First Quarter 2020 Financial Results

May 6, 2020

Alnylam® PHARMACEUTICALS

Agenda

Welcome
- Christine Lindenboom
  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 a 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; 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 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, 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 expense and unrealized gain on marketable equity securities. 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 because the Company believes this item is a one-time event occurring outside the ordinary course of the Company's business.

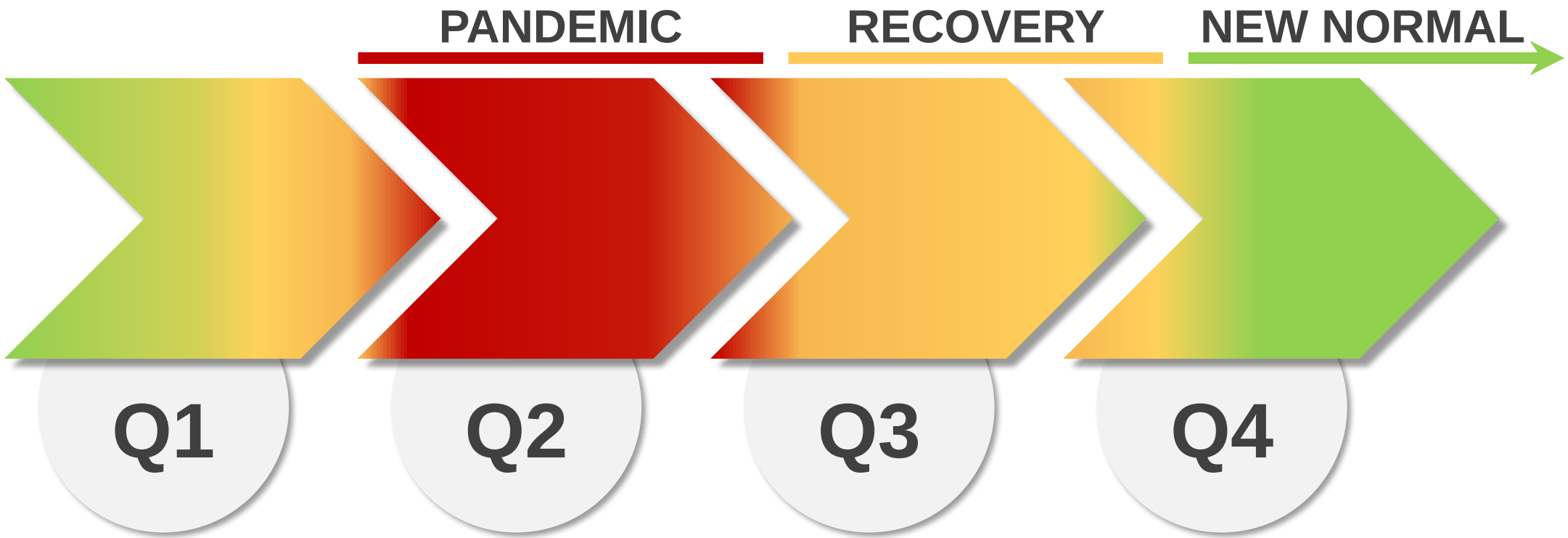
John Maraganore, Ph.D.

Chief Executive Officer

Overview

COVID-19 Planning Framework

Anticipated Business Impacts Through 2020



Alnylam Q1 Context

Building a Top-Tier Biopharmaceutical Company

Strong Commercial Progress

Productive Organic Pipeline

Secured Bridge Toward Self-Sustainability

Barry Greene

President

Commercial/Med Affairs Highlights

ONPATTRO® Launch Update: Q1 2020

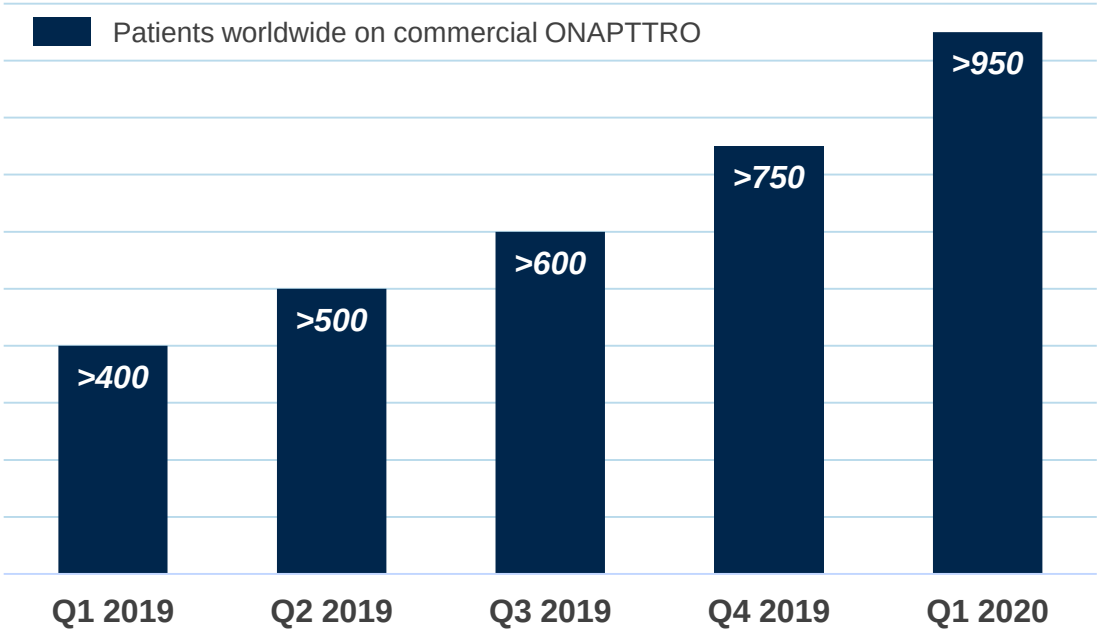
Strong Performance with Significant Growth

