Glaucienne
Living with AHP (Brazil)

Fourth Quarter and Full Year 2020 Financial Results

February 11, 2021

Alnylam® PHARMACEUTICALS

Agenda

Welcome

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

Overview

- John Maraganore, Ph.D.
  Chief Executive Officer

Commercial/Medical Affairs 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 ability to achieve our “Alnylam P5x25” strategy, the potential expansion of the ATTR amyloidosis franchise, plans for additional global regulatory filings and the continuing product launches of our approved products, the achievement of additional pipeline and regulatory milestones, expectations regarding FDA review of inclisiran, conditions at the third party manufacturer where inclisiran is manufactured and the expected timing of resubmission of the inclisiran NDA by Novartis, 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 and the expected range of net product revenues and net revenues from collaborations and royalties 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 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, 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 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, Regeneron and Vir; the outcome of litigation; the risk of government investigations; and unexpected expenditures; as well as those risks more fully discussed in the “Risk Factors” filed with our most recent Annual Report on Form 10-K 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, unrealized losses (gains) on marketable equity securities, costs associated with our strategic financing collaboration, loss/net loss on contractual settlement, change in estimate of contingent liabilities and a gain on the change in fair value of a liability obligation. 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, loss/net loss on contractual settlement, change in estimate of contingent liabilities and a gain on the change in fair value of a liability obligation because we believe these items are non-recurring transactions outside the ordinary course of our business. We have excluded the impact of the unrealized losses (gains) on marketable equity securities because we do not believe these adjustments accurately reflect the performance of our ongoing operations for the period in which such gains or losses are reported as their sole purpose is to adjust amounts on the balance sheet.

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

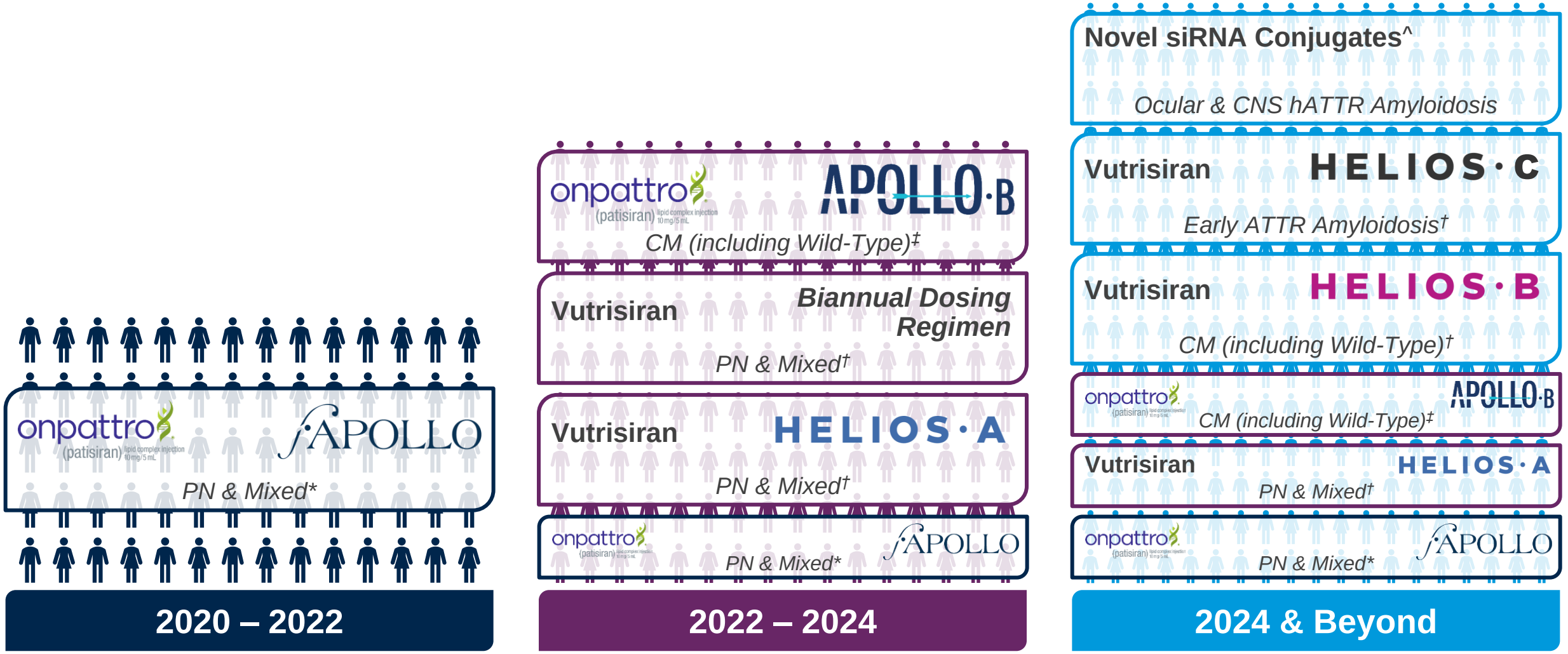
Pipeline: Over 20 clinical programs, with 10+ in late stages and 4+ INDs per year

