Third Quarter 2016 Financial Results

November 2, 2016

Alnylam® PHARMACEUTICALS

Agenda

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

Q3 2016 Overview
- John Maraganore, Ph.D.
  Chief Executive Officer

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

Financial Results
- Michael Mason
  Vice President, Finance and Treasurer

2016 Goal Update
- Barry Greene
  President

Q&A Session

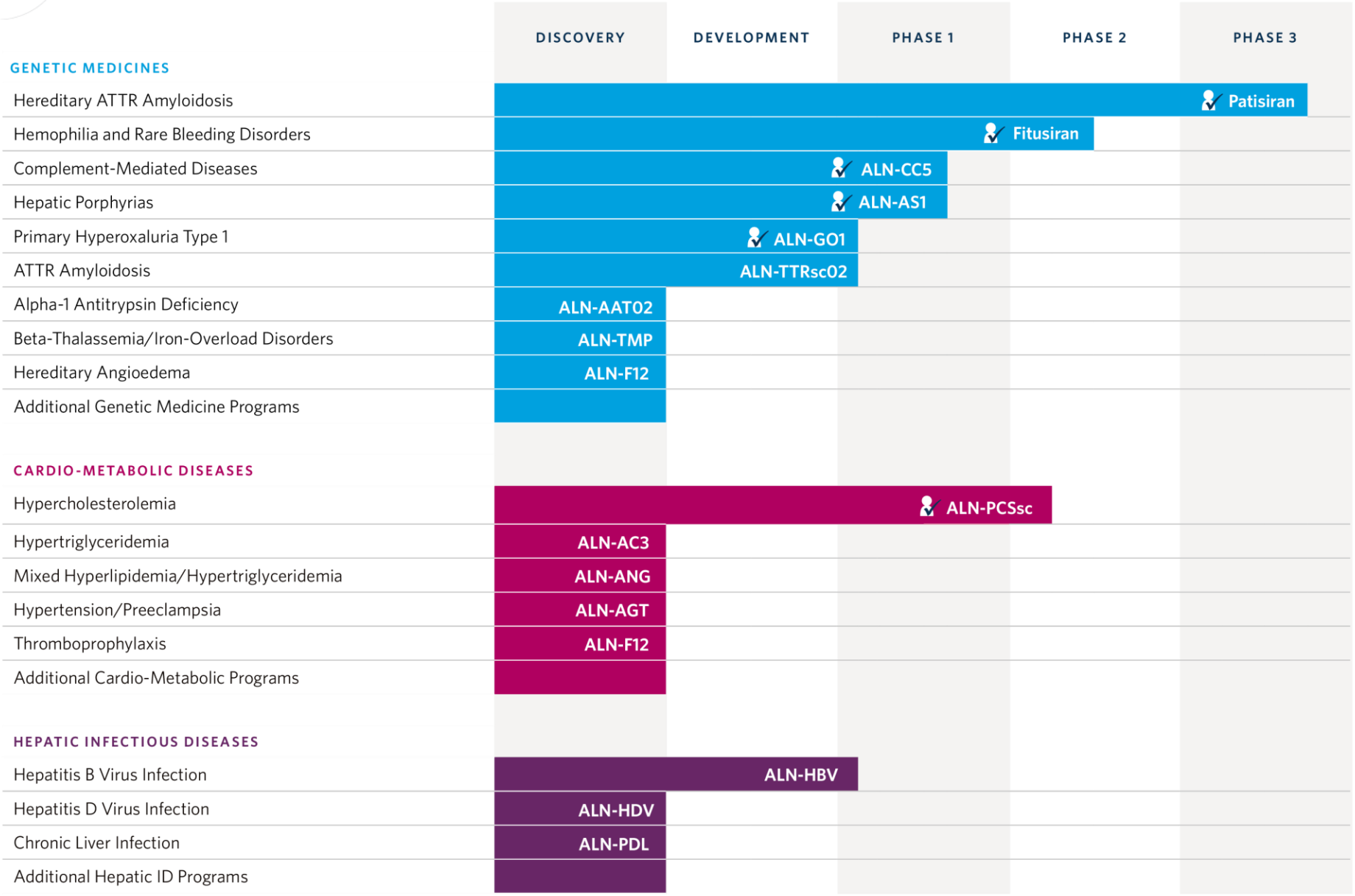
Alnylam Forward Looking Statements

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.

