Third Quarter 2019 Financial Results

October 31, 2019

Alnylam® PHARMACEUTICALS

Agenda

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

Q3 2019 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

2019 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 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; our ability to obtain, maintain and protect intellectual property, enforce our intellectual property rights and defend our patent portfolio; our ability to obtain and maintain regulatory approval, pricing and reimbursement for products; our progress in establishing a commercial and ex-United States infrastructure; our ability to successfully launch, market and sell our approved products globally; our ability to successfully expand the indication for ONPATTRO® (patisiran) in the future; competition from others using similar technology and developing products for similar uses; our ability to manage our growth and operating expenses, obtain additional funding to support our business activities and establish and maintain business alliances; the outcome of litigation; and the risk of government investigations; as well as those risks more fully discussed in our most recent quarterly report on Form 10-Q under the caption “Risk Factors.” 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 contains non-GAAP financial measures, including expenses adjusted to exclude certain non-cash expenses and non-recurring gains outside the ordinary course of the Company’s business. These measures are not in accordance with, or an alternative to, GAAP, and may be difference 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 presented herein are stock-based compensation expense and the gain on litigation settlement. 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 gain on litigation settlement 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

Q3 2019 Overview

Alnylam Snapshot

Sustainable Value Creation Potential

Strong Launch Progress

Productive R&D Engine

Positioned for Future Growth

On Path Toward Financial Self-Sustainability

Alnylam Named #1 Employer in *Science* 2019 Top Employer Survey

Barry Greene
President

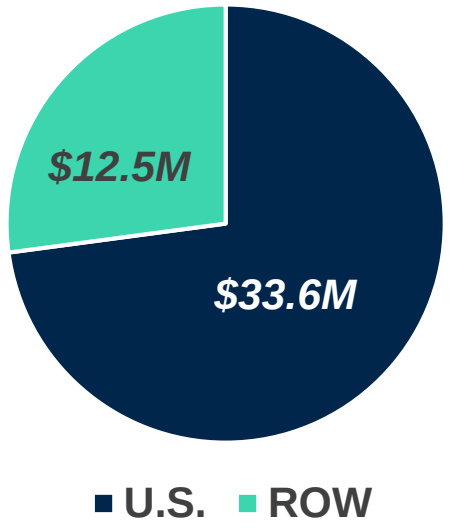
Commercial/Med Affairs Highlights

ONPATTRO® Global Launch Update: Q3 2019

Strong Performance with Significant Growth Potential

$46.1M

ONPATTRO Global Q3 Net Product Revenues



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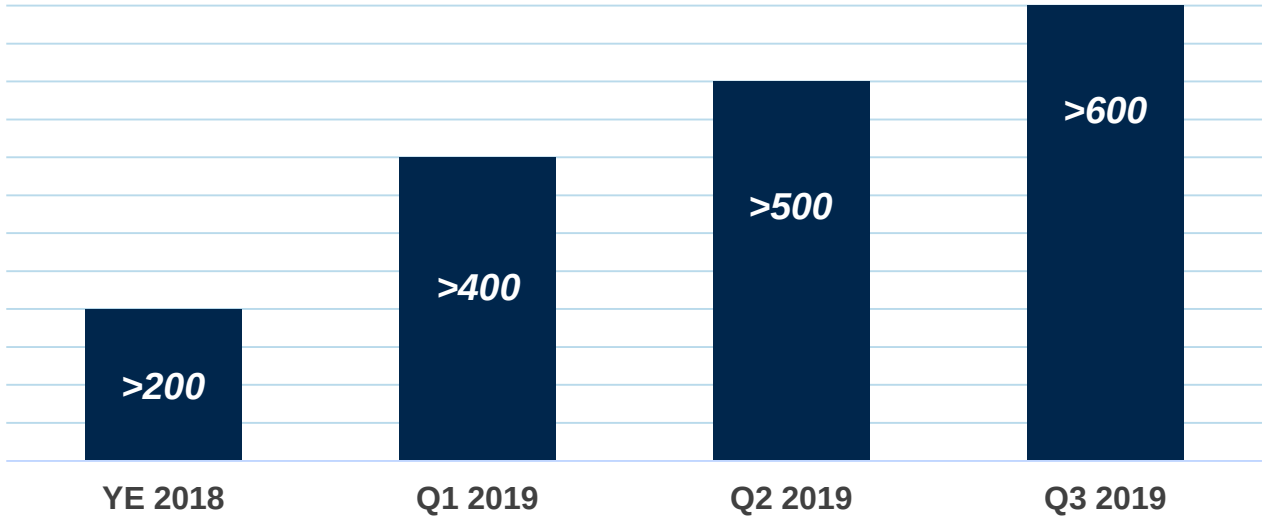
Patients Worldwide on Commercial ONPATTRO at Q3 2019