Performance: ≥40% revenue CAGR through YE 2025

Profitability: Achieve sustainable non-GAAP profitability within period

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 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
‡ 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

Tolga Tanguler

Chief Commercial Officer

Commercial/Med Affairs Highlights

ONPATTRO® Launch Update: Year End 2020

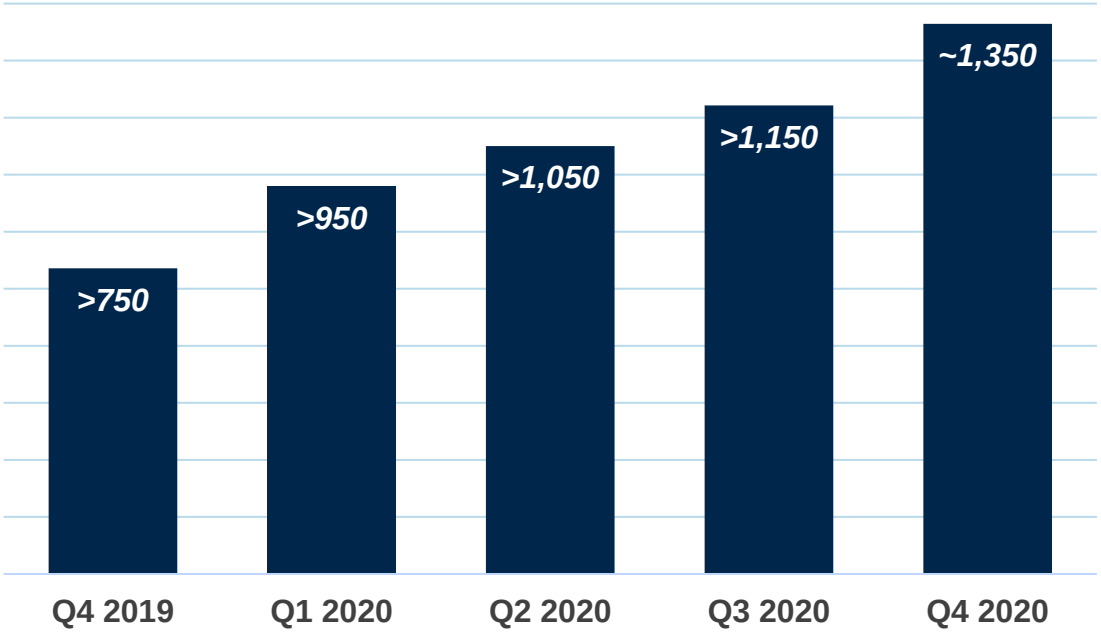
Strong Year 2 Performance with Continued Growth

