



Third Quarter 2020 Financial Results

November 5, 2020

Agenda

Welcome

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

Overview

- John Maraganore, Ph.D.
Chief Executive Officer

Commercial/Med Affairs Highlights

- Andy Orth
Senior Vice President, Head of U.S. Business

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
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. 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 any 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, including ONPATTRO® (patisiran), GIVLAARI® (givosiran), inclisiran, lumasiran and vutrisiran; 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 and GIVLAARI; 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; 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, 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, 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 gain on marketable equity securities, costs associated with our strategic financing collaboration, loss on contractual settlement and change in estimate of contingent liabilities. 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, loss on contractual settlement and change in estimate of contingent liabilities 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

Alnylam Q3 Context

Building a Top-Tier Biopharmaceutical Company



**Strong Commercial
Progress**



**Productive Organic
Pipeline**



**Moving Toward
Self-Sustainability**



2020*

3 STArS	→	4
3 Marketed Products	→	4
10 Clinical Programs	→	12
4 Late Stage Programs	→	6

* Numbers represent expectations as of 11/5/20

SAVE THE DATE

Alnylam R&D Day

December 15-16, 2020

Virtual Event



Andy Orth

Senior Vice President, Head of U.S. Business

Commercial/Med Affairs Highlights

ONPATTRO® Launch Update: Q3 2020

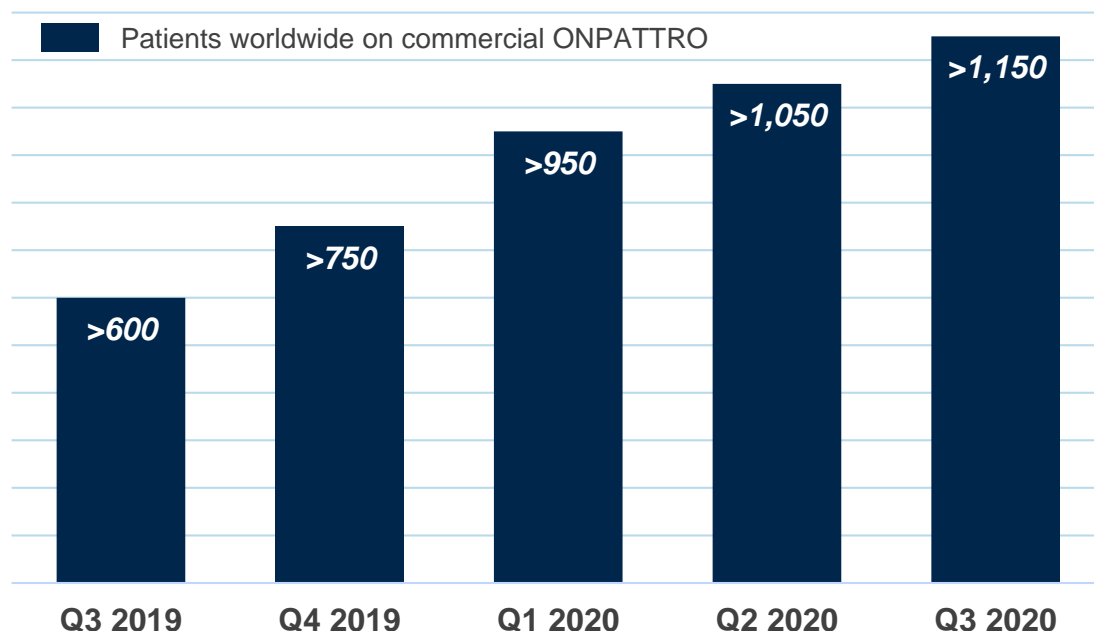
Strong Performance with Significant Growth

\$82.5M

ONPATTRO Global Q3
Net Product Revenues

>1,150

Patients Worldwide on Commercial
ONPATTRO at end of Q3 2020



Q3 U.S. Highlights



Notable demand increase and strong compliance



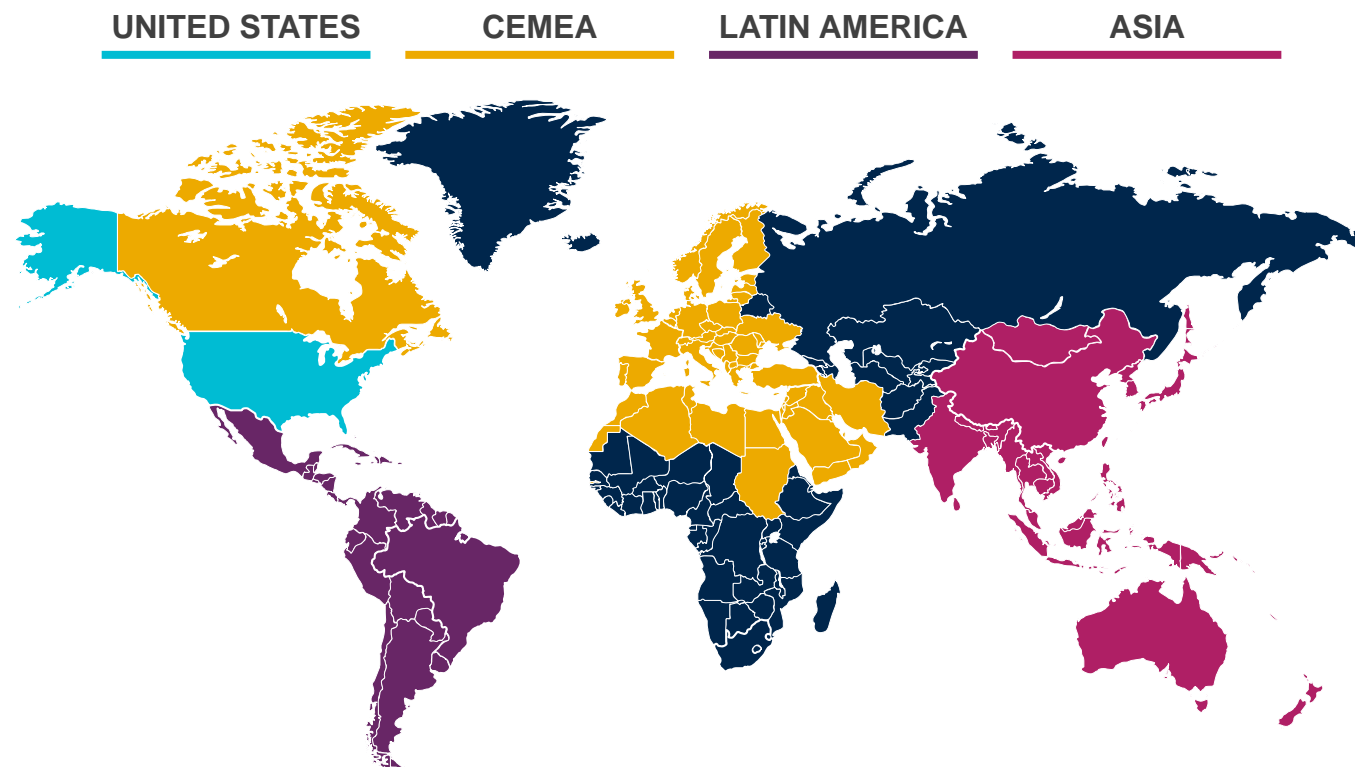
Cardiologists make up more than half of new prescribing physicians



