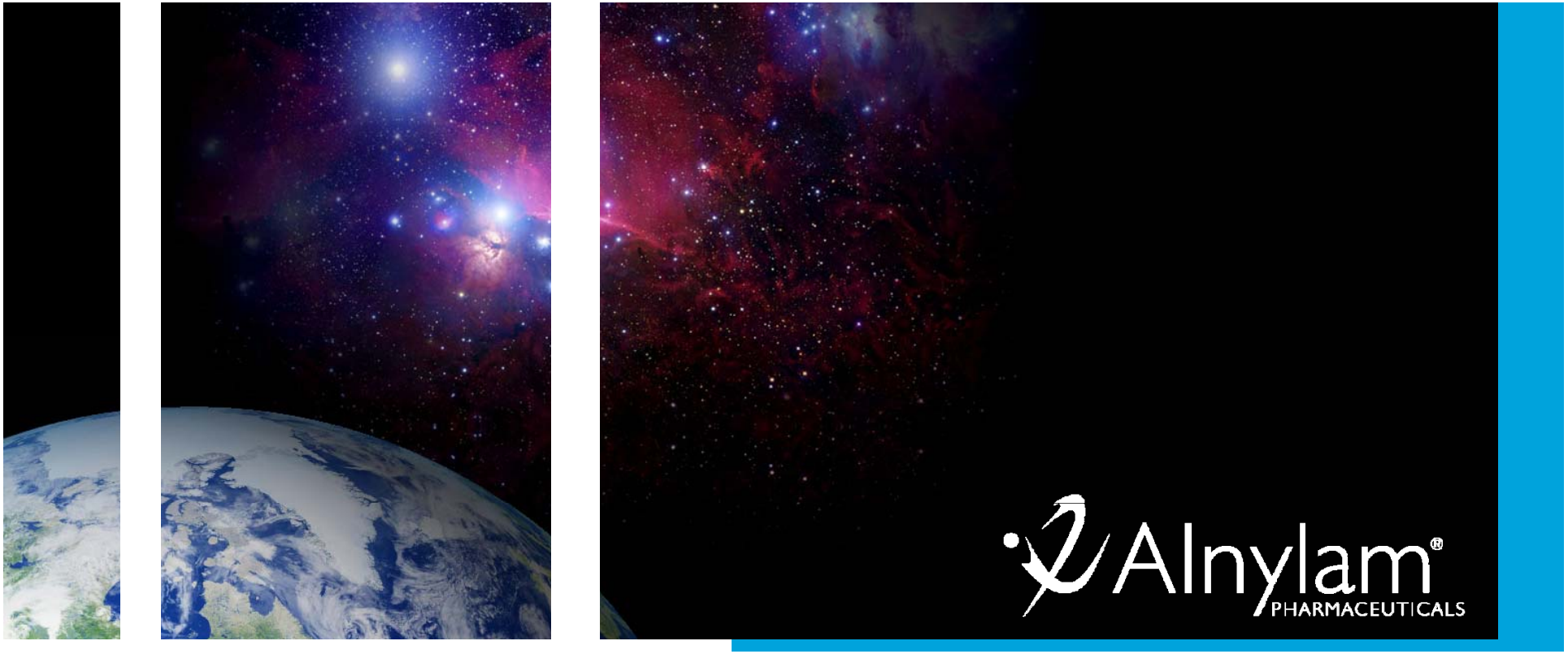


Piper Jaffray
22nd Annual Health Care Conference

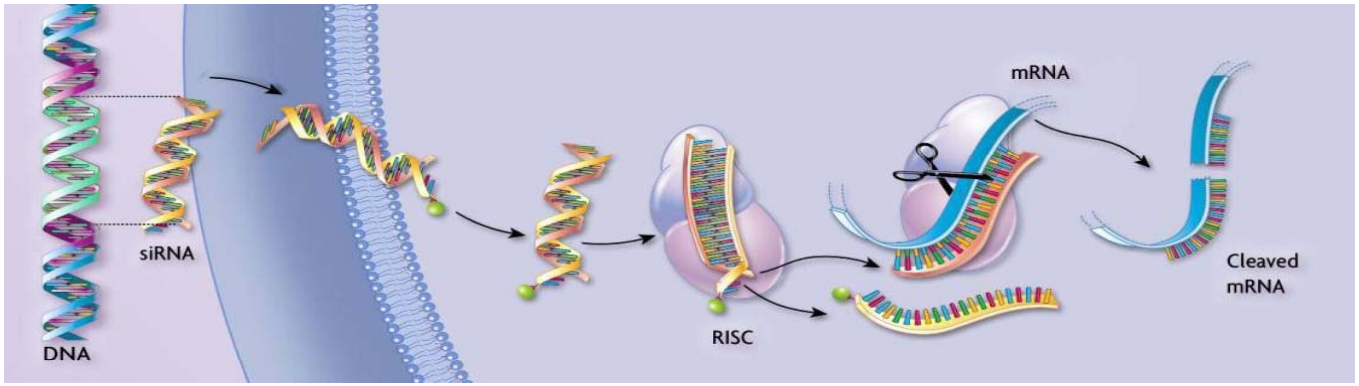
November 30, 2010

Alnylam Forward Looking Statements

This presentation contains forward-looking statements. 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 those that we discuss 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.

RNA Interference (RNAi)

A "Discovery that Happens Only Every Decade or So"



Potential for a whole new class of drugs

- Harness natural pathway
  - » Catalytic mechanism
  - » Mediated by small interfering RNAs or "siRNAs"
- Achieve therapeutic gene silencing
  - » Any gene in genome

Major breakthroughs in delivery achieved