$306M

ONPATTRO Global 2020 Net Product Revenues

~1,350

Patients Worldwide on Commercial ONPATTRO at YE 2020



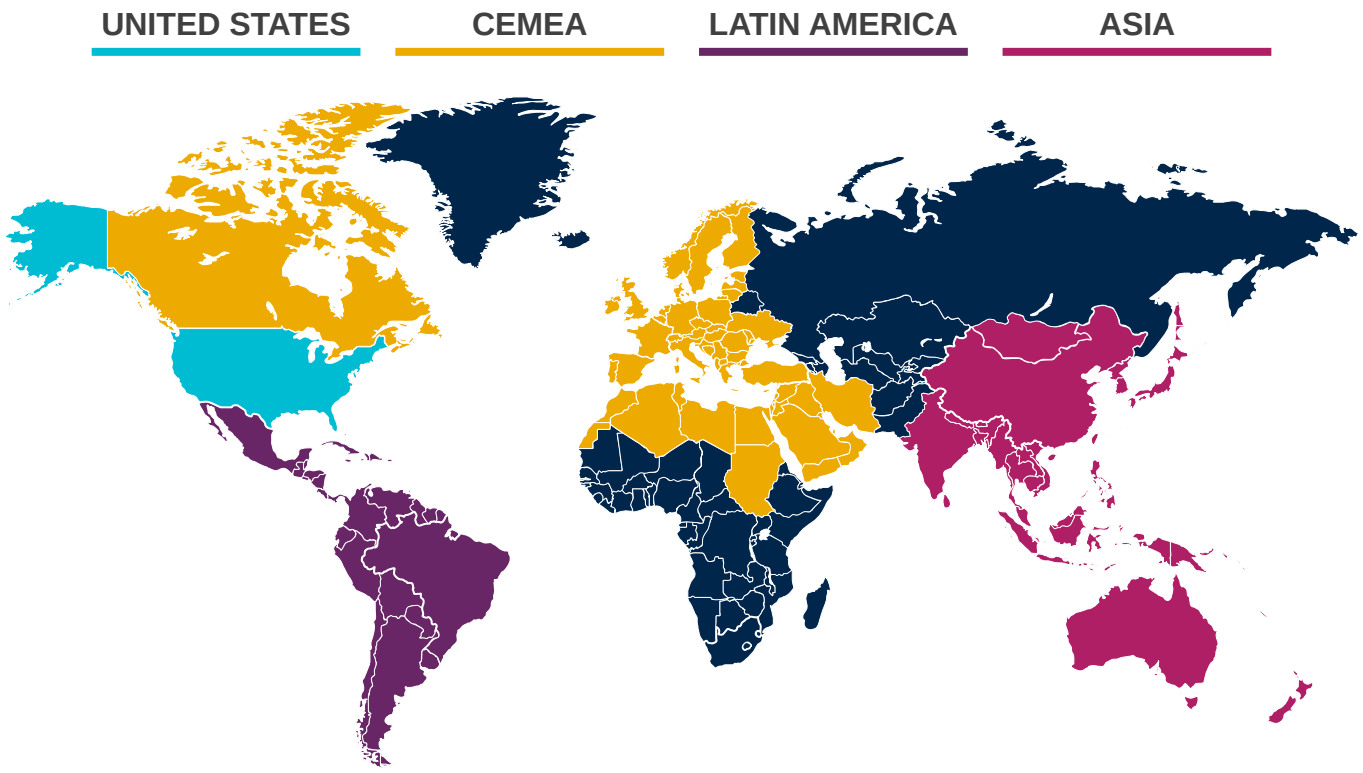
Q4 U.S. Highlights

- Continued strength in demand and treatment compliance
- Steady growth of ONPATTRO for polyneuropathy in mixed phenotype hATTR patients with concomitant TTR stabilizer therapy

ONPATTRO Global Commercialization

Increasing Access and Value Recognition

- Significant progress with global ONPATTRO availability
  - Recent launches in Denmark, Sweden, and Bulgaria
  - Achieved regulatory approval in Taiwan
  - Over 20 countries outside U.S. now selling ONPATTRO through direct reimbursement, named patient sales, or reimbursed expanded access
  - Uptake observed from both first-line treatment in hATTR patients with PN and switching from other products, including stabilizers

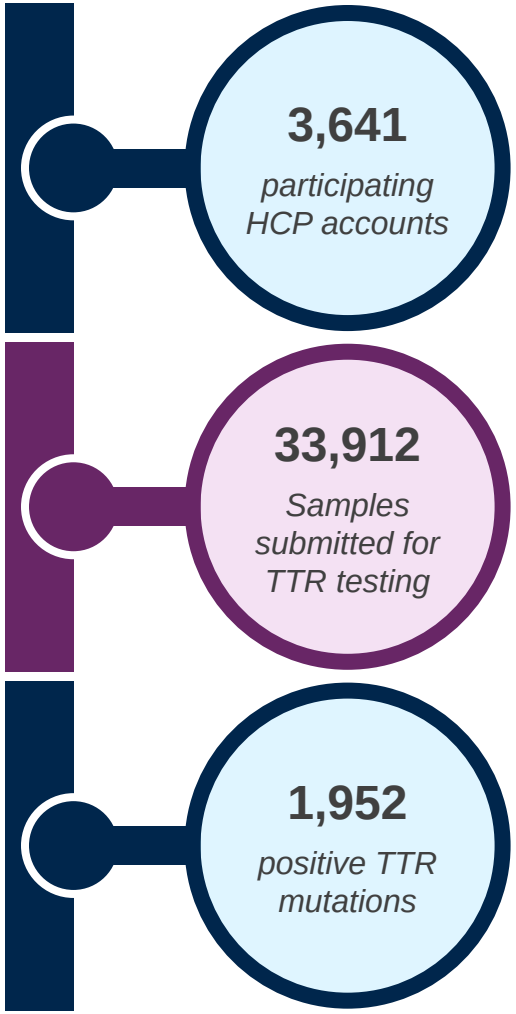


onpattro® (patisiran) lipid complex injection 10 mg/5 mL

CEMEA: Canada, Europe, Middle East, North Africa

Alnylam Act® – hATTR Amyloidosis

Third-Party Genetic Testing and Counseling Program Sponsored by Alnylam



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

Tests and services are performed by independent third parties

Available in U.S., Canada and Brazil (genetic counseling service available in U.S.)

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

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

Data as of January 2021

At no time does Alnylam receive patient-identifiable information. Alnylam receives contact information for healthcare professionals who use this program