ONPATTRO Global Commercialization

Increasing Access and Value Recognition

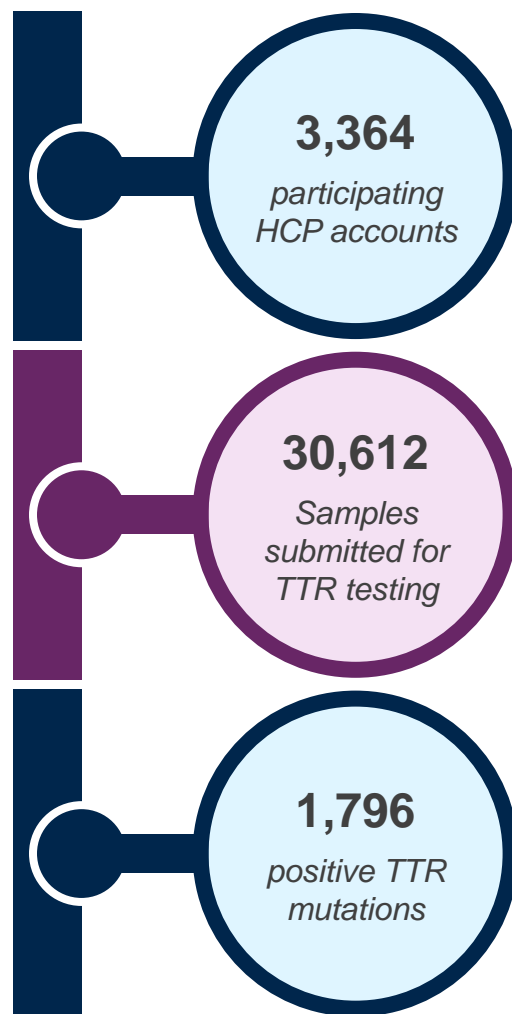
- Significant progress with global ONPATTRO availability
 - Recent launch in Portugal
 - Conclusion of price negotiations in France
 - Completion of initial access agreement in Canada
 - Achievement of regulatory approval in Israel
 - About 20 countries outside U.S. now selling ONPATTRO through direct reimbursement, named patient sales, or reimbursed expanded access
 - Uptake observed from both first-line treatment and switching from other products, including stabilizers
 - >50% of new patients outside U.S. have switched from stabilizers