$66.7M

ONPATTRO Global Q1 Net Product Revenues

>950

Patients Worldwide on Commercial ONPATTRO at end of Q1 2020



U.S. Demand/Adherence, Prescriber Mix, and Access

>250	Unique prescribing physicians since launch
57%	Demand from neurologists[1]
26%	Demand from cardiologists[1]
17%	Demand from other specialties[1]
>90%	Adherence on commercial ONPATTRO[2]
99%	U.S. lives with confirmed access to ONPATTRO, if prescribed[3]

[1] Based on total Start Forms submitted in Q1 2020. Start Forms are an incomplete picture of U.S. demand

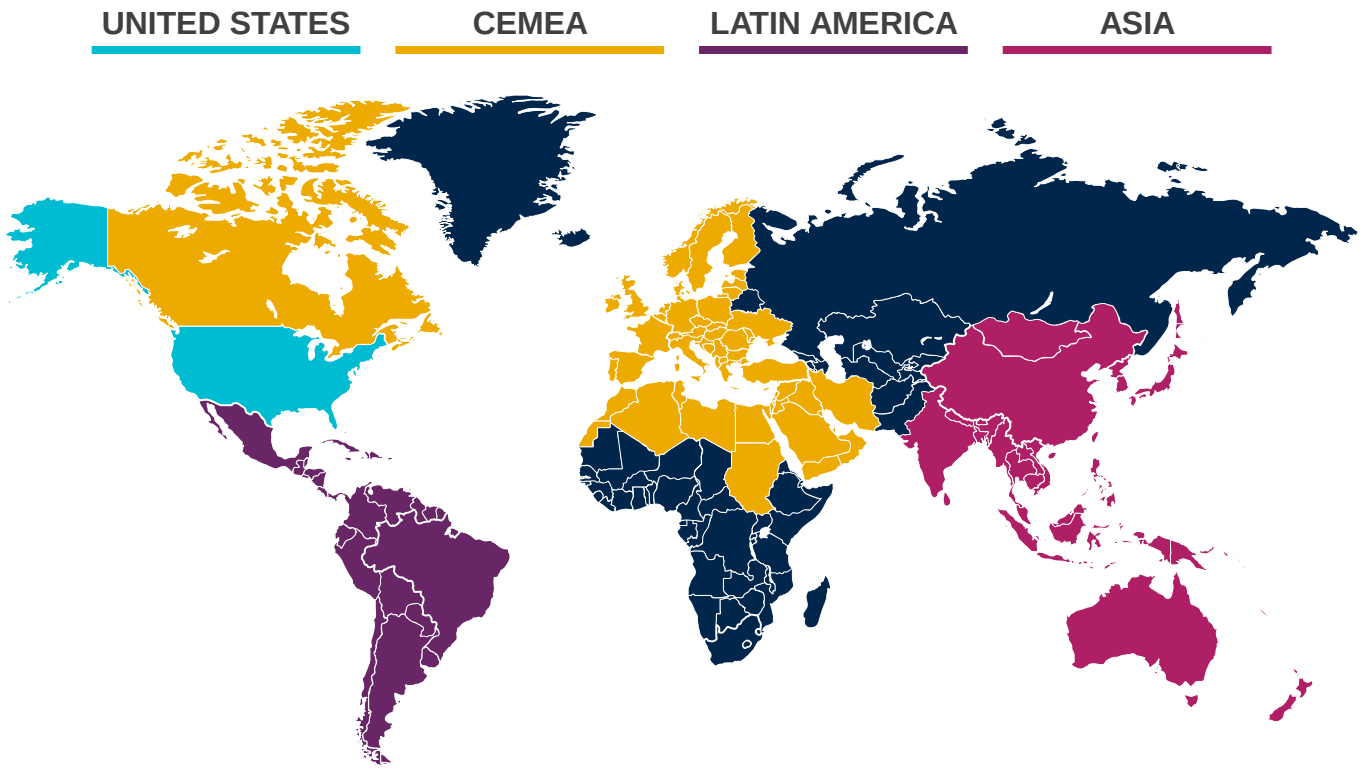
[2] Based on 12-month rolling average

[3] Across commercial, Medicare, Medicaid, and other government payer categories (DKP PayerScope® August 1, 2018 through March 31, 2020)

ONPATTRO Global Commercialization

Increasing Access and Value Recognition

- Significant progress with global ONPATTRO availability
  - Launch expanded to Italy, Sweden, Israel, Turkey, and Spain
  - Reimbursement achieved in Portugal
  - Almost 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
- Additional countries and regions advancing
  - Latin America plans progressing, with recent approval in Brazil