GIVLAARI® Launch Update: Year End 2020

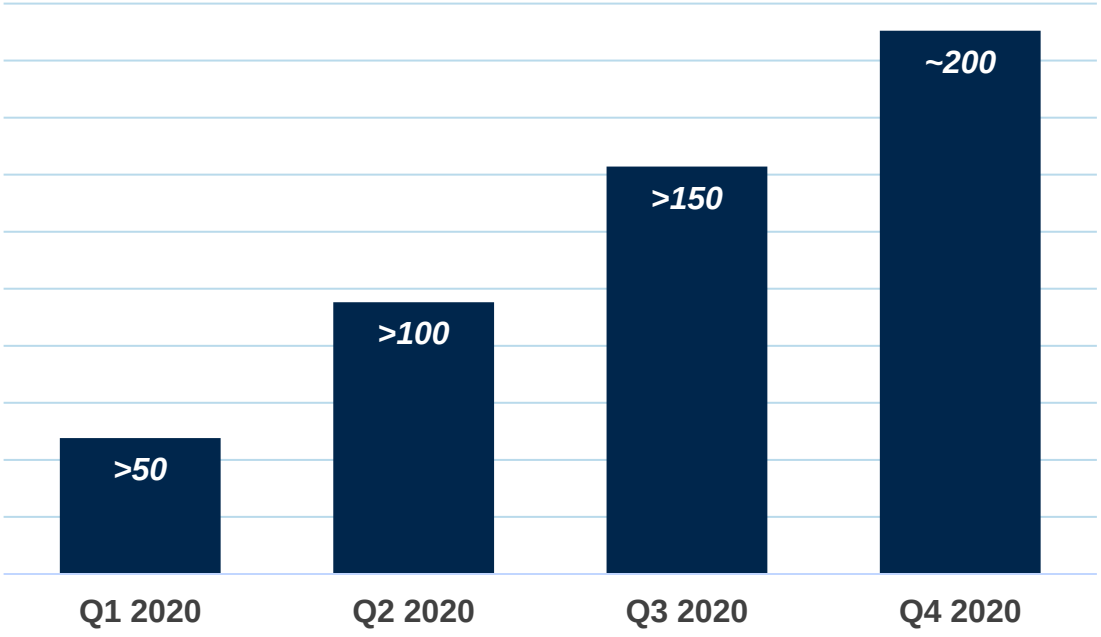
Strong First Year Performance

$55M

GIVLAARI Global 2020
Net Product Revenues

~200

Patients on Commercial
GIVLAARI at YE 2020



U.S. Demand and Access

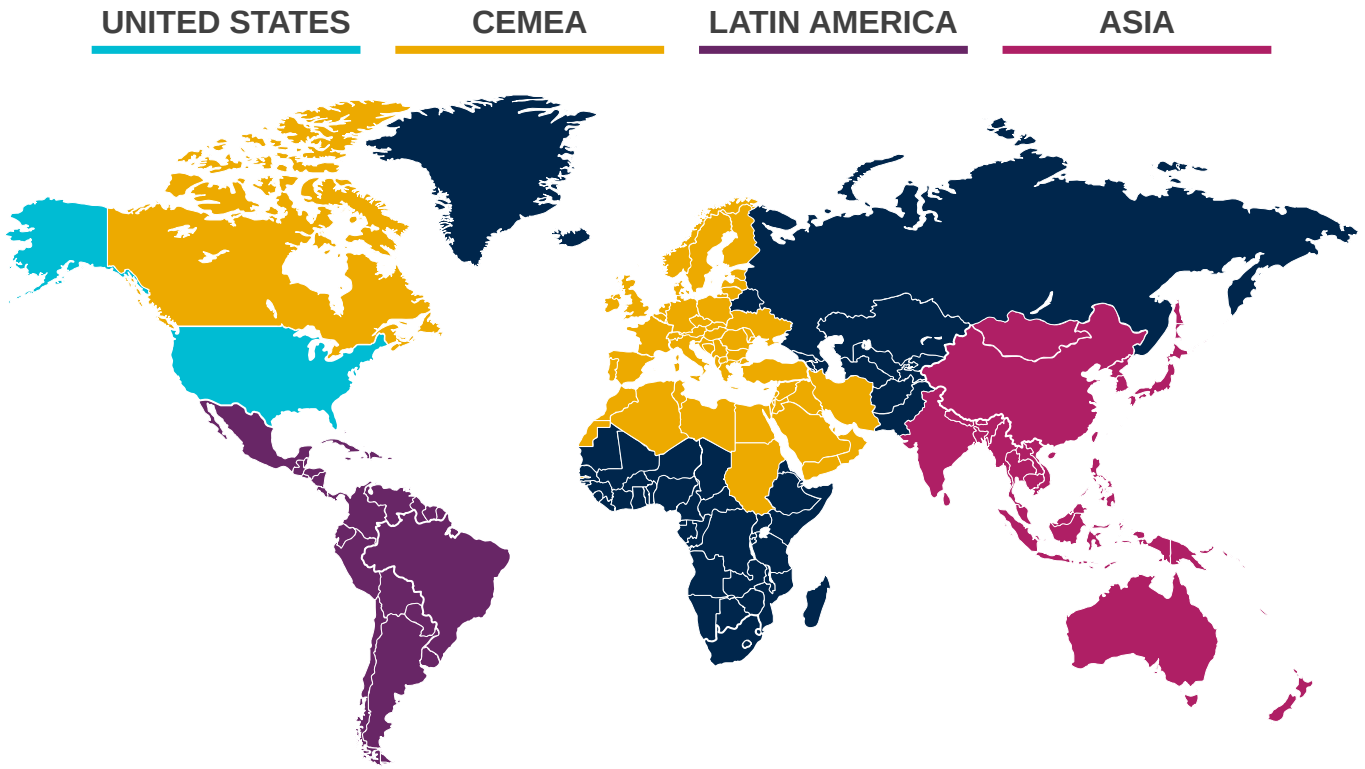
>10 Value-Based Agreements (VBAs) finalized