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

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



ONPATTRO® Wins 2020 Prix Galien USA Award Best Biotechnology Product

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



GIVLAARI® Launch Update: Q3 2020

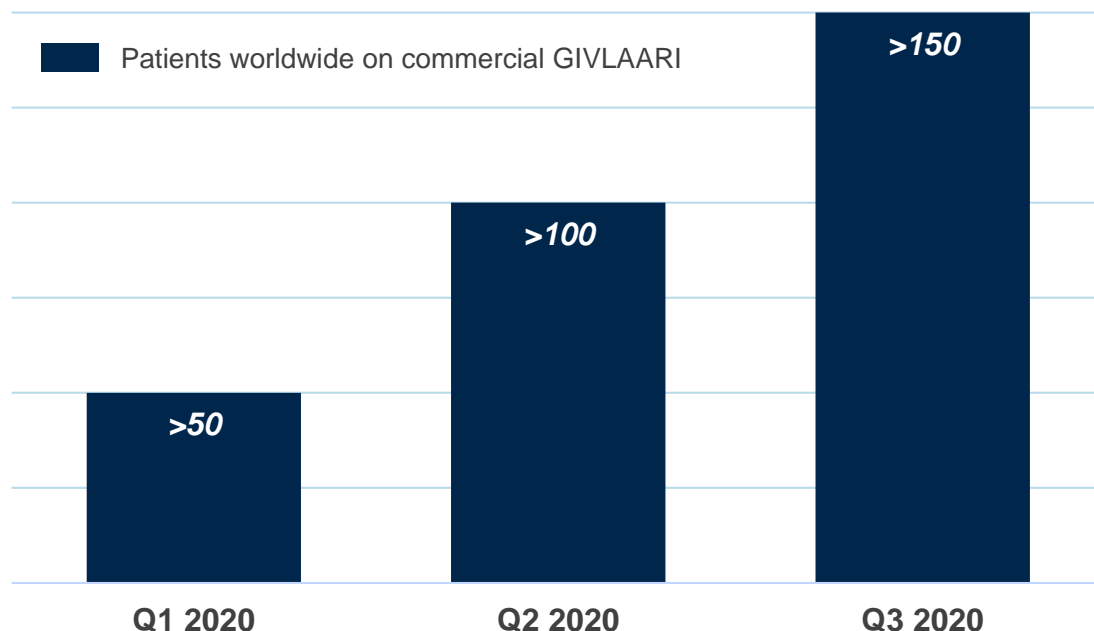
Strong Initial Performance

\$16.7M

GIVLAARI Q3
Net Product Revenues

>150

Patients on Commercial GIVLAARI
at end of Q3 2020



U.S. Demand and Access

10

Value-Based Agreements (VBAs) finalized

>90%

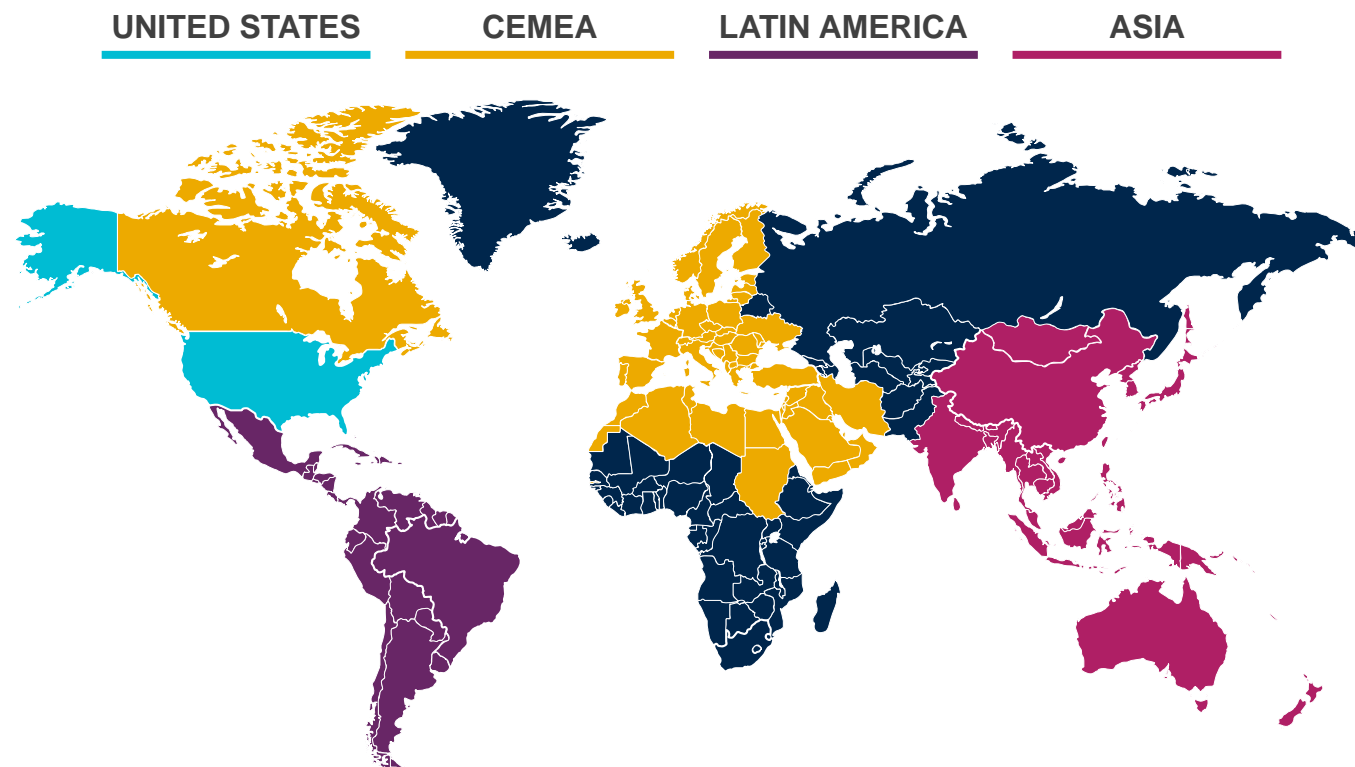
U.S. lives with confirmed access to
GIVLAARI, if prescribed



GIVLAARI Global Commercialization

Ensuring GIVLAARI Availability Around the World

- Successful ongoing launch in Germany
- Named patient sales in France and other countries
- Strong start for market access in CEMEA
 - ASMR II granted by HAS in France
 - “Considerable Added Benefit” rating obtained in Germany
 - Strong HTA rating secured in Italy
- Recent approval in Canada
- Submitted JNDA in Japan



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

The third RNAi therapeutic has received **POSITIVE CHMP OPINION***



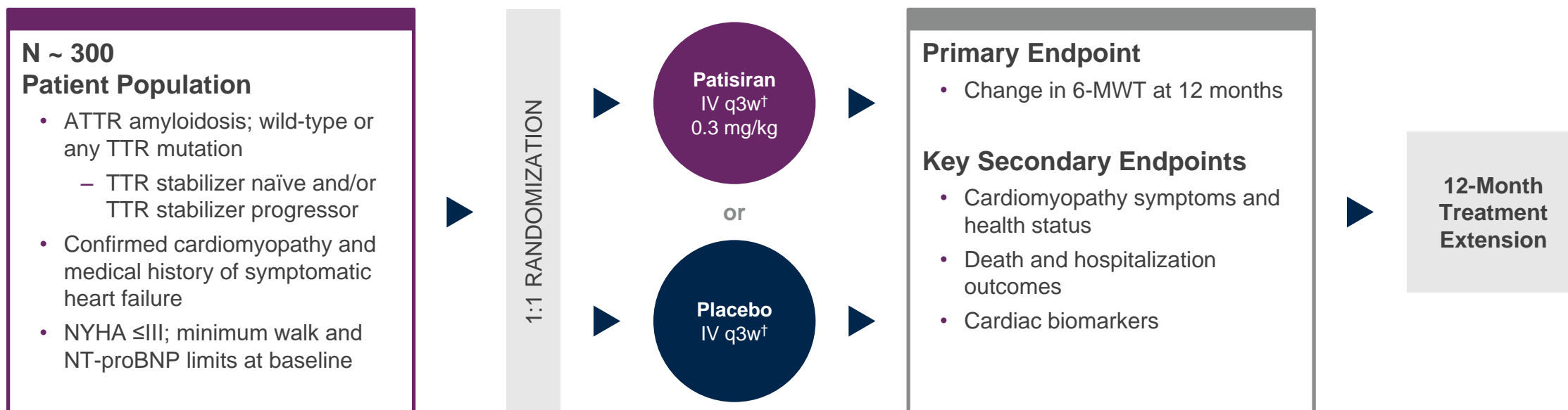
Akshay Vaishnaw, M.D., Ph.D.

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



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 Hereditary & Wild-Type ATTR Amyloidosis

