Fourth Quarter and Full Year 2016 Financial Results

February 8, 2017

Alnylam® PHARMACEUTICALS

Agenda

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

Q4 2016 Overview
- John Maraganore, Ph.D.
  Chief Executive Officer

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

Financial Results
- Michael Mason
  Vice President, Finance and Treasurer

2017 Goals Update
- Barry Greene
  President

Q&A Session

Alnylam Forward Looking Statements

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; 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.

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John Maraganore, Ph.D.
Chief Executive Officer

Q4 2016 Overview

Akshay Vaishnaw, M.D., Ph.D.,
Executive Vice President of R&D

Alnylam Clinical Pipeline

Alnylam ATTR Amyloidosis Portfolio

Committed to Continued Innovation for Patients

Patisiran

- IV administration
- Phase 2 completed
- APOLLO Phase 3 trial ongoing; fully enrolled with top-line results expected in mid-2017
- APOLLO-OLE study ongoing

ALN-TTRsc02

- ESC “second generation” chemistry
- Anticipate quarterly SC dose regimen
- Phase 1 ongoing; initial positive data presented December 2016

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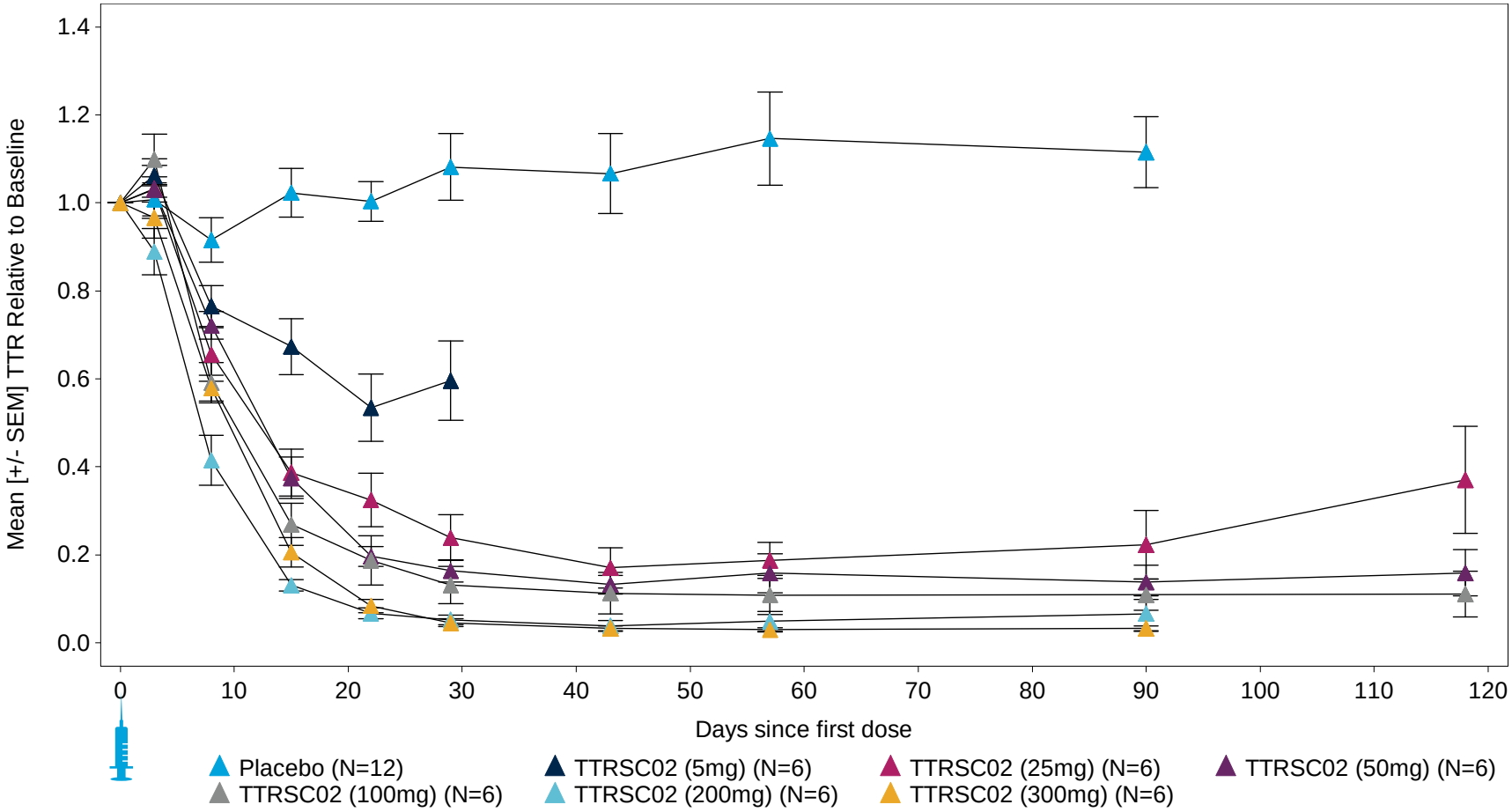
ALN-TTRsc02 Phase 1 Preliminary Study Results*