John Maraganore, Ph.D.
Chief Executive Officer

Q3 2016 Overview

Alnylam Development Pipeline



Updated October 10, 2016

Human Proof of Concept Achieved

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

Alnylam Clinical Pipeline

Decision to Discontinue Revusiran Development
Description of Safety Findings as of October 4, 2016

Following ISA in July 2016, reports of new onset or worsening peripheral neuropathy in some revusiran Phase 2 OLE patients

- Diligence with independent neurology experts led to conclusion that events likely consistent with disease
- Data reviewed with ENDEAVOUR DMC; no changes to conduct of study recommended
- Regulatory authorities and study investigators notified

Subsequently, additional reports of peripheral neuropathy and elevated blood lactate levels in Phase 2 OLE

At Company request, ENDEAVOUR DMC met October 4, 2016 to review Phase 3 data in light of new safety information and to assess overall benefit-risk profile of revusiran

- DMC reported no conclusive evidence of drug-related peripheral neuropathy signal
- However, recommended suspension of dosing based on lack of favorable benefit-risk
- Company subsequently reviewed unblinded ENDEAVOUR data which revealed imbalance of mortality in revusiran arm vs. placebo

Decision to discontinue all ongoing studies and further development of revusiran

Conducting comprehensive evaluation of revusiran data - further update on progress of evaluation expected at December 16th R&D Day

No evidence of drug-related peripheral neuropathy or cardiovascular mortality signal based on current assessment of safety data from >800 subjects/patients dosed across 9 other clinical programs, with exposure of up to 34 months (as of Sep 30, 2016)

