Second Quarter 2020 Financial Results

August 6, 2020

Alnylam® PHARMACEUTICALS

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Agenda

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

Overview
- John Maraganore, Ph.D.
  Chief Executive Officer

Commercial/Med Affairs Highlights
- Barry Greene
  President

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

Financial Summary and Guidance
- Jeff Poulton
  Chief Financial Officer

2020 Goals Update
- Yvonne Greenstreet, MBChB, MBA
  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. 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 direct or indirect impact of the COVID-19 global pandemic or a future pandemic, such as the scope and duration of the outbreak, government actions and restrictive measures implemented in response, material delays in diagnoses of rare diseases, initiation or continuation of treatment for diseases addressed by our products, or in patient enrollment in clinical trials, potential supply chain disruptions, and other potential impacts to our business, the effectiveness or timeliness of steps taken by us to mitigate the impact of the pandemic, and our ability to execute business continuity plans to address disruptions caused by the COVID-19 or any future pandemic; our ability to discover and develop novel drug candidates and delivery approaches and successfully demonstrate the efficacy and safety of our product candidates, including vutrisiran, ALN-AGT, ALN-HSD, ALN-APP and ALN-COV; 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 and our partner's ability to obtain regulatory approval for our product candidates, including lumasiran and inclisiran, and our ability 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, and achieve net product revenues for ONPATTRO within our further revised expected range during 2020; 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 within the reduced ranges of guidance provided by us through implementation of further discipline in operations to moderate spend and our ability to achieve a self-sustainable financial profile in the future without the need for future equity financing; our ability to establish and maintain business alliances, including completing an agreement for funding by Blackstone of certain R&D activities for vutrisiran and ALN-AGT; our dependence on third parties, including Novartis, for the development, manufacture and commercialization of inclisiran, Regeneron, for development, manufacture and commercialization of certain products, including eye and CNS products such as ALN-APP, Ironwood, for assistance with the education about and promotion of GIVLAARI, and Vir for the development of ALN-COV and other potential RNAi therapeutics targeting SARS-CoV-2 and host factors for SARS-CoV-2; the outcome of litigation; and the risk of government investigations; as well as those risks and other factors more fully discussed in our most recent annual, quarterly and current reports filed with the SEC. 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.

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 gain on marketable equity securities, costs associated with our strategic financing collaboration, a gain on litigation settlement, and a gain on the change in fair value of a liability obligation. 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 unrealized gain on marketable equity securities, costs associated with our strategic financing collaboration, the gain on litigation settlement, and a gain on the change in fair value of a liability obligation because the Company believes these items are non-recurring transactions outside the ordinary course of the Company's business.

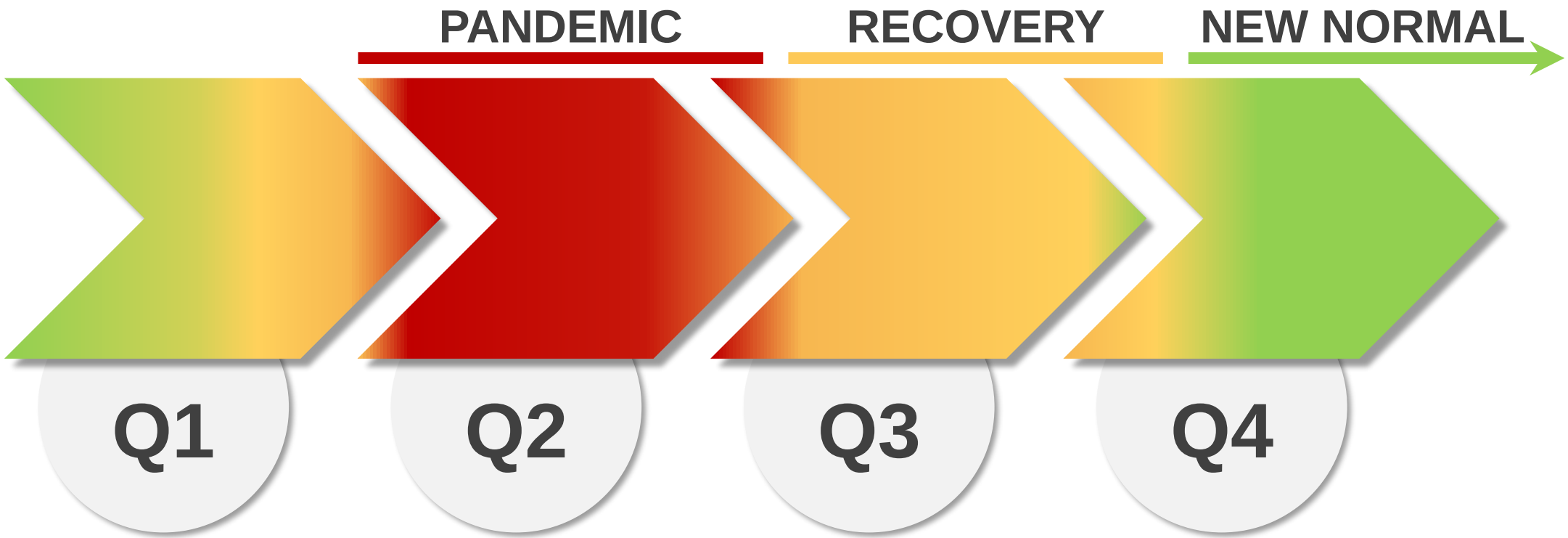
John Maraganore, Ph.D.

