Alnylam Forward Looking Statements & Non-GAAP Financial Measures

This presentation contains forward-looking statements, within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. There are a number of important factors that could cause actual results to differ materially from the results anticipated by these forward-looking statements. These important factors include: the direct or indirect impact of the COVID-19 global pandemic or a future pandemic, such as the scope and duration of the outbreak, government actions and restrictive measures implemented in response, material delays in diagnoses of rare diseases, initiation or continuation of treatment for diseases addressed by our products, or in patient enrollment in clinical trials, potential supply chain disruptions, and other potential impacts to our business, the effectiveness or timeliness of steps taken by us to mitigate the impact of the pandemic, and our ability to execute business continuity plans to address disruptions caused by the COVID-19 or a future pandemic; our ability to discover and develop novel drug candidates and delivery approaches and successfully demonstrate the efficacy and safety of our product candidates; pre-clinical and clinical results for our product candidates; actions or advice of regulatory agencies; delays, interruptions or failures in the manufacture and supply of our product candidates and our marketed products; intellectual property matters including potential patent litigation relating to our platform, products or product candidates; and our partner’s ability to obtain regulatory approval for our product candidates, including lumasiran and inclisiran, and our ability to maintain regulatory approval and obtain pricing and reimbursement for products, including ONPATTRO® (patisiran) and GIVLAARI® (givosiran); our progress in continuing to establish a commercial and ex-United States infrastructure; our ability to successfully launch, market and sell our approved products globally, including ONPATTRO and GIVLAARI, and achieve net product revenues for ONPATTRO within our revised expected range during 2020; our ability to successfully expand the indication for ONPATTRO in the future; competition from others using similar technology and developing products for similar uses; our ability to manage our growth and operating expenses within the reduced ranges of guidance provided by us through implementation of further discipline in operations to moderate spend and our ability to achieve a self-sustainable financial profile in the future without the need for future equity financing; our ability to establish and maintain business alliances, including completing an agreement for funding by Blackstone of certain R&D activities for vutrisiran and ALN-AGT; our dependence on third parties, including Novartis, for the development, manufacture and commercialization of inclisiran, Regeneron, for development, manufacture and commercialization of certain products, including eye and CNS products, Ironwood, for assistance with the education about and promotion of GIVLAARI, and Vir for the development of ALN-COV and other potential RNAi therapeutics targeting SARS-CoV-2 and host factors for SARS-CoV-2; the outcome of litigation; and the risk of government investigations; as well as those risks and other factors more fully discussed in our most recent annual, quarterly and current reports filed with the SEC. If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. All forward-looking statements speak only as of the date of this presentation and, except as required by law, we undertake no obligation to update such statements.

This presentation references non-GAAP financial measures. These measures are not in accordance with, or an alternative to, GAAP, and may be different from non-GAAP financial measures used by other companies. The items included in GAAP presentations but excluded for purposes of determining non-GAAP financial measures for the periods referenced herein are stock-based compensation expense and unrealized gain on marketable equity securities. The Company has excluded the impact of stock-based compensation expense, which may fluctuate from period to period based on factors including the variability associated with performance-based grants for stock options and restricted stock units and changes in the Company’s stock price, which impacts the fair value of these awards. The Company has excluded the impact of the unrealized gain on marketable equity securities because the Company believes this item is a one-time event occurring outside the ordinary course of the Company’s business.
RNAi Therapeutics: New Class of Innovative Medicines
Clinically Proven Approach with Transformational Potential

- Nobel Prize-winning science
- Silence any gene in genome
- Potent and durable mechanism of action
- Product engine for sustainable innovation
- Multiple products impacting patients globally
The first RNAi therapeutic is **APPROVED IN U.S., EU, CANADA, JAPAN, SWITZERLAND & BRAZIL**
**ATTR Amyloidosis**

**Rare, Progressively Debilitating, and Often Fatal Disease**

**Description**

Caused by misfolded TTR protein that accumulates as amyloid deposits in multiple tissues including heart, nerves, and GI tract

<table>
<thead>
<tr>
<th>Hereditary ATTR (hATTR) Amyloidosis</th>
<th>~50,000 patients worldwide*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wild-Type ATTR (wtATTR) Amyloidosis</td>
<td>~200,000 – 300,000 patients worldwide</td>
</tr>
</tbody>
</table>


ONPATTRO® Launch Update: Q1 2020
Strong Performance with Significant Growth

$66.7M
ONPATTRO Global Q1
Net Product Revenues

>950
Patients Worldwide on Commercial
ONPATTRO at end of Q1 2020

ROW
U.S.