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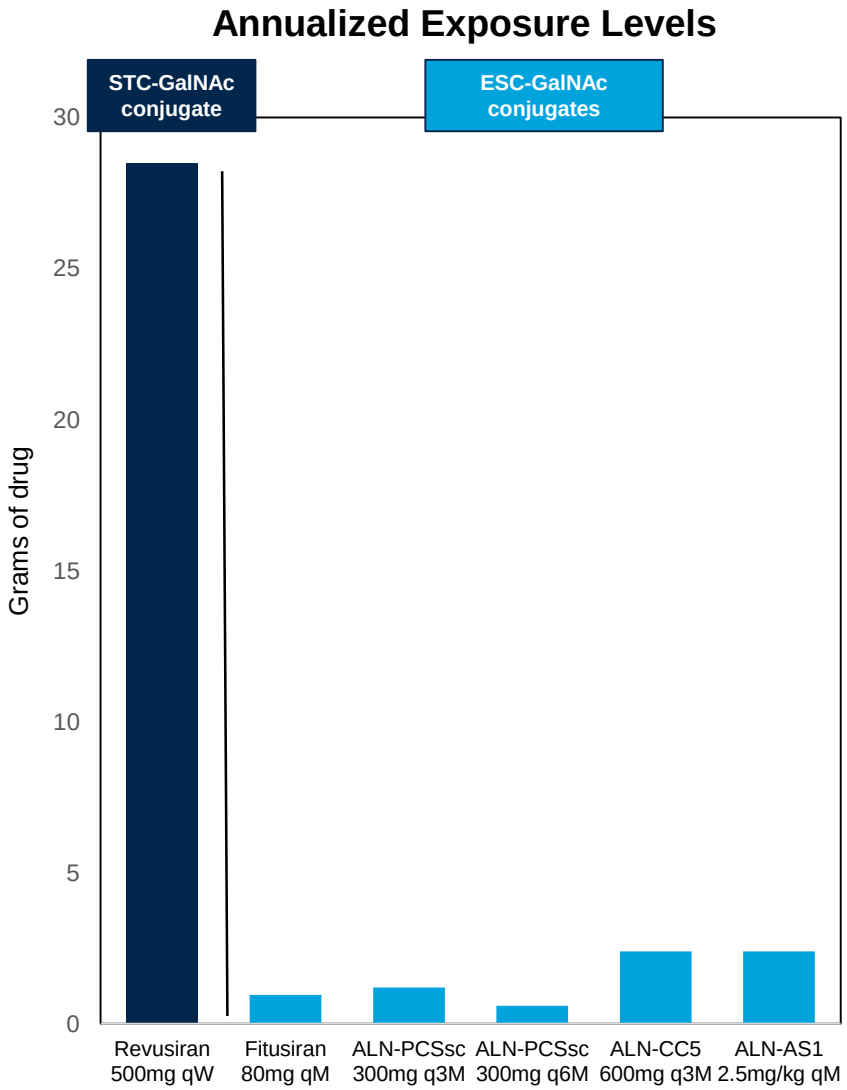
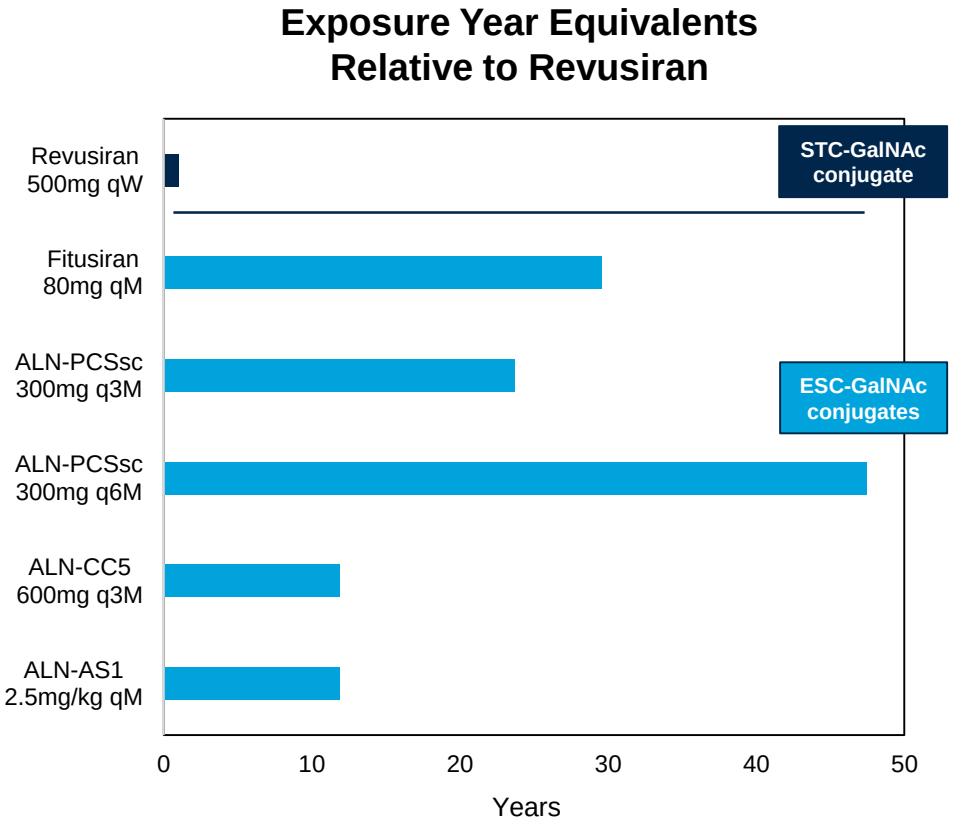
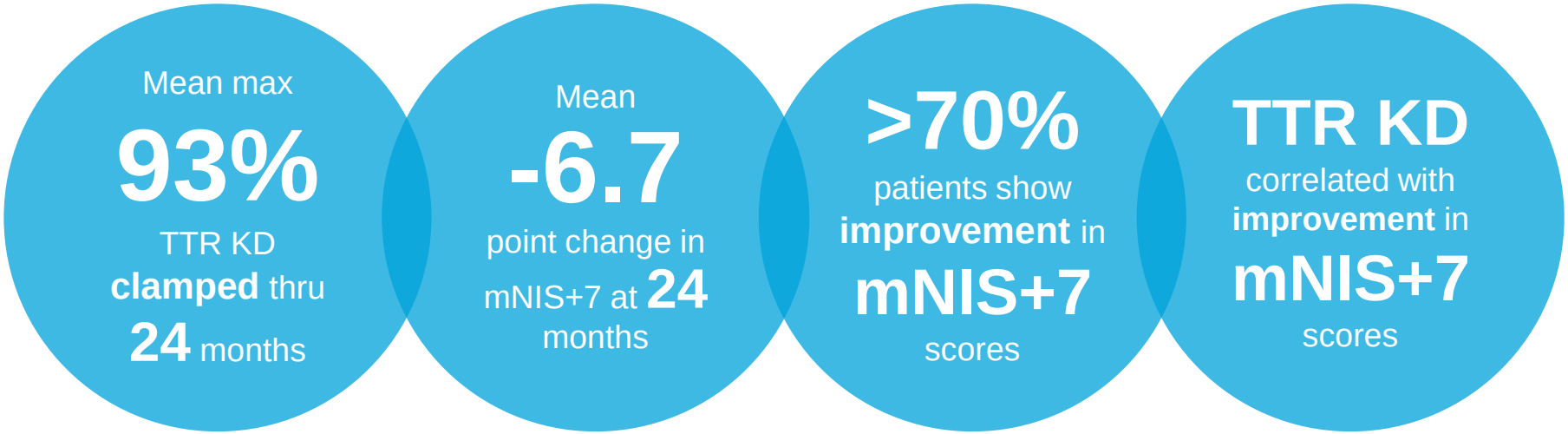
Exposure Levels with Revusiran Significantly Higher than other GalNAc Conjugate Programs





