Patisiran and Revusiran, Investigational RNAi Therapeutics for the Treatment of Transthyretin (TTR)-Mediated Amyloidosis

August 20, 2015
Agenda

Welcome
• Joshua Brodsky
  Senior Manager, Investor Relations and Corporate Communications

Introduction
• Barry Greene
  President, Chief Operating Officer

Overview of Transthyretin (TTR)-Mediated Amyloidosis
• Philip Hawkins, Ph.D., FRCP, FRCPath, FMedSci, Head, National Amyloidosis Centre, and Head, Periodic Fever Syndrome Service/Honorary consultant physician

Patient Advocacy: Amyloidosis Patient Perspective
• Isabelle Lousada, President & CEO, Amyloidosis Research Consortium, and Chairman, Amyloidosis Foundation

Q&A Session
• With Dr. Hawkins and Isabelle Lousada

Patisiran and Revusiran Programs
• Eric Green, Vice President, General Manager, TTR Program
• Jared Gollob, M.D., Vice President, Clinical Research

Q&A Session
Reminders

- Event will run for approximately 90 minutes
- Q&A Session at end of each presentation
  - Submit questions at bottom of webcast screen
  - Questions may be submitted at any time
- Replay, slides and audio available at www.alnylam.com
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, successfully demonstrate the efficacy and safety of our drug candidates, obtain, maintain and protect intellectual property, enforce our patents and defend our patent portfolio, obtain regulatory approval for products, establish and maintain business alliances; our dependence on third parties for access to intellectual property; and the outcome of litigation, 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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Q&A Session
Alnylam RNAi Therapeutics Strategy
A Reproducible and Modular Path for Innovative Medicines

1. Liver-expressed target gene
   - Involved in disease with high unmet need
   - Validated in human genetics
   - GalNAc-siRNA enables SC dosing with wide therapeutic index

2. POC achieved in Phase 1
   - Blood-based biomarker with strong disease correlation
     - e.g., Serum TTR, thrombin generation, hemolytic activity, LDL-C, HBsAg levels

3. Definable path to approval and market
   - Established endpoints
   - Focused trial size
   - Large treatment effect
   - Collaborative approach with physicians, regulators, patient groups, and payers
# Development Pipeline

## Genetic Medicines

<table>
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*Updated August 2, 2015*
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Q&A Session
Amyloid

- Abnormal extracellular protein deposit composed of amyloid fibrils
- Diagnostic Congo red staining in tissue sections
- Different fibril proteins in different types of amyloid but all derived by a similar protein misfolding mechanism and have similar final structure
Amyloid deposits
Amyloidosis

- Disease caused by accumulation of amyloid deposits in various organs: local or systemic
- Systemic amyloidosis usually fatal
- Causes ~1 per 1,000-1,500 deaths; AL type most frequently diagnosed
- Diagnosis usually late
- Treatment very challenging
- Major recent advances in understanding pathogenesis
- Major unmet medical need
Pathogenicity & treatment of amyloidosis

- Amyloid deposits are directly damaging by their physical presence
- No amyloid: no disease
  More amyloid: disease progression & death
  Amyloid regression: clinical benefit, survival
- Early diagnosis, amyloid awareness
- Maintenance of organ function
- Reduce supply of fibril precursor
Hereditary transthyretin (ATTR) amyloidosis

Fibrils derived from mutant TTR

Familial Amyloid Polyneuropathy (FAP)
5-10,000 cases worldwide; 100 different mutations

TTR Met30 most prevalent worldwide
  Younger patients, typically < 40 years of age
  Peripheral & autonomic neuropathy; cardiac involvement rare.
  Death 10-15 years.

TTR Ala60 most prevalent in British Caucasians
  Autonomic neuropathy and cardiac involvement
  Typically present ~60 years of age
  Peripheral neuropathy less prominent. Cardiac deaths in 5-10 yrs.

Familial Amyloid Cardiomyopathy (FAC)
  TTR Ile122 variant in ~4% of black Africans (i.e. ~1.5 million in US)
  Penetrance unknown; likely to be much under-diagnosed
  Cardiac amyloidosis after ~60 years of age. Death in <5 years.
Clinical course of FAP

Progressive impairment of sensation and strength from toes moving upwards.

Stage I  Ambulant
Stage II  Ambulant with assistance
Stage III No longer ambulant

Autonomic symptoms of weight loss, constipation, diarrhoea, difficulty eating meals, difficulty passing urine; low blood pressure and fainting
Stages of FAP

Stage 1: 4-5 yrs
Stage 2: Early: 2-3 yrs
Stage 2: Late: 1-2 yrs
Stage 3
Clinical course of FAC

Progressive heart failure with diastolic dysfunction followed by systolic dysfunction

Symptoms of left and right heart failure, including: fatigue, shortness of breath, poor exercise tolerance, fluid retention in legs and abdomen, liver enlargement, loss of appetite, nausea

Conduction abnormalities leading to cardiac arrhythmias

Frequent hospitalizations for cardiovascular decompensation in later stages of disease
Cardiac ATTR amyloidosis

Restrictive cardiomyopathy, preserved ejection fraction
Echocardiography

Diffusely thickened heart wall
$^{99m}$Tc-DPD scans in cardiac ATTR amyloid

<table>
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<tr>
<th>Healthy</th>
<th>Grade 1</th>
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<td>![Healthy Image]</td>
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- **Grade 1** = Mild cardiac uptake no attenuation of bone uptake
- **Grade 2** = Moderate cardiac uptake with bone attenuation
- **Grade 3** = Strong cardiac uptake with little or no bone signal

- Very sensitive
- Grade 2 or 3 uptake in all patients with cardiac ATTR amyloidosis
- Cheap, potentially universally available
Therapeutic strategies in amyloidosis

- Precursor protein
- Amyloid

- Reversion to native fold

- Fibril formation

- Stabilise precursor proteins
- Inhibit GAG binding
- β sheet breakers

- Reduce supply of amyloid precursor protein

- Immunotherapy
- Destabilise by SAP depletion
Treatment of amyloidosis

Reduce supply of fibril precursor protein

**AA**  control inflammation to reduce SAA protein production by the liver

**AL**  chemotherapy for plasma cell dyscrasias to reduce monoclonal light chain protein production in the bone marrow

**ATTR**  liver transplantation to remove the source of genetically variant amyloid-forming TTR protein
Regression of AA amyloid
Whole body scintigraphy with $^{123}\text{I}$-labelled SAP

in spleen and liver of a patient whose underlying rheumatoid arthritis was well suppressed by anti-inflammatory treatment

1999  2001
Natural turnover & clearance of amyloid deposits

More than 50% of existing AA and AL amyloid deposits can be cleared in one year when amyloid precursor protein supply is cut-off.