Chief Executive Officer

Overview

COVID-19 Planning Framework

Anticipated Business Impacts Through 2020



Alnylam Q2 Context

Building a Top-Tier Biopharmaceutical Company

Strong Commercial Progress

Productive Organic Pipeline

Secured Bridge Toward Self-Sustainability

Organizational Updates

Barry Greene, President,
to Depart at End of Q3

COO Yvonne Greenstreet
Appointed President and COO as of Oct 1st


Alnylam®
PHARMACEUTICALS
2020
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4 Late Stage Programs 6

Barry Greene

President

Commercial/Med Affairs Highlights

ONPATTRO® Launch Update: Q2 2020

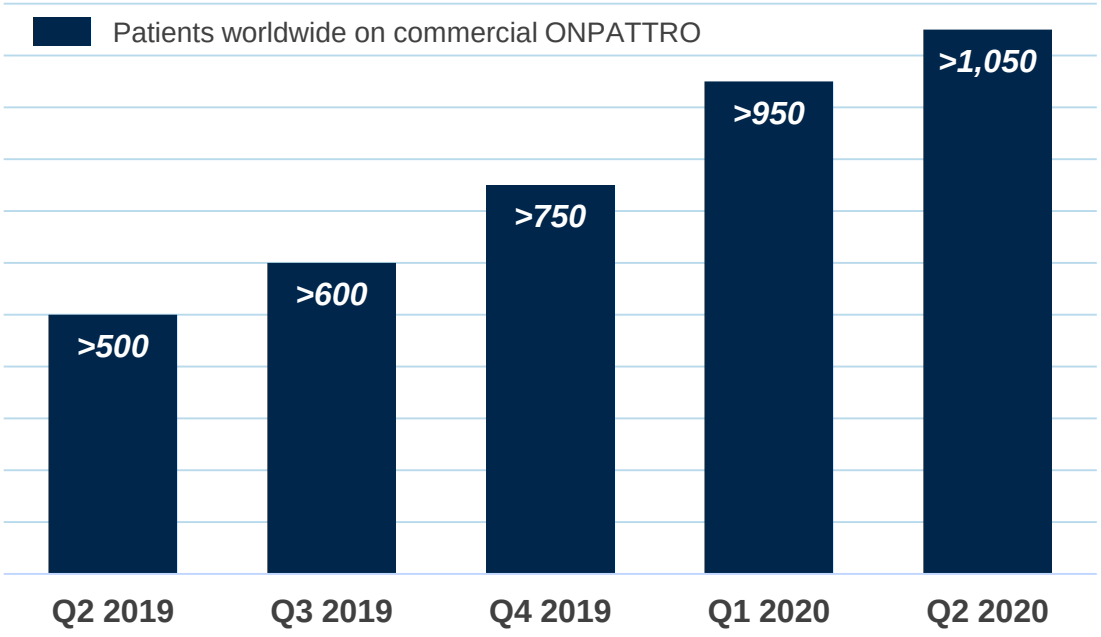
Strong Performance with Significant Growth

$66.5M

ONPATTRO Global Q2 Net Product Revenues

>1,050

Patients Worldwide on Commercial ONPATTRO at end of Q2 2020



U.S. Demand and Access

40% Demand from new writers[1]

98% U.S. lives with confirmed access to ONPATTRO, if prescribed[2]