HELIOS



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

Enrollment complete

Topline results expected
early 2021



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

Enrollment ongoing

Study includes optional
interim analysis

Opportunity for q6M Vutrisiran Dosing Regimen

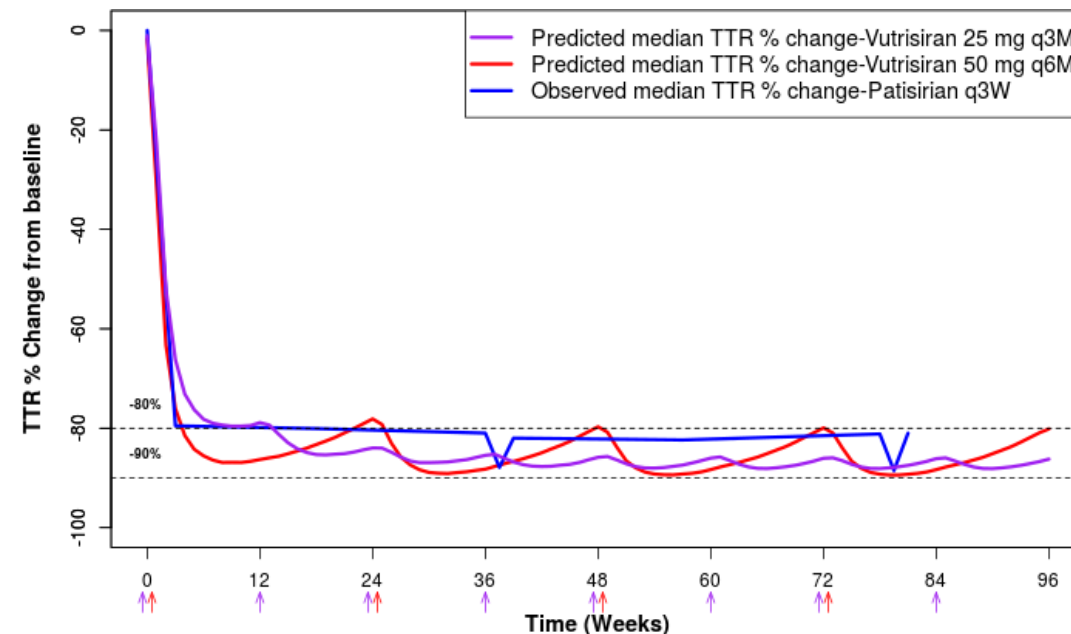
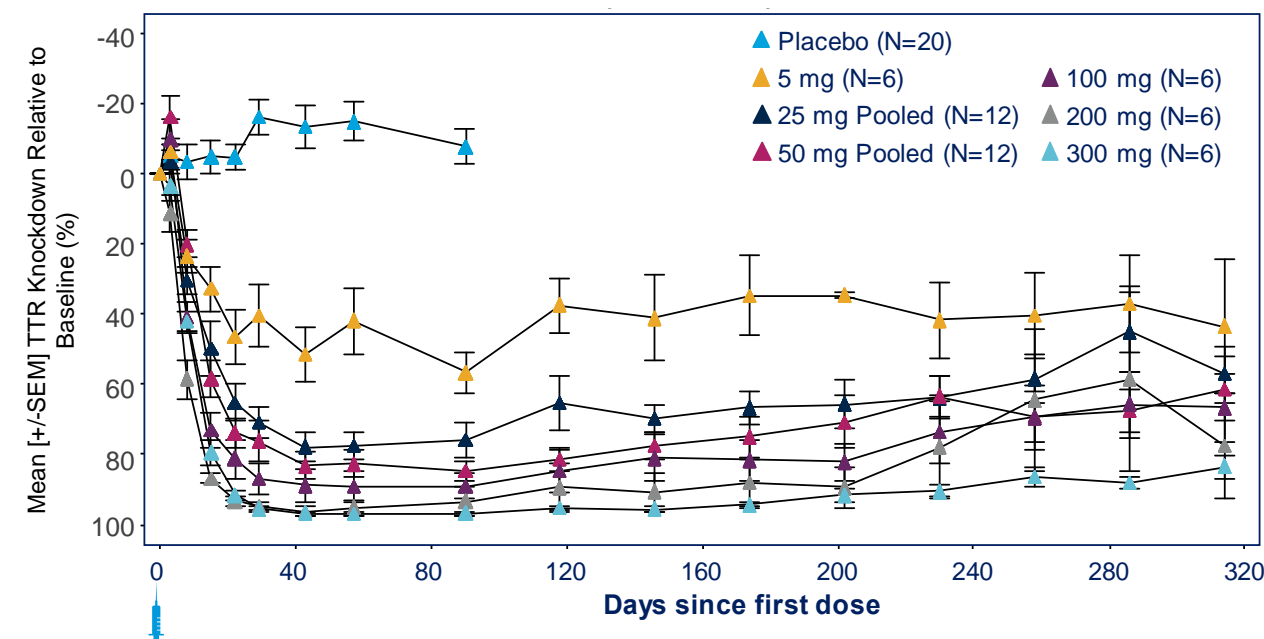
Modeling Supports Potential Biannual 50mg Dosing Regimen in Addition to Quarterly 25mg Dosing Regimen

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
- 50mg q6M vutrisiran dosing predicted to have similar TTR reduction as 0.3mg/kg q3W patisiran
- Comparable average TTR reduction at steady state predicted for both 25mg and 50mg repeat dosing

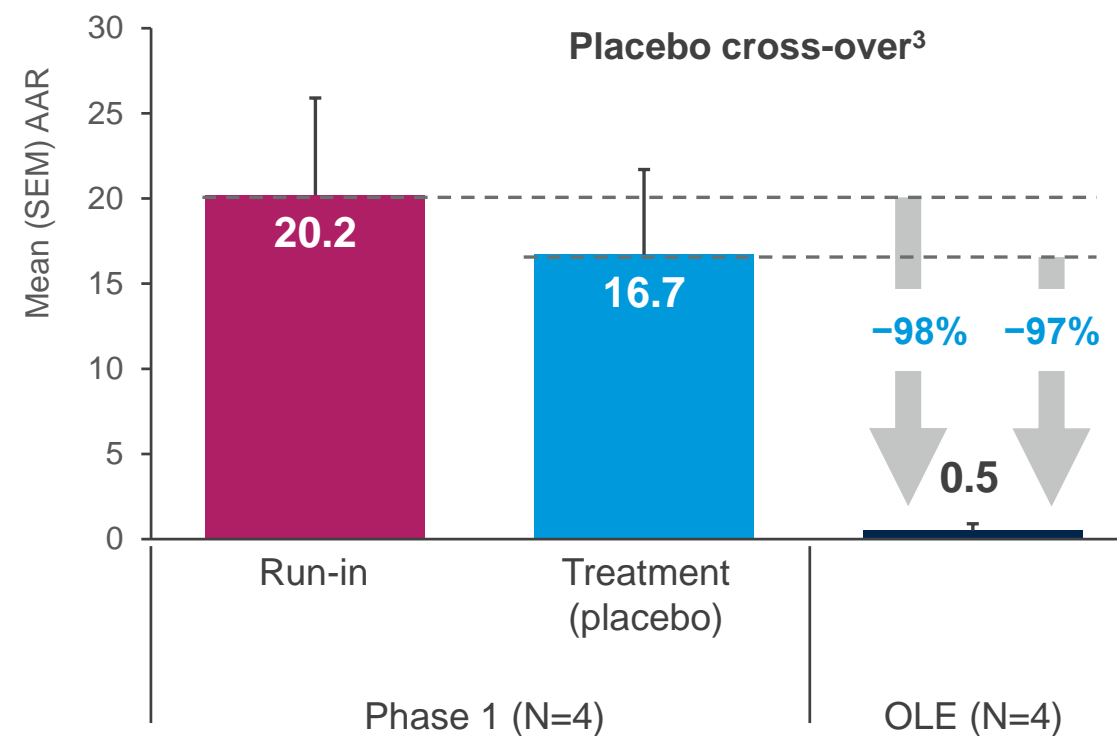
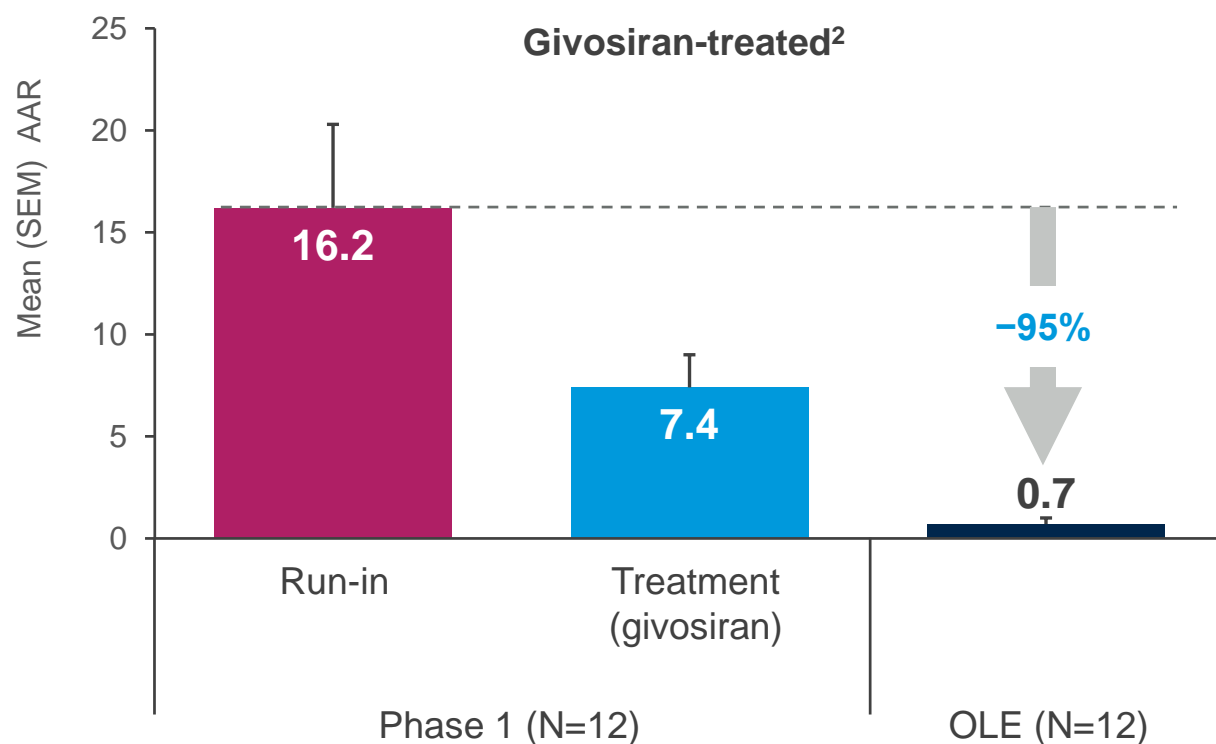