Expect steady and continued growth with new patient finding, global expansion, and evidence-generating activities

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

Q3 2019 Selected Metrics

50%	First-time ONPATTRO prescribers*
55%	Demand from neurologists*
33%	Demand from cardiologists*
12%	Demand from other specialties*
>90%	Adherence on commercial ONPATTRO
98%	U.S. lives with confirmed access to ONPATTRO, if prescribed†

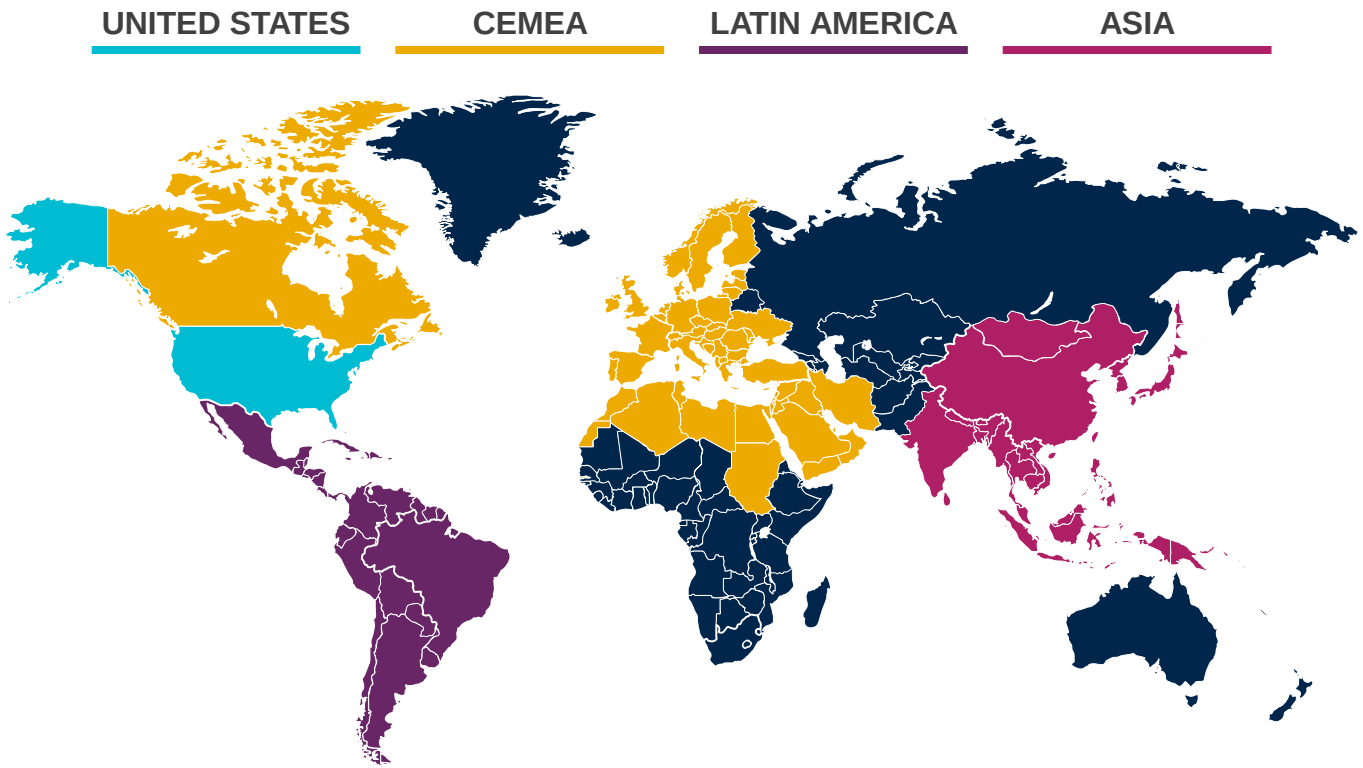
* Based on total Start Forms submitted in Q3 2019. Start Forms are an incomplete picture of U.S. demand.

† Across commercial, Medicare, Medicaid, and other government payer categories (DKP PayerScope® August 1, 2018 through September 30, 2019).