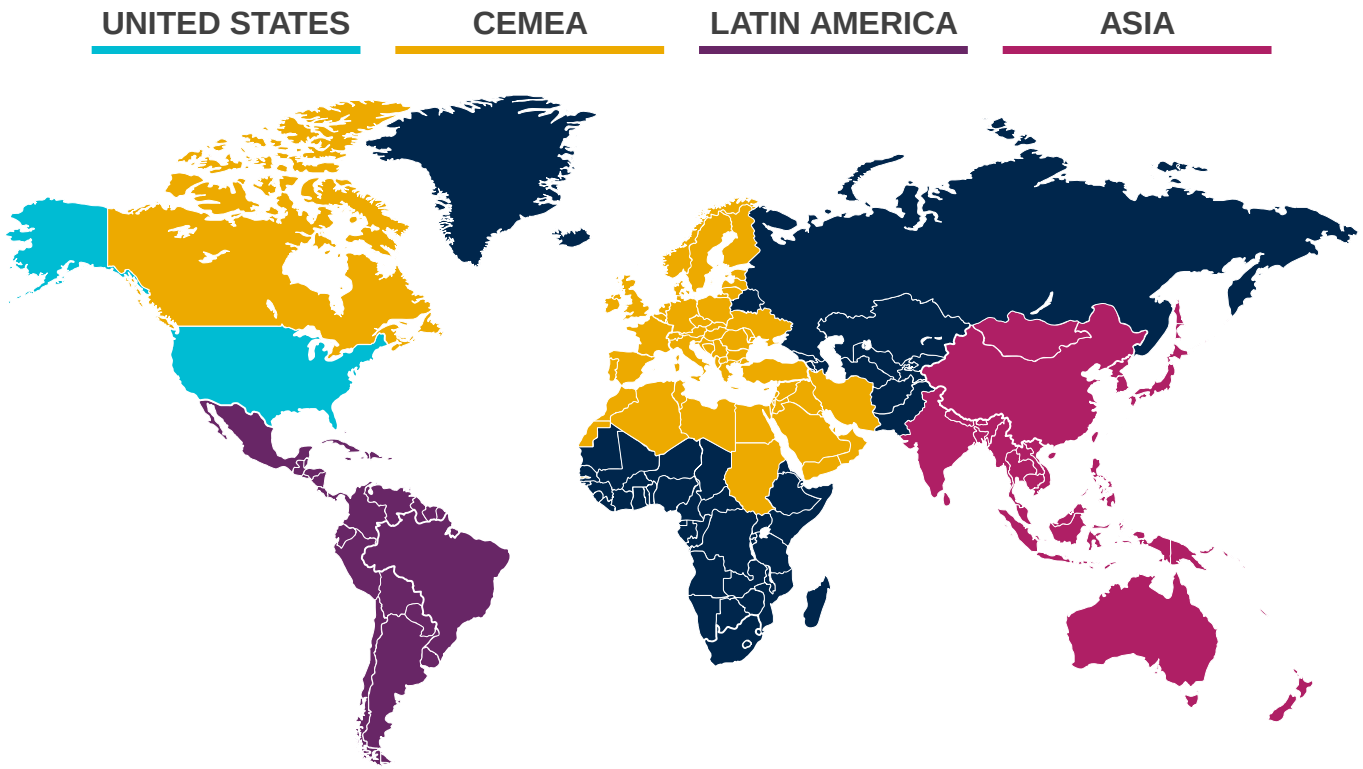
[1] Based on total Start Forms submitted in Q2 2020. Start Forms are an incomplete picture of U.S. demand

[2] Across commercial, Medicare, Medicaid, and other government payer categories (DKP PayerScope® August 1, 2018 through June 30, 2020)

ONPATTRO Global Commercialization

Increasing Access and Value Recognition

- Significant progress with global ONPATTRO availability
  - Recent launches in Spain and Italy
  - Reimbursement achieved in France
  - Access achieved in “big five” Western European markets, plus Portugal, Sweden, The Netherlands, and Belgium.
  - About 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 and switching from other products, including stabilizers
- Strength coming from Japan
  - Now represents second largest country for ONPATTRO revenue

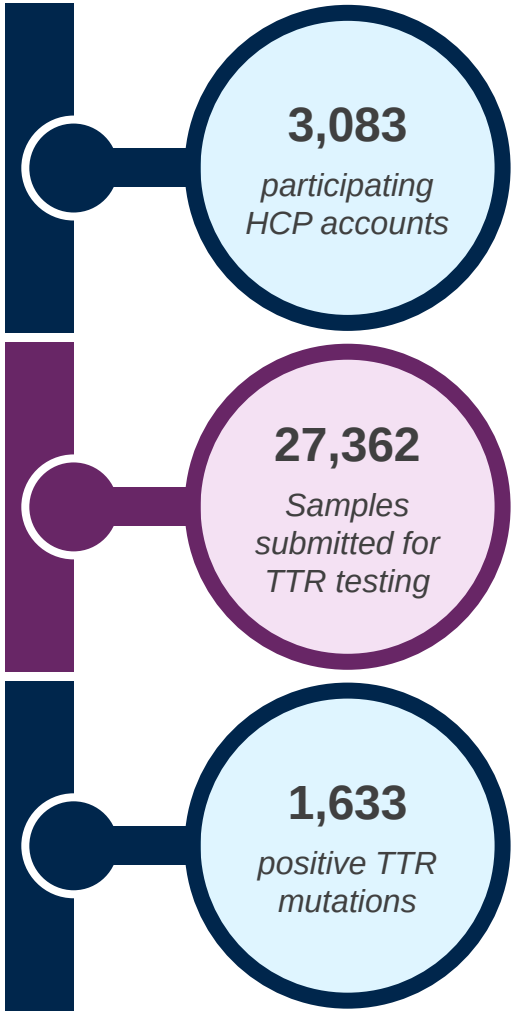


onpattro® (patisiran) lipid complex injection 10 mg/5 mL

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 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 July 2020