Rate of clearance varies from patient to patient.

Without treatment, clearance of amyloid is almost always slower than the on-going rate of new amyloid deposition.

Any degree of reduction in the supply of the respective precursor protein will slow down disease progression.

A 50% reduction can completely halt disease progression.
Management of FAP

- Symptom relief for neuralgic pain, gastrointestinal symptoms associated with autonomic disease, cardiac failure

- Liver transplantation to remove source of genetically variant amyloid forming TTR protein variants
  - Improved survival and stabilization of disease in early stage V30M patients
  - Progressive amyloid deposition occurs in heart and other sites due to normal TTR continuing to build up on the pre-existing template of variant TTR amyloid, especially in patients with later stage disease and non-V30M mutations
  - Only 6 liver transplants in UK for FAP past 5 yr.

- TTR tetramer stabilizers tafamidis and diflunisal show modest effect on neuropathy progression
  - Tafamidis: Approved in EU only for early stage FAP; not approved in US
  - Diflunisal: Positive Phase 3 study results in trial conducted by academic centre
Management of FAC

- Symptom relief for congestive heart failure, chiefly just with diuretics and fluid balance management.

- Liver transplantation has no role.

- Cardiac transplantation in highly selected cases; most patients too old.
Case History
FAP associated with TTR Met30

36 yr old Greek Cypriot woman
2 yr history of painful peripheral neuropathy
Loss of bladder control and self-catheterization
No cardiac amyloidosis

2 year wait for liver transplantation, associated with progression of peripheral neuropathy and weight loss

Stabilization during 5 yr follow-up, weight gain, slight recovery of bladder control
59 yr old Afro-Carribean man presented with congestive heart failure in 2003
Thick walled heart on echo with well preserved ejection fraction
Suspicion of amyloid supported by genetic testing – homozygous for TTR Ile122 variant
Amyloidosis confirmed by cardiac biopsy

Marked deterioration over following year; accepted for cardiac transplant 2004
Remains well; no cardiac amyloid on DPD scan.
Prospects for treatment of ATTR amyloidosis

Serious disease with substantial unmet need

Liver transplantation for FAP patients with early symptoms associated with TTR Met30. Amyloidogenic property of wild-type TTR limits this approach in patients with cardiac involvement

TTR stabilization shows some promise, though limited clinical efficacy demonstrated to date in FAP

Management of FAC largely limited to supportive care

Robust rationale for reducing the supply of TTR in the plasma to treat FAP and FAC, a strategy that has proved to be highly effective in other types of amyloidosis
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Q&A Session
Challenges in advancing the treatment of amyloidosis and the role of patient advocacy
Rare Diseases

Common ground in rare diseases

- 7,000 rare diseases
- 1 in 10 affected by a rare disease
- More than 25 Million Americans have one
- 80% are genetic in origin
- Delayed diagnosis
- Small patient pool
- Lack of natural history studies
- Challenges of clinical trials in small populations
“If patients were a drug, it would be the blockbuster drug of the century and malpractice not to use it”

Leonard Kish (digital strategist) – 2012
Evolution of Patient Engagement

We are at a crossroads in the history of patient engagement

- March of Dimes 1938
- Nuremberg Code 1947
- Patients’ Bill of Rights 1973
- HIV/AIDS 1980s
- PCORI 2010
- PDUFA 2012
- 21st Century Cures 2014
The Road Map

Patient Group Engagement Across the Clinical Trial Continuum

Pre-Discovery
- Interest of research question to patient community
- Provide data on unmet need and therapeutic burden
- Direct funding and fundraising for research or product development
- Understanding mechanisms of action relevant to disease and symptom burden

Pre-Clinical
- Direct funding and fundraising for research or product development
- Natural history database/registry support
- Help define eligibility criteria within the study protocol
- Feedback on meaningful clinical endpoints
- Assist in creating the informed consent form
- Advise on study recruitment
- Accompany sponsor to FDA to advocate study design

Phase 1
- Network recruitment/outreach
- Direct funding and fundraising for research or product development
- Infrastructure support
- Provide input on study design (barriers to participation)
- Support trial awareness and recruitment
- Peer advocate during informed consent procedure

Phase 2/3
- Direct funding and fundraising for trial operations support
- Network recruitment/outreach
- Serve on Data Safety Monitoring Board
- Report on patient feedback regarding sites, investigators, and study participant experience

FDA Review & Approval
- Serve on FDA advisory committees
- Provide testimony at FDA hearings
- Feedback on meaningful clinical endpoints

PAS/Outcomes
- Natural history database/registry support
- Provide feedback on how the patient community views results
- Help return study results to participants
- Write newsletter articles or blog about results
- Co-present results
- Serve on post-market surveillance initiatives

Challenges in advancing the treatment of amyloidosis and the role of patient advocacy
Adapted from Parkinson’s Disease Foundation materials in 2013 by patient advocate members of CTTI
Challenges in Clinical Trials in ATTR

Standing out from the crowd

- Complex multi-system disease
- Heterogeneous population
- Delayed diagnosis
- Hard to reach population
- Small patient pool
- Lack of awareness about clinical trials
- Limited understanding of Amyloidosis at regulatory level
- Single novel agent evaluated in different divisions of FDA
- Length of trials
- Lack of surrogate endpoints or biomarkers
Education is Key

Engaging patients is critical to the success of trials

- 73% believe, somewhat to absolutely, that participating in a clinical trial would enhance their overall care
- 49% of patients say they have no or little access to information on clinical trials which pertain to them
- 45% say that if they were well informed about a clinical trial they would consider taking part
- 73% of patients say they are unsure how to enroll in a clinical trial
The Amyloidosis Group

Supporting patients and families while promoting research, education and awareness

An engaging and educational tool that connects patients with clinical trials

Accelerating the development of advanced diagnostic tools and effective treatment for systemic amyloidosis
“There are no problems we cannot solve together, and very few we can solve by ourselves”