ONPATTRO Global Commercialization

Increasing Access and Value Recognition

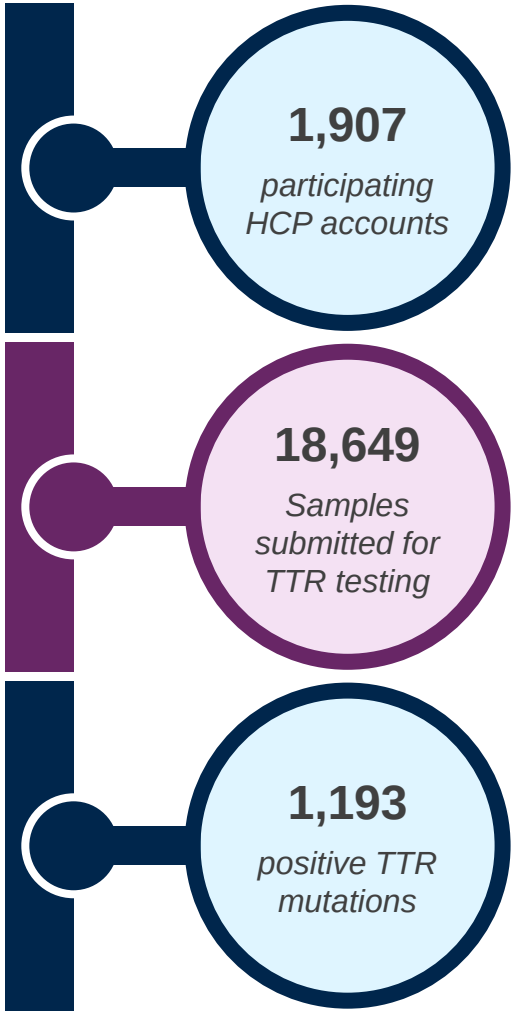
- Significant progress with global ONPATTRO availability
  - Officially launched in Japan and Canada
  - Reimbursement achieved in United Kingdom, Belgium and Germany
  - Over 10 countries outside U.S. now selling ONPATTRO through direct reimbursement, named patient sales, or reimbursed expanded access
  - Uptake observed from both first-line treatment and switching from stabilizer
- Additional countries and regions advancing
  - Latin America plans progressing, with Brazil marketing authorization application submitted and undergoing priority review



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. 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

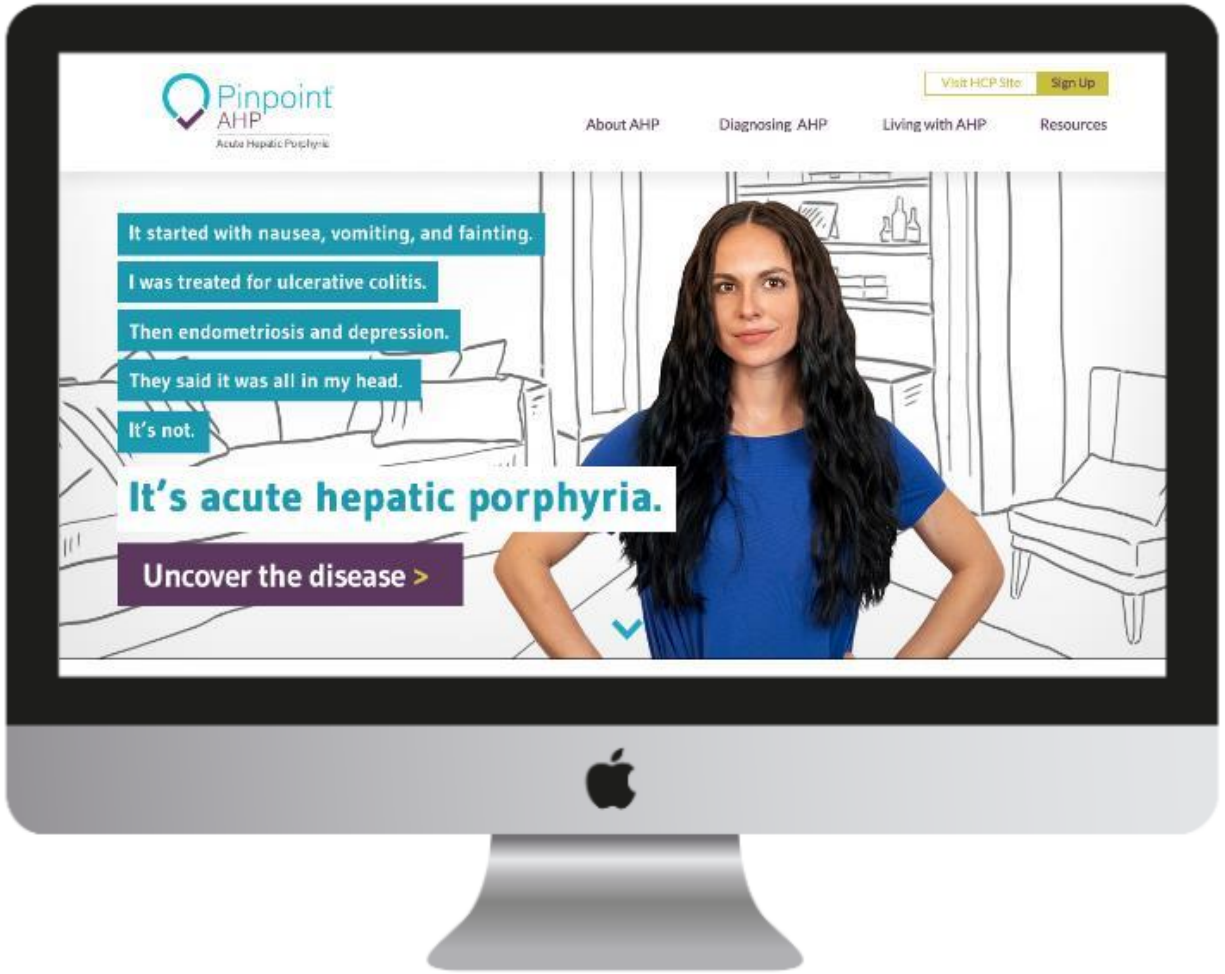
More information regarding this program available at: **www.alnylamact.com**

