	$ 109,611	241,875	217,843
Reconciliation of GAAP to Non-GAAP operating loss:				
GAAP operating loss	$ (146,160)	$ (198,859)	(332,414)	(409,017)
Add: Stock-based compensation expenses	32,078	33,755	87,768	68,333
Add: Costs associated with the strategic financing collaboration	—	320	—	320
Non-GAAP operating loss	$ (114,082)	$ (164,784)	(244,646)	(340,364)

Please note that the figures presented may not sum exactly due to rounding