Lyndon B. Johnson
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Transthyretin-Mediated Amyloidosis (ATTR) Program
Unmet Need and Product Opportunity

Progressive, debilitating monogenic disease
- ATTR is significant orphan disease
  - ~50,000 Patients worldwide
- Clinical pathology
  - Onset ~40 to >60 yr; fatal within 2-15 years
  - Two predominant forms
    - Familial amyloidotic polyneuropathy (FAP)
    - Familial amyloidotic cardiomyopathy (FAC)
- Halting disease progression remains unmet need
  - Liver transplantation required early
  - TTR stabilizers provide modest benefit

Mutant transthyretin (TTR) is genetic cause
- Autosomal dominant with >100 defined mutations
- Misfolds and forms amyloid deposits in nerves, heart, other tissues

RNAi opportunity as potentially transformative therapy
- Knockdown disease-causing protein
- Aim to halt progression, possibly achieve regression
- Value proposition supported by pharmacoeconomics and cost of disease burden
- Concentrated provider base and active patient community
RNAi Therapeutics for ATTR Amyloidosis
Patisiran and Revusiran

**Patisiran for Familial Amyloidotic Polyneuropathy (FAP)**
- Intravenous administration
- Positive Phase 2 results in FAP patients
- Phase 2 Open-Label Extension (OLE) study ongoing
  - Clinical endpoints every 6 months
  - Positive 12-month data reported at AAN, April 2015
  - 18-month data expected in late 2015
- APOLLO Phase 3 trial ongoing
  - Over 40 sites in over 15 countries
  - Expect APOLLO to enable NDA submission ~2017
  - APOLLO-OLE ongoing

**Revusiran for Familial Amyloidotic Cardiomyopathy (FAC)**
- Subcutaneous administration
  - STC “first generation” chemistry
- Positive Phase 2 study results
  - TTR cardiac amyloidosis patients
- Phase 2 Open-Label Extension (OLE) study ongoing
  - Clinical endpoints every 6 months
  - Report data at least once annually
- DISCOVERY study ongoing
  - Prevalence of TTR mutations in suspected cardiac amyloidosis
  - Multi-center study; up to 1,000 patients
- ENDEAVOUR Phase 3 trial ongoing
- Also advancing ALN-TTRsc02
  - ESC “second generation” chemistry
  - Data and guidance at OTS, October 2015
Therapeutic Hypothesis

Production of mutant and wild type TTR

Unstable circulating TTR tetramers reduced

Organ deposition of monomers, amyloid (β-pleated) fibril prevented, clearance promoted

Neuropathy, cardiomyopathy

Patisiran and revusiran act to knock down both mutant and wild type TTR production
Patisiran Phase 2 Study Results

Robust knockdown of both wild-type and mutant TTR in FAP patients

- Open label, multi-center, multi-dose, dose escalation study
- Results (n=29) show up to 96% TTR knockdown; 84% and 87% mean TTR knockdown after 1st and 2nd doses in 0.30 mg/kg q3w cohort (p<0.001 vs. 0.01 mg/kg)
- 1:1 knockdown of wild-type and mutant TTR; similar knockdown in patients with TTR stabilizers

Dose Response and Duration of TTR Knockdown

Knockdown in Wild Type vs. Mutant

Cohorts 0.01-0.30 mg/kg q4w
Cohort 0.30 mg/kg q3w

*Excludes post-day 28 data from one patient that experienced drug extravasation during second infusion

Int'l Symp. FAP, Nov. 2013; Updated at ISA, Apr. 2014
Patisiran Open-Label Extension (OLE) Study

FAP patients dosed in Phase 2 trial eligible for Phase 2 OLE study

• Clinical endpoints evaluated every 6 months for up to 2 years
  ◦ Clinical endpoints same as APOLLO Phase 3 study
  ◦ Dosing at 0.30 mg/kg IV every 3 weeks

• Study objectives
  ◦ Primary: Safety and tolerability of long-term dosing with patisiran
  ◦ Secondary: Effects on neurologic impairment (mNIS+7), quality of life, mBMI, disability, mobility, nerve fiber density in skin biopsies, and serum TTR levels

Status

- Ongoing; enrollment completed (N=27)
- 12-month mNIS+7 patient data
  ◦ Presented at AAN, April 18-25, 2015 (N=20)
  ◦ Full dataset planned to be presented at ANA, September 27-29, 2015
- Expect to report 18-month data in late 2015

Clinicaltrials.gov # NCT01961921
### Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>N=27 (includes 11 patients in cardiac subgroup)</td>
</tr>
<tr>
<td>Median age</td>
<td>64.0 years (range 29-77)</td>
</tr>
<tr>
<td>Gender</td>
<td>18 males, 9 females</td>
</tr>
<tr>
<td>TTR genotype</td>
<td>• Val30Met (V30M) = 20&lt;br&gt;• Ser77Tyr (S77Y) = 2&lt;br&gt;• Ser77Phe (S77F) = 2</td>
</tr>
<tr>
<td></td>
<td>• Tyr116Ser (Y116S) = 1&lt;br&gt;• Phe64Leu (F64L) = 1&lt;br&gt;• Arg54Thr (R54T) = 1</td>
</tr>
<tr>
<td>FAP stage/PND score</td>
<td>• Stage 1: 24&lt;br&gt;• Stage 2: 3</td>
</tr>
<tr>
<td></td>
<td>• I: 14&lt;br&gt;• II: 10&lt;br&gt;• IIIa: 2&lt;br&gt;• IIIb: 1</td>
</tr>
<tr>
<td>Concurrent tetramer stabilizer use at baseline</td>
<td>13 tafamidis, 7 diflunisal, 7 none</td>
</tr>
<tr>
<td>Current tetramer stabilizer use¹</td>
<td>12 tafamidis, 6 diflunisal, 9 none</td>
</tr>
<tr>
<td>Total doses administered</td>
<td>511</td>
</tr>
<tr>
<td>Median doses/patient to date</td>
<td>19 (range 13-24)</td>
</tr>
<tr>
<td>Mean treatment duration</td>
<td>12.8 months (range 8.4-16.7)</td>
</tr>
</tbody>
</table>

¹ 2 subjects: one on diflunisal, one on tafamidis, reported stabilizer use at the time of first dose but had subsequently stopped using stabilizer.