94% U.S. lives with confirmed access to GIVLAARI, if prescribed

GIVLAARI Global Commercialization

Ensuring GIVLAARI Availability Around the World

- Successful ongoing launch in Germany
- ATU supply in France
- Strong start for market access in CEMEA
- Achieved market access in Italy
- Named patient sales in other countries
- Recent approval in Canada
- Japan JNDA under review



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

CEMEA: Canada, Europe, Middle East, North Africa

The third RNAi therapeutic is

NOW APPROVED IN THE EU & U.S.

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

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

APOLLO-B

Study initiated
September 2019

Enrollment completion expected
early 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

HELIOS-A Positive Topline Results

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

Positive results for all Month 9 primary and secondary efficacy endpoints, relative to APOLLO placebo

Endpoint	P-value
Neuropathy Impairment (mNIS+7) Primary	3.54×10^{-12}
Quality of Life (Norfolk QoL-DN) Key Secondary	5.43×10^{-9}
Gait Speed (10-MWT) Secondary	3.10×10^{-5}

Evidence of reversal of polyneuropathy manifestations

- Majority of patients showed improvement in neuropathy impairment and QOL, relative to baseline

Positive exploratory cardiac endpoint result

- Improvement in NT-proBNP biomarker, relative to placebo ($p<0.0001$*); additional cardiac data at Month 18 in Late 2021

Encouraging safety and tolerability profile

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

* Nominal p-value

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

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
Now Enrolling

Study includes optional interim analysis

ILLUMINATE Phase 3 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

Full results presented
June 2020

ILLUMINATE•B

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

Full results presented
October 2020

ILLUMINATE•C

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

Enrollment completed;
Topline results expected
in **mid-2021**

Phase 2 study in recurrent renal stones expected to initiate in 2021

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

CRL in U.S. related to inspection; no efficacy, safety concerns raised; Novartis response to be submitted Q2-Q3 2021

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]

Two of three Phase 3 studies fully enrolled

Dosing resumed in ATLAS studies[4]

Sanofi to evaluate tailored dosing regimen[5]

[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; [4] Previous reports of thromboembolic events were associated with high levels of antithrombin reduction to < 10% of normal; [5] Sanofi to evaluate once-every-2 monthly 50 mg dosing regimen for fitusiran that can be titrated up in frequency to once-monthly and in dose to 80 mg depending on antithrombin levels achieved.

RNAi Therapeutics Profile Supports Expansion to Prevalent Diseases

- Durability
- Clamped pharmacology
- Established safety profile
- Improved access

RARE

ONPATTRO-PN
GIVLAARI
OXLUMO
Vutrisiran-PN
Fitusiran
ALN-AAT02
ALN-APP
ALN-HTT

SPECIALTY

ONPATTRO-CM
Vutrisiran-CM
Cemdisiran

PREVALENT

Leqvio® (inclisiran)
ALN-HBV02 (VIR-2218)
ALN-AGT
ALN-HSD
ALN-XDH
ALN-KHK

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
- ALN-VIR2 (ACE2)
- ALN-VIR3 (TMPRSS2)