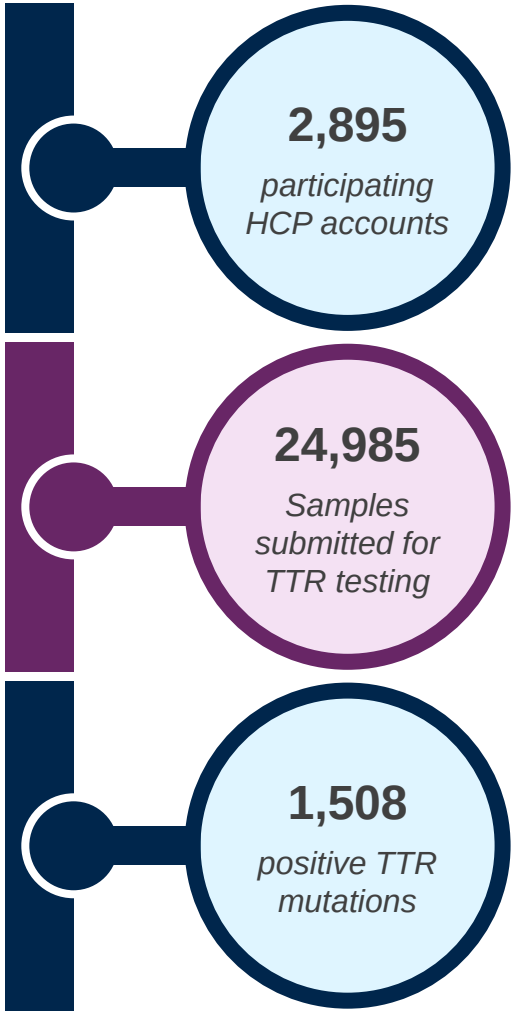


onpattro® (patisiran) lipid complex injection 10 mg/5 mL

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 April 2020

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

GIVLAARI® Launch Update: Q1 2020

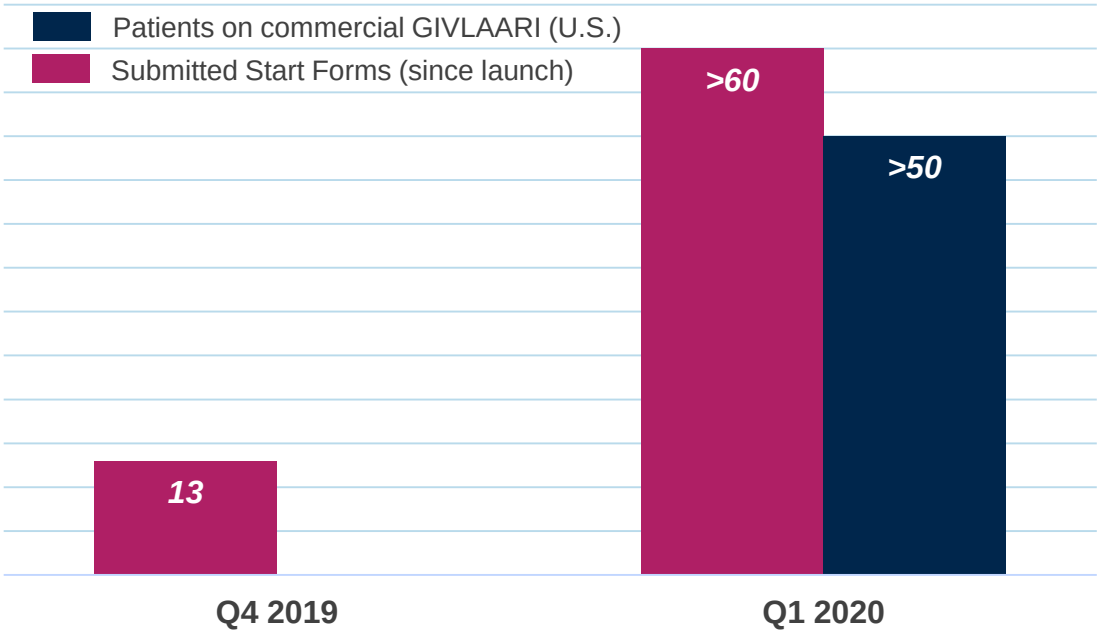
Strong Initial Demand in U.S.

$5.3M

GIVLAARI Q1
Net Product Revenues

>50

Patients on Commercial GIVLAARI
at end of Q1 2020 (U.S.)



U.S. Demand and Access

>60 Start Forms submitted since launch*

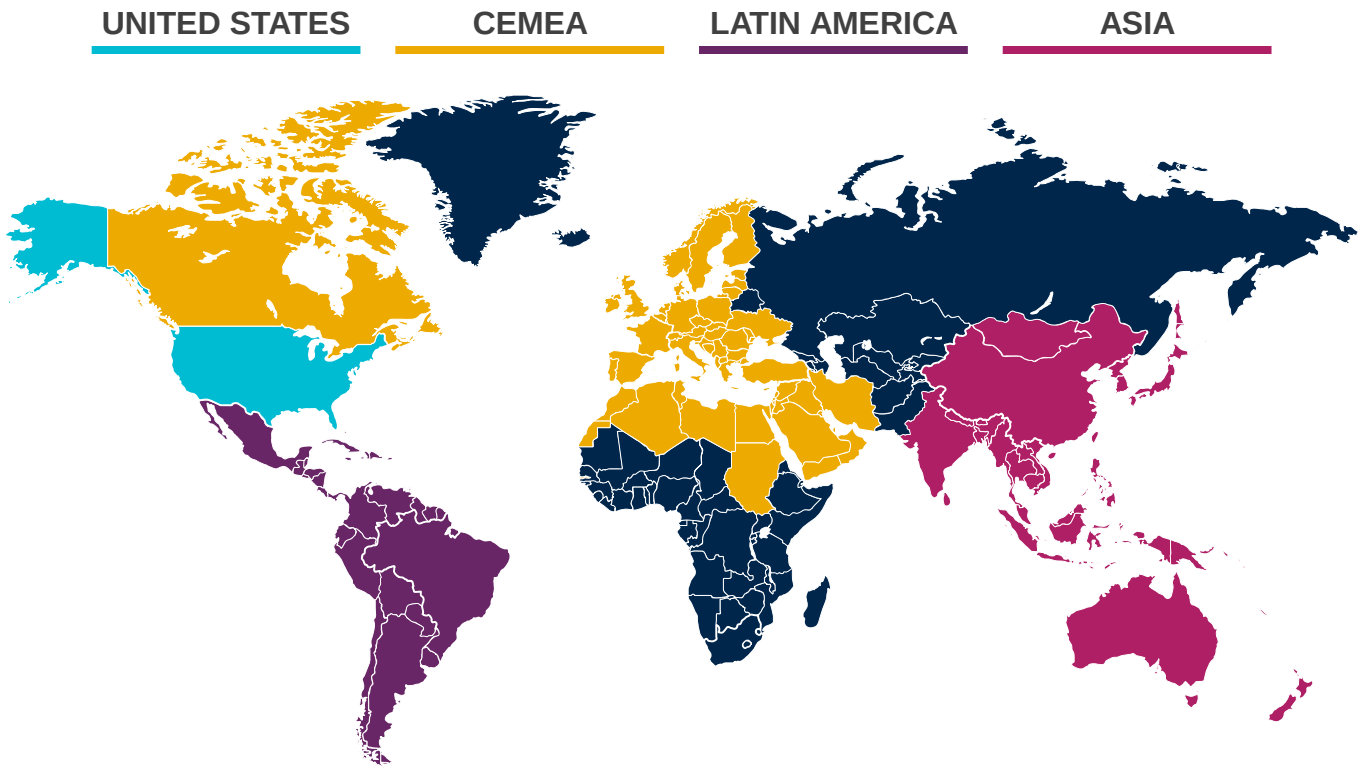
1-2 Average weeks from Start Form to treatment