*Data as of March 13, 2015
Patisiran Phase 2 OLE Preliminary Study Results*
Safety and Tolerability - TEAEs Related or Possibly Related

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>n (%)</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flushing</td>
<td>6 (22.2%)</td>
<td>Mild</td>
</tr>
<tr>
<td>Infusion-related reaction</td>
<td>5 (18.5%)</td>
<td>Mild</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (7.4%)</td>
<td>Mild-Moderate</td>
</tr>
<tr>
<td>Peripheral Edema</td>
<td>2 (7.4%)</td>
<td>Mild</td>
</tr>
<tr>
<td>Ectropion</td>
<td>1 (3.7%)</td>
<td>Moderate</td>
</tr>
<tr>
<td>Fatigue</td>
<td>1 (3.7%)</td>
<td>Moderate</td>
</tr>
<tr>
<td>Infusion site irritation</td>
<td>1 (3.7%)</td>
<td>Moderate</td>
</tr>
<tr>
<td>Neuralgia</td>
<td>1 (3.7%)</td>
<td>Mild</td>
</tr>
<tr>
<td>Impairment of taste</td>
<td>1 (3.7%)</td>
<td>Mild</td>
</tr>
<tr>
<td>Insomnia</td>
<td>1(3.7%)</td>
<td>Mild</td>
</tr>
<tr>
<td>Alopecia</td>
<td>1 (3.7%)</td>
<td>Mild</td>
</tr>
</tbody>
</table>

- All TEAEs mild to moderate in severity
- No clinically significant changes in liver function tests, renal function, or hematologic parameters
- No study discontinuations
- 3 subjects with 4 SAEs (unrelated to study drug): One subject with 2 separate events (distal femur/proximal tibia fracture with osteonecrosis and dehydration/acute renal failure), one subject with ankle/foot fracture with osteonecrosis, and one subject with a lower limb venous thrombosis

*Data as of March 13, 2015
Patisiran Phase 2 OLE Preliminary Study Results*
Serum TTR Knockdown

- Similar TTR knockdown in patients on patisiran alone or on patisiran + TTR tetramer stabilizers

*Data as of March 13, 2015
* One Day 273 value removed for subject that missed two consecutive doses immediately prior to measurement
Neuropathy Impairment Scores Used in FAP Trials

**mNIS+7**
(304 points)

<table>
<thead>
<tr>
<th>Component</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postural BP or HRdb (2)</td>
<td></td>
</tr>
<tr>
<td>Σ 5 NCS (10)</td>
<td></td>
</tr>
<tr>
<td>Reflexes (20)</td>
<td></td>
</tr>
<tr>
<td>QST (80)</td>
<td></td>
</tr>
</tbody>
</table>

**NIS**
(244 points)

<table>
<thead>
<tr>
<th>Component</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reflexes (20)</td>
<td></td>
</tr>
<tr>
<td>Sensation (32)</td>
<td></td>
</tr>
<tr>
<td>Motor strength/weakness (192)</td>
<td></td>
</tr>
</tbody>
</table>

Higher score indicates worsening of disease.

BP: Blood Pressure
HRdb: Heart Rate response to Deep Breathing
NCS: Nerve Conduction Studies
QST: Quantitative Sensory Testing
Partial imputation was used to recover two mNIS+7 datapoints: A subject missing QST at Baseline, and another subject missing NIS-W (one replicate) and Postural BP (other replicate) at 12 mos.

<table>
<thead>
<tr>
<th>mNIS+7 component</th>
<th>Change from Baseline to Month 6 (n=27)</th>
<th>Change from Baseline to Month 12 (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SEM)</td>
<td>Median (range)</td>
</tr>
<tr>
<td>Total</td>
<td>-1.4 (2.1)</td>
<td>-2.0 (-25.4, 22)</td>
</tr>
<tr>
<td>NIS-weakness</td>
<td>0.2 (1.2)</td>
<td>0 (-9.9, 16)</td>
</tr>
<tr>
<td>NIS-reflexes</td>
<td>-0.7 (0.5)</td>
<td>0 (-8, 3)</td>
</tr>
<tr>
<td>QST#</td>
<td>-1.1 (1.5)</td>
<td>-1.5 (-15, 16)</td>
</tr>
<tr>
<td>NCS Σ5</td>
<td>0.2 (0.1)</td>
<td>0 (-1.5, 1.5)</td>
</tr>
<tr>
<td>Postural BP+</td>
<td>0 (0.1)</td>
<td>0 (-1, 1)</td>
</tr>
</tbody>
</table>

Partial imputation was used to recover two mNIS+7 datapoints: A subject missing QST at Baseline, and another subject missing NIS-W (one replicate) and Postural BP (other replicate) at 12 mos. * QST: N=26, 19 for 6 and 12-mo. comparisons, respectively.  * Postural BP: N=19 for 12-mo. comparison

*Data as of March 13, 2015*
### Patisiran Phase 2 OLE Preliminary Study Results*
Comparison of $\Delta NIS$ and $\Delta mNIS+7$ Across FAP Studies

<table>
<thead>
<tr>
<th>12 Months</th>
<th>Natural History (linear)</th>
<th>Natural History (nonlinear)*</th>
<th>Tafamidis Fx1A-201§</th>
<th>Diflunisal Phase 3+</th>
<th>Patisiran Phase 2 OLE†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SEM)</td>
<td>NA</td>
<td>17.8 (8.5)</td>
<td>Prestudy: 17.3 (3.5)</td>
<td>Drug: 6.6 (3.7)</td>
<td>PBO: 12.6 (4.0)</td>
</tr>
<tr>
<td>$\Delta mNIS+7$^</td>
<td>NA</td>
<td></td>
<td>Drug: 5.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SEM)</td>
<td>NA</td>
<td>14.3 (6.8)</td>
<td>Prestudy: 13.9 (2.8)</td>
<td>Drug: 5.3 (3.0)</td>
<td>PBO: 10.1 (3.2)</td>
</tr>
<tr>
<td>$\Delta NIS$</td>
<td></td>
<td></td>
<td>Drug: 4.1</td>
<td></td>
<td>0.4 (1.2)</td>
</tr>
</tbody>
</table>

* Data as of March 13, 2015; comparisons drawn from studies in patients with similar baseline characteristics and not based on head-to-head studies

^ Translated algebraically from NIS (Natural History study, Tafamidis study) or NIS+7 (Diflunisal study)