Q1 2019 Q2 2019 Q3 2019 Q4 2019 Q1 2020
$26.3M $38.2M $46.1M $55.8M $66.7M

$26.3M $38.2M $46.1M $55.8M $66.7M

Q1 2019 Q2 2019 Q3 2019 Q4 2019 Q1 2020
$26.3M $38.2M $46.1M $55.8M $66.7M

Q1 2019 Q2 2019 Q3 2019 Q4 2019 Q1 2020
>400 >500 >600 >750 >950

Patients worldwide on commercial ONPATTRO

Q1 2019 Q2 2019 Q3 2019 Q4 2019 Q1 2020
Potential to Expand Value to Patients Globally for Many Years to Come

* ONPATTRO is approved in the U.S. and Canada for the treatment of the polyneuropathy of hATTR amyloidosis in adults, in the EU, Switzerland and Brazil for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy, and in Japan for the treatment of transthyretin (TTR) type familial amyloidosis with polyneuropathy; † ONPATTRO has not been approved by the FDA, EMA, or any other regulatory agency for cardiac manifestations of amyloidosis. No conclusions can or should be drawn regarding its safety or effectiveness in this population. ‡ Vutrisiran is an investigational agent and has not been approved by the FDA, EMA, or any other regulatory agency and no conclusions can or should be drawn regarding its safety or effectiveness; additional studies and future development possible; ^ Novel siRNA conjugate development candidates for ocular or CNS hATTR amyloidosis not yet selected.

Intended to be illustrative and not intended to represent specific estimates of patient numbers.
The second RNAi therapeutic is NOW APPROVED IN THE U.S. & EU
Acute Hepatic Porphyria (AHP)
Family of Rare Genetic Diseases with Significant Disease Burden

Description
Causes potentially life-threatening attacks and chronic manifestations that negatively impact quality of life

Predominantly
female
commonly misdiagnosed

Patient Population
~3,000
diagnosed in U.S./EU with active disease¹,²

Central Nervous System
- Confusion
- Anxiety
- Depression
- Memory loss
- Fatigue
- Hallucinations
- Seizures

Autonomic Nervous System
- Severe abdominal pain
- Nausea/vomiting
- Hypertension
- Tachycardia
- Constipation
- Hyponatremia

Peripheral Nervous System
- Neuropathic pain
- Sensory loss
- Muscle weakness
- Paralysis
- Respiratory failure

Cutaneous†
- Lesions on sun-exposed skin

Long-term Complications
- Hepatocellular carcinoma
- Chronic kidney disease
- Hypertension
- Neuropathy


† Symptoms specific to hereditary coproporphyria and variegate porphyria
GIVLAARI® Launch Update: Q1 2020
Strong Initial Demand in U.S.

$5.3M
GIVLAARI Q1
Net Product Revenues

>50
Patients on Commercial GIVLAARI at end of Q1 2020 (U.S.)

$0.2M
$5.3M
Q4 2019
Q1 2020

13
Q4 2019
Q1 2020

 Patients on commercial GIVLAARI (U.S.)
 Submitted Start Forms* (since launch)

* Start Forms are an incomplete picture of U.S. demand
GIVLAARI® (givosiran) Market Opportunity
Ultra-Rare Orphan Disease with Significant Disease Burden and Limited Treatment Options

**PREVALENCE**
~3,000 patients in U.S./EU, diagnosed with active disease\(^1,2\)

**DIAGNOSIS**
~20-50% currently diagnosed; delays up to 15 years

**DISEASE BURDEN**
65% recurrent attack patients with chronic symptoms\(^3\)

**COST BURDEN**
$400–650K average annual expenditure, recurrent attack patients\(^4\)

GIVLAARI | ACUTE HEPATIC PORPHYRIA

>$500M potential market opportunity

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2 Data on file, IBM MarketScan Commercial Claims and Medicare Supplemental Database
3 Gouya, et al. EASL 2018
4 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.
### Multiple Launches Planned in Next 12-24 Months

<table>
<thead>
<tr>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>Partnered programs*: 2020-2021</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ONPATTRO</strong></td>
<td><strong>GIVLAARI</strong></td>
<td><strong>Lumasiran</strong></td>
<td><strong>Vutrisiran</strong></td>
<td>Inclisiran</td>
</tr>
<tr>
<td>Onpattro (patisiran)</td>
<td>Givlaari (givosiran)</td>
<td>Primary hyperoxaluria type 1 Ph3 ✓</td>
<td>ATTR amyloidosis</td>
<td>Hypercholesterolemia Ph3 ✓</td>
</tr>
<tr>
<td>ONPATTRO is indicated in the U.S. for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults*</td>
<td>GIVLAARI is indicated in the U.S. for the treatment of adults with acute hepatic porphyria†</td>
<td>NDA and MAA accepted (PDUFA date 12/3/2020)</td>
<td>Phase 3 enrolling</td>
<td>NDA and MAA accepted Phase 3 enrolling</td>
</tr>
</tbody>
</table>