Single Ascending Dose Study in Healthy Volunteers



Max TTR knockdown of 98.4% with mean max of 97.1 ± 0.5%
Most potent Alnylam investigational RNAi therapeutic to date

*Data cut-off 26Oct2016; reported at Alnylam R&D Day in December 2016; no SAEs or discontinuations due to AEs; all AEs mild or moderate

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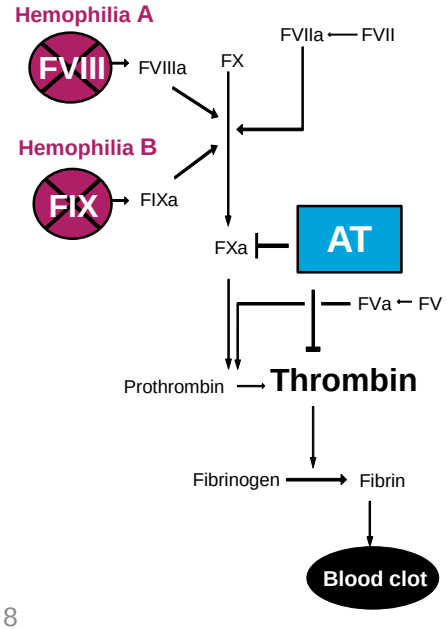
Fitusiran for Hemophilia

Potential to Restore Hemostasis in Hemophilia

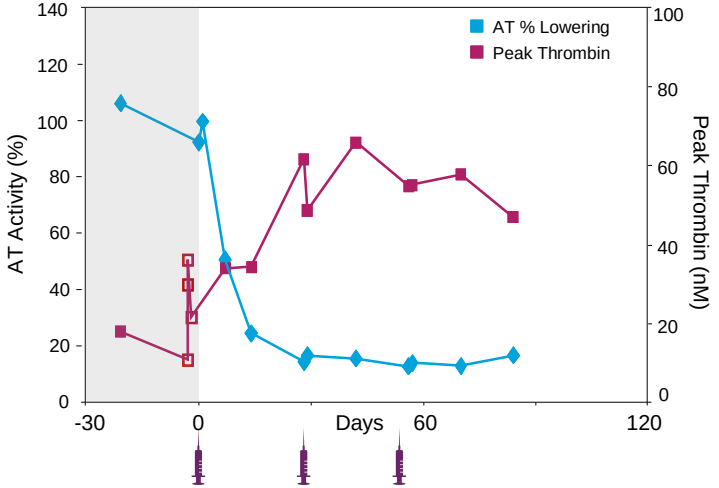
Genetically validated, liver-expressed target gene

Biomarker for POC in Phase 1

Definable path to approval and patient access



Plasma Biomarkers
AT Lowering, Thrombin Generation



Established Endpoint
Annualized Bleeding Rate (ABR)