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

GIVLAARI® Launch Update: Q2 2020

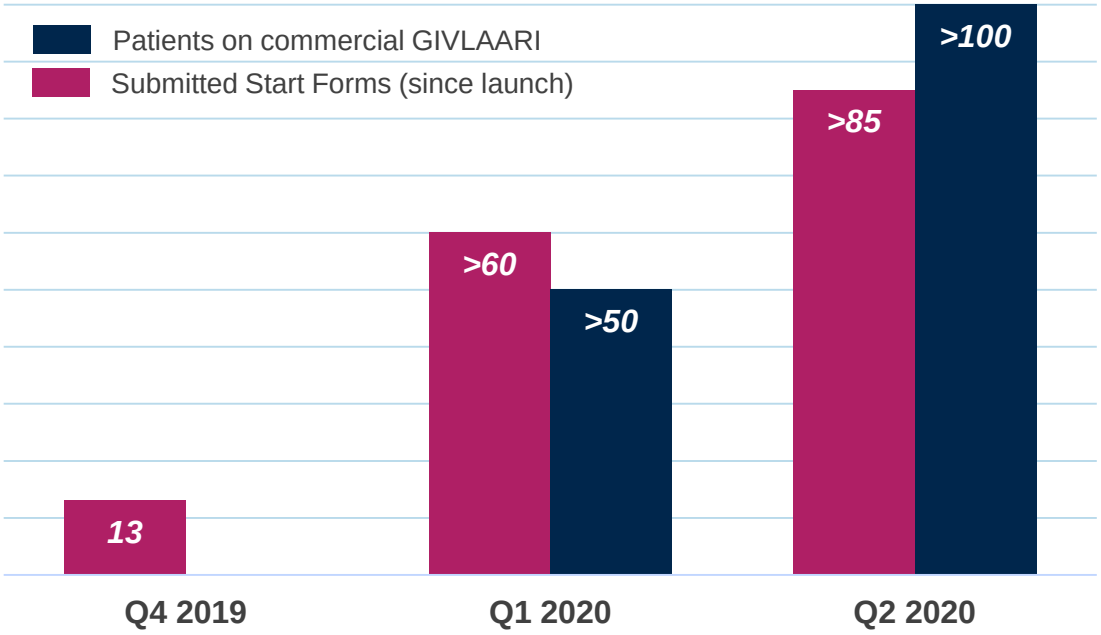
Strong Initial Demand in U.S.

$11.0M

GIVLAARI Q2
Net Product Revenues

>100

Patients on Commercial GIVLAARI
at end of Q2 2020



U.S. Demand and Access

76% New U.S. starts from new writers*

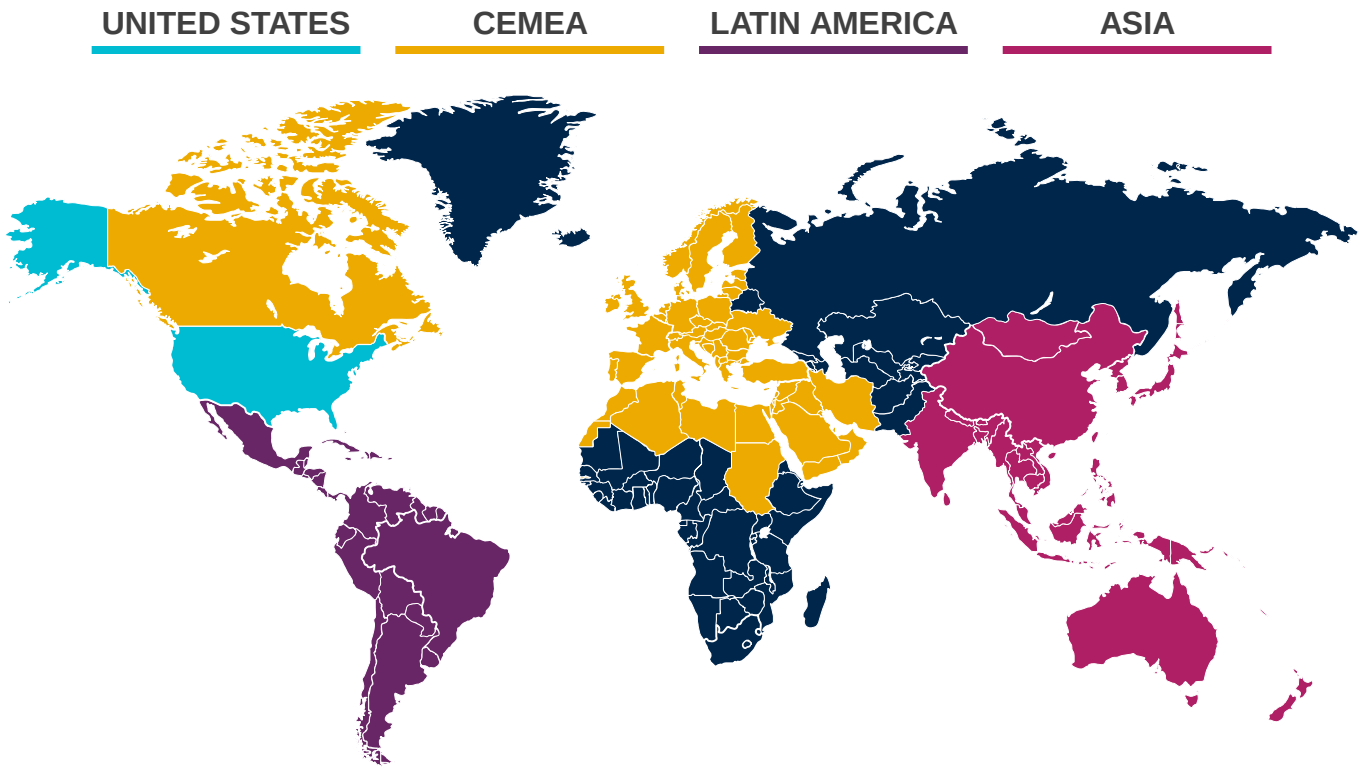
>75% U.S. lives with confirmed access to GIVLAARI, if prescribed