Patisiran Interim Phase 2 OLE Study Results*

Ongoing Study in hATTR-PN Patients



Evidence for Potential Halting or Improvement of Neuropathy Progression

Safety: Generally well tolerated out to 25 months

- 9 non-drug related SAEs in 6 patients
- Majority of AEs mild to moderate, including mild flushing (22.2%) and mild infusion-related reactions (18.5%)
- No significant lab findings, including platelets, and no drug-related discontinuations

PLANNED NEXT STEPS

36-month Phase 2 OLE data in **2017**

*Preliminary Phase 2 OLE results based on data in database as of May 12, 2016; Suhr, *ISA*, July 2016

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APOLLO Phase 3 Study Design

Enrollment Complete

N=225

Patient Population
- hATTR-PN: any TTR mutation, Stages 1 and 2
- Neurological impairment score (NIS) of 5-130
- Prior tetramer stabilizer use permitted

2:1 RANDOMIZATION

Patisiran IV q3W, 0.3 mg/kg

OR

Placebo IV q3W

Primary Endpoint at 18 months
- mNIS+7

Key Secondary Endpoints
- Norfolk QOL-DN
- NIS-weakness
- mBMI
- 10-meter walk

All completers eligible for patisiran treatment on Phase 3 OLE study (APOLLO-OLE)

Enrollment completed; mid-2017 data readout, supporting 2017 NDA and MAA if positive

Statistical Considerations

- Placebo-estimated mNIS+7 progression rate of 17.8 points/year derived from natural history study of 283 hATTR-PN patients
- 90% Power to detect as little as 37.5% difference in ΔmNIS+7 between treatment groups with 2-sided alpha=0.05
  - Based on original target enrollment of 200 patients

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Clinicaltrials.gov # NCT01960348

Fitusiran Interim Phase 1 Study Results*

Ongoing Study in Hemophilia A & B Patients, Including Inhibitors

Up to **91%** AT lowering

Up to **mean 290%** increase in thrombin generation

Median estimated ABR of **0** in non-inhibitor patients

AT lowering, **thrombin generation increases**, and preliminary evidence of **reduced bleeding** in first inhibitor cohort