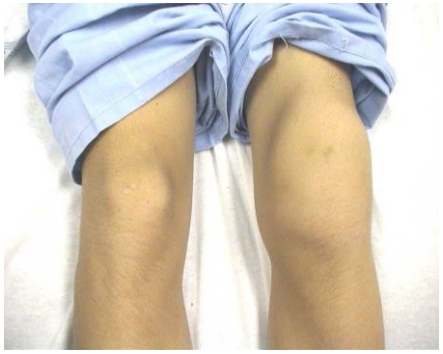
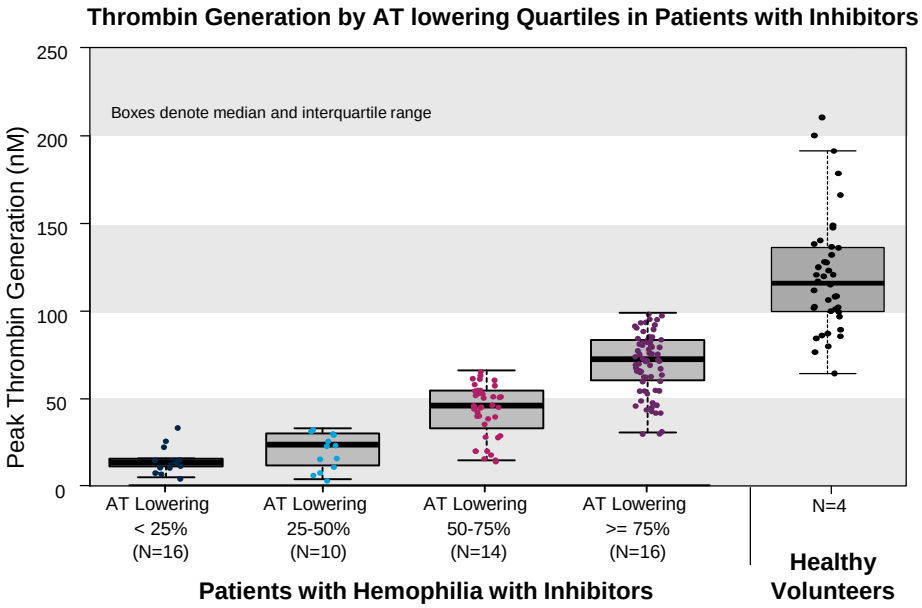
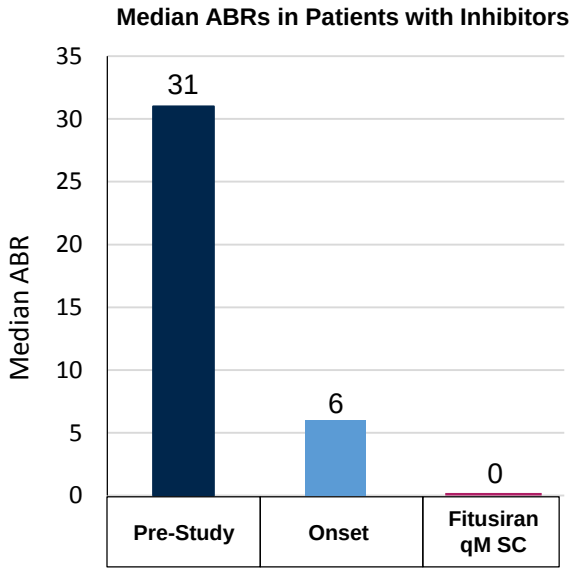


Photo courtesy of Guy Young, M.D.
Director, Hemostasis & Thrombosis Center at Children's Hospital Los Angeles and Professor of Pediatrics, USC Keck School of Medicine

Fitusiran Phase 1 results: Pasi *et al.*, *WFH*, July 2016

Fitusiran Interim Phase 1 Study Results*
Ongoing Study in Hemophilia A & B Patients, Including Inhibitors





DURABILITY

Monthly SC fixed dose regimen

Initial Evidence for Potential Restoration of Hemostasis in Severe Hemophilia A and B

Safety: Generally well tolerated with up to **14 months** of dosing (N=32)

- No drug-related SAEs; all AEs mild or moderate in severity
  - Mild ISRs in 11 (34%) patients
- No thromboembolic events; no lab evidence for pathologic clot formation
- ALT increases >3x ULN observed in 6 (19%) patients
  - All asymptomatic, with no concurrent elevations of bilirubin >2x ULN
  - Reversible; all patients had medical history of HCV
- No instances of anti-drug antibody formation