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

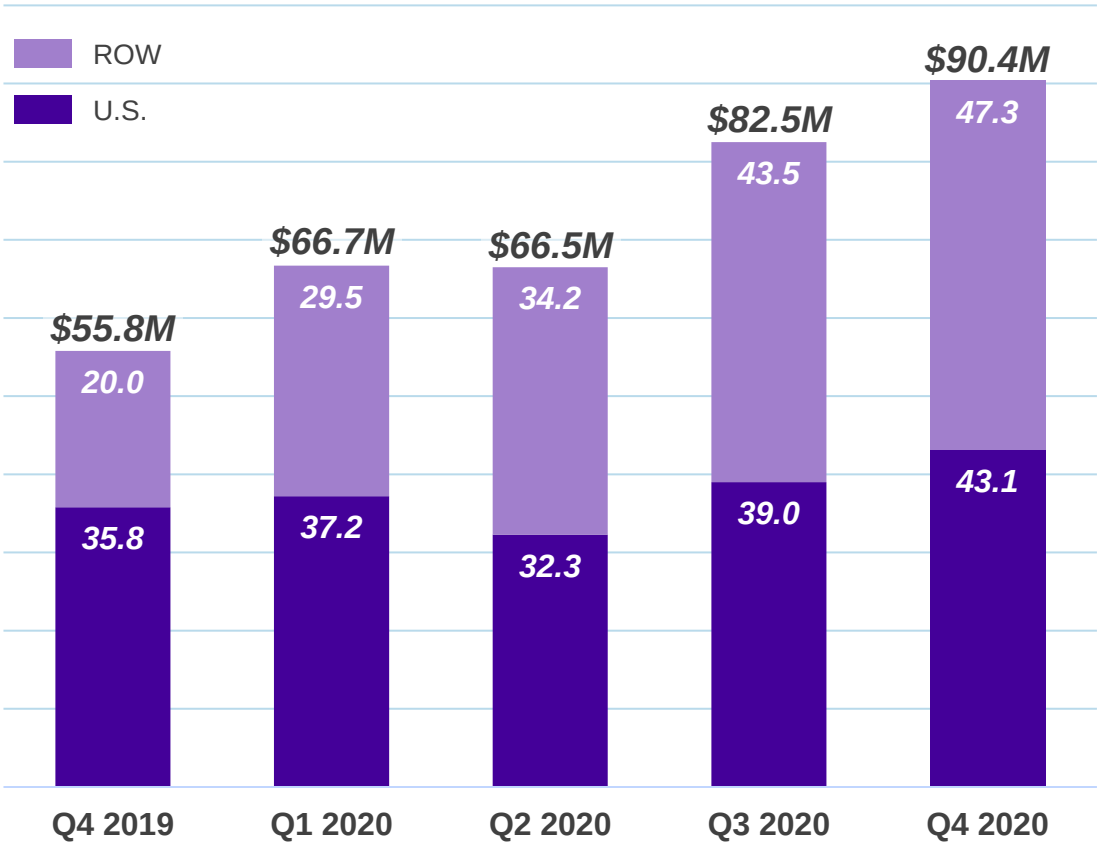
Jeff Poulton

Chief Financial Officer

Financial Summary and Guidance

Global ONPATTRO Q4 2020 Performance

Revenue ($M)



Q4 Highlights

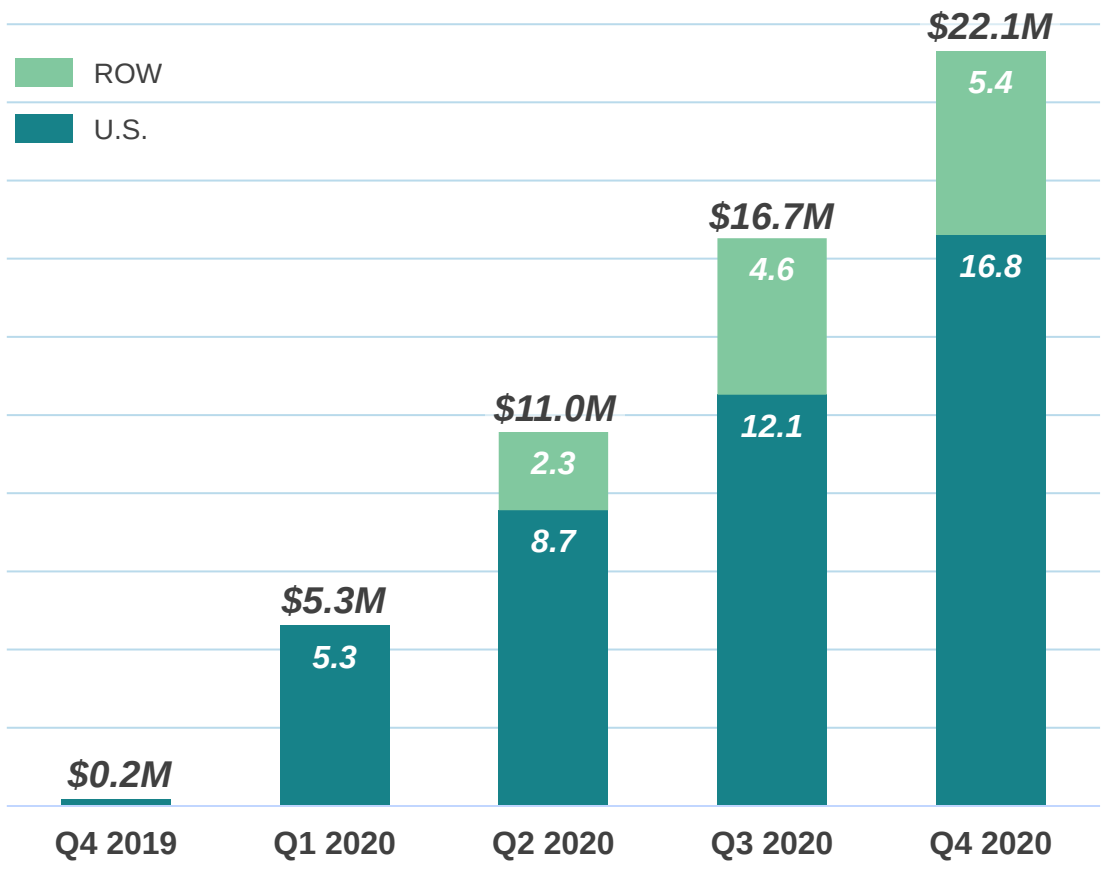
	YoY % Growth	QoQ % Growth
U.S.	20%	10%
ROW	136%	9%
Global	62%	10%