Data as of October 2019

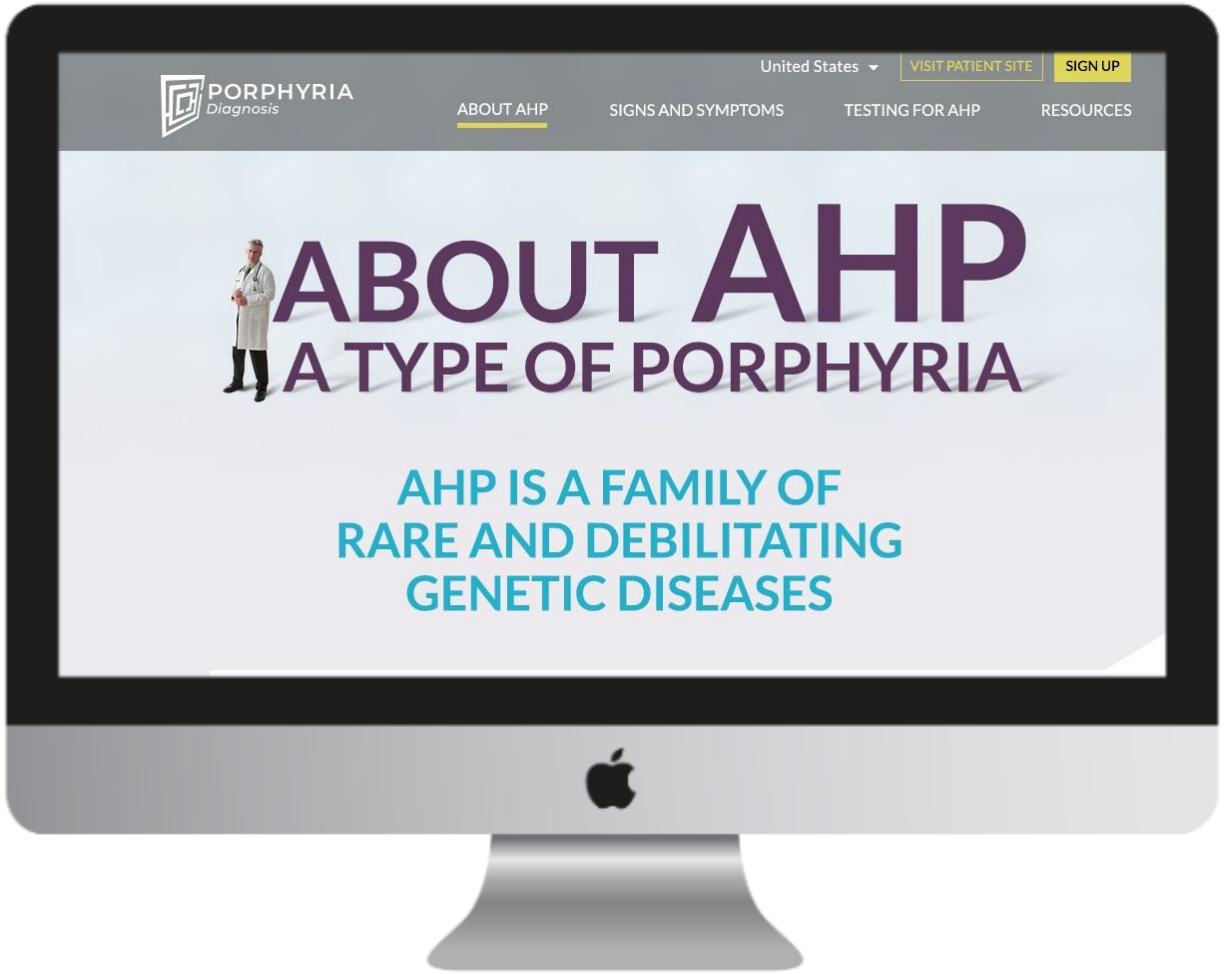
At no time does Alnylam receive patient-identifiable information. Alnylam receives contact information for healthcare professionals who use this program.