DURABILITY

Monthly SC fixed dose regimen

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

Safety: Generally well tolerated

- No SAEs; majority of AEs mild or moderate
  - Mild ISRs in 11 (35%) patients
- One discontinuation due to AE considered severe, possibly drug-related
  - Non-cardiac chest pain; associated transient increases in LFTs, D-dimer, CRP
  - Extensive evaluation unremarkable; VTE excluded
  - Event resolved with symptomatic management; antacids, analgesics
- No thromboembolic events; no lab evidence for pathologic clot formation

PLANNED NEXT STEPS

Additional data at **ASH in December 2016**

Start Phase 3 studies in **early 2017**

*Interim Phase 1 study results as of July 11, 2016; Pasi *et al.*, *WFH*, July 2016

ALN-AS1 Interim Phase 1 Study Results*

Ongoing Study in Asymptomatic & Symptomatic Porphyria Patients

Up to **64%** silencing of ALAS-1 mRNA

Up to **86%** lowering of **ALA**

Up to **95%** lowering of **PBG**

Durable ALA and PBG reductions, with effects lasting **>10** months after single dose

DURABILITY

Monthly and possibly **quarterly** SC dose regimen

Potent and Durable Lowering of Toxic Heme Synthesis Intermediates that Mediate Attacks

Safety: Generally well tolerated

- 3 SAEs all deemed unlikely related to study drug, and no discontinuations
- Majority of AEs reported were mild-moderate in severity
- No clinically significant laboratory abnormalities related to study drug

PLANNED NEXT STEPS

Recurrent attack patient data

at **ASH in December 2016**

Start Phase 3

in **2017**

*Interim Phase 1 study results as of June 28, 2016; Sardh *et al.*, *SSIEM*, September 2016

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ALN-GO1 Initial Phase 1/2 Part A Results

Ongoing Study in Primary Hyperoxaluria Type 1 (PH1)

DESCRIPTION

Genetic mutations lead to excessive oxalate production, resulting in recurrent kidney stones and extensive renal damage

DRUG MECHANISM

ALN-GO1 targets glycolate oxidase (GO), an enzyme upstream from the genetic defect, for potential lowering of oxalate levels

DURABILITY

Monthly and possibly **quarterly** SC dose regimen

PATIENT POPULATION*

~5,000 worldwide

Primarily affects children

Sustained through 85 days at highest dose

Up to 8-fold increase in plasma glycolate in healthy volunteers

Safety: Generally well tolerated in healthy adult volunteers

- No SAEs or discontinuations due to AEs
- All AEs mild or moderate, with exception of one subject with transient, asymptomatic CPK elevation deemed unrelated to study drug