PLANNED NEXT STEPS

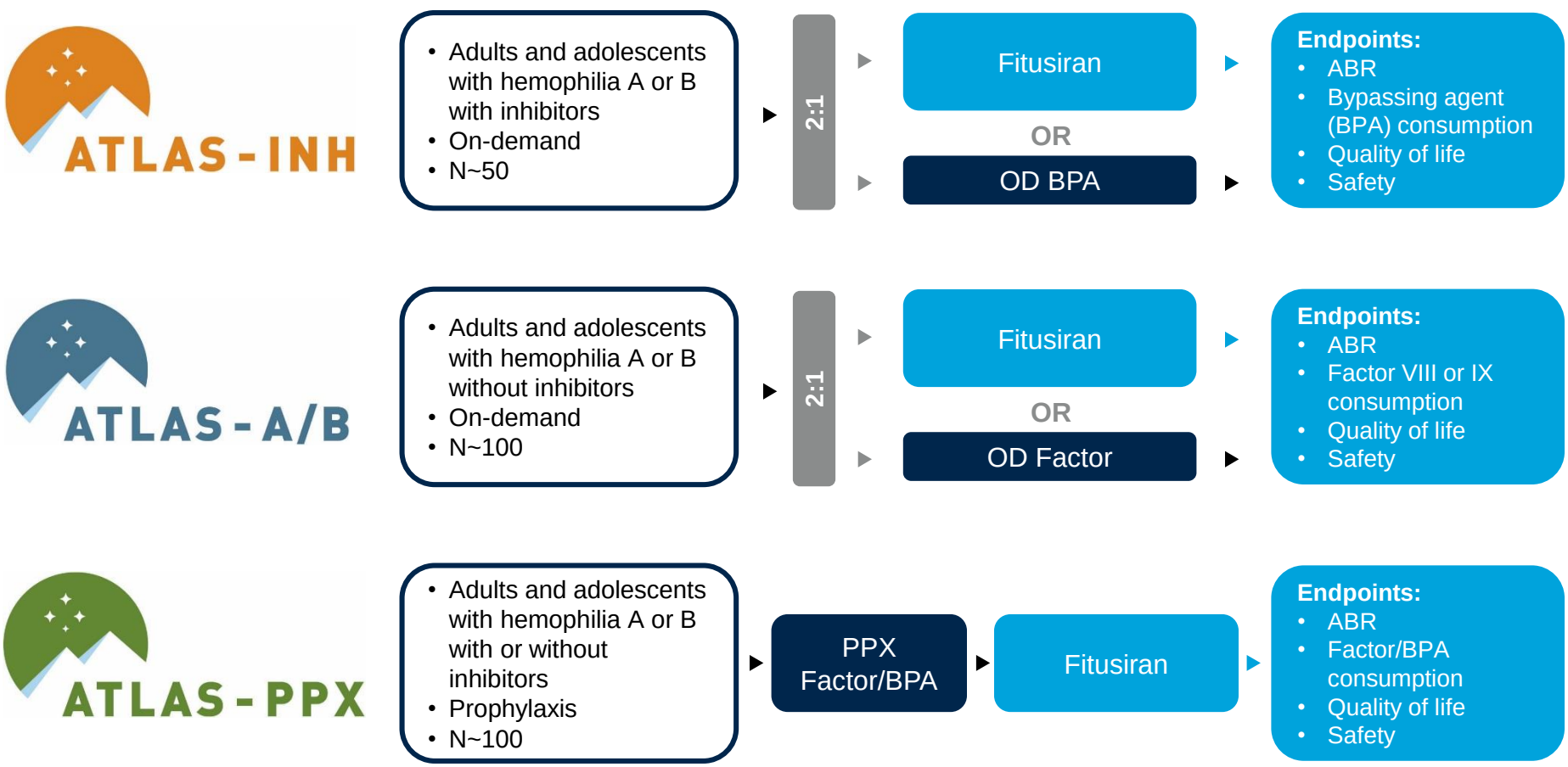
Start ATLAS Phase 3 studies

in **early 2017**

Alnylam, Sanofi Genzyme 50-50 US/Can/Western Europe; Sanofi Genzyme ROW

*Clinical results as of Oct 6, 2016; Pasi *et al.*, Ragni *et al., ASH*, December 2016

Preliminary Fitusiran ATLAS Phase 3 Program*
Plan to Initiate in Early 2017



All completers will be eligible for fitusiran treatment in Phase 3 OLE study (ATLAS-OLE)

*Preliminary plans subject to further diligence and health authority feedback

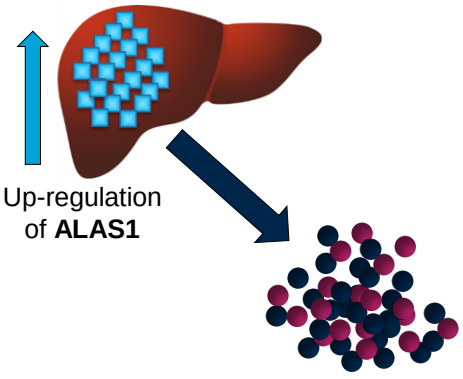
Givosiran for Acute Hepatic Porphyrias
Potential to Prevent Debilitating Attacks

Genetically validated, liver-expressed target gene

Biomarker for POC in Phase 1

Definable path to approval and patient access

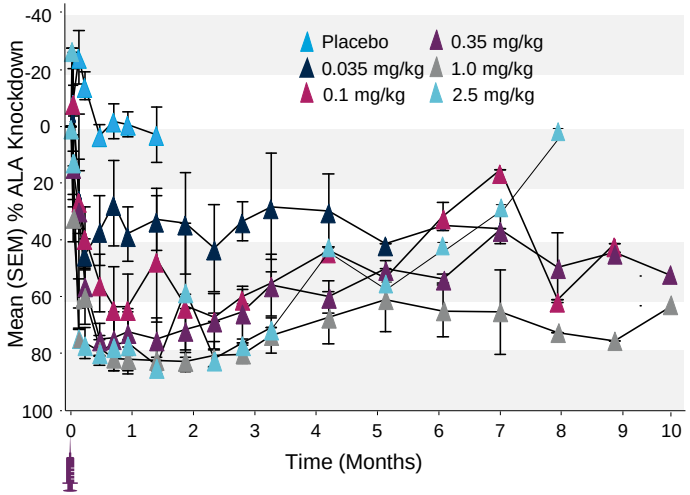
ALAS1
upstream of genetic defect



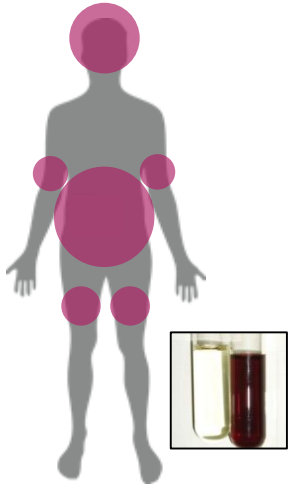
Up-regulation of **ALAS1**

Accumulation of toxic intermediates **ALA** and **PBG**

Serum and Urinary Biomarkers
ALA and PBG



Potential Endpoints
- **Annualized attack rate**
- **ALA and PBG levels**



Givosiran Interim Phase 1 results: Sardh *et al.*, *ASH*, December 2016

Givosiran Interim Phase 1 Study Results*

Ongoing Randomized, Double-Blind, Placebo-Controlled Study in Recurrent Attack Porphyria Patients