* Linear interpolation between 0 and 12 month progression for median NIS value (from Gompertz curve fit)

# Predicted progression of median NIS value from Gompertz curve fit

§ Estimated from prestudy rate of change; drug rate as reported

† Linear interpolation from 2-year NIS progression measurement in longitudinal analysis set

† N=20; patisiran results similar in patients with/without concurrent TTR stabilizer therapy; mNIS+7 using full mNIS+7 set (with partial imputation for 2 patients)

SEM: Standard Error of the Mean

---

Adams D et al., XIVth ISA (2014)
Tafamidis EMA assessment report (2011)
Patisiran Phase 2 OLE Preliminary Study Results*

Patisiran generally well tolerated in FAP patients out to 17 months
- 511 doses administered, median of 19 doses/pt, mean treatment duration of 13 mo
- No drug-related SAEs
- Low incidence of mild flushing (22.2%) and IRRs (18.5%)
- No clinically significant LFT or renal function changes
- No study discontinuations
- Includes patients on concurrent tetramer stabilizers

Sustained mean serum TTR knockdown of approximately 80%, with mean knockdown up to 88% between doses, for approximately 16 months

Neuropathy impairment scores stable through 12 months
- Mean change in mNIS+7 and NIS of -2.5 and +0.4 points, respectively
- Compares favorably to 10-18 point increase in mNIS+7 or NIS estimated at 12 months from prior FAP studies in patient population with similar baseline NIS
- Similar results in patients with or without concurrent tetramer stabilizers

In aggregate, results consistent with therapeutic hypothesis that TTR knockdown has potential to halt neuropathy progression

*Data as of March 13, 2015
Phase 3 Study Design

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

**Primary Endpoint**
- mNIS+7 at 18 months

**Secondary Endpoints**
- Norfolk QOL-DN
- NIS-weakness
- mBMI
- 10-meter walk test
- COMPASS-31

**Exploratory Endpoints**
- EQ-5D QOL
- NIS+7
- Serum TTR levels
- Cardiac assessments
- Grip strength
- Rausch-built Overall Disability Scale

**Statistical Considerations**
- Placebo-estimated mNIS+7 progression rate of 17.8 points/yr derived from natural history study of 283 FAP patients
- Study with 90% power to detect as little as 37.5% difference in ΔmNIS+7 between treatment groups with 2-sided alpha=0.05
- Blinded interim analysis (IA) of variance for sample size adjustment
- Potential IA for efficacy under consideration; regulatory discussions pending

Clinicaltrials.gov # NCT01960348
GalNAc-siRNA Conjugates Subcutaneous RNAi Therapeutics

Asialoglycoprotein Receptor (ASGPR)
- Highly expressed in hepatocytes
- High rate of uptake
- Recycling time ~15 minutes
- Conserved across species

Revusiran, ALN-AT3, ALN-PCSsc, ALN-CC5…
- siRNA conjugated to N-acetylgalactosamine (GalNAc) ligand
- Efficient delivery to hepatocytes following subcutaneous administration
- Wide therapeutic index
- “Enhanced stabilization chemistry” (ESC) used with all programs after revusiran
  - Significantly improved potency and durability
Revusiran Non-Clinical Safety Summary

**Rat**
- IND enabling tox (6-weeks, 10 doses)
  - Liver was only target organ of toxicity (dose-dependent minimal to moderate hepatocellular vacuolation)
  - Non-adverse basophilic granules in proximal kidney tubules at ≥30 mg/kg
  - NOAEL set conservatively at 30 mg/kg; based on liver pathology associated with reversible minor increase in liver transaminases at ≥100 mg/kg
- Chronic 6-month tox
  - No new target organ pathologies identified
  - Transient, non-adverse edema seen at injection sites at 100 mg/kg
  - Liver and kidney findings did not progress in severity or incidence with chronic dosing
  - Same NOAEL as 6-week study: 30 mg/kg

**NHP**
- IND enabling tox (6-weeks, 10 doses)
  - No target organs of toxicity were identified
  - NOAEL in NHP (pharmacologically relevant species) was ≥ highest dose tested (>300 mg/kg)
- Chronic 9-month tox
  - No meaningful changes in hematology, coagulation, serum chemistry or urinalysis
  - Transient, non-adverse edema seen at injection sites at 200 mg/kg
  - NOAEL ≥200 mg/kg (highest dose tested)
- CV/Respiratory Safety Pharmacology Study
  - NOEL ≥100 mg/kg
Revusiran Phase 1 Study
Serum TTR lowering in multi-dose weight based (mg/kg) cohorts

- Rapid, dose-dependent, consistent, and durable knockdown of serum TTR
  - Maximum knockdown of serum TTR up to 95%; mean knockdown up to 92.4%
  - Doses of ≥ 5 mg/kg: > 85% mean TTR knockdown

<table>
<thead>
<tr>
<th>Dose Level [mg/kg]</th>
<th>Mean % kd (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>58.2 (11.1)</td>
</tr>
<tr>
<td>5</td>
<td>87.5 (7.2)</td>
</tr>
<tr>
<td>7.5</td>
<td>87.9 (1.2)</td>
</tr>
<tr>
<td>10</td>
<td>92.4 (1.5)</td>
</tr>
</tbody>
</table>

Zimmerman, Heart Failure Society of America 2013
Manoharan, TIDES 2014
Revusiran Phase 2 Study Design

**Study Design**
- Open-label, multi-dose study in patients with TTR cardiac amyloidosis
  - NYHA class ≤ 3 (stable CHF)
  - Concomitant tafamidis, diflunisal, doxycycline/TUDCA allowed
  - Dose/regimen: 5.0 or 7.5 mg/kg, daily x 5, followed by weekly x 5

**Primary Objective**
- Evaluate safety and tolerability of multiple doses of revusiran

**Secondary Objectives**
- Assess PK of revusiran in patients with TTR cardiac amyloidosis
- Assess PD effect on serum TTR

**Exploratory Clinical Measurements**
- NT-proBNP and troponin T and I, Echo, CMR, 6-MWT, NYHA class, mBMI, KCCQ, Quality of Life (EQ-5D-5L)
## Revusiran Phase 2 Study Results