PLANNED NEXT STEPS

Oxalate lowering data in PH1 patients in **2017**

* Cochat *et al., N Engl J Med,* 2013

Milliner *et al., IPNA,* September 2016

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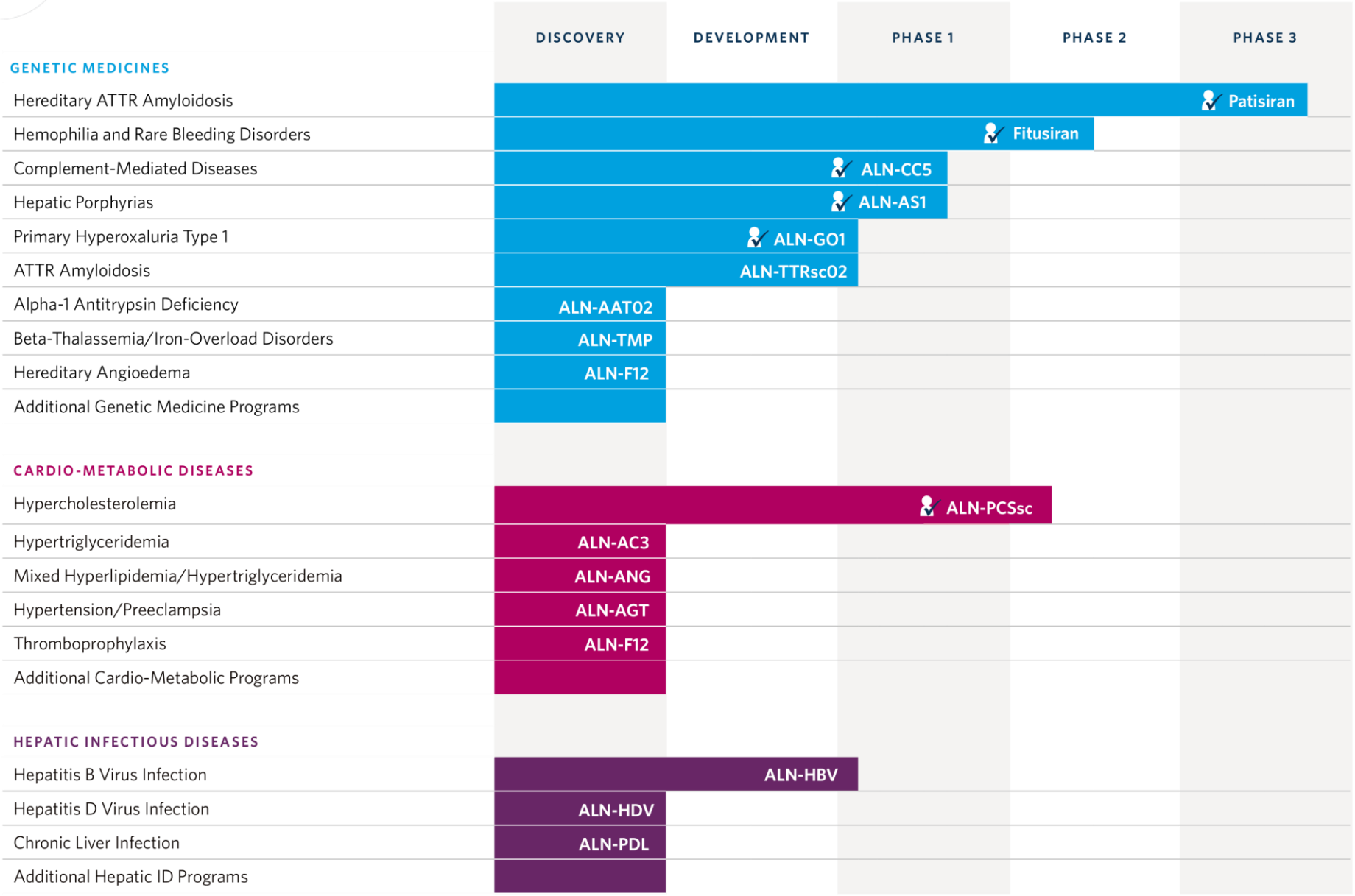

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Human Proof of Concept Achieved

Michael Mason

Vice President, Finance and Treasurer

Q3 2016 Financial Results

Financial Summary and Guidance

2016 Q3 Financial Results

- Cash ~$1.2B
  - Includes $150.0 million in restricted investments
- GAAP Revenues $13.7M
- Total GAAP Operating Expenses $120.3M
  - Research and Development Expense $97.9M
  - General and Administrative Expense $22.4M
- GAAP Net Loss of $104.1M
- Shares Outstanding ~85.8M

2016 Guidance

- Year-end cash >$1.0B
  - Includes $150.0 million of restricted investments received from credit agreements related to build out of new drug substance manufacturing facility

Barry Greene

President

2016 Goals Update

Select Scientific and Clinical Meetings
Late 2016

	Conference	Date (Location)	Expected Presentation(s)
ALN-PCSsc	American Heart Association (AHA) Scientific Sessions	November 15 (New Orleans)	ALN-PCSsc ORION-1 Phase 2
Fitusiran ALN-CC5 ALN-AS1	American Society of Hematology (ASH) Annual Meeting	December 3-6 (San Diego)	Fitusiran Phase 1, Parts C and D (highest and fixed dose cohorts, including inhibitor patients); Initial Fitusiran Phase 1/2 OLE;
			ALN-CC5 Phase 1/2 (PNH patients);
			ALN-AS1 Phase 1, Initial Part C data (recurrent attack patients)
ALN-TTRsc02 Corporate	R&D Day 2016	December 16 (New York)	ALN-TTRsc02 Phase 1

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Q&A Session

Thank you

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