Driving AHP Awareness

Education Initiatives Tailored to Physician and Patient Communities



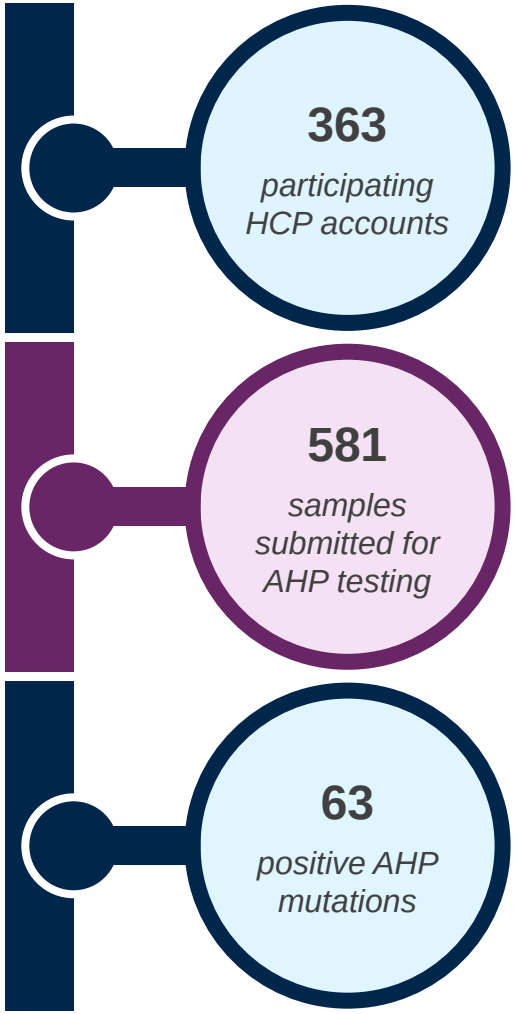
PinpointAHP.com



PorphyriaDiagnosis.com

Alnylam Act – Acute Hepatic Porphyria

Third-Party Genetic Testing and Counseling Program Sponsored by Alnylam



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Collaboration with Ironwood

U.S. Gastroenterologist Disease Awareness and Promotional Agreement

Rationale

- Gastroenterologists are one of the most frequently seen specialty group due to GI manifestations of AHP*
  - ~20% of AHP patients receive diagnosis from a gastroenterologist
  - Diagnosed patients typically see > 3 gastroenterologists during their journey
  - ~40% of AHP patients have received a prior diagnosis of IBS

Overview

- Ironwood will provide disease education to gastroenterologists to support accurate diagnosis of AHP patients
- If givosiran is approved, Ironwood clinical sales specialists will begin promotional efforts

