



Alnylam: Lessons Learned in Transitioning from Transformative R&D to WW launch

Theresa Heggie
October 17, 2019

The Alnylam Epic Journey



Alnylam Journey is a Three-Act Play

Based on Nobel-Prize winning science, focused on rare genetic diseases, invested and investing in Europe



Extra copies of same gene = Cosuppression

Alnylam was founded in 2002 with a vision to turn RNA interference (RNAi), a Nobel-Prize winning discovery, into a new class of medicines

1. Science

Among RNAi's broad potential, Alnylam has made the deliberate, scientifically guided choice of focusing on diseases where the unmet medical need is high, primarily rare genetic diseases

2. Innovation

Alnylam continues to invest in Europe and around the world through clinical research, job creation and partnerships with the health community to improve patients' lives

3. Impact

Alnylam Today: the Leader in RNAi Therapeutics

~25 sites in 18 countries

- Includes: US, Switzerland, UK, France, Portugal, Spain, Germany, Austria, Italy, Benelux, Japan, Brazil, Canada
- >1200 employees

Global commercial company

- ONPATTRO for hATTR amyloidosis w/ polyneuropathy
- Approved in U.S., EU, Japan, Canada, Switzerland

Robust product portfolio

- Focus on 4 Strategic Therapeutic Areas (STARs)
 - Genetic Medicines, Cardio-Metabolic Disease, Hepatic Infectious Disease, and CNS/Ocular Disease
- 10 Programs in clinical development
 - 1 in Phase 4, 1 in Registration, 4 in Phase 3

Leaders in RNAi technology

- Design, synthesis, characterization, and delivery

Leading IP estate

- Robust fundamental, delivery and product-specific patent protection

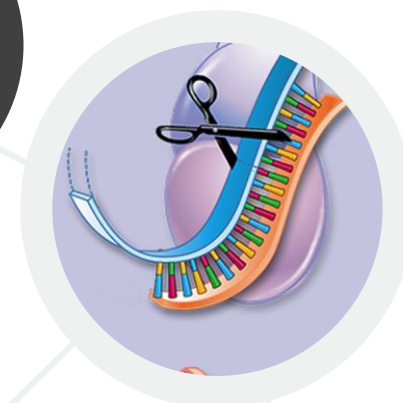
Industry-leading partnerships and collaborations

- >12 major partnerships with Pharma/Biotech

Well-capitalized and strong balance sheet

- Raised ~\$5.3B, invested ~\$3B since inception
- ~\$8B market cap; Q2'19 cash ~\$2B