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

GIVLAARI Global Commercialization

Ensuring GIVLAARI Availability Around the World

- Initial launch underway in Germany
- Working with physicians in multiple regions to provide pre-approval access via Expanded Access Program (EAP)

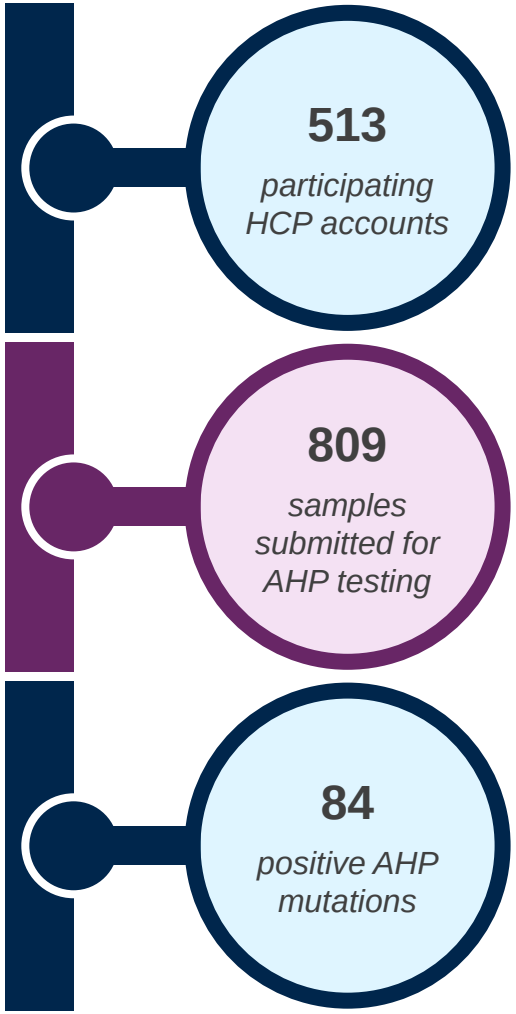


GIVLAARI® (givosiran) injection for subcutaneous use 189 mg/mL

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

Tests and services are performed by independent third parties

Available in U.S. and Canada (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

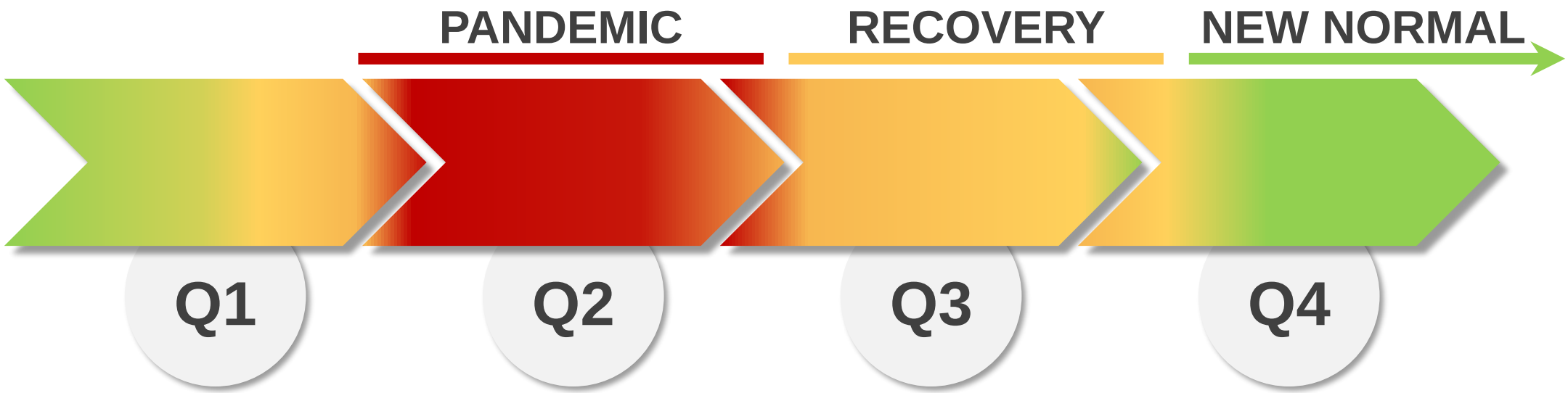
More information regarding this program available at: **www.alnylamact.com**

Data as of April 2020

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

COVID-19 Outlook

Potential Risks and Mitigations for Supply Chain and Commercial Activities



Supply Chain	Sufficient inventory of commercial product, drug product, drug substance, raw materials; No significant exposure to manufacturing in foreign countries to date		
Global Field Operations	Virtual interactions with HCPs, payers, patients		Continued use of virtual solutions to complement in-person visits
Continuity of Care	Expanded efforts to assist with site-of-care logistics	Continued site optimization; gradual return to clinics	Integrate expanded site optimization capabilities into normal operations

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

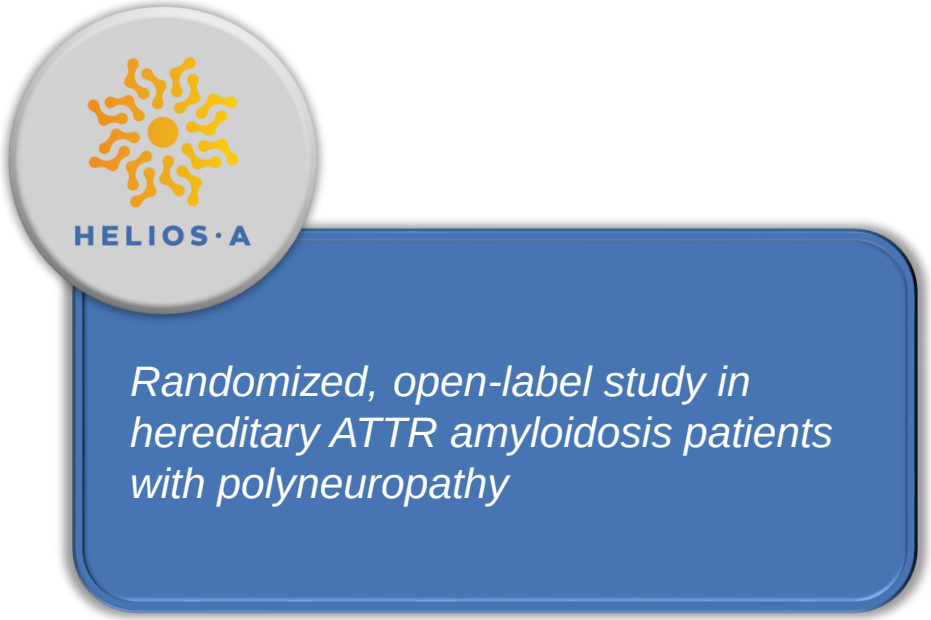
Enrollment completion shifted to **2021** due to COVID-19