Terms

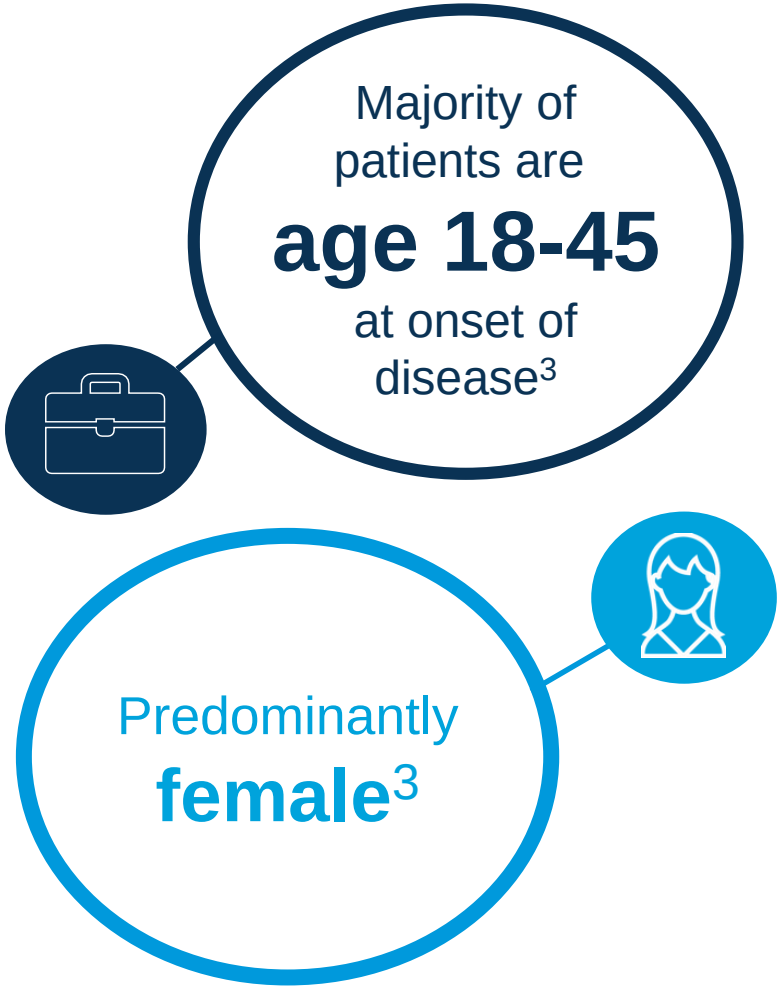
- Ironwood receives fixed payments and, subject to regulatory approval of givosiran, royalties on net sales generated from prescriptions or referrals from certain HCPs related to Ironwood's promotional efforts
- Alnylam retains responsibility for all other aspects of givosiran, including global development and commercial rights

* Alnylam market research

AHP Patient Population

Rare Disease Disproportionately Impacting Female Patients of Working and Childbearing Age

- Consensus estimated global prevalence of 2-5 per 100,000[1]
- Estimated ~1,000 severely affected patients with recurrent attacks in U.S./EU[2]
- Many more estimated to have sporadic attacks (~5,000 patients in U.S./EU[2]) and yet additional patients may have chronic symptoms and impaired quality of life
- AHP are challenging to diagnose, and most patients with active disease currently remain undiagnosed
  - Internal estimates of ~3,000 patients with active disease currently diagnosed in U.S./EU, with ~1,000 in urgent need with frequent attacks



1. Anderson KE, Metabolic & Molecular Bases of Inherited Disease, 2001
2. ORPHANET; The Porphyria Consortium
3. Bissell DM et al. N Engl J Med. 2017;377:862-872

Givosiran Market Opportunity

Ultra-Rare Orphan Disease with Significant Disease Burden and Essentially No Competition

PREVALENCE

~1,000 *recurrent attacks*

~5,000 *sporadic attacks*

patients in U.S./EU[1]

DIAGNOSIS

~20%

currently diagnosed;
delays up to 15 years

DISEASE BURDEN

65%

recurrent attack patients
with chronic symptoms[2]

COST BURDEN

$400–650K

average annual expenditure,
recurrent attack patients[3]

GIVOSIRAN | ACUTE HEPATIC PORPHYRIA

>$500M potential market opportunity

[1] ORPHANET; The Porphyrias Consortium
[2] Gouya et al. EASL 2018
[3] EXPLORE Natural History Study (includes patients with ≥ 3 attacks per year). Annual expenditure per patient; based on both hospitalization charges (amount billed) and costs (amount paid) from published data sources in U.S.

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

* Concomitant use of local standard of care allowed during study, including TTR stabilizer
† To reduce likelihood of infusion-related reactions, patients receive following premedication or equivalent at least 60 min. before each study drug infusion: 10 mg (low dose) dexamethasone; oral acetaminophen; H1 and H2 blockers
NYHA: New York Heart Association; NT-proBNP: N-terminal pro b-type natriuretic peptide; 6-MWT: 6-Minute Walk Test

Vutrisiran HELIOS·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

1:1 RANDOMIZATION

Vutrisiran
SC q3M
25 mg

or

Placebo
SC q3M

Primary Endpoint

- Composite outcome of all-cause mortality and recurrent CV hospitalizations (when last patient reaches Month 30)

Secondary Endpoints

- 6-MWT distance
- Kansas City Cardiomyopathy Questionnaire (KCCQ OS) score
- Mean left ventricular (LV) wall thickness
- Global longitudinal strain
- Composite of all-cause mortality and recurrent all-cause hospitalizations
- All-cause mortality
- Recurrent CV hospitalizations
- NT-proBNP

HELIOS·B

HELIOS-B expected to initiate
late 2019

Study includes optional interim analysis

Lumasiran ILLUMINATE•A Phase 3 Study

Randomized, Double-Blind Study in Primary Hyperoxaluria Type 1 Patients

ENROLLMENT COMPLETED

Patient Population

- Adults & children ≥6 years
- Urinary oxalate excretion ≥0.7 mmol/24hr/1.73m^2
- Confirmed alanine glyoxalate aminotransferase (*AGXT*) mutations
- eGFR >30 mL/min/1.73m^2