- Q4 represents 2nd consecutive quarter of double-digit growth in U.S. & highest quarterly sales since launch
- U.S. growth favorably impacted by increase in demand (*+13%*) with patient compliance rates remaining at pre-pandemic levels
- U.S. inventory levels decreased during Q4 ending year with ~1 week in channel
- ROW growth driven by increase in patients on therapy broadly across Europe and Japan and increase in inventory in Japan

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

Global GIVLAARI Q4 2020 Performance

Revenue ($M)



Q4 Highlights

	QoQ % Growth
U.S.	38%
ROW	18%
Global	33%

- ~200 global patients on therapy since launch
- Continued progress with VBAs in U.S. with >10 finalized, and confirmed access for 94% of covered lives
- Continued progress with market access efforts across the CEMEA region, with ongoing launch in Germany, ATU supply in France, and named patient sales in other countries

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

Q4 and Full Year 2020 Financial Summary

Financial Results ($ millions)	Q4 2020	Q4 2019	YoY % Change	FY 2020	FY 2019	YoY % Change
ONPATTRO Net Product Revenues	$90.4	$55.8	61.9%	$306.1	$166.4	84.0%
GIVLAARI Net Product Revenues	$22.1	$0.2	N/A	$55.1	$0.2	N/A
OXLUMO Net Product Revenues	$0.3	-	N/A	$0.3	-	N/A
Net Revenues from Collaborations	$50.7	$15.7	222.4%	$131.3	$53.2	146.8%
Total Revenues	$163.6	$71.7	128.2%	$492.9	$219.8	124.3%
Cost of Goods Sold	$23.0	$12.2	89.1%	$78.1	$25.1	211.4%
GM as % of Total Revenues[1]	*85.9%*	*83.0%*	-	*84.2%*	*88.6%*	-
Non-GAAP R&D Expenses[2]	$153.5	$166.5	(7.8%)	$594.4	$566.2	5.0%
Non-GAAP SG&A Expenses[2]	$136.7	$124.9	9.5%	$469.1	$393.1	19.3%
Non-GAAP Operating Loss[2]	($149.7)	($231.9)	-	($648.6)	($764.6)	-

Financial Results ($ millions)	Dec 31, 2020	Dec 31, 2019
Cash & Investments[3]	$1,874.4	$1,536.2

[1] GM as a % of Product Sales for Q4 2020 is 80.7%, Q4 2019 is 78.2%, FY 2020 is 79.5%, FY 2019 is 85.0% (Q4 2020 excludes $1.2M and FY 2020 excludes $3.9M in COGS associated with revenue from collaborations, respectively).
[2] Non-GAAP R&D expense, SG&A expense, and non-GAAP operating loss primarily exclude costs related to stock-based compensation expense and a change in estimate of contingent liabilities
[3] Cash, cash equivalents and marketable securities
See Appendix for a reconciliation between GAAP and non-GAAP measures

2021 Full Year Guidance

	FY 2020 Actuals	FY 2021 Guidance	Projected 2021 Growth (using mid-point of guidance)
Net Product Revenues (ONPATTRO, GIVLAARI, OXLUMO)	$361.5M	$610M – $660M	+76%
Net Revenues from Collaborations & Royalties	$131.3M	$150M – $200M	+33%
Non-GAAP Combined R&D and SG&A Expenses[1,2]	$1,063.4M	$1,175M – $1,275M	+15%

[1] 2020 Non-GAAP Combined R&D and SG&A Expenses primarily exclude costs related to stock-based compensation expense and a change in estimate of contingent liabilities. See appendix for reconciliation between GAAP and non-GAAP expenses