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

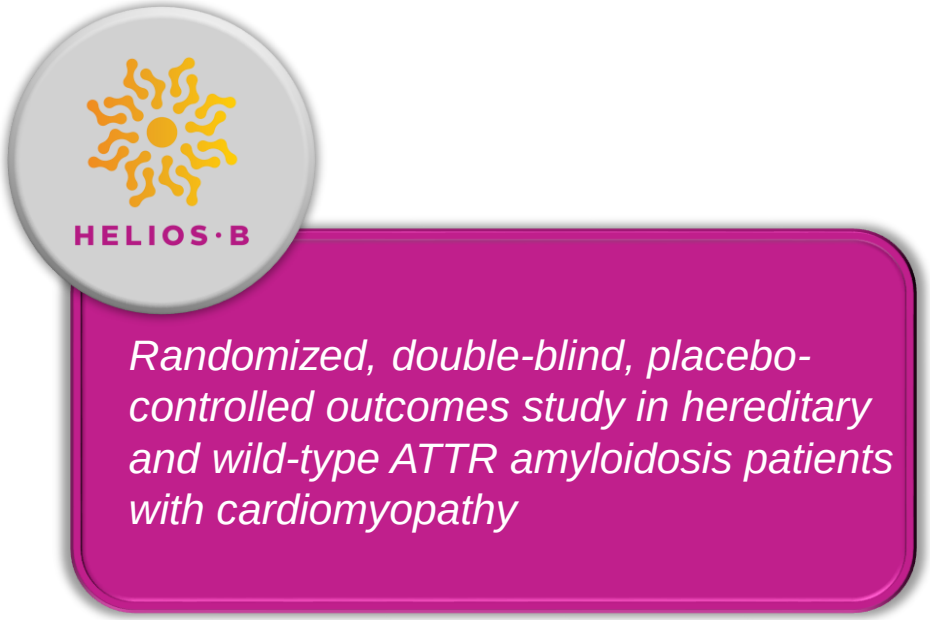
Robust Registrational Program to Evaluate Vutrisiran in Heredtiary & Wild-Type ATTR Amyloidosis

HELIOS



Enrollment complete

Topline results expected
early 2021



Enrollment ongoing

Study includes optional
interim analysis

Lumasiran NDA and MAA Filed

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

Topline results in Dec 2019;
Full results planned to be reported in **June 2020**

ILLUMINATE•B

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**

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 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

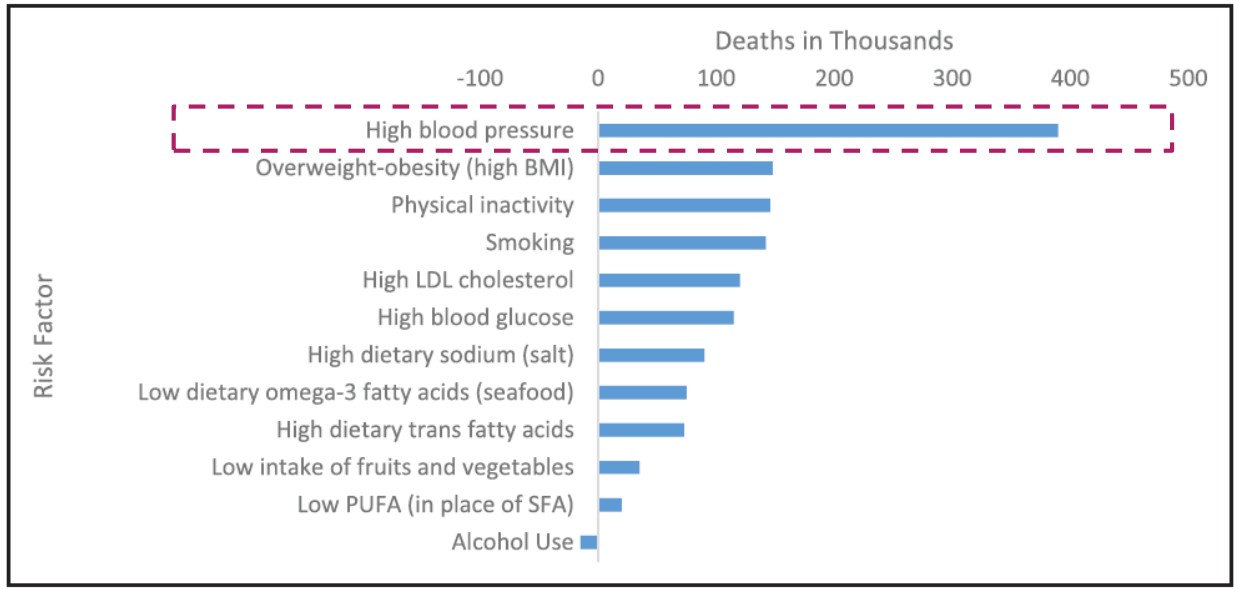
[2] Consumer Awareness, Trial, and Usage study among patients conducted over 359 Adult patients and caregivers surveyed online in April 2019, of which 131 were Adult Hemophilia A patients and 78 were Hemophilia A caregivers. Patients who switched to emicizumab answered questions specific to their treatment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