2:1 RANDOMIZATION

Lumasiran
3xqM loading dose, then q3M
3.0 mg/kg SC†

or

Placebo
3xqM loading dose, then q3M SC

Primary Endpoint

- Percent change in urinary oxalate excretion from baseline (average percent change from baseline across months 3 through 6)

Open-Label Extension

ILLUMINATE•A

FDA Breakthrough and EMA PRIME Designations

Topline ILLUMINATE-A results expected in **late 2019**

NDA submission planned in **early 2020** (assuming positive results)

NCT03681184; EudraCT Number: 2018-001981-40

† 3.0 mg/kg once monthly for 3 consecutive months (loading dose phase) followed by 3.0 mg/kg once every 3 months (maintenance phase) starting 1 month after last loading dose

Other Clinical and Late Pre-Clinical Programs

Large Number of Additional Programs Across Orphan and Prevalent Diseases

PROGRAM	INDICATION	PREVALENCE	STAGE	EXPECTED MILESTONE	PARTNER
Inclisiran	*Hypercholesterolemia*	**~31 million** in U.S. with LDL-C levels >240 mg/dl	**Phase 3**	**Late 2019** File NDA	The Medicines Company
Fitusiran	*Hemophilia and Rare Bleeding Disorders*	**~200,000** worldwide	**Phase 3**	**2019** support Sanofi	SANOFI
Cemdisiran	*Complement-Mediated Diseases*	**>100,000** total complement-mediated diseases	**Phase 2**	**2019** advance Phase 2 IgA nephropathy study	REGENERON
Cemdisiran/ Pozelimab Combo	*Complement-Mediated Diseases*	**>100,000** total complement-mediated diseases	**Phase 1 planned**	**2019** advance combo studies	REGENERON
ALN-AAT02	*Alpha-1 Liver Disease*	**~12,000** worldwide	**Phase 1/2**	**Late 2019** initial Phase 1/2 data	Alnylam PHARMACEUTICALS
ALN-HBV02 (VIR-2218)	*Hepatitis B Virus Infection*	**~400 million** worldwide with chronic disease	**Phase 1/2**	**Late 2019** initial Phase 1/2 data	VIR
ALN-AGT	*Hypertension*	**~9.1 million** in U.S. with resistant Hypertension	**Phase 1**	**Late 2019** initial Phase 1 data	Alnylam PHARMACEUTICALS

Alnylam R&D Day

Friday, November 22, 2019

Westin Times Square

New York City

Alnylam® PHARMACEUTICALS

CHALLENGE ACCEPTED

Jeff Poulton
Chief Financial Officer

Financial Summary and Guidance

Third Quarter 2019 Financial Summary

Financial Results	Three Months Ended Sept. 30,		Nine Months Ended Sept. 30,	
	2019	2018	2019	2018
ONPATTRO Net Product Revenues	$46.1M	$0.5M	$110.6M	$0.5M
Total Revenues	$70.1M	$2.1M	$148.1M	$53.9M
Total GAAP Operating Costs and Expenses	$286.4M	$256.6	$789.4M	$648.2M
• *R&D Expenses*	*$160.8M*	*$139.9M*	*$453.8M*	*$374.4M*
• *SG&A Expenses*	*$120.4M*	*$116.5M*	*$322.7M*	*$273.7M*
• *Cost of Goods Sold*	*$5.2M*	*$0.1M*	*$12.9M*	*$0.1M*
Non-GAAP Expenses				
• *Non-GAAP R&D Expenses**	*$138.1M*	*$94.2M*	*$399.7M*	*$306.8M*
• *Non-GAAP SG&A Expenses**	*$97.1M*	*$74.4M*	*$268.2M*	*$211.4M*
GAAP Net Loss	$208.5M	$245.3M	$609.9M	$550.1M
Non-GAAP Net Loss**	$162.5M	$157.3M	$510.7M	$440.8M

* Non-GAAP operating expenses exclude stock-based compensation expenses.
** Non-GAAP net loss excludes stock-based compensation expenses, a gain on the change in fair value of a liability obligation, and a gain on litigation settlement.
See Appendix for a reconciliation between GAAP and non-GAAP measures.