Up to **86%** **lowering of ALA,** **95%** **lowering of PBG** in ASHE subjects

74% Mean Decrease in **Annualized Attack Rate**

75% Mean Decrease in **Annualized Hemin Use**

Maximum **Attack Free Interval** **10.5x** Relative to Run-In

DURABILITY

Monthly and possibly **quarterly** SC dose regimen

Initial Evidence for Clinical Activity in Recurrent Attack Porphyria Patients

Safety: Generally well tolerated (N=8)

- No discontinuations due to AEs
- Majority of AEs mild-moderate in severity
- No clinically significant changes in vital signs, EKG, clinical laboratory parameters or physical examination
- After data transfer date, one patient in blinded cohort experienced SAE of acute pancreatitis complicated by pulmonary embolism resulting in death, considered unlikely related to givosiran or placebo

PLANNED NEXT STEPS

Additional data from Phase 1 in mid-**2017**

Start Phase 3 in late **2017**

Alnylam retains global rights to the givosiran program

*Interim Phase 1 study results as of Nov 7, 2016; Sardh *et al.*, *ASH*, December 2016

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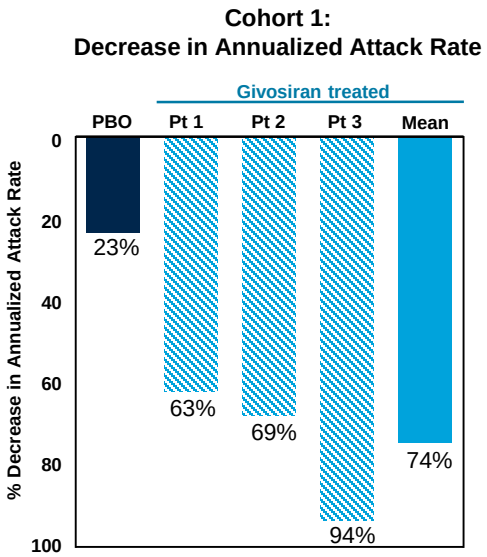
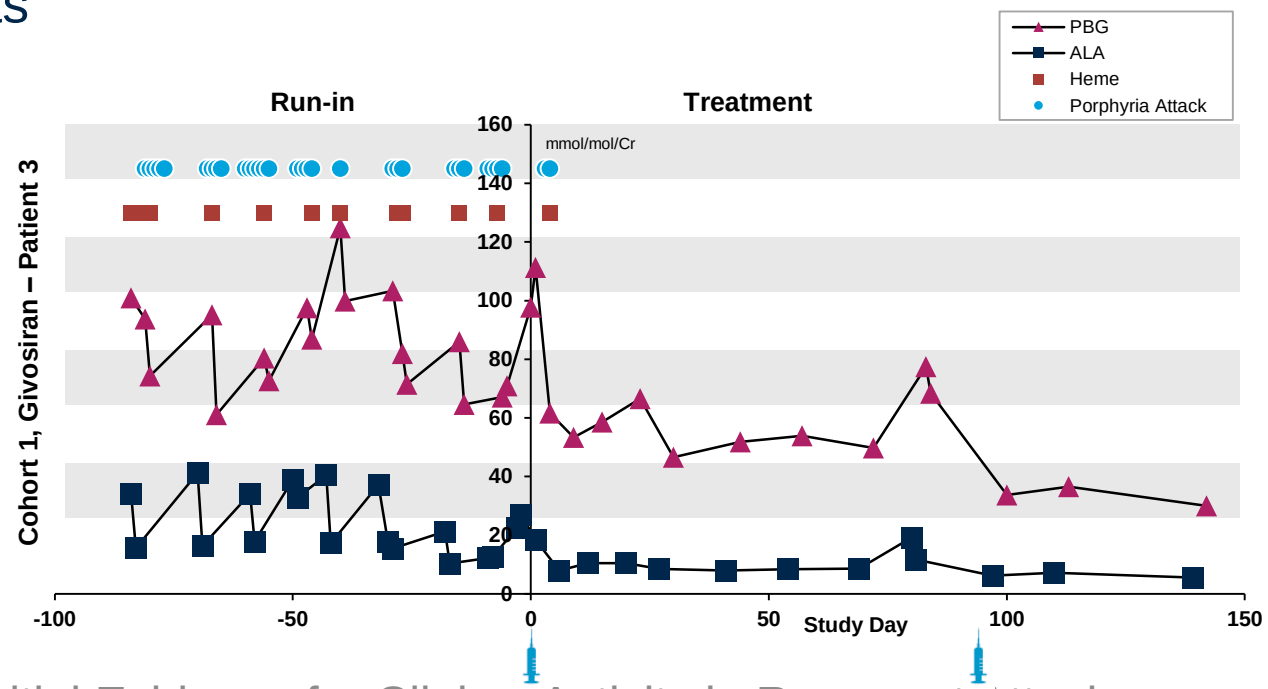
Givosiran Interim Phase 1 Study Results*