[†] Taubel J, et al. Phase 1 Study of ALN-TTRsc02, a Subcutaneously Administered Investigational RNAi Therapeutic for the Treatment of Transthyretin-Mediated Amyloidosis. ISA 2018: XVIIIth International Symposium of Amyloidosis; Kumamoto, Japan; March 2018 (poster)

Givosiran Phase 1/2 OLE Study

Maintenance and Potential Enhancement of Clinical Activity with Continuous Monthly Dosing

Annualized Attack Rate¹



¹ Attacks requiring hospitalization, urgent healthcare visit, or IV hemin at home

² Aggregated across all dose groups. Mean time in Phase 1 run-in and treatment of 103 days and 165 days, respectively; mean time in OLE of 822 days

³ Mean time in Phase 1 run-in and treatment of 77 days and 175 days, respectively; mean time in OLE of 913 days

Lumasiran **ILLUMINATE•B** Phase 3 Study (*Interim Results*)

Efficacy Results and Safety Profile in Pediatric Patients Similar to Those Observed in ILLUMINATE-A

Rapid and sustained reduction in spot urinary oxalate:creatinine ratio across all weight groups

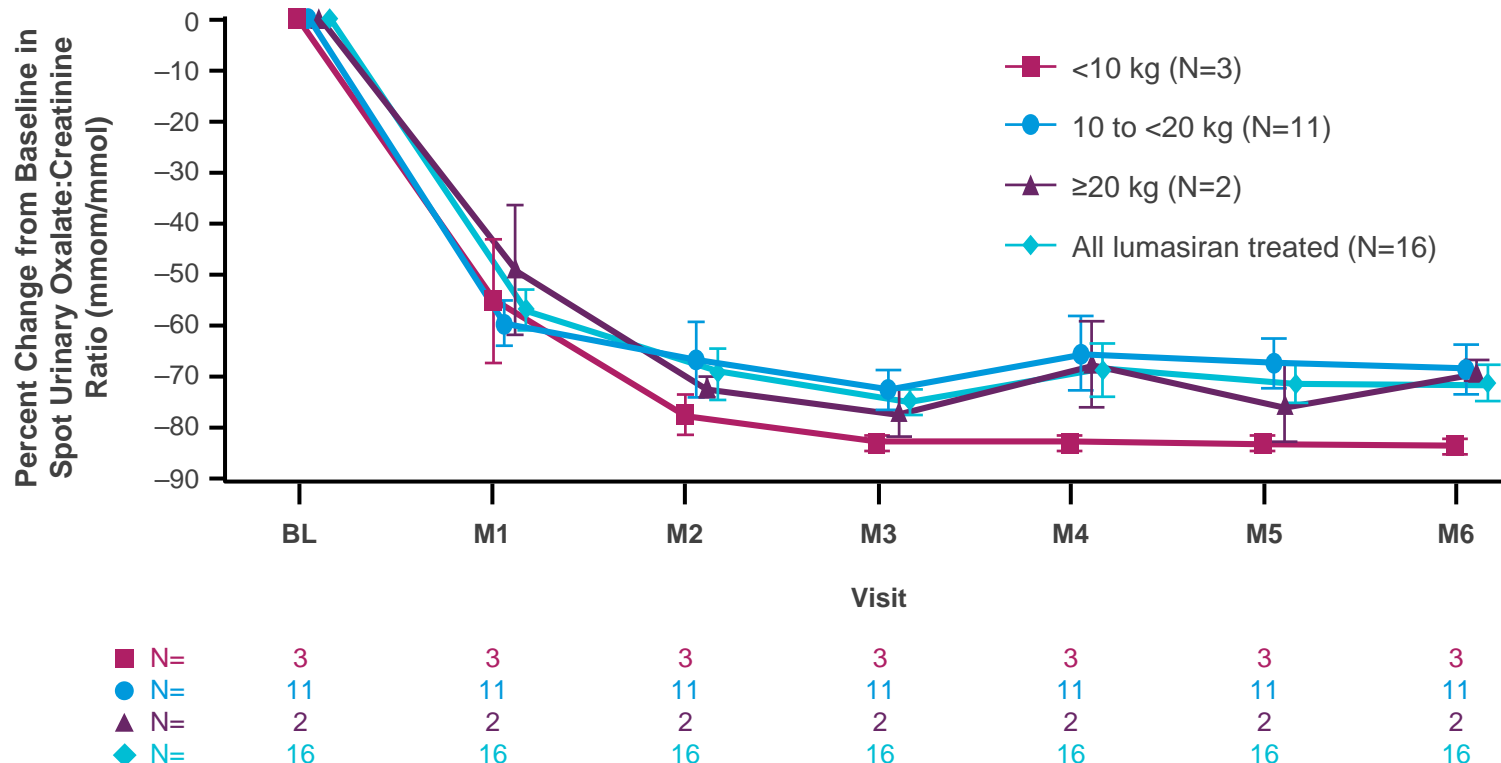
Primary Endpoint Result

-71%

LS mean reduction in spot urinary oxalate:creatinine ratio from BL to M6 (average change of M3-M6)

Safety

- No deaths, discontinuations or withdrawals, or severe AEs
- One serious AE occurred, considered not related to lumasiran¹
- Most common related AE was injection-site reactions
 - All mild and transient in severity
- No clinically relevant changes in laboratory measures, vital signs, or electrocardiograms related to lumasiran observed
- No hepatic events reported



Data in graph are presented as mean ± SEM of observed values.