* Novartis is leading and funding development of inclisiran and will commercialize inclisiran, assuming regulatory approvals; Sanofi Genzyme is leading and funding development of fitusiran and will commercialize fitusiran, if successful

† ONPATTRO is approved in Canada for the polyneuropathy of HATTR amyloidosis in adults, the EU, Switzerland and Brazil for the treatment of HATTR amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy, and Japan for the treatment of transthyretin (TTR) type familial amyloidosis with polyneuropathy; For additional information on ONPATTRO, see Full Prescribing Information

† GIVLAARI is approved in the EU for the treatment of acute hepatic porphyria (AHP) in adults and adolescents over 12 years old; Alnylam has filed for marketing authorization for givosiran in Brazil and plans to file in Japan and other countries in 2020; For additional information on GIVLAARI, see Full Prescribing Information

Anticipated dates of launch based on current development timelines for investigational therapeutics and assuming positive pivotal study data and regulatory approval

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Robust pipeline fuels sustainable product launches **beyond 2021**, leveraging global commercial infrastructure.
### Alnylam Commercial Products and Late Stage Clinical Development Pipeline

<table>
<thead>
<tr>
<th>Focused in 4 Strategic Therapeutic Areas (STArS):</th>
<th>BREAKTHROUGH DESIGNATION</th>
<th>LATE STAGE (Phase 2-Phase 3)</th>
<th>REGISTRATION</th>
<th>COMMERCIAL RIGHTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic Medicines</td>
<td>hATTR Amyloidosis¹</td>
<td></td>
<td></td>
<td>Global</td>
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<tr>
<td>Cardio-Metabolic Diseases</td>
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<tr>
<td>Infectious Diseases</td>
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<tr>
<td>CNS/Ocular Diseases</td>
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</tbody>
</table>

**hATTR Amyloidosis¹**

- Approved in the U.S. and Canada for the polyneuropathy of hATTR amyloidosis in adults, in the EU, Switzerland and Brazil for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy, and in Japan for the treatment of transthyretin (TTR) type familial amyloidosis with polyneuropathy.

**Acute Hepatic Porphyria²**

- Approved in the U.S. for the treatment of adults with acute hepatic porphyria (AHP), and in the EU for the treatment of AHP in adults and adolescents aged 12 years and older.

**Lumasiran**

- Approved in the U.S. for the treatment of primary hyperoxaluria type 1.

**Inclisiran**

- Approved in the U.S. for the treatment of hypercholesterolemia.

**Patisiran**

- Approved in the U.S. for the treatment of ATTR amyloidosis label expansion.

**Fitusiran**

- Approved in the U.S. for the treatment of hemophilia and rare bleeding disorders.

**Vutrisiran**

- Approved in the U.S. for the treatment of ATTR amyloidosis.

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¹ Approved in the U.S. and Canada for the polyneuropathy of hATTR amyloidosis in adults, in the EU, Switzerland and Brazil for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy, and in Japan for the treatment of transthyretin (TTR) type familial amyloidosis with polyneuropathy.

² Approved in the U.S. for the treatment of adults with acute hepatic porphyria (AHP), and in the EU for the treatment of AHP in adults and adolescents aged 12 years and older.

³ As part of Blackstone strategic financing collaboration, 50% of inclisiran royalty revenue will be payable to Blackstone.

As of May 2020
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

Primary Endpoint
- Change in 6-MWT at 12 months

Key Secondary Endpoints
- Cardiomyopathy symptoms and health status
- Death and hospitalization outcomes
- Cardiac biomarkers

Study initiated
September 2019
Enrollment completion shifted to 2021 due to COVID-19

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
Phase 3 Study Results
Encouraging Evidence for Patisiran’s Potential in ATTR Cardiomyopathy

~50% Reduction in all-cause hospitalization and mortality in post-hoc analysis

Cardiac Safety Data in Entire APOLLO Study Population:

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo(^2) (n=77)</th>
<th>Patisiran(^2) (n=148)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>6.2 (2.5 – 12.7)</td>
<td>3.2 (1.4 – 6.2)</td>
</tr>
<tr>
<td>All-cause hospitalization</td>
<td>69.7 (54.3 – 87.7)</td>
<td>32.9 (25.9 – 41.1)</td>
</tr>
<tr>
<td>Cardiac hospitalization</td>
<td>15.6 (9.0 – 24.9)</td>
<td>8.2 (5.0 – 12.6)</td>
</tr>
<tr>
<td>Hospitalization and/or death</td>
<td>71.8 (56.1 – 90.1)</td>
<td>34.7 (27.5 – 43.1)</td>
</tr>
<tr>
<td>Cardiac hospitalization and/or death</td>
<td>18.7 (11.4 – 28.8)</td>
<td>10.1 (6.4 – 14.9)</td>
</tr>
</tbody>
</table>

\(^1\) Patisiran has not been approved by the FDA, EMA, or any other regulatory agency for cardiac manifestations of amyloidosis. No conclusions can or should be drawn regarding its safety or effectiveness in this population

\(^2\) For any hospitalization/death analysis: negative binomial regression rate ratio (RR) 0.49 [0.30, 0.79]; Anderson-Gill hazard ratio (HR) 0.48 [0.34, 0.69]

\(^\dagger\) nominal p<0.01; \(^\ddagger\) nominal p<0.05; Solomon S, et al. Circulation 2018
Patisiran Treatment of hATTR Amyloidosis

Evidence for Potential Cardiac Amyloid Regression

Recent uncontrolled case series

Recently published similar findings by Nienhuis et al.

Patisiran treatment may be associated with cardiac remodeling and/or amyloid regression

Cardiac effects to be further assessed in randomized, controlled trials

1 Patisiran has not been approved by the FDA, EMA, or any other regulatory agency for cardiac manifestations of amyloidosis. No conclusions can or should be drawn regarding its safety or effectiveness in this population.

2 Gillmore, OTS Munich 2019

3 Mayo Clinic Proceedings, 2019
Vutrisiran Opportunity
Advancing Continued Innovation to Patients with ATTR Amyloidosis

Mean max TTR KD of 83% after single 25 mg dose*

Phase 1 Study – Healthy Volunteers†

Safety (N=80):
- No SAEs and no discontinuations due to AEs
- All AEs mild or moderate in severity

Vutrisiran

4 DOSES PER YEAR

~90% peak TTR KD predicted after repeat dosing

* Taubel J, et al. Phase 1 Study of ALN-TTRsc02, a Subcutaneously Administered Investigational RNAi Therapeutic for the Treatment of Transthyretin-Mediated Amyloidosis. ISA 2018: XVIIth International Symposium of Amyloidosis; Kumamoto, Japan; March 2018 (poster)
† As of data cutoff on May 31, 2017
Vutrisiran Phase 3 Program
Robust Registrational Program to Evaluate Vutrisiran in Hereditary & Wild-Type ATTR Amyloidosis

**HELIOS**

**HELIOS·A**
Randomized, open-label study in hereditary ATTR amyloidosis patients with polyneuropathy

- Enrollment complete
- Topline results expected early 2021

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

- Enrollment ongoing
- Study includes optional interim analysis
Randomized, Open-Label Study in Hereditary ATTR Amyloidosis Patients

N ~ 160

Patient Population
- hATTR amyloidosis; any TTR mutation
- Neuropathy Impairment Score (NIS) of 5-130
- Prior tetramer stabilizer use permitted

3:1 RANDOMIZATION

Vutrisiran SC q3M 25 mg

or

Reference Comparator (patisiran)

Efficacy Assessments vs. APOLLO placebo arm

Co-Primary Endpoints
- Change in mNIS+7 from baseline
- Change in Norfolk QOL-DN from baseline

9-Month Efficacy^ 
- Assessment vs. APOLLO placebo arm

18-Month Efficacy
- Assessment vs. APOLLO placebo arm

Open-Label Extension

HELIOS-A Phase 3 study enrollment complete
Topline results expected early 2021

^ Primary endpoint for the study is at 9 months
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

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

Select Secondary Endpoints
- 6-MWT distance
- Kansas City Cardiomyopathy Questionnaire (KCCQ OS) score
- Echocardiographic parameters
- All-cause mortality and recurrent all-cause hospitalizations
- All-cause mortality
- Recurrent CV hospitalizations
- NT-proBNP

Vutrisiran SC q3M 25 mg
or
Placebo SC q3M

HELIOS-B Phase 3 study
now enrolling
Study includes optional interim analysis
Primary Hyperoxaluria Type 1

Lumasiran

Description
Rare autosomal recessive disorder of increased oxalate synthesis resulting in kidney stones and renal failure, with subsequent oxalate accumulation in extra-renal tissues

Onset generally pediatric
very limited treatment options

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>~3,000 – 5,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S./EU</td>
<td></td>
</tr>
</tbody>
</table>