Ongoing Randomized, Double-Blind, Placebo-Controlled Study in Recurrent Attack Porphyria Patients





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PLANNED NEXT STEPS

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Start Phase 3

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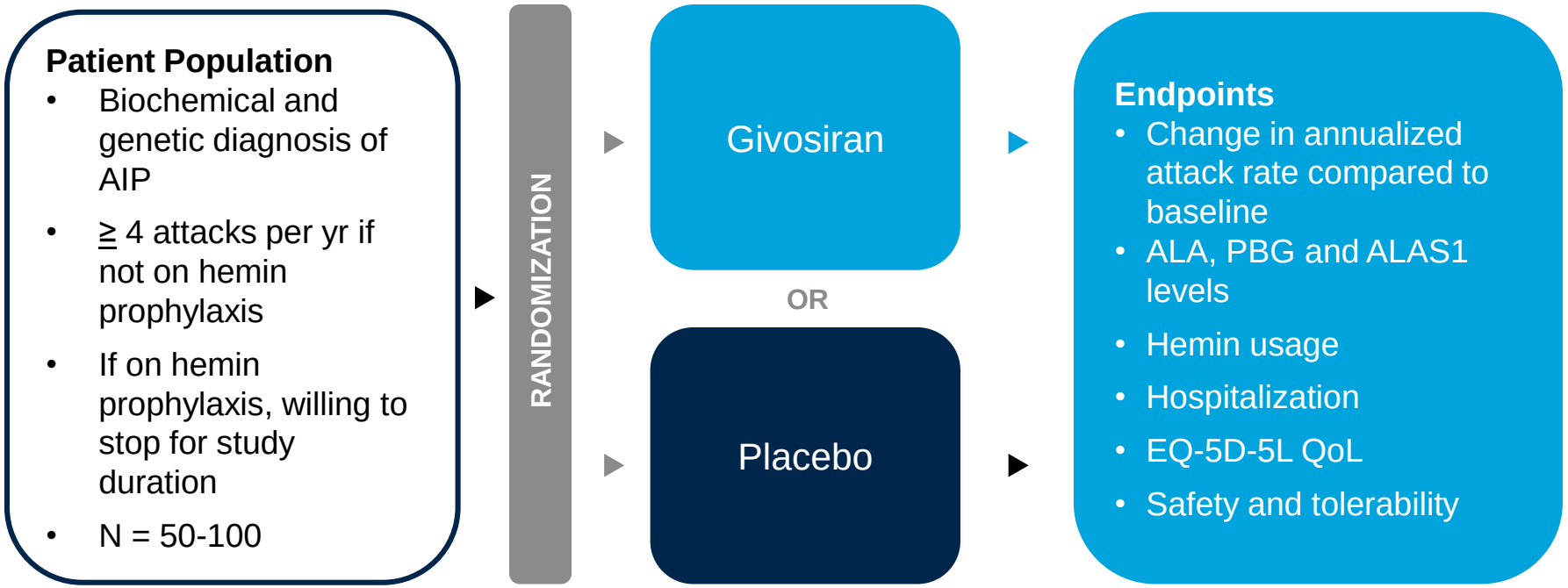
*Interim Phase 1 study results as of Nov 7, 2016; Sardh *et al.*, *ASH*, December 2016

Potential Phase 3 Study Design for Givosiran*
Initial Focus on Prophylaxis for Recurrent Attack Acute Intermittent Porphyria (AIP) Patients