¹ Viral infection, considered not related to the study drug by the Investigator

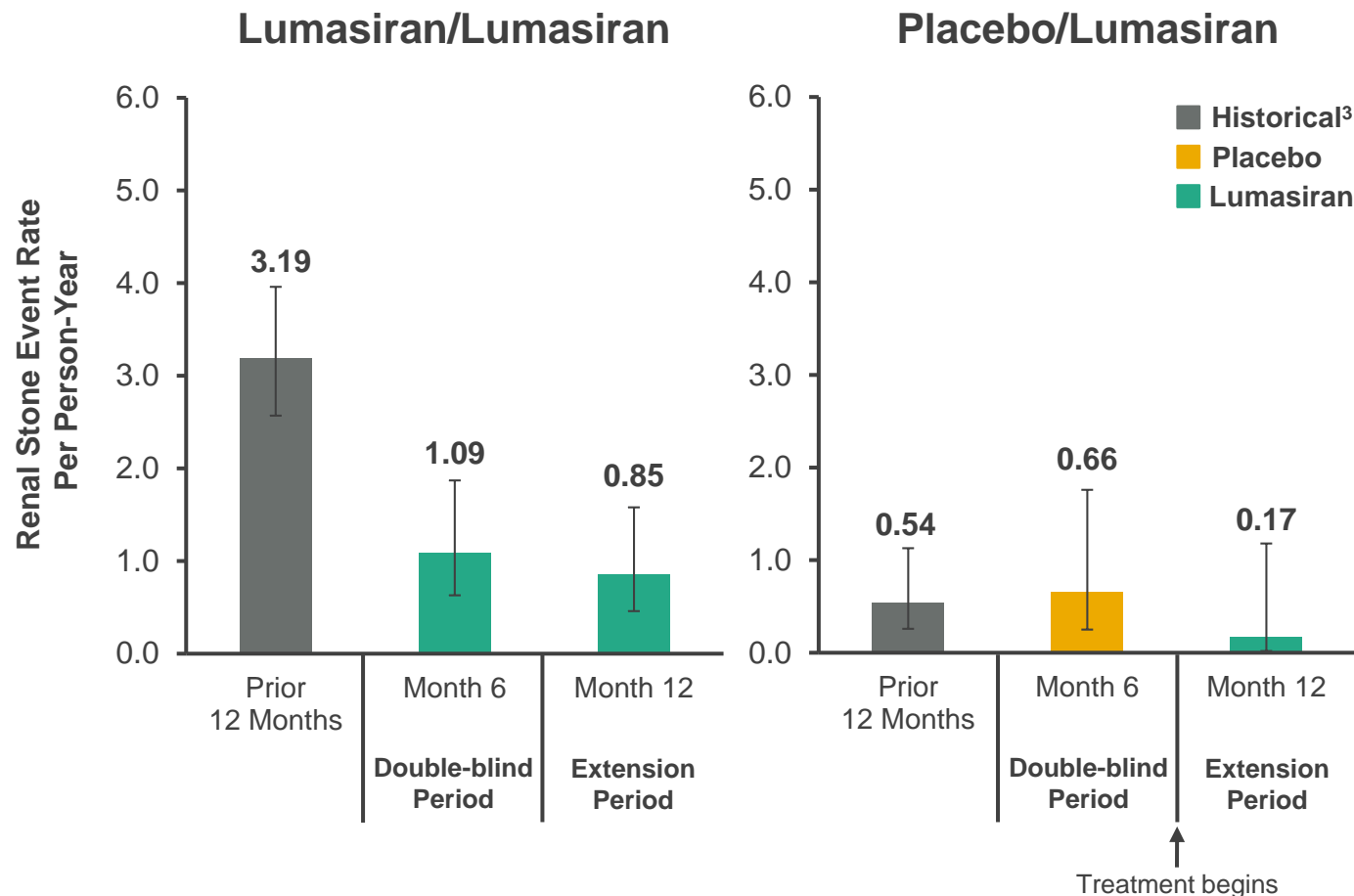
BL, baseline; M, month; SEM, standard error of the mean; ULN, upper limit of normal; AE, adverse event; SAE, serious adverse event



Renal Stone Events¹

Lower Renal Stone Event Rates Were Seen After 6–12 Months of Treatment²

- In the Lumasiran/Lumasiran group, renal stone event rates decreased with lumasiran treatment through Month 12
- In the Placebo/Lumasiran crossover group, renal stone event rates decreased after 6 months of treatment with lumasiran
- Renal stone event rate data will continue to be collected in the Extension Period of ILLUMINATE-A



¹ A renal stone event is defined as an event that includes at least one of the following: visit to healthcare provider because of a renal stone, medication for renal colic, stone passage, or macroscopic hematuria due to a renal stone. ² Randomization was not stratified by renal stone events at baseline. ³ Patient reported history of renal stone events

Error bars represent 95% confidence interval



Exploratory Endpoints: Renal Stones and Nephrocalcinosis

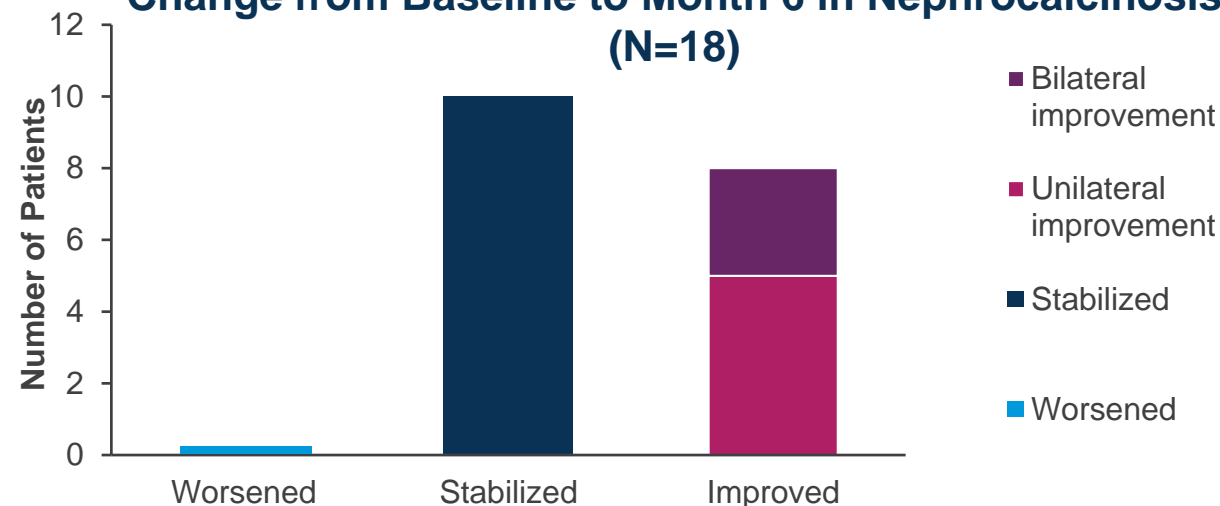
No Change in Renal Stone Event Rates after Lumasiran Treatment;
Improved Nephrocalcinosis in 8/18 Patients