Vision:
*Harnessing a
revolution in
biology for
human health®*

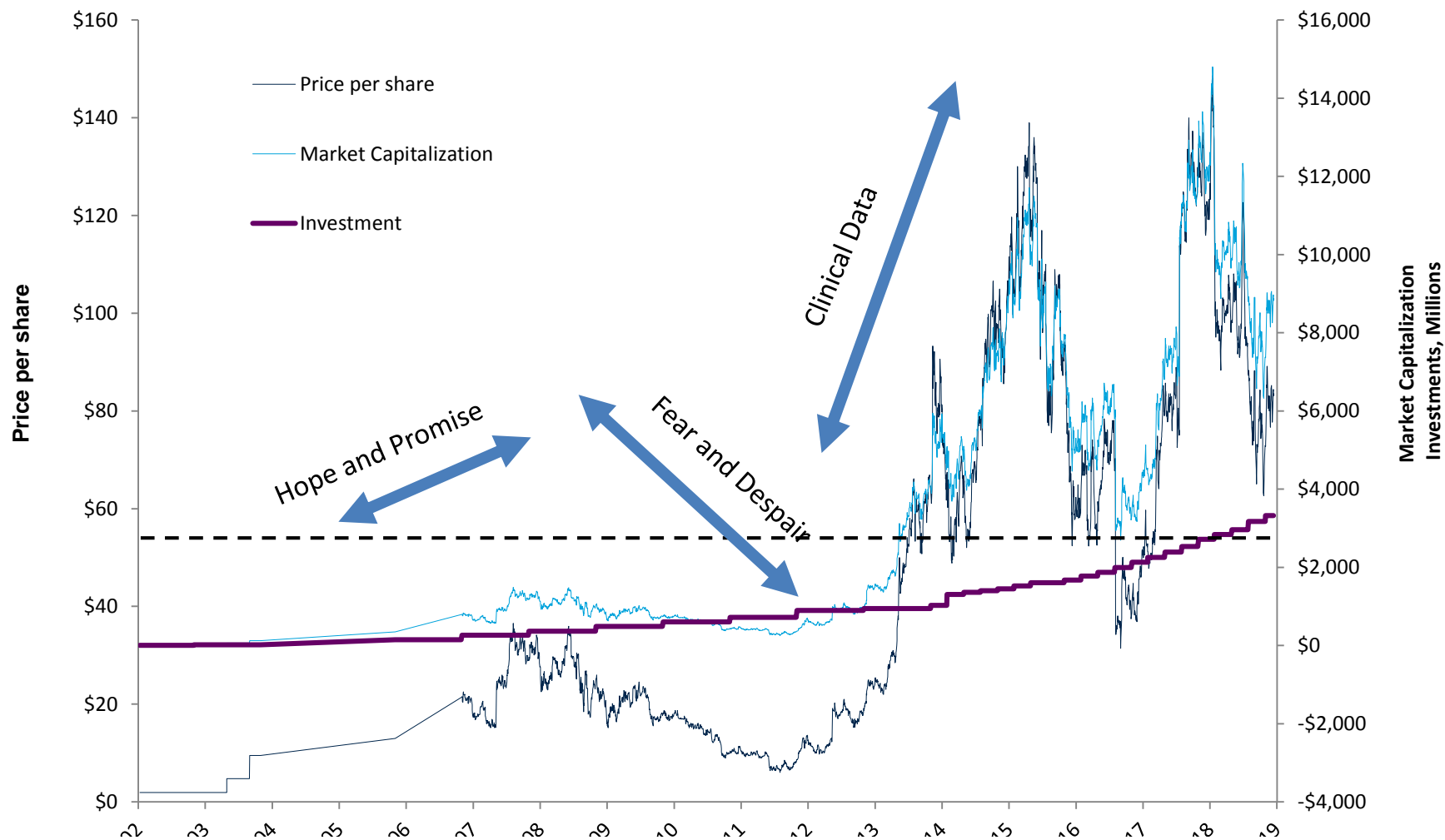


Mission:
*Build a top-tier,
independent
biopharmaceutical
company founded
on RNAi*

ALNY Value Since Inception

ALNY Value Since Inception

PPS / Market Cap / Enterprise Value / Investment



The first RNAi therapeutic is APPROVED IN U.S., EU, CANADA & JAPAN and SWITZERLAND



onpattro®
(patisiran) lipid complex injection
10 mg/5 mL

onpattro®
2 mg/mL concentrate for solution
for infusion patisiran

オンパットロ®
パチシランナトリウム注射液2mg/mL



Israel Filing

MAA submitted June 2019



Brazil Filing

NDA submitted October 2019

Supporting ONPATTRO® Success Globally

Alnylam Commitment to Medical and Commercial Excellence



Alnylam: Building a Biotech Leader

Global commercial-stage biotech with emerging self-sustainability

- Address patient unmet needs around world
- Transitioning toward profitability over next 3-5 years

Deep clinical pipeline of transformative medicines to fuel robust growth

- Rich pipeline with large number of late-stage programs
- Essentially annual product launches for foreseeable future

Product engine to fuel organic and sustainable innovation for future

- Reproducible and modular approach for discovery
- Leadership in advancing a whole new class of medicines

Culture and team in place for long-term success

- Industry leadership and recognition
- Commitment to patients and excellence

Anylam Clinical Development Pipeline

Focused in 4 Strategic Therapeutic Areas (STArS):

- Genetic Medicines
- Cardio-Metabolic Diseases
- Hepatic Infectious Diseases
- CNS/Ocular Diseases

HUMAN
POC¹










BREAKTHROUGH
DESIGNATION

EARLY STAGE
(IND or CTA Filed-Phase 2)

LATE STAGE
(Phase 2-Phase 4)

REGISTRATION/
COMMERCIAL³

COMMERCIAL
RIGHTS

	hATTR Amyloidosis ²						Global
Givosiran	Acute Hepatic Porphyria						Global
Patisiran	ATTR Amyloidosis Label Expansion						Global
Fitusiran	Hemophilia and Rare Bleeding Disorders						15-30% royalties
Inclisiran	Hypercholesterolemia						Milestones & up to 20% royalties
Lumasiran	Primary Hyperoxaluria Type 1						Global
Vutrisiran	ATTR Amyloidosis						Global
Cemdisiran	Complement-Mediated Diseases						50-50
Cemdisiran/Pozelimab Combo ⁴	Complement-Mediated Diseases						Milestone/Royalty
ALN-AAT02	Alpha-1 Liver Disease						Global
ALN-HBV02 (VIR-2218)	Hepatitis B Virus Infection						50-50 option rights post-Phase 2
ALN-AGT	Hypertension						Global

- 3 STArS with Clinical Programs
- 1 Marketed Product
- 10 Clinical Programs
- 5 Late-Stage Programs
- 3 Breakthrough Designations
- Substantial Global Rights

¹ POC, proof of concept – defined as having demonstrated target gene knockdown and/or additional evidence of activity in clinical studies

² Approved in the U.S. and Canada for the polyneuropathy of hATTR amyloidosis in adults, in the EU 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


³ Includes marketing application submissions

⁴ Cemdisiran is currently in Phase 2 development and pozelimab is currently in Phase 1 development; Anylam and Regeneron are evaluating potential combinations of these two investigational therapeutics
As of September 2019

Reflections on our 16-year Journey

- Founded on and stayed committed to a **BOLD** Vision and Mission
- Committed to scientific and business **EXCELLENCE** in everything we've done
- Pioneered new frontiers of medicine advancing a **WHOLE NEW DRUG CLASS**
- Took major **RISKS** and conquered key technology **HURDLES**
- Clear partnership principles that bring **COMPLIMENTARY CAPABILITIES**
- **GREAT** people and “**CHALLENGE ACCEPTED**” culture were key success factors
- Pursued **BREADTH** of opportunity, but **FOCUSED** when needed
- Great at **THINKING LONG-TERM**; making decisions not just for today but how to grow from a product perspective and geographically
- Always kept **PATIENTS** front and center





To those who say “impossible,
impractical, unrealistic,” we say:

CHALLENGE ACCEPTED