Third Quarter 2019 Cash, Investments, and Full-Year Financial Guidance

Cash and Investments	Q3 2019	YE 2018
Cash and Cash Equivalents	$923.3M	$420.1M
Restricted Cash	$2.4M	$2.5M
Restricted Investments	$14.8M	$44.8M
Marketable Debt Securities	$797.8M	$662.8M
TOTAL	**$1,738.3M**	**$1,130.2M**

Reaffirming 2019 Financial Guidance

- Annual Non-GAAP Operating Expenses:
  - Non-GAAP R&D Expenses* in the range of $550M to $575M
  - Non-GAAP SG&A Expenses* in the range of $390M to $400M
- Current cash, cash equivalents, and marketable debt securities expected to support company operations for multiple years based on current operating plan

* Non-GAAP operating expenses exclude stock-based compensation expenses.

Yvonne Greenstreet, MBChB, MBA
Chief Operating Officer

2019 Goals Update

Alnylam 2019 Goals

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

		2019*		
		Early	Mid	Late
onpattro® (patisiran) lipid complex injection 10 mg/5 mL (ATTR Amyloidosis)	Commercial Execution	✓	✓	✓
	Japan Launch			✓
	Additional Country Launches	✓	✓	✓
	Start APOLLO-B Cardiomyopathy Phase 3		✓	
VUTRISIRAN (ATTR Amyloidosis)	HELIOS-A Polyneuropathy Phase 3 Enrollment	✓	✓	✓
	Start HELIOS-B Cardiomyopathy Phase 3			●
GIVOSIRAN (Acute Hepatic Porphyria)	ENVISION Phase 3 Topline Results	✓		
	File NDA		✓	
	File MAA		✓	
LUMASIRAN (Primary Hyperoxaluria Type 1)	Complete ILLUMINATE-A Phase 3 Enrollment		✓	
	ILLUMINATE-A Phase 3 Topline Results			●
	Start ILLUMINATE-B & C Phase 3 Studies	✓		●
ADDITIONAL CLINICAL PROGRAMS	Continue to advance early/mid-stage pipeline; File new INDs; Present clinical data	✓	✓	●
PARTNERED PROGRAMS				
INCLISIRAN (Hypercholesterolemia)	ORION-9, 10, & 11 Phase 3 Topline Results		✓	✓
	File NDA			●
FITUSIRAN (Hemophilia and RBD)	Support Sanofi on ATLAS Phase 3	✓	✓	✓

Q3 2019 Financial Results

Q&A Session

Alnylam PHARMACEUTICALS

Q3 2019 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
Reconciliation of GAAP to Non-GAAP Research and Development:	**2019**	**2018**	**2019**	**2018**
GAAP Research and Development	$ 160,796	$ 139,945	$ 453,813	$ 374,384
Less: Stock-Based Compensation Expenses	(22,737)	(45,784)	(54,144)	(67,537)
Non-GAAP Research and Development	$ 138,059	$ 94,161	$ 399,669	$ 306,847
Reconciliation of GAAP to Non-GAAP Selling, General and Administrative:				
GAAP Selling, General and Administrative	$ 120,351	$ 116,545	$ 322,728	$ 273,671
Less: Stock-Based Compensation Expenses	(23,272)	(42,170)	(54,500)	(62,242)
Non-GAAP Selling, General and Administrative	$ 97,079	$ 74,375	$ 268,228	$ 211,429
Reconciliation of GAAP to Non-GAAP Operating Expenses:				
GAAP Operating Expenses	$ 286,360	$ 256,627	$ 789,427	$ 648,192
Less: Stock-Based Compensation Expenses	(46,009)	(87,954)	(108,644)	(129,779)
Non-GAAP Operating Expenses	$ 240,351	$ 168,673	$ 680,783	$ 518,413
Reconciliation of GAAP to Non-GAAP Net Loss:				
GAAP Net Loss	$ (208,535)	$ (245,282)	$ (609,931)	$ (550,056)
Add: Stock-Based Compensation Expenses	46,009	87,954	108,644	129,779
Less: Change in Fair Value of Liability Obligation	-	-	(9,422)	-
Less: Gain on Litigation Settlement	-	-	-	(20,564)
Non-GAAP Net Loss	$ (162,526)	$ (157,328)	$ (510,709)	$ (440,841)
Reconciliation of GAAP to Non-GAAP Net Loss per Common Share - Basic and Diluted:				
GAAP Net Loss per Common Share - Basic and Diluted	$ (1.92)	$ (2.43)	$ (5.63)	$ (5.48)
Add: Stock-Based Compensation Expenses	0.42	0.87	1.01	1.29
Less: Change in Fair Value of Liability Obligation	-	-	(0.09)	-
Less: Gain on Litigation Settlement	-	-	-	(0.20)
Non-GAAP Net Loss per Common Share - Basic and Diluted	$ (1.50)	$ (1.56)	$ (4.71)	$ (4.39)

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