Renal stone events

	Reported History (12 Months Prior to Consent)	Lumasiran Treated Period (6 Months)
Patients with renal stone events	3	2
Total renal stone events	4	2
Renal stone event rate (person-year) ¹	0.24 (95% CI 0.09, 0.63)	0.24 (95% CI 0.06, 0.96)

- A renal stone event was defined as one of the following: visit to healthcare provider because of a renal stone, medication for renal colic, stone passage, macroscopic hematuria due to a renal stone
- The low rates of renal stone events in these patients were unchanged between the 12-month historical recall and the first 6 months of treatment

Change from Baseline to Month 6 in Nephrocalcinosis (N=18)



- Nephrocalcinosis was graded on a standardized 4-point scale² as ascertained by renal ultrasound at baseline and Month 6, centrally read by a radiologist blinded to the timepoint
- 14/18 patients had nephrocalcinosis at baseline
- After 6 months of lumasiran treatment, no patient worsened, 10 remained stable, and 8 showed improvement in nephrocalcinosis
- Of improved patients, 3 improved in both kidneys, 5 in one kidney

Late Stage Partnered Program Opportunities

INCLISIRAN



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 goal¹

**Positive CHMP opinion received;
FDA approval anticipated by YE 2020**

FITUSIRAN



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 dosing³

~90%

Emicizumab patients experienced acute bleeds²

Two of three Phase 3 studies fully enrolled

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	<i>Complement-Mediated Diseases</i>					50-50 (Regeneron)
Cemdisiran/Pozelimab Combo²	<i>Complement-Mediated Diseases</i>					Milestone/Royalty (Regeneron)
ALN-AAT02 (DCR-A1AT)³	<i>Alpha-1 Liver Disease</i>					Ex-U.S. option post-Phase 3 (Dicerna)
ALN-HBV02 (VIR-2218)	<i>Hepatitis B Virus Infection</i>					50-50 option post-Phase 2 (Vir)
ALN-AGT	<i>Hypertension</i>					Global
ALN-HSD	<i>NASH</i>					50-50 (Regeneron)

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

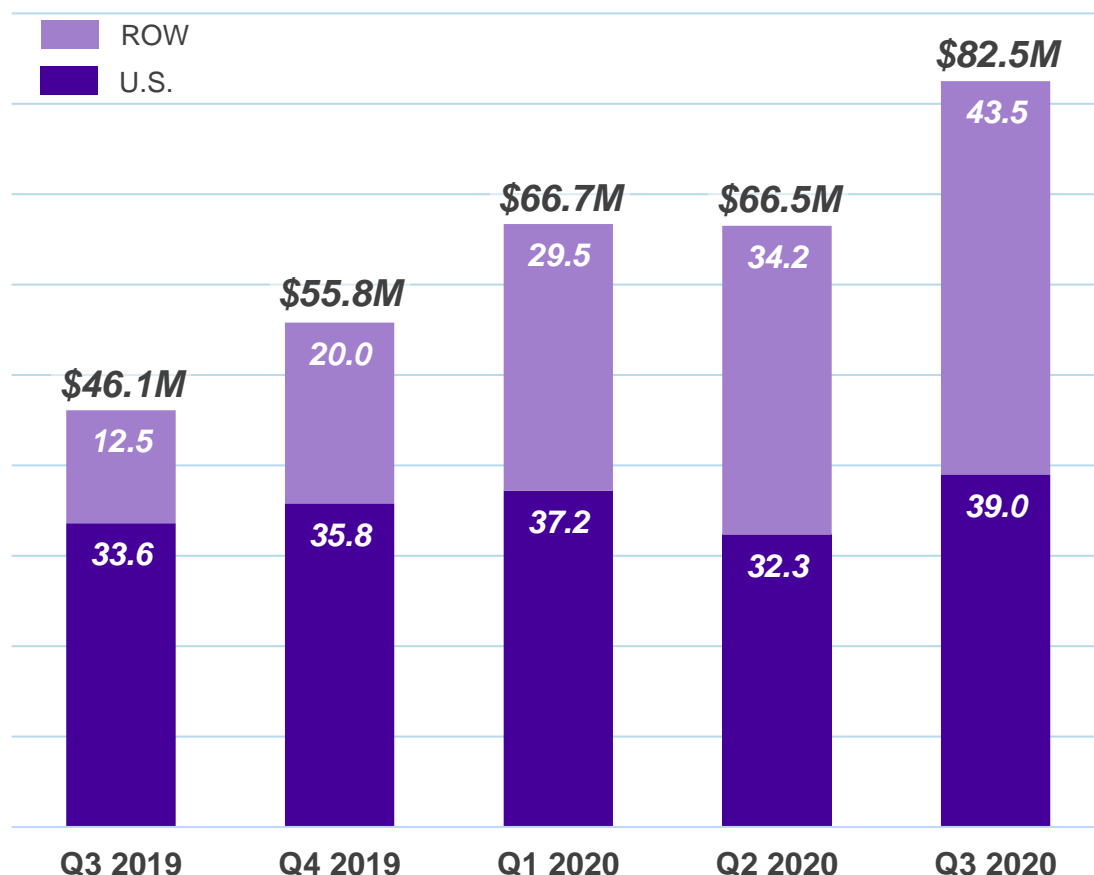
Jeff Poulton

Chief Financial Officer

Financial Summary and Guidance

Global ONPATTRO Performance

Revenue (\$M)



Highlights

	YoY % Growth	QoQ % Growth
U.S.	16%	21%
ROW	249%	27%
Global	79%	24%

- U.S. QoQ growth was favorably impacted by the following:
 - Increase in patient demand due to addition of new patients on therapy and improved patient compliance (+14%)
 - Increase in channel inventory in Q3 compared with decrease in Q2 offset by modest increase in gross to net sales deductions (+7%)
- ROW QoQ growth was favorably impacted by the following:
 - Increase in patient demand primarily from strength across EU5 major markets, initial Portugal launch, and Japan (+19%)
 - One-time benefits associated with finalizing price in France and initial access agreement in Canada (+8%)