- Retinal Oxalosis
- Cardiomyopathy
- Nephrocalcinosis
- Renal stones
- ESRD
- Skeletal Involvement
Lumasiran NDA and MAA Accepted
Robust Registrational Program to Evaluate Lumasiran Across all Ages and Full PH1 Disease Spectrum

**ILLUMINATE**

**ILLUMINATE-A**

Double-blind, placebo-controlled trial in PH1 patients at least 6 years old with preserved renal function

Full results presented June 2020; FDA approval anticipated by YE 2020

**ILLUMINATE-B**

Single arm, open-label study in PH1 patients less than 6 years old with preserved renal function

Enrollment complete; Topline results expected in mid-2020

**ILLUMINATE-C**

Single arm, open-label study in PH1 patients with impaired renal function, including advanced disease

Topline results expected in 2021

Expanded Access Protocol (EAP) for PH1 patients at least 6 years old with preserved renal function initiated in U.S. and Europe
Lumasiran ILLUMINATE·A Phase 3 Study
Met Primary and All Tested Secondary Endpoints with Encouraging Safety and Tolerability Profile

Rapid and sustained reduction in 24hr urinary oxalate levels from baseline to Month 6

Majority of patients achieved near-normalization (≤1.5 x ULN) or normalization (≤ULN) in 24hr urinary oxalate levels at Month 6

Safety
- No deaths, severe, or serious AEs. All AEs mild or moderate
- Most common related AEs were injection-site reactions
  - All transient and mild in severity; no treatment interruption or discontinuation
  - Most common symptoms: erythema, pain, pruritus, or discomfort at injection site
- No hepatic AEs reported in either group
- No clinically relevant changes in laboratory measures, vital signs, and electrocardiograms related to lumasiran observed

Difference in LS mean average M3-M6 (Lumasiran-Placebo) (p=1.7 x 10^{-14})
-53.5%

Mean maximal reduction
-76.0%

Dosing
 Patients (N) 13 26 12 26 13 24 13 23 13 25 13 25

BL, baseline; BSA, body surface area; hr, hour; LS, least squares; M, month; ULN, upper limit of normal; AE, adverse event

*p-value is based on Cochran–Mantel–Haenszel test stratified by baseline 24 hr urinary oxalate corrected for BSA (≤1.70 vs >1.70 mmol/24 hr/1.73 m²)
Lumasiran Market Opportunity
First-in-Class Target Product Profile in Ultra-Rare Orphan Disease

<table>
<thead>
<tr>
<th>PREVALENCE</th>
<th>DIAGNOSIS</th>
<th>DISEASE BURDEN</th>
<th>COST BURDEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>~3–5K patients</td>
<td>~50% currently diagnosed; mean time to diagnosis ~6 years</td>
<td>30–65% reach end-stage renal disease before diagnosis</td>
<td>$1M+ average cost (transplant &amp; lifelong immunosuppression)</td>
</tr>
</tbody>
</table>

LUMASIRAN | PRIMARY HYPEROXALURIA TYPE 1

>$500M potential market opportunity

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Late Stage Partnered Program Opportunities

<table>
<thead>
<tr>
<th>INCLISIRAN</th>
<th>FITUSIRAN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypercholesterolemia</strong></td>
<td><strong>Hemophilia A or B, with and without inhibitors</strong></td>
</tr>
<tr>
<td><strong>40%</strong> Adults WW with high LDL-C; ASCVD leading cause of death WW</td>
<td><strong>~200K</strong> Patients WW with hemophilia A or B, with and without inhibitors</td>
</tr>
<tr>
<td><strong>&gt;50M</strong> Patients in key markets with ASCVD or FH on current SOC not at goal</td>
<td><strong>~75%</strong> Patients switched to emicizumab due to convenience (less frequent dosing, SC)²</td>
</tr>
<tr>
<td><strong>7%</strong> Treated patients statin intolerant</td>
<td><strong>&lt;10%</strong> Emicizumab patients on monthly dosing³</td>
</tr>
<tr>
<td><strong>&gt;60%</strong> Patients treated with statins +/- ezetimibe do not meet goal¹</td>
<td><strong>~90%</strong> Emicizumab patients experienced acute bleeds²</td>
</tr>
</tbody>
</table>

**NDA and MAA accepted; FDA approval anticipated by YE 2020**

**Topline results expected in H1 2021 per Sanofi**

¹ Boekholt et al. Very Low LDL-C levels and CVD Risk JACC VOL 64.No5 2014:485-94
² Consumer Awareness, Trial, and Usage study among patients conducted over 359 Adult patients and caregivers surveyed online in April 2019, of which 131 were Adult Hemophilia A patients and 78 were Hemophilia A caregivers. Patients who switched to emicizumab answered questions specific to their treatment experience
³ 2019 Specialty Pharmacy data obtained through Specialty Pharmacy Distributors, Hemophilia Alliance HTCs and Direct HTCs
Alnylam Early Stage Clinical Development and 2020 IND Pipeline