### Demographics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>FAC (n=14)</th>
<th>SSA (n=12)</th>
<th>Total (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean Age</strong></td>
<td>65.0</td>
<td>71.8</td>
<td>68.1</td>
</tr>
<tr>
<td><strong>Gender (M/F)</strong></td>
<td>11/3</td>
<td>12/0</td>
<td>23/3</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td>10 White, 4 African American</td>
<td>12 White</td>
<td>22 White, 4 African American</td>
</tr>
<tr>
<td><strong>Mean Weight [kg]</strong></td>
<td>77.8</td>
<td>83.1</td>
<td>80.3</td>
</tr>
<tr>
<td><strong>TTR Type</strong></td>
<td>T60A (7) V122I (5) S77Y (1) I84S (1)</td>
<td>WT (12)</td>
<td>T60A (7) V122I (5) S77Y (1) I84S (1) WT (12)</td>
</tr>
<tr>
<td><strong>NYHA Class:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1 (7.1%)</td>
<td>1 (8.3%)</td>
<td>2 (7.7%)</td>
</tr>
<tr>
<td>2</td>
<td>12 (85.7%)</td>
<td>9 (75%)</td>
<td>21 (80.8%)</td>
</tr>
<tr>
<td>3</td>
<td>1 (7.1%)</td>
<td>2 (16.7%)</td>
<td>3 (11.5%)</td>
</tr>
<tr>
<td><strong>Karnofsky 60/70/80/90</strong></td>
<td>4/0/5/5</td>
<td>0/1/8/3</td>
<td>4/1/13/8</td>
</tr>
<tr>
<td><strong>Concurrent Stabilizer Use</strong>*</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

* Diflunisal 250 mg BID
### Revusiran Phase 2 Study Results

#### Safety and Tolerability

**Treatment Emergent Adverse Events Possibly or Definitely Related ≥10%**

<table>
<thead>
<tr>
<th></th>
<th>5.0 mg/kg (n=23)</th>
<th>7.5 mg/kg (n=3)</th>
<th>Total (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LFT elevation^</td>
<td>4 (17%)</td>
<td>0</td>
<td>4 (15%)</td>
</tr>
<tr>
<td>Injection site erythema</td>
<td>3 (13%)</td>
<td>0</td>
<td>3 (12%)</td>
</tr>
</tbody>
</table>

^ Preferred Terms: LFT abnormal (1), ALT increased (2), alkaline phosphatase increased (1)

- All related TEAEs mild in severity
  - Injection site reactions occurred in 4 (15%) patients, including erythema (3) and rash (1)
  - Transient mild liver function test (LFT) changes
    - In 3 of 4 patients (<1.5 x ULN ALT) with uninterrupted dosing
    - 1 possibly related SAE for LFT changes (~4 x ULN ALT/AST), which resolved during continued dosing; graded mild in severity
- 2 unrelated SAEs (non-cardiac chest pain, AICD placement)
- No study discontinuations
- No significant changes in renal function, other laboratory chemistries, or hematologic parameters
Revusiran Phase 2 Study Results
Serum TTR Lowering by Dose Group

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Individual Max KD (%)</th>
<th>Mean ± SD Max KD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>26</td>
<td>98.2</td>
<td>85.9 ± 9.2</td>
</tr>
<tr>
<td>5.0 mg/kg</td>
<td>23</td>
<td>97.7</td>
<td>85.1 ± 9.3</td>
</tr>
<tr>
<td>7.5 mg/kg</td>
<td>3</td>
<td>98.2</td>
<td>92.1 ± 5.4</td>
</tr>
</tbody>
</table>

Revusiran (mg/kg), qd x5; qw x5

Genetic Medicines

ACC Annual Meeting, 2015
Revusiran Open-Label Extension (OLE) Study

Patients dosed in Phase 2 trial eligible for Phase 2 OLE study

- **Dosing for up to 2 years**
  - Fixed subcutaneous dose of 500 mg; QDx5 followed by QW
- **Study objectives**
  - Primary: Safety and tolerability of long-term dosing with revusiran
  - Secondary: Effects on mortality, hospitalization, and serum TTR levels
  - Additional exploratory clinical endpoints evaluated every 6 months: 6MWD, Cardiac imaging (echo and MRI), amyloid burden by technetium scans and fat pad aspirates, cardiac biomarkers (BNP, troponins), NYHC, and QOL

**Status**
- Ongoing; enrollment completed (N=25)
- Expect to report 6-month data in late 2015
  - ~15 patients in initial analysis
- Generally well tolerated in majority of patients; three (3) patients discontinued due to injection site reactions (ISRs), including some with associated diffuse rash*

* As of August 5, 2015
Clinicaltrials.gov # NCT02292186
Injection Site Reactions with Oligonucleotides
Experience with Antisense Oligonucleotides (ASOs)

**Mipomersen**
- Pooled Phase 3 experience in patients with hyperlipidemia (N=261): ISRs in 84% with weekly SC dosing
  - Most common signs/symptoms include: erythema, pain, hematoma, pruritus, swelling, and discoloration
  - Most events mild-moderate in severity (severe in 2-3%)

**Drisapersen**
- Phase 2 experience in Duchenne muscular dystrophy (N=35): ISRs in 78-88% with weekly SC dosing
  - Most common signs/symptoms include: discoloration, erythema, hematoma, pain, pruritus, and swelling
  - All events mild-moderate in severity

---

1 Mipomersen FDA Briefing Document (NDA 203568), October 2012
**Patient Population**
- Documented TTR mutation, including V122I or other
- Amyloid deposits on biopsy (cardiac or non-cardiac)
- History of heart failure
- Evidence of cardiac amyloid involvement by echocardiogram

**Co-Primary Endpoints**
- Change in 6-MWD at 18 months compared to baseline
- Percent reduction in serum TTR over 18 months

**Secondary Endpoints**
- Composite CV mortality and CV hospitalization
- Change in NYHA class
- Change in Kansas City Cardiomyopathy Questionnaire (KCCQ)

**Statistical Considerations**
- Placebo-estimated decline in 6-MWD of ~140 meters over 18 months in natural history study of 137 FAC patients (N=39 for 6-MWD data)
- 90% Power to detect as little as 39% difference in 18 mo change from baseline 6-MWD between treatment groups with significance level of $p < 0.05$
- Un-blinded interim analysis for futility when ~50% of patients reach 18 mos

---

*All completers eligible for revusiran treatment on Phase 3 OLE study*
## Change in 6-MWD Over 18 Months
### FAC Natural History Study