* Based on Start Forms submitted. Start Forms are an incomplete picture of U.S. demand

GIVLAARI Global Commercialization

Ensuring GIVLAARI Availability Around the World

- Now approved in Brazil
- Initial launch underway in Germany
- Named patient sales in France and other countries
    - ASMR II granted by HAS in France
- Working with physicians in multiple regions to provide pre-approval access via Expanded Access Program (EAP)
- MAAs submitted in Switzerland and Israel
- Planned JNDA submission in Japan in late 2020

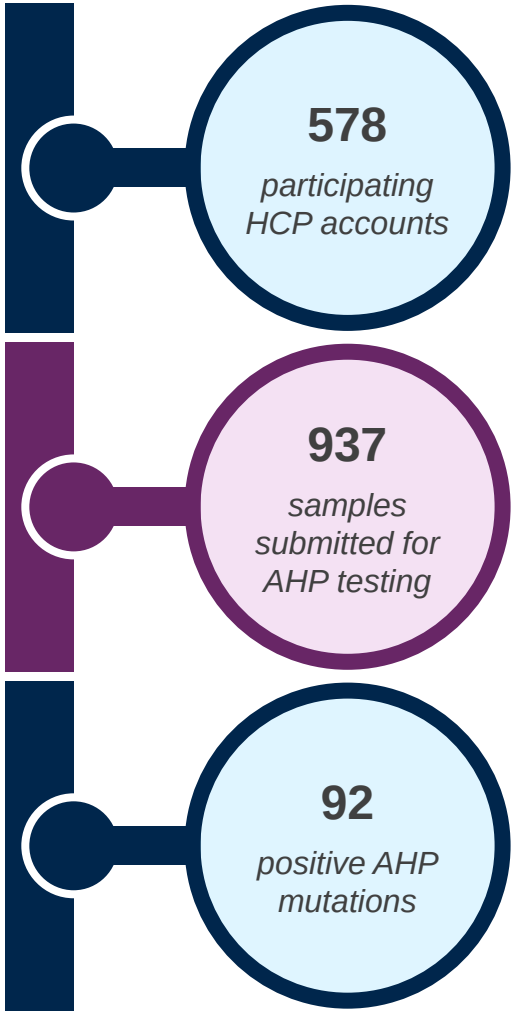


GIVLAARI® (givosiran) injection for subcutaneous use 189 mg/mL

CEMEA: Canada, Europe, Middle East, North Africa

Alnylam Act – Acute Hepatic Porphyria

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

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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
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

Vutrisiran Phase 3 Program

Robust Registrational Program to Evaluate Vutrisiran in Heredtiary & Wild-Type ATTR Amyloidosis

HELIOS

HELIOS·A

Randomized, open-label study in hereditary ATTR amyloidosis patients with polyneuropathy

Enrollment complete

Topline results expected
early 2021

HELIOS·B

Randomized, double-blind, placebo-controlled outcomes study in hereditary and wild-type ATTR amyloidosis patients with cardiomyopathy

Enrollment ongoing

Study includes optional interim analysis

Givosiran Phase 3 Data Published in *The New England Journal of Medicine*

The NEW ENGLAND JOURNAL of MEDICINE

Phase 3 Trial of RNAi Therapeutic Givosiran for Acute Intermittent Porphyria

Manisha Balwani, M.D., Eliane Sardh, M.D., Ph.D., Paolo Ventura, M.D., Paula Aguilera Peiró, M.D., David C. Rees, F.R.C.P., Ulrich Stölzel, M.D., D. Montgomery Bissell, M.D., Herbert L. Bonkovsky, M.D., Jerzy Windyga, M.D., Ph.D., Karl E. Anderson, M.D., Charles Parker, M.D., Samuel M. Silver, M.D., Ph.D., et al., for the ENVISION Investigators*