Focused in 4 Strategic Therapeutic Areas (STArs):
- Genetic Medicines
- Cardio-Metabolic Diseases
- Infectious Diseases
- CNS/Ocular Diseases

<table>
<thead>
<tr>
<th></th>
<th>HUMAN POC¹</th>
<th>BREAKTHROUGH DESIGNATION</th>
<th>2020 IND CANDIDATES</th>
<th>EARLY STAGE (Phase 1-Phase 2)</th>
<th>COMMERCIAL RIGHTS</th>
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<tbody>
<tr>
<td>Cemdisiran</td>
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<td>50-50 (Regeneron)</td>
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<td>Complement-Mediated Diseases</td>
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<tr>
<td>Cemdisiran/Pozelimab Combo²</td>
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<td>Milestone/Royalty (Regeneron)</td>
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<td>Complement-Mediated Diseases</td>
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<td>ALN-AAT02 (DCR-A1AT)³</td>
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<td>Ex-U.S. option post-Phase 3 (Dicerna)</td>
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<td>Alpha-1 Liver Disease</td>
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<tr>
<td>ALN-HBV02 (VIR-2218)</td>
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<td>50-50 option post-Phase 2 (Vir)</td>
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<tr>
<td></td>
<td>Hepatitis B Virus Infection</td>
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<td>ALN-AGT</td>
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<td></td>
<td>Hypertension</td>
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<td>ALN-HSD</td>
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<td></td>
<td></td>
<td>Milestone/Royalty (Regeneron)</td>
</tr>
<tr>
<td></td>
<td>NASH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALN-COV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>50-50 option post-Phase 2 (Vir)</td>
</tr>
<tr>
<td>(VIR-2703)</td>
<td>COVID-19</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2-4 INDs per year planned from organic product engine

¹ POC, proof of concept – defined as having demonstrated target gene knockdown and/or additional evidence of activity in clinical studies
² Cemdisiran is currently in Phase 2 development and pozelimab is currently in Phase 1 development; Alnylam and Regeneron are evaluating potential combinations of these two investigational therapeutics
³ Dicerna is leading and funding development of ALN-AAT02 and DCR-A1AT and will select which candidate to advance in development

As of May 2020
ALN-AGT for Hypertension
Unmet Need, Mechanism of Action, and Initial Phase 1 Topline Results

Initial Phase 1 Topline Results (N=48)\(^2\)

- >90% AGT knockdown
- >10 mmHg reduction in mean 24-h systolic blood pressure relative to placebo
- Durability supportive of once quarterly and possibly less frequent dosing
- Encouraging safety and tolerability profile with no drug-related SAEs

Results to be presented at scientific meeting in **late 2020**

---

\(^1\) McClellan et al., Circulation, 2019

\(^2\) As of April 29, 2020 data transfer date
COVID-19 Targeting Strategy

Broad, Multifaceted RNAi Therapeutics Effort with Vir

**Virus**
- SARS-CoV-2 RNA genome and viral transcripts
- Selected development candidate, ALN-COV (VIR-2703), with potent and highly cross-reactive activity; plan for accelerated IND filing at or around year-end 2020

**Host Factors**
- ACE2: viral entry receptor for SARS-CoV-2 and other coronaviruses
- TMPRSS2: cleaves SARS-CoV-2 spike protein to facilitate cellular attachment to ACE2
- Third target expected from Vir’s functional genomics efforts to identify novel host factors pertinent to coronaviral infection

Sources: Song et al., *Viruses*, 2019; Jiang et al., *Emerging Microbes and Infections*, 2012; *The Economist*
RNAi Therapeutics for CNS and Ocular Diseases
Expand Alnylam Opportunities Beyond Liver

Devastating diseases with enormous burden and unmet need

- Alzheimer’s disease
- Amyotrophic lateral sclerosis (ALS)
- Cerebral amyloid angiopathy
- Frontotemporal dementia
- Huntington’s disease
- Multi-system atrophy
- Parkinson’s disease
- Spinocerebellar ataxia
- AMD, dry
- AMD, wet
- Birdshot chorioretinopathy
- Dominant retinitis pigmentosa 4
- Fuch’s dystrophy
- hATTR amyloidosis
- Hereditary and sporadic glaucoma
- Stargardt’s disease