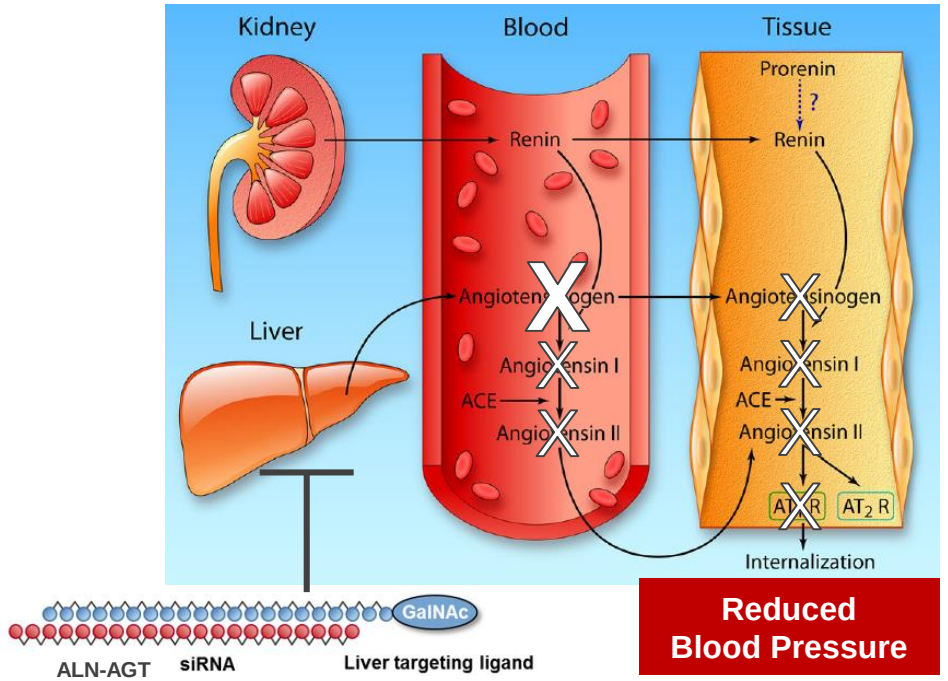
[3] 2019 Specialty Pharmacy data obtained through Specialty Pharmacy Distributors, Hemophilia Alliance HTCs and Direct HTCs

ALN-AGT for Hypertension

Unmet Need, Mechanism of Action, and Initial Phase 1 Topline Results

Preventable Causes of Death in the U.S.[1]





Initial Phase 1 Topline Results (N=48)[2]

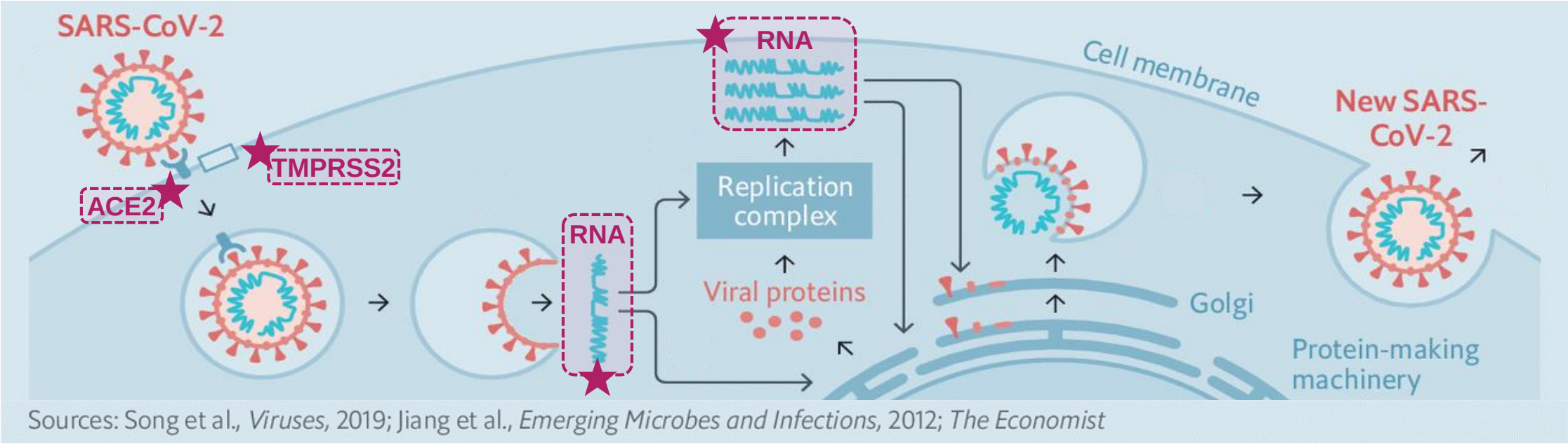
- >90% AGT knockdown
- >10 mmHg reduction in mean 24-h systolic blood pressure relative to placebo
- Durability supportive of once quarterly and possibly less frequent dosing
- Encouraging safety and tolerability profile with no drug-related SAEs

Results to be presented at scientific meeting in **late 2020**

[1] McClellan et al., Circulation, 2019
[2] As of April 29, 2020 data transfer date

COVID-19 Targeting Strategy

Broad, Multifaceted RNAi Therapeutics Effort with Vir



Virus

- SARS-CoV-2 RNA genome and viral transcripts
- Selected development candidate, ALN-COV (VIR-2703), with potent and highly cross-reactive activity; plan for accelerated IND filing at or around year-end 2020