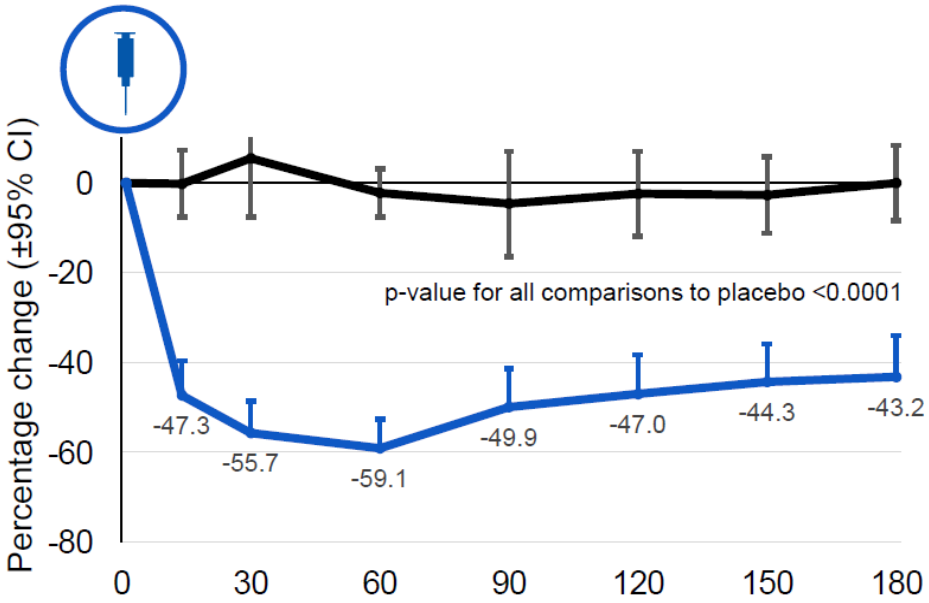


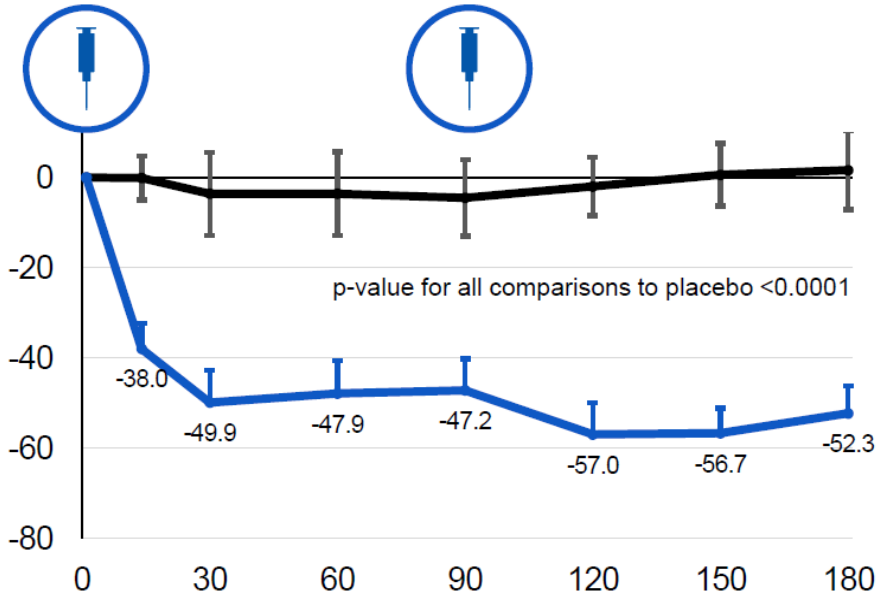
All completers will be eligible for givosiran treatment in Phase 3 OLE study

*Preliminary plans subject to further diligence and health authority feedback

One Dose and Two Doses of Inclisiran up to Day 180*

Efficacy of 300mg versus Placebo on LDL-C





Days from first injection

Placebo (N=22) 300mg (N=21)

Placebo (N=23) 300mg (N=28)

Available data as of 25 Oct 2016

*Preliminary Phase 2 study results; Ray *et al.*, AHA, November 2016

Inclisiran also known as "ALN-PCSsc" and "PCSK9si"

The Medicines Company is leading and funding development of inclisiran from Phase 2 onward and will commercialize the program, if successful

Other Programs to Watch

ALN-CC5
for Complement-Mediated Diseases

Sustained control of disease hemolysis with up to

67%

reduction in eculizumab dose in PNH patients[1]

Safety (N=6):
- No SAEs, no discontinuations due to AEs
- 1 AE of hemolysis in setting of URI; moderate in severity and considered unrelated to study drug
- 1 AE of asymptomatic, transient grade 3 elevation of LFTs; considered possibly related

ALN-GO1
for Primary Hyperoxaluria 1 (PH1)

Up to

8-fold

increase in plasma glycolate in healthy volunteers[2]

Safety (N=32):
- No SAEs, no discontinuations due to AEs
- All AEs mild or moderate, with exception of one subject with transient, asymptomatic CPK elevation considered unrelated to study drug