Investigational RNAi therapeutics demonstrate potent, widely distributed, and highly durable effects

**ALN-APP**
Targeting amyloid precursor protein (APP) for hereditary cerebral amyloid angiopathy (hCAA)

- hCAA caused by APP mutations leading to arteriolar Aβ deposition with microbleeds and intracranial hemorrhages
- Multiple CSF and radiologic biomarkers for early readout
- Study of hCAA potential gateway to larger indications (e.g., sporadic CAA, EOFAD, AD)

**ALN-HTT**
Targeting huntingtin gene (HTT) for early manifest Huntington’s disease

- Autosomal dominant, gain-of-function genetic disease with 100% age-related penetrance
- Patients present with progressive motor, cognitive and psychiatric decline
- Affects ~30,000 in U.S. with disease duration of 15-20 years
Guidance, Goals, & Perspective
## Alnylam 2020 Goals

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

<table>
<thead>
<tr>
<th>Product</th>
<th>2020*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early</td>
</tr>
<tr>
<td><strong>onpattro</strong> (patisiran)</td>
<td></td>
</tr>
<tr>
<td>(ATTR Amyloidosis)</td>
<td></td>
</tr>
<tr>
<td>Global Commercial Execution</td>
<td>✓</td>
</tr>
<tr>
<td>Brazil Approval</td>
<td>✓</td>
</tr>
<tr>
<td>Additional Country Launches</td>
<td>✓</td>
</tr>
<tr>
<td>APOLLO-B Enrollment</td>
<td>✓</td>
</tr>
<tr>
<td><strong>GIVLAARI</strong> (givosiran)</td>
<td></td>
</tr>
<tr>
<td>(Acute Hepatic Porphyria)</td>
<td></td>
</tr>
<tr>
<td>EMA Approval</td>
<td>✓</td>
</tr>
<tr>
<td>Global Commercial Execution</td>
<td>✓</td>
</tr>
<tr>
<td>Additional ENVISION Results</td>
<td></td>
</tr>
<tr>
<td>Additional Country Filings and Approvals</td>
<td>✓</td>
</tr>
<tr>
<td><strong>VUTRISIRAN</strong> (ATTR Amyloidosis)</td>
<td>Complete HELIOS-A Enrollment</td>
</tr>
<tr>
<td>HELIOS-B Enrollment</td>
<td>✓</td>
</tr>
<tr>
<td><strong>LUMASIRAN</strong> (Primary Hyperoxaluria Type 1)</td>
<td>File NDA and MAA</td>
</tr>
<tr>
<td>FDA/EMA Approval</td>
<td></td>
</tr>
<tr>
<td>ILLUMINATE-B Phase 3 Topline</td>
<td></td>
</tr>
<tr>
<td><strong>ADDITIONAL CLINICAL PROGRAMS</strong></td>
<td>Continue to advance early/mid-stage pipeline; File 2-4 new INDs; Present clinical data</td>
</tr>
<tr>
<td><strong>PARTNERED PROGRAMS</strong></td>
<td></td>
</tr>
<tr>
<td><strong>INCLISIRAN</strong> (Hypercholesterolemia)</td>
<td>FDA Approval</td>
</tr>
<tr>
<td>MAA Filing</td>
<td></td>
</tr>
<tr>
<td>ORION-4 CVOT Phase 3 Enrollment (<em>paused due to COVID-19</em>)</td>
<td></td>
</tr>
<tr>
<td><strong>FITUSIRAN</strong> (Hemophilia)</td>
<td>Support Sanofi on ATLAS Phase 3</td>
</tr>
</tbody>
</table>
Productivity of Alnylam RNAi Therapeutic Platform

Comparison of Historical Industry Metrics to Alnylam Portfolio

Past rates of Alnylam and industry respectively may not be predictive of the future.

1 Wong et al., Biostatistics (2019) 20, 2, pp. 273–286

Probability of Success (POS) by Phase Transition

- % POS, Phase 1 to 2
- % POS, Phase 2 to 3
- % POS, Phase 3
- % POS, Cumulative

Alnylam programs biomarker-driven at all stages of development (100%).