June 11, 2020
N Engl J Med 2020; 382:2289-2301
DOI: 10.1056/NEJMoa1913147

Lumasiran NDA and MAA Accepted

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

ILLUMINATE

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

Full results presented June 2020;
FDA approval anticipated
by **YE 2020**

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

Enrollment complete;
Topline results expected
in **mid-2020**

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 initiated in U.S. and Europe

Late Stage Partnered Program Opportunities

INCLISIRAN

NOVARTIS

Hypercholesterolemia

Blackstone

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 and MAA accepted;
FDA approval anticipated by YE 2020

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]

Topline results expected in H1 2021 per Sanofi

[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

Alnylam Early Stage Clinical Development and 2020 IND Pipeline

Focused in 4 Strategic Therapeutic Areas (STArs):

- Genetic Medicines
- Cardio-Metabolic Diseases
- 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 (DCR-A1AT)[3]	*Alpha-1 Liver Disease*	✓			●	Ex-U.S. option post-Phase 3 **(Dicerna)**
ALN-HBV02 (VIR-2218)	*Hepatitis B Virus Infection*	✓			●	50-50 option post-Phase 2 **(Vir)**
ALN-AGT	*Hypertension*	✓			●	Global
ALN-HSD	*NASH*				●	50-50 **(Regeneron)**
ALN-COV (VIR-2703)	*COVID-19*			○		50-50 option post-Phase 2 **(Vir)**

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
[3] Dicerna is leading and funding development of ALN-AAT02 and DCR-A1AT and will select which candidate to advance in development

As of August 2020

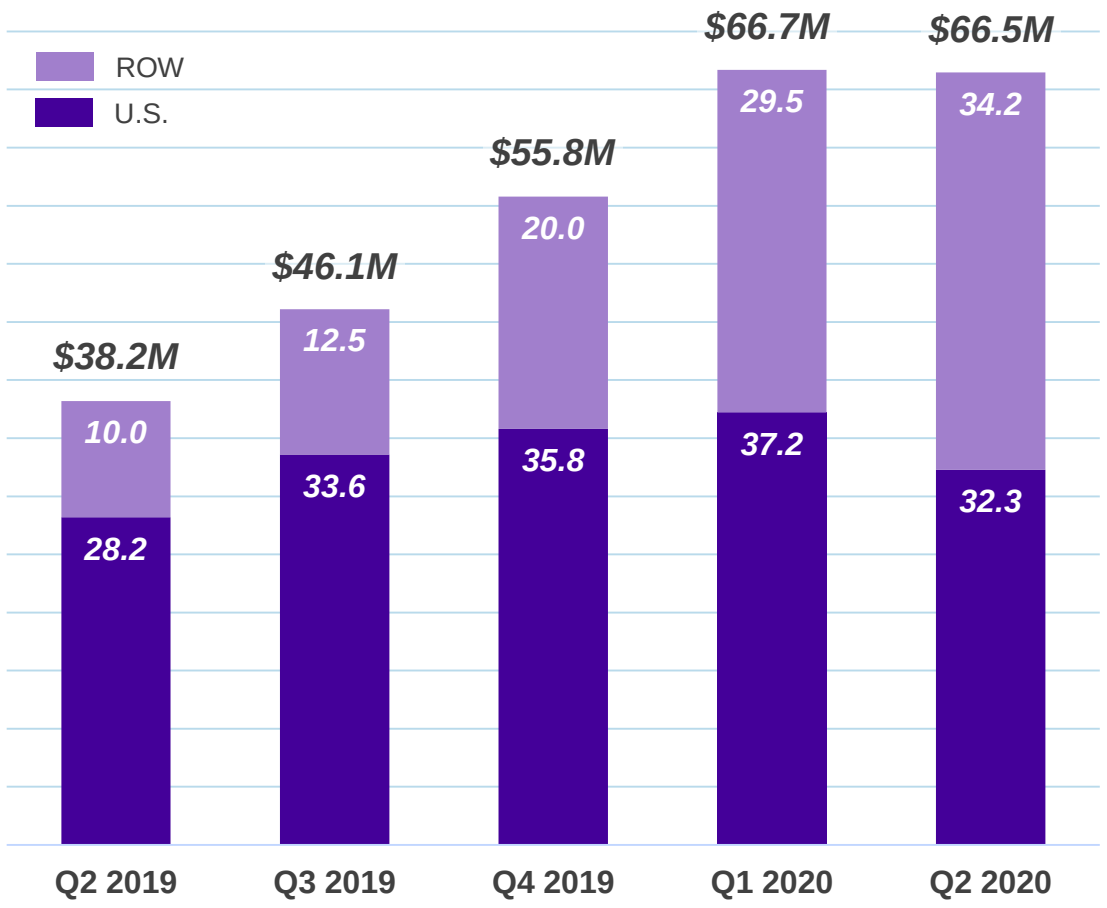
Jeff Poulton

Chief Financial Officer

Financial Summary and Guidance

Global ONPATTRO Performance

Revenue ($M)