ALN-HBV
for Hepatitis B Virus (HBV) Infection

Pre-clinical results:[3]

up to

3.6 $\log_{10}$

HBsAg reduction

[1]Phase 1/2 Study; Hill *et al.*, *ASH*, Dec 2016

[2]Phase 1/2 Study; Milliner *et al.*, *IPNA*, Sep 2016

[3]Mouse model; Sepp-Lorenzino *et al.*, *Liver Meeting*, Nov 2015

Michael Mason

Vice President, Finance and Treasurer

Q4-YE 2016 Financial Results

Financial Summary and Guidance

2016 Q4 Financial Results

- Cash ~$1.1B
  - Includes $150.0 million in restricted investments
- GAAP Revenues $17.5M
- Total GAAP Operating Expenses $132.9M
  - Research and Development Expense $105.0M
  - General and Administrative Expense $27.9M
- GAAP Net Loss of $112.9M
- Shares Outstanding ~85.9M

2017 Guidance

- Year-end cash >$700M
  - Includes $150.0 million of restricted investments

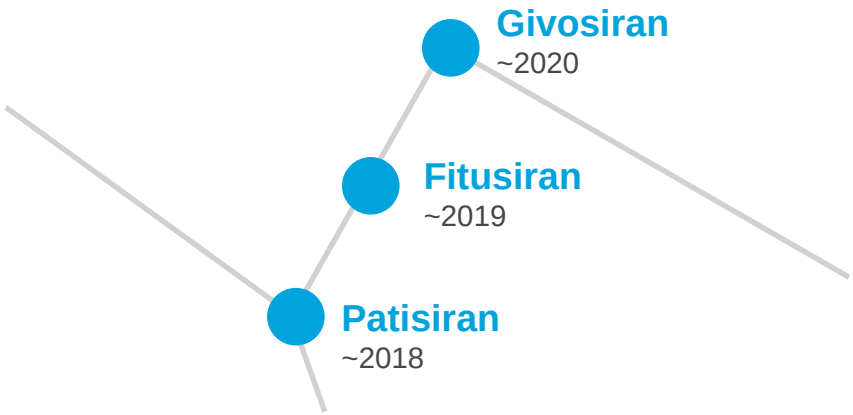
Barry Greene

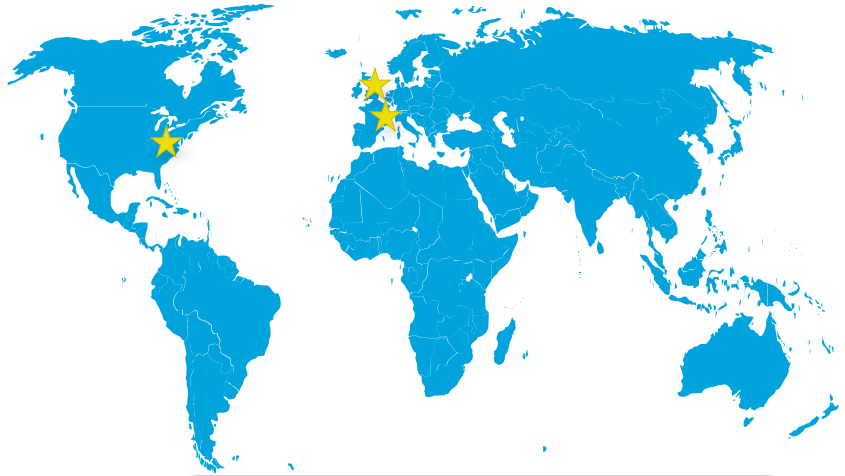
President

2017 Goals Update

Transition to Potential Commercialization

Planned Rapid Launch Succession





Building commercial capabilities to prepare for upcoming product launches

- Patisiran in US, Canada, and Western Europe
- Fitusiran co-develop/co-commercialize in US, Canada, and Western Europe
- Givosiran globally

Manufacturing build-out to ensure consistent drug supply underway

- Alewife facility fully operational and ready for patisiran launch
- Norton drug substance facility expected to be commercially operational in 2020

Alnylam 2017 Pipeline Goals

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

		2017*		
		Early	Mid	Late
PATISIRAN (hATTR Amyloidosis)	Phase 2 OLE data	●		●
	APOLLO Phase 3 top-line		●	
	APOLLO Phase 3 results			●
	NDA/MAA filing			●
FITUSIRAN (Hemophilia and RBD)	Phase 2 OLE data		●	●
	ATLAS Phase 3 program start	●		
GIVOSIRAN (Acute Hepatic Porphyrias)	Phase 1, Part C data		●	
	Phase 3 study start			●
INCLISIRAN** (Hypercholesterolemia)	ORION-1 Phase 2 data	●		
	ORION-2 HoFH study start	✔		
	ORION-3 Phase 2 OLE study start	✔		
	ASCVD Phase 3 study start		●	
ADDITIONAL CLINICAL PROGRAMS	Continue to advance early/mid-stage pipeline; Present clinical data	●	●	●

**Based on The Medicines Company guidance as of January 2017

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Q4-YE 2016 Financial Results

Q&A Session

Thank You

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