Industry (biomarker-driven programs) 100%

Industry (overall)
Path to Self-Sustainability

A Top Priority for Alnylam

Strong Q1 2020 balance sheet of $1.37B*
- $2B strategic partnership with Blackstone anchors path toward self-sustainable financial profile without need for future equity financing

Focused on key levers affecting pathway
- Topline growth
- Disciplined investment

2019 projected to be peak non-GAAP NOL year

* including cash, cash equivalents, marketable debt and equity investments and restricted investments

# Late Stage Programs:

- 2015: 2
- 2016: 1
- 2017: 4
- 2018: 6
- 2019: 6
- 2020: 6

# Commercial Products:

- 2015: 0
- 2016: 0
- 2017: 0
- 2018: 1
- 2019: 2
- 2020: 4
# Building a Top-Tier Biotech

Potential for Significant Transformation of Alnylam over Next 6 Years

<table>
<thead>
<tr>
<th>Today</th>
<th>2025</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approved Products</td>
<td>8+ Approved Products</td>
</tr>
<tr>
<td>Late Stage Programs</td>
<td>10+ Late Stage Programs</td>
</tr>
<tr>
<td>STArs</td>
<td>4+ STArs</td>
</tr>
<tr>
<td>10+ Markets</td>
<td>Global</td>
</tr>
<tr>
<td>~1K Employees</td>
<td>~2.5K Employees</td>
</tr>
<tr>
<td>CMOs</td>
<td>Norton + CMOs</td>
</tr>
</tbody>
</table>

**Top 5 independent, global biopharma company**
admired for its dedication to
patients, corporate culture, scientific innovation, social responsibility, and commercial excellence with numerous RNAi products across orphan and large disease areas.
Financial Summary and Guidance as of May 6, 2020

<table>
<thead>
<tr>
<th>Financial Results ($ millions)</th>
<th>Three Months Ended March 31, 2020</th>
<th>Three Months Ended March 31, 2019</th>
<th>Full Year 2020 Guidance (as of May 6, 2020)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ONPATTRO Net Product Revenues</td>
<td>$66.7</td>
<td>$26.3</td>
<td>$270 - $300</td>
</tr>
<tr>
<td>GIVLAARI Net Product Revenues</td>
<td>$5.3</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Net Revenue from Collaborations</td>
<td>$27.5</td>
<td>$7.0</td>
<td>$100M - $150M</td>
</tr>
<tr>
<td>Total Revenues</td>
<td>$99.5</td>
<td>$33.3</td>
<td></td>
</tr>
<tr>
<td>Costs of Goods Sold</td>
<td>$13.3</td>
<td>$3.3</td>
<td></td>
</tr>
<tr>
<td>Gross Margin (% of net product revenues)</td>
<td>82%</td>
<td>87%</td>
<td></td>
</tr>
<tr>
<td>GAAP R&amp;D Expenses</td>
<td>$169.6</td>
<td>$129.1</td>
<td></td>
</tr>
<tr>
<td>GAAP SG&amp;A Expenses</td>
<td>$126.8</td>
<td>$89.6</td>
<td></td>
</tr>
<tr>
<td>Combined GAAP R&amp;D and SG&amp;A Expenses</td>
<td>$296.3</td>
<td>$218.7</td>
<td>$1,155 - $1,250</td>
</tr>
<tr>
<td>Non-GAAP R&amp;D Expenses¹</td>
<td>$153.5</td>
<td>$113.0</td>
<td></td>
</tr>
<tr>
<td>Non-GAAP SG&amp;A Expenses¹</td>
<td>$108.2</td>
<td>$73.7</td>
<td></td>
</tr>
<tr>
<td>Combined Non-GAAP R&amp;D and SG&amp;A Expenses¹</td>
<td>$261.8</td>
<td>$186.7</td>
<td>$1,000 - $1,075</td>
</tr>
<tr>
<td>GAAP Operating Income/(Loss)</td>
<td>($210.2)</td>
<td>($188.8)</td>
<td></td>
</tr>
<tr>
<td>Non-GAAP Operating Income/(Loss)²</td>
<td>($175.6)</td>
<td>($156.8)</td>
<td></td>
</tr>
<tr>
<td>Cash &amp; Investments³</td>
<td>$1,366.9</td>
<td>$1,551.0</td>
<td></td>
</tr>
</tbody>
</table>

Some negative impact from COVID-19 expected in Q2 2020 with ONPATTRO revenues potentially decreasing by ~10% vs. Q1 2020; improvement and growth expected in second half of 2020

$2 billion strategic financing collaboration with Blackstone expected to enable Alnylam’s achievement of a self-sustainable financial profile without need for future equity financing

Guidance and cash expectations as of May 6, 2020: $600 million in cash added to balance sheet in Q2 2020 with close of Blackstone strategic financing

¹ Non-GAAP R&D and SG&A expenses exclude stock-based compensation expenses; ² Non-GAAP net loss excludes stock-based compensation expenses and unrealized gains on marketable equity securities

³ Cash, cash equivalents, marketable debt and equity securities, and restricted investments
To those who say “impossible, impractical, unrealistic,” we say:

CHALLENGE ACCEPTED