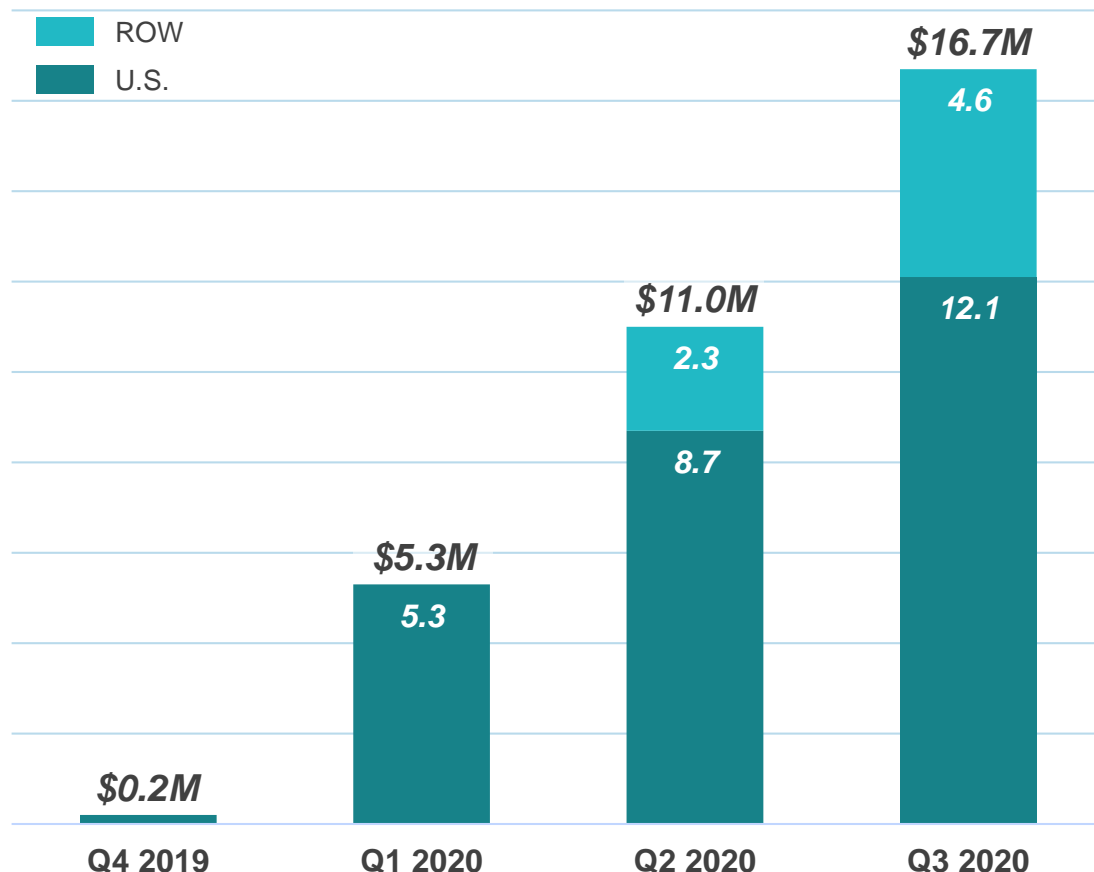


 (patisiran) lipid complex injection

 10 mg/5 mL

Global GIVLAARI Performance

Revenue (\$M)



Highlights

	QoQ % Growth
U.S.	40%
ROW	96%
Global	52%

- >150 global patients on therapy since launch
- Continued progress with VBAs in U.S. with 10 signed and confirmed access for over 90% of covered lives
- Continued progress with market access efforts across the CEMEA region, with ongoing launch in Germany, cohort ATU supply in France, and named patient sales in other countries



Third Quarter 2020 Financial Summary

Financial Results (\$ millions)	Q3 2020	Q3 2019	Q2 2020	YoY % Change	QoQ % Change
ONPATTRO Net Product Revenues	\$82.5	\$46.1	\$66.5	79.1%	24.0%
GIVLAARI Net Product Revenues	\$16.7	-	\$11.0	N/A	51.8%
Net Revenues from Collaborations	\$26.6	\$24.0	\$26.4	11.1%	0.8%
Total Revenues	\$125.9	\$70.1	\$104.0	79.6%	21.1%
Cost of Goods Sold	\$21.8	\$5.2	\$19.9	318.1%	9.4%
<i>GM as % of Total Revenues¹</i>	<i>82.7%</i>	<i>92.6%</i>	<i>80.8%</i>	-	-
Non-GAAP R&D Expenses ²	\$148.1	\$138.1	\$139.2	7.3%	6.4%
Non-GAAP SG&A Expenses ²	\$114.5	\$97.1	\$109.6	17.9%	4.5%
Non-GAAP Operating Loss ²	(\$158.5)	(\$170.3)	(\$164.8)	-	-

Financial Results (\$ millions)	Sep 30, 2020	Dec 31, 2019
Cash & Investments ³	\$1,833.9	\$1,536.2

¹ GM as a % of Product Sales for Q3 2020 is 79.0%, Q3 2019 is 88.7%, Q2 2020 is 76.4% (Q3 '20 excludes \$1.0M and Q2'20 excludes \$1.7M in COGS associated with revenue from collaborations).

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

Updated 2020 Full-Year Guidance

	Prior FY 2020 Guidance	Updated FY 2020 Guidance ²
ONPATTRO Net Product Revenues	\$280M - \$300M	\$295M - \$310M
GIVLAARI Net Product Revenues	No guidance provided	Unchanged
Net Revenues from Collaborations	\$100M - \$150M	Unchanged
GAAP Combined R&D and SG&A Expenses	\$1,130M - \$1,225M	\$1,160M - \$1,255M
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 operating expenses exclude \$160-\$180 million (previously \$130-\$150 million) primarily related to stock-based compensation and a change in estimate of contingent liabilities from estimated GAAP R&D and SG&A expenses

² As of November 5, 2020

Yvonne Greenstreet, MBChB, MBA
President and 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
	Global Commercial Execution	✓	✓	●
	Brazil Approval	✓		
	Additional Country Launches	✓	✓	✓
	APOLLO-B Enrollment	✓	✓	●
	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	✗	✓	●
FITUSIRAN (Hemophilia)	Support Sanofi on ATLAS Phase 3	✓	✓	●

Q3 2020 Financial Results

Q&A Session



To those who say “impossible, impractical,
unrealistic,” we say:

CHALLENGE ACCEPTED

Q3 2020 Financial Results

Appendix

Anylam Pharmaceuticals, Inc.

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

	Three Months Ended	
	September 30, 2020	September 30, 2019
Reconciliation of GAAP to Non-GAAP research and development:		
GAAP Research and development	\$ 161,783	\$ 160,796
Less: Stock-based compensation expenses	(13,703)	(22,737)
Non-GAAP Research and development	<u>\$ 148,080</u>	<u>\$ 138,059</u>
Reconciliation of GAAP to Non-GAAP selling, general and administrative:		
GAAP Selling, general and administrative	\$ 167,472	\$ 120,351
Less: Stock-based compensation expenses	(23,561)	(23,272)
Less: Costs associated with the strategic financing collaboration	(763)	—
Less: Loss on contractual settlement	(650)	—
Less: Change in estimate of contingent liabilities	(28,000)	—
Non-GAAP Selling, general and administrative	<u>\$ 114,498</u>	<u>\$ 97,079</u>
Reconciliation of GAAP to Non-GAAP operating loss:		
GAAP operating loss	\$ (225,199)	\$ (216,299)
Add: Stock-based compensation expenses	37,264	46,009
Add: Costs associated with the strategic financing collaboration	763	—
Add: Loss on contractual settlement	650	—
Add: Change in estimate of contingent liabilities	28,000	—
Non-GAAP operating loss	<u>\$ (158,522)</u>	<u>\$ (170,290)</u>