<table>
<thead>
<tr>
<th>Visit</th>
<th>Actual Value (meters)</th>
<th>Change from Baseline (meters)</th>
<th>Percentage Change from Baseline (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>Mean (+/−) SEM 281 (20)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>N=39</td>
<td>Range 46, 485</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 6</td>
<td>Mean (+/−) SEM 233 (25)</td>
<td>-36 (23)</td>
<td>-6% (12)</td>
</tr>
<tr>
<td>N=32</td>
<td>Range 0, 465</td>
<td>-426, 209</td>
<td>-100%, 261%</td>
</tr>
<tr>
<td>Month 12</td>
<td>Mean (+/−) SEM 178 (24)</td>
<td>-106 (24)</td>
<td>-34% (7)</td>
</tr>
<tr>
<td>N=27</td>
<td>Range 0, 432</td>
<td>-449, 32</td>
<td>-100%, 15%</td>
</tr>
<tr>
<td>Month 18</td>
<td>Mean (+/−) SEM 158 (35)</td>
<td>-140 (39)</td>
<td>-46% (12)</td>
</tr>
<tr>
<td>N=16</td>
<td>Range 0, 421</td>
<td>-485, 80</td>
<td>-100%, 50%</td>
</tr>
</tbody>
</table>

### Change From Baseline (m)

- 180
- 150
- 120
- 90
- 60
- 30
- 0

### Months from 1st visit

- 0
- 6
- 12
- 18

### Change From Baseline (%)

- 100%
- 50%
- 15%
- 10%
- 5%
- 0%
- 5%

---

*ABC Membership Meeting, March 2015*
Screening Study

**Rationale:**
- Determine frequency of TTR mutations in subjects suspected of having cardiac amyloidosis
- Subjects diagnosed with FAC may be eligible for enrollment in Phase 3 study

**Design:**
- 75 sites, up to 1500 patients
- Sequencing of TTR gene in subjects with HF suspected to have cardiac amyloidosis with 2 or more of the following criteria:
  - Heart failure signs and/or symptoms
  - IVS > 12mm
  - Left ventricular diastolic dysfunction
  - Low voltage ECG
  - History of CTS
- Patients positive for TTR mutation will have follow-up visit
  - Medical history of prior 12-months, echocardiogram, cardiac biomarkers
  - Tissue biopsy and 6-Minute Walk test (optional)

Clinicaltrials.gov # NCT02252653
Alnylam ATTR Amyloidosis Programs Summary

Patisiran for FAP
- Phase 2 OLE study showing sustained TTR knockdown of approximately 80% and evidence for potential halting of neuropathy progression at 12 months, with favorable safety profile out to 17 months
  - Study ongoing
  - Complete 12-month data planned to be presented at ANA meeting in late September
  - Expect to present initial 18-month data in late 2015
- APOLLO Phase 3 on track to enable NDA submission ~2017
  - Potential IA for efficacy under consideration; regulatory discussions pending
  - Enrollment into APOLLO and APOLLO-OLE ongoing

Revusiran for FAC
- “First generation” STC chemistry that enables SC dose administration
- Phase 2 study in TTR cardiac amyloidosis showed robust, sustained >80% TTR knockdown
  - Favorable safety profile with low frequency of mild, transient ISRs and LFT changes, and no flu-like symptoms or changes in renal function
- Phase 2 OLE study ongoing, with plan to report initial 6-month data in late 2015
  - Generally well-tolerated in majority of patients; 3 discontinuations due to ISRs not associated with flu-like symptoms, anti-drug antibodies, or attenuation of TTR lowering
- ENDEAVOUR Phase 3 trial in FAC enrolling
- DISCOVERY screening study ongoing

Advancing ALN-TTRsc02 for ATTR amyloidosis
- ESC “second generation” chemistry
- Expected to enable once-monthly and possibly once-quarterly SC dose administration
- Data and guidance planned at OTS, October 2015
Upcoming Patisiran and Revusiran Events

Upcoming planned presentations
• American Neurological Association (ANA) - Patisiran
  • September 27-29 (Chicago)
• European Congress of ATTR Amyloidosis* - Patisiran and Revusiran
  • November 2-3 (Paris)
• American Heart Association (AHA)* - Revusiran
  • November 7-11 (Orlando)

Upcoming planned milestones
• Continued enrollment in APOLOLO and ENDEAVOUR Phase 3 trials

* Pending abstract acceptance
Agenda

Welcome
• Joshua Brodsky
  Senior Manager, Investor Relations and Corporate Communications

Introduction
• Barry Greene
  President, Chief Operating Officer

Overview of Transthyretin (TTR)-Mediated Amyloidosis
• Philip Hawkins, Ph.D., FRCP, FRCPath, FMedSci, Head, National Amyloidosis Centre, and Head, Periodic Fever Syndrome Service/Honorary consultant physician

Patient Advocacy: Amyloidosis Patient Perspective
• Isabelle Lousada, President & CEO, Amyloidosis Research Consortium, and Chairman, Amyloidosis Foundation

Q&A Session
• With Dr. Hawkins and Isabelle Lousada

Patisiran and Revusiran Programs
• Eric Green, Vice President, General Manager, TTR Program
• Jared Gollob, M.D., Vice President, Clinical Research

Q&A Session
Upcoming RNAi Roundtables

**ALN-GO1 for the treatment of Primary Hyperoxaluria Type 1 (PH1)**  
*Tuesday, September 8, 9:00 – 10:00 a.m. ET*  
- David Erbe, Ph.D., Director, Research  
- Moderator: Barry Greene, President and Chief Operating Officer  
- Guest Speaker: Sally-Anne Hulton, M.D., FRCPCH, MRCP, FCP, MBCh, Consultant Paediatric Nephrologist and Clinical Lead, Birmingham Children’s Hospital NHS Trust

**ALN-PCSsc for the treatment of Hypercholesterolemia**  
*Wednesday, September 16, 9:30 – 10:30 a.m. ET*  
- Kevin Fitzgerald, Ph.D., Vice President, Research  
- David Kallend, MBBS, Vice President and Global Medical Director, The Medicines Company  
- Moderator: Barry Greene, President and Chief Operating Officer  
- Guest Speaker: Marc S. Sabatine, M.D., M.P.H., Chairman, Thrombolysis in Myocardial Infarction (TIMI) Study Group at Brigham and Women’s Hospital, Lewis Dexter, MD Distinguished Chair in Cardiovascular Medicine, and Professor of Medicine, Harvard Medical School