Highlights

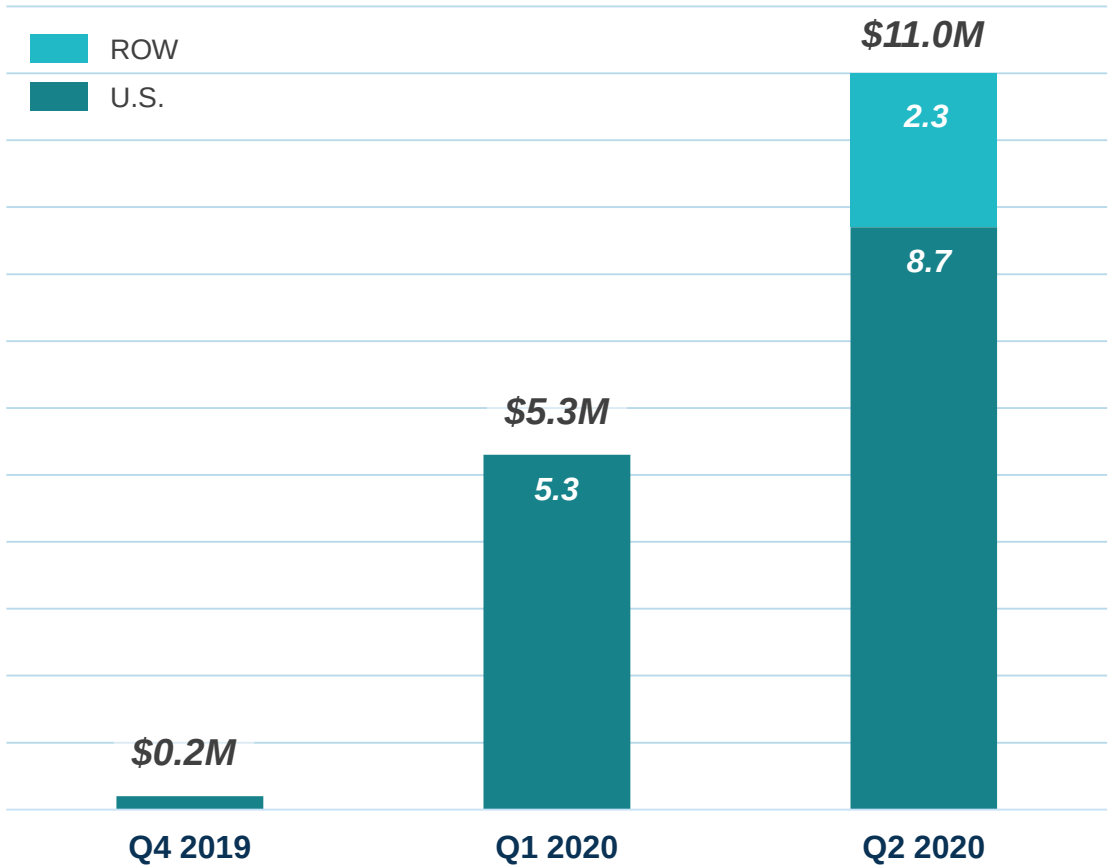
	YoY % Growth	QoQ % Growth
U.S.	14%	(13%)
ROW	241%	16%
Global	74%	(0%)

- U.S. QoQ growth was negatively impacted during Q2 '20 by the following:
  - Reduction in patient demand due to reduced adherence associated with COVID-19 pandemic *(-4%)*
  - Reduction in inventory in channel to ~1.5 weeks on hand *(-8%)*
  - Modest increase in gross to net sales deductions *(-1%)*
- Strength in international results driven by recent launches in Italy and Spain and continued strong growth in Japan

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

Global GIVLAARI Performance

Revenue ($M)



Highlights

	QoQ % Growth
U.S.	64%
ROW	N/A
Global	109%

- >85 U.S. Start Forms[1], >100 global patients on therapy since launch
- Good progress with VBAs, now have confirmed access for over 75% of covered U.S. lives
- Initial contribution from our international markets with successful launch in Germany and named patient sales in other countries, including France