[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

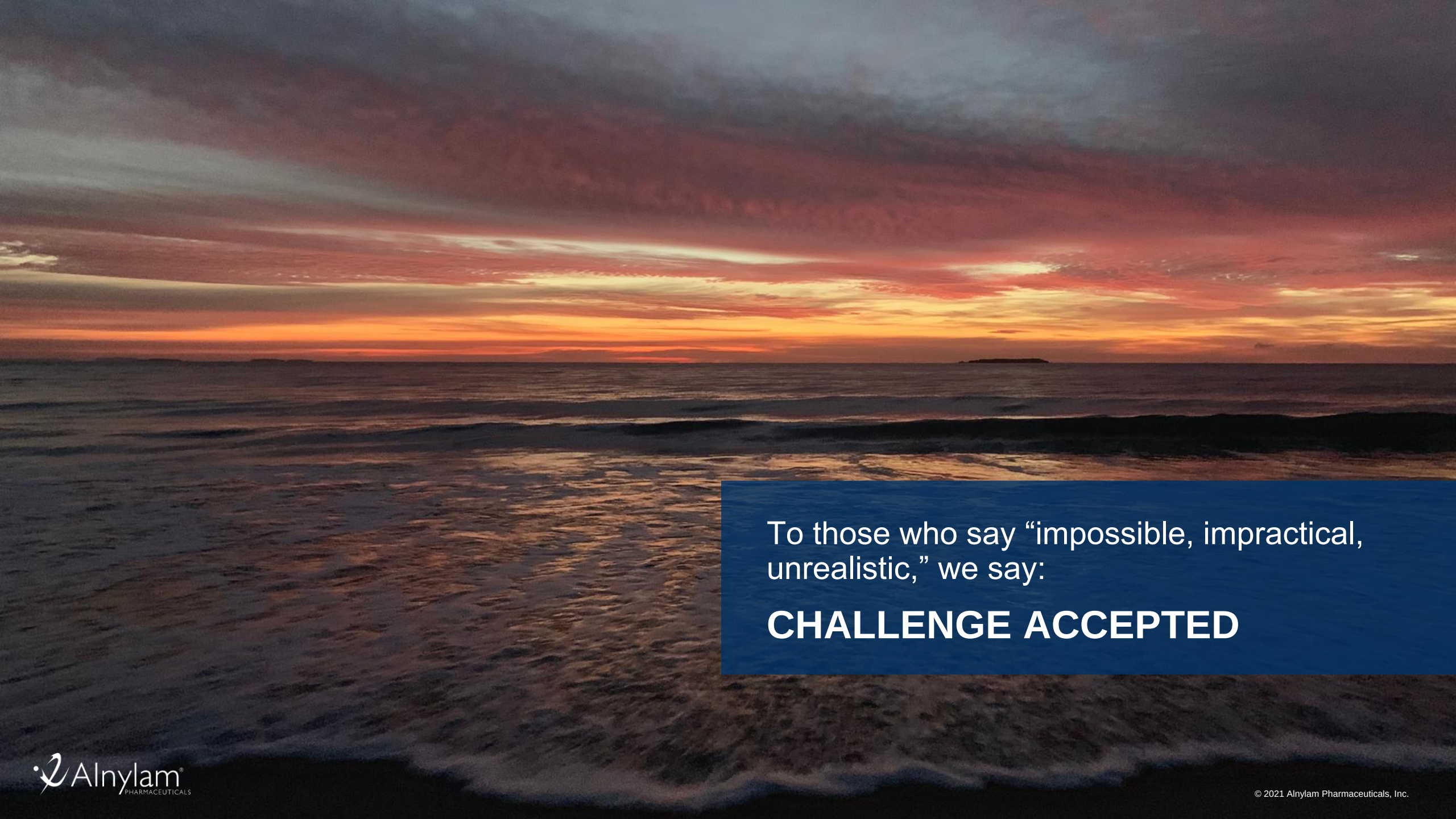
Alnylam 2021 Goals

		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 Endpoint	✓		
	File NDA	●		
	Initiate q6M Dose Regimen Study	●		
	HELIOS-A Phase 3 Topline – 18 Month Endpoint (incl. cardiac)			●
	HELIOS-B Phase 3 Enrollment	●	●	●
ALN-AGT (Uncontrolled Hypertension)	Initiate KARDIA-1 and -2 Phase 2 Studies		●	
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 (guidance pending)			
	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	●	●	●

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

Q4 and Full Year 2020 Financial Results

Q&A Session



Alnylam PHARMACEUTICALS

Q4 and Full Year 2020 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

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

	Three Months Ended		Twelve Months Ended	
	December 31, 2020	December 31, 2019	December 31, 2020	December 31, 2019
Reconciliation of GAAP to Non-GAAP research and development:				
GAAP Research and development	$ 168,469	$ 201,301	$ 654,819	$ 655,114
Less: Stock-based compensation expenses	(14,922)	(34,786)	(60,464)	(88,930)
Non-GAAP Research and development	$ 153,547	$ 166,515	$ 594,355	$ 566,184
Reconciliation of GAAP to Non-GAAP selling, general and administrative:				
GAAP Selling, general and administrative	$ 166,291	$ 156,277	$ 588,420	$ 479,005
Less: Stock-based compensation expenses	(19,354)	(31,411)	(79,409)	(85,911)
Less: Costs associated with the strategic financing collaboration	—	—	(1,083)	—
Less: Loss on contractual settlement	—	—	(650)	—
Less: Change in estimate of contingent liabilities	(10,216)	—	(38,216)	—
Non-GAAP Selling, general and administrative	$ 136,721	$ 124,866	$ 469,062	$ 393,094
Reconciliation of GAAP to Non-GAAP operating loss:				
GAAP operating loss	$ (194,222)	$ (298,073)	$ (828,438)	$ (939,431)
Add: Stock-based compensation expenses	34,276	66,197	139,873	174,841
Add: Costs associated with the strategic financing collaboration	—	—	1,083	—
Add: Loss on contractual settlement	—	—	650	—
Add: Change in estimate of contingent liabilities	10,216	—	38,216	—
Non-GAAP operating loss	$ (149,730)	$ (231,876)	$ (648,616)	$ (764,590)

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