**ALN-AS1 for the treatment of Acute Hepatic Porphyrias**  
*Tuesday, September 24, 11:00 a.m. – 12:00 p.m. ET*  
- Bill Querbes, Ph.D., Associate Director, Research  
- Moderator: John Maraganore, Ph.D., Chief Executive Officer  
- Guest Speaker: Robert J. Desnick, M.D., Ph.D., Dean for Genetics and Genomic Medicine, Professor and Chair Emeritus, Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai Hospital

Replays, presentations, transcripts of all RNAi Roundtables available at www.alnylam.com/capella
Speaker Biographies

Barry Greene
President and Chief Operating Officer, Alnylam
Barry Greene joined Alnylam in 2003, and brings over 25 years of experience in healthcare, pharmaceutical, and biotechnology industries. Prior to Alnylam, he was General Manager of Oncology at Millennium Pharmaceuticals, Inc., where he led the company’s global strategy and execution for its oncology business including strategic business direction and execution, culminating in the successful approval and launch of VELCADE™ (bortezomib) in mid 2003. Prior to joining Millennium in February 2001, Barry served as Executive Vice President and Chief Business Officer for Mediconsult.com. Prior to Mediconsult.com, his past experiences include Vice President of Marketing and Customer Services for AstraZeneca, formerly AstraMerck; Vice President Strategic Integration with responsibility for the AstraZeneca North American post merger integration; and Partner, Andersen Consulting responsible for the pharmaceutical/biotechnology marketing and sales practice. Barry received his B.S. in Industrial Engineering from University of Pittsburgh and served as Senior Scholar at Duke University, Fuqua School of Business. Barry also serves on the Boards of Acorda Therapeutics and Karyopharm Therapeutics.

Philip Hawkins, Ph.D., FRCP, FRCPath, FMedSci
Head, National Amyloidosis Centre, and Head, Periodic Fever Syndrome Service/Honorary consultant physician
Philip Hawkins studied medicine at St. George’s Hospital Medical School, London where he qualified with double distinction in 1982. After training in general internal medicine at St. George’s, he undertook specialist training in rheumatology at the Royal Postgraduate Medical School, Hammersmith Hospital where he subsequently obtained his Ph.D. for studies on the pathogenesis, diagnosis and treatment of amyloidosis during a Medical Research Council Training Fellowship under the supervision of Professor Mark Pepys. He was appointed Senior Lecturer at the Royal Postgraduate Medical School in 1990, and was promoted to Reader in 1994. He has co-held a Medical Research Council Programme Grant with Mark Pepys since 1994, and received a Wellcome Trust University Award in 1997 for his work on amyloidosis. In 1999, he was appointed Professor of Medicine at University College London, and Clinical Director of the NHS National Amyloidosis Centre at the Royal Free Hospital, which was newly commissioned by the UK Department of Health to provide diagnostic and management services for the national amyloidosis caseload. He was awarded the Goulstonian Lectureship of the Royal College of Physicians in 1994 and was elected Fellow of the Academy of Medical Sciences in 2004. His clinical research program is focused on diagnosis, pathogenesis, monitoring and treatment of amyloidosis and inherited autoinflammatory diseases with an emphasis on translational, early phase and otherwise novel approaches. The cohort of amyloid patients referred to the National Amyloidosis Centre is now by far the largest and most diverse in the world.

Isabelle Lousada
President & CEO, Amyloidosis Research Consortium, and Chairman, Amyloidosis Foundation
Isabelle graduated as an architect from University College, London. In her work she focused on public buildings and large scale International Projects. In 1996, she was diagnosed with AL Amyloidosis, and she underwent a successful stem cell transplant. As a patient, she is committed to empowering other patients through knowledge, raising awareness of the disease, and building relations with the scientific community to improve outcomes. Isabelle previously served on the boards of the International Myeloma Foundation and MyelomaUK, where she was active in building their amyloidosis programs. Isabelle has served as the Board Chairman of the Amyloidosis Foundation since 2007. She is also the founder and CEO of the recently formed Amyloidosis Research Consortium, a partner organization with the AF. As CEO of ARC, Isabelle will oversee the Clinical Trials Finder for patients, while focusing on increasing the development of advanced diagnostic tools and effective treatments for systemic amyloidosis.
Speaker Biographies

**Eric Green**  
*Vice President and General Manager, TTR Program, Alnylam*

Mr. Green joined Alnylam in 2015, having most recently worked at Synageva BioPharma, where he was Vice President of Program and Alliance Management. In that role he was responsible for the oversight, management, and leadership of the company’s lead compound being developed as an enzyme replacement therapy for an ultra-orphan genetic disease. Prior to Synageva, he worked as Senior Director, Product Development and Program Management at Infinity Pharmaceuticals, where he developed the clinical and commercial product strategy and led the operational execution for the development of a small molecule product being investigated in non-small cell lung cancer. Before working at Infinity, he spent over eight years at Genzyme Corporation, where he served in roles of increasing responsibility in program and brand management for multiple commercial oncology products. Eric received his Bachelor of Science in Chemical Engineering from the University of Michigan, a Masters in Chemical Engineering from the Massachusetts Institute of Technology (MIT), and an MBA from the MIT Sloan School of Management.

**Jared Gollob, M.D.**  
*Vice President, Clinical Research, Alnylam*

Dr. Gollob joined Alnylam in 2007 and has been responsible for management of the clinical development organization, in addition to serving in a program leadership role for the company’s ALN-TTR programs. Prior to Alnylam, he was an Associate Professor of Medicine and Director of the Biologic Therapy Program at Duke University Medical Center, with a secondary appointment as Associate Professor of Immunology. He was also concurrently Head of Hematology/Oncology at the Duke VA Medical Center. Jared received his A.B. and M.D. from Columbia University, and then completed his clinical training at Massachusetts General Hospital, Harvard Medical School, and the Dana-Farber Cancer Institute. Jared is a board certified Medical Oncologist with interests in tumor biology and development of new treatments for renal cell carcinoma and melanoma. Previously, he has advised Chiron, Schering-Plough, Bayer, and Novartis on their oncology programs.
Thank You

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