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

[1] Start Forms are an incomplete picture of U.S. demand

Second Quarter 2020 Financial Summary

Financial Results ($ millions)	Q2 2020	Q2 2019	Q1 2020	YoY % Change	QoQ % Change
ONPATTRO Net Product Revenues	$66.5	$38.2	$66.7	74.0%	(0.2%)
GIVLAARI Net Product Revenues	$11.0	-	$5.3	N/A	108.5%
Net Revenue from Collaborations	$26.4	$6.5	$27.5	307.7%	(4.0%)
Total Revenues	$104.0	$44.7	$99.5	132.5%	4.5%
Cost of Goods Sold	$19.9	$4.3	$13.3	360.7%	49.8%
GM as % of Total Revenues[1]	*80.8%*	*90.3%*	*86.6%*	-	-
Non-GAAP R&D Expenses[2]	$139.2	$148.6	$153.5	(6.3%)	(9.3%)
Non-GAAP SG&A Expenses[3]	$109.6	$97.4	$108.2	12.5%	1.3%
Non-GAAP Operating Loss[3]	($164.8)	($205.7)	($175.6)	-	-

Financial Results ($ millions)	Jun 30, 2020	Dec 31, 2019
Cash & Investments[4]	$1,950.3	$1,551.0

[1] GM as a % of Product Sales for Q2 2020 is 76.4%, Q2 2019 is 88.7%, Q1 2020 is 81.5% (Q2 2020 GM % of Product Sales excludes $1.7M in COGS associated with revenue from collaborations).
[2] Non-GAAP R&D expense excludes stock-based compensation expenses
[3] Non-GAAP SG&A expense and non-GAAP operating loss exclude stock-based compensation expense and costs associated with our strategic financing collaboration
[4] Cash, cash equivalents, marketable debt and equity securities, and restricted investments
See Appendix for a reconciliation between GAAP and non-GAAP measures

Updated 2020 Full-Year Guidance

	Prior FY 2020 Guidance	Updated FY 2020 Guidance[2]
ONPATTRO Net Product Revenues	$270M - $300M	$280M - $300M
GIVLAARI Net Product Revenues	No guidance provided	Unchanged
Net Revenues from Collaborations	$100M - $150M	Unchanged
GAAP Combined R&D and SG&A Expenses	$1,155M - $1,250M	$1,130M - $1,225M
Non-GAAP Combined R&D and SG&A Expenses[1]	$1,000M - $1,075M	Unchanged

$2 billion strategic financing collaboration with Blackstone expected to enable Alnylam's achievement of a self-sustainable financial profile without need for future equity financing

[1] Non-GAAP combined R&D and SG&A expenses exclude $130-$150 million (previously $155-$175 million) of stock-based compensation and costs associated with the strategic financing collaboration from estimated GAAP R&D and SG&A expenses

[2] As of August 6, 2020

Yvonne Greenstreet, MBChB, MBA

Chief Operating Officer

2020 Goals Update

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 10 mg/5 mL (ATTR Amyloidosis)	Global Commercial Execution	✓	●	●
	Brazil Approval	✓		
	Additional Country Launches	✓	✓	●
	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 NDA and MAA	✓		
	FDA/EMA Approval			●
	ILLUMINATE-B Phase 3 Topline		●	
ADDITIONAL CLINICAL PROGRAMS	Continue to advance early/mid-stage pipeline; File 2-4 new INDs; Present clinical data	✓	✓	●
PARTNERED PROGRAMS				
INCLISIRAN (Hypercholesterolemia)	FDA Approval			●
	MAA Filing	✓		
	ORION-4 CVOT Phase 3 Enrollment (*paused due to COVID-19*)	✗	✗	●
FITUSIRAN (Hemophilia)	Support Sanofi on ATLAS Phase 3	✓	●	●

Upcoming RNAi Roundtables

Lumasiran, in Development for the Treatment of Primary Hyperoxaluria Type 1

- Monday, August 10, 2:00 pm ET

Patisiran and Vutrisiran, in Development for the Treatment of ATTR Amyloidosis

- Date TBD

Givosiran, for the Treatment of Acute Hepatic Porphyria

- Monday, September 14

Additional details for upcoming RNAi Roundtables will be provided on the Capella section of the Company's website, www.alnylam.com/capella

Q2 2020 Financial Results

Q&A Session

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Q2 2020 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

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

	Three Months Ended		
	June 30, 2020	**June 30, 2019**	**March 31, 2020**
Reconciliation of GAAP to Non-GAAP research and development:			
GAAP Research and development	154,996	163,890	169,571
Less: Stock-based compensation expenses	(15,790)	(15,282)	(16,049)
Non-GAAP Research and development	139,206	148,608	153,522
Reconciliation of GAAP to Non-GAAP selling, general and administrative:			
GAAP Selling, general and administrative	127,896	112,769	126,761
Less: Stock-based compensation expenses	(17,965)	(15,321)	(18,529)
Less: Costs associated with the strategic financing collaboration	(320)	—	—
Non-GAAP Selling, general and administrative	109,611	97,448	108,232
Reconciliation of GAAP to Non-GAAP operating loss:			
GAAP operating loss	(198,859)	(236,271)	(210,158)
Add: Stock-based compensation expenses	33,755	30,603	34,578
Add: Costs associated with the strategic financing collaboration	320	—	—
Non-GAAP operating loss	(164,784)	(205,668)	(175,580)

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