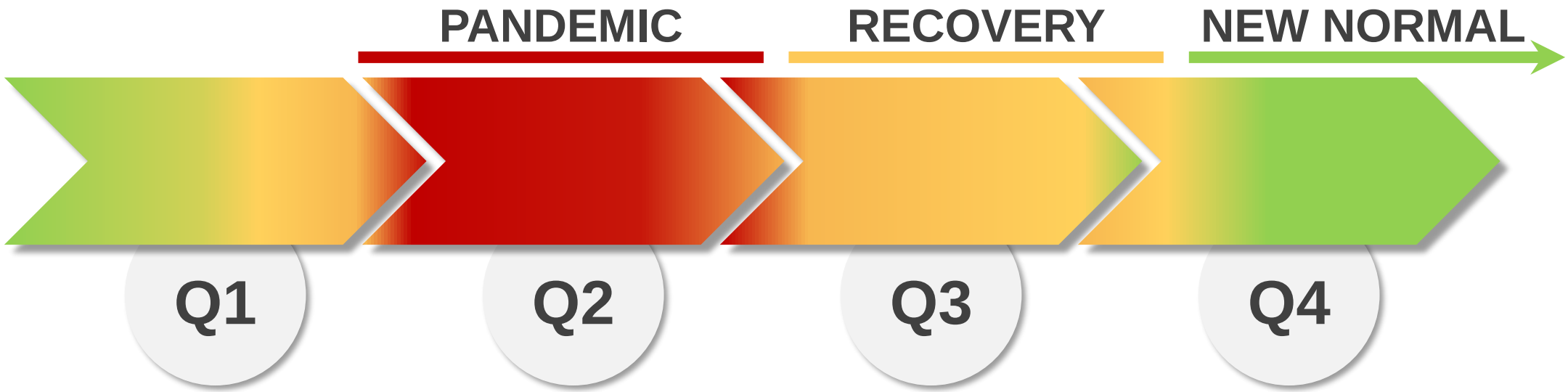
Host Factors

- ACE2: viral entry receptor for SARS-CoV-2 and other coronaviruses
- TMPRSS2: cleaves SARS-CoV-2 spike protein to facilitate cellular attachment to ACE2
- Third target expected from Vir's functional genomics efforts to identify novel host factors pertinent to coronaviral infection

Vir to lead development of potential coronavirus RNAi therapeutic candidates discovered by Alnylam, with Alnylam retaining option for 50-50 participation

COVID-19 Outlook

Potential Risks and Mitigations for Clinical Development



Study Integrity	Widened assessment windows; supplemental case report forms to capture COVID-19 impacts; sensitivity analyses in SAPs		
Patient Continuity	Expanded efforts for home administration; widened visit windows and virtual visits; remote lab and AE collection		Continue to support flexibility to ensure patient continuity and safety
Trial Enrollment	Enrollment delays globally; continuing site activation efforts where possible	Gradual recovery in patient enrollment	Return to pre-pandemic levels

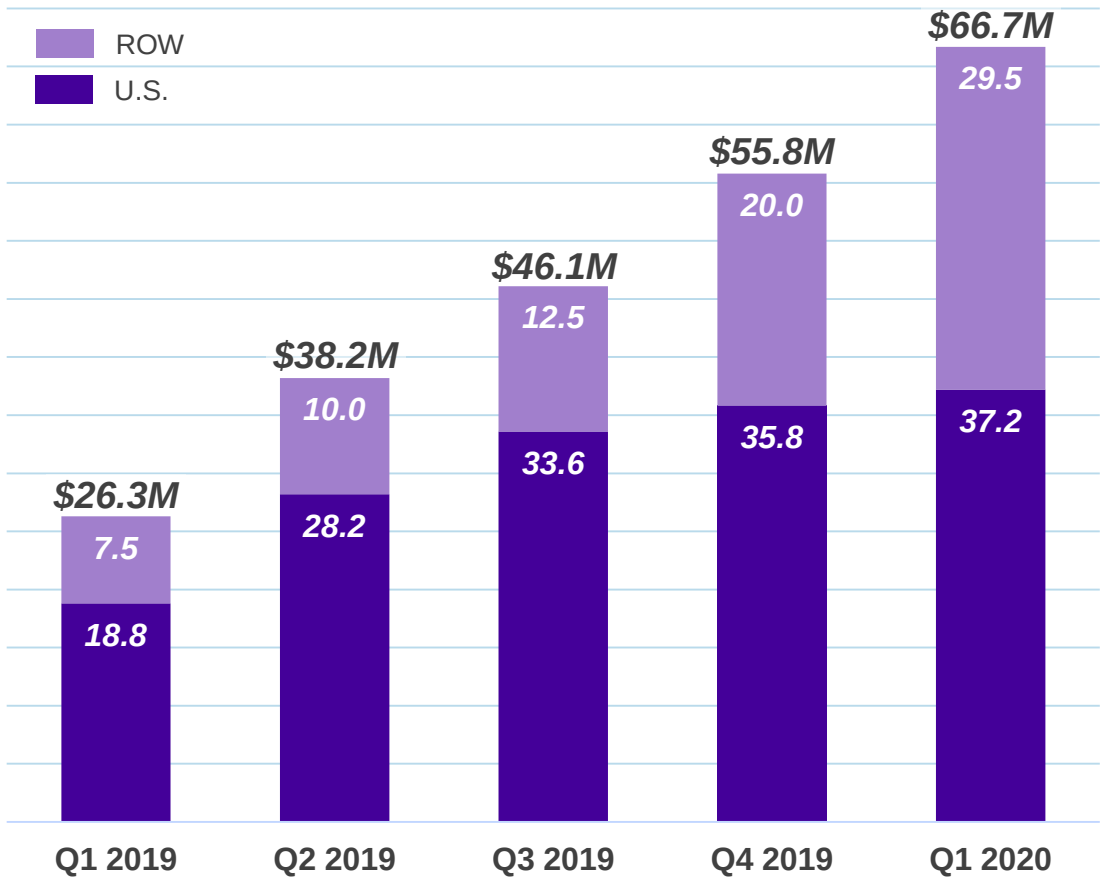
Jeff Poulton

Chief Financial Officer

Financial Summary and Guidance

Global ONPATTRO Performance

Revenue ($M)



Highlights

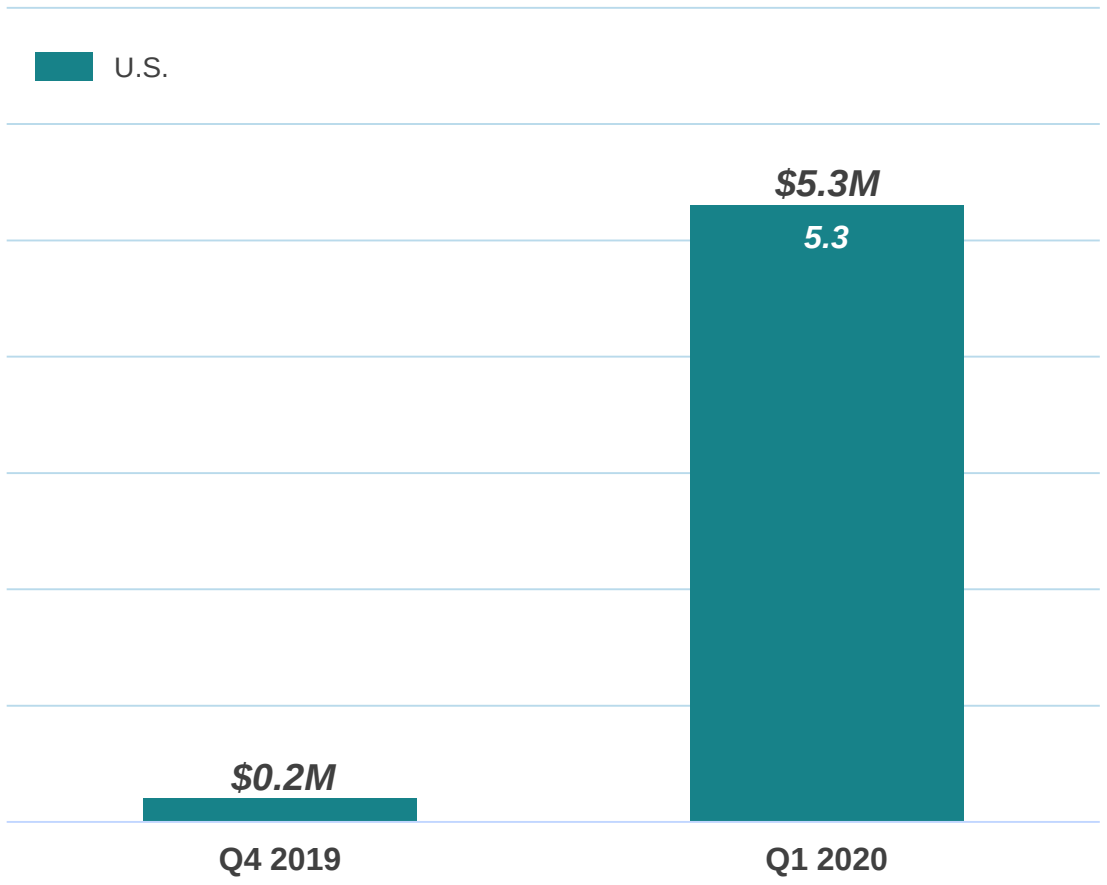
	YoY % Growth	QoQ % Growth
U.S.	98%	4%
ROW	292%	47%
Global	154%	19%

- U.S. QoQ growth negatively impacted by ~8% due to decrease in Q1 2020 channel inventory of ~$0.8M compared to increase of ~$1.8M in Q4 2019
- U.S. QoQ growth positively impacted by ~6% due to decrease in Q1 2020 gross-to-net deductions compared to Q4 2019
- Strength in international results broadly across markets in both Europe and Japan
- Minimal COVID-19 impact on Q1 product sales

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

Global GIVLAARI Performance

Revenue ($M)



Highlights

- >60 Start Forms, >50 patients on commercial therapy drive strong U.S. launch
- International launch (Germany) expected in Q2 2020
- Minimal COVID-19 impact on Q1 product sales

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

First Quarter 2020 Financial Summary

Financial Results ($ millions)	Q1 2020	Q1 2019	YoY % Change
ONPATTRO Net Product Revenues	$66.7	$26.3	154%
GIVLAARI Net Product Revenues	$5.3	-	n/a
Net Revenue from Collaborations	$27.5	$7.0	293%
Total Revenues	$99.5	$33.3	199%
Cost of Goods Sold	$13.3	$3.3	297%
Gross Margin (% of net product revenues)	*82%*	*87%*	-
GAAP R&D Expenses	$169.6	$129.1	31%
Non-GAAP R&D Expenses[1]	$153.5	$113.0	36%
GAAP SG&A Expenses	$126.8	$89.6	41%
Non-GAAP SG&A Expenses[1]	$108.2	$73.7	47%
GAAP Operating Income/(Loss)	($210.2)	($188.8)	
Non-GAAP Operating Income/(Loss)[2]	($175.6)	($156.8)	
Cash & Investments[3]	$1,366.9	$1,551.0	

[1] Non-GAAP R&D and SG&A expenses exclude stock-based compensation expenses
[2] Non-GAAP net loss excludes stock-based compensation expenses and unrealized gains on marketable equity securities
[3] 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	$285M - $315M	$270M - $300M
GIVLAARI Net Product Revenues	No guidance provided	Unchanged
Net Revenues from Collaborations	$100M - $150M	Unchanged
Total Non-GAAP Combined R&D + SG&A Expenses[1]	$1,025M - $1,125M	$1,000M - $1,075M

Some negative impact from COVID-19 expected in Q2 2020 with ONPATTRO revenues potentially decreasing by ~10% vs. Q1 2020; improvement and growth expected in second half of 2020

$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 operating expenses exclude $155-175 million of stock-based compensation from estimated GAAP R&D and SG&A expenses

[2] As of May 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	●	●	●

Q1 2020 Financial Results

Q&A Session

Alnylam PHARMACEUTICALS

Q1 2020 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

Reconciliation of Selected GAAP Measures to Non-GAAP Measures
(In thousands, except per share amounts)

	Three Months Ended March 31,	
	2020	**2019**
Reconciliation of GAAP to Non-GAAP Research and development:		
GAAP Research and development	169,571	129,127
Less: Stock-based compensation expenses	(16,049)	(16,125)
Non-GAAP Research and development	153,522	113,002
Reconciliation of GAAP to Non-GAAP Selling, general and administrative:		
GAAP Selling, general and administrative	126,761	89,608
Less: Stock-based compensation expenses	(18,529)	(15,907)
Non-GAAP Selling, general and administrative	108,232	73,701
Reconciliation of GAAP to Non-GAAP operating loss:		
GAAP operating loss	(210,158)	(188,788)
Add: Stock-based compensation expenses	34,578	32,032
Non-GAAP operating loss	(175,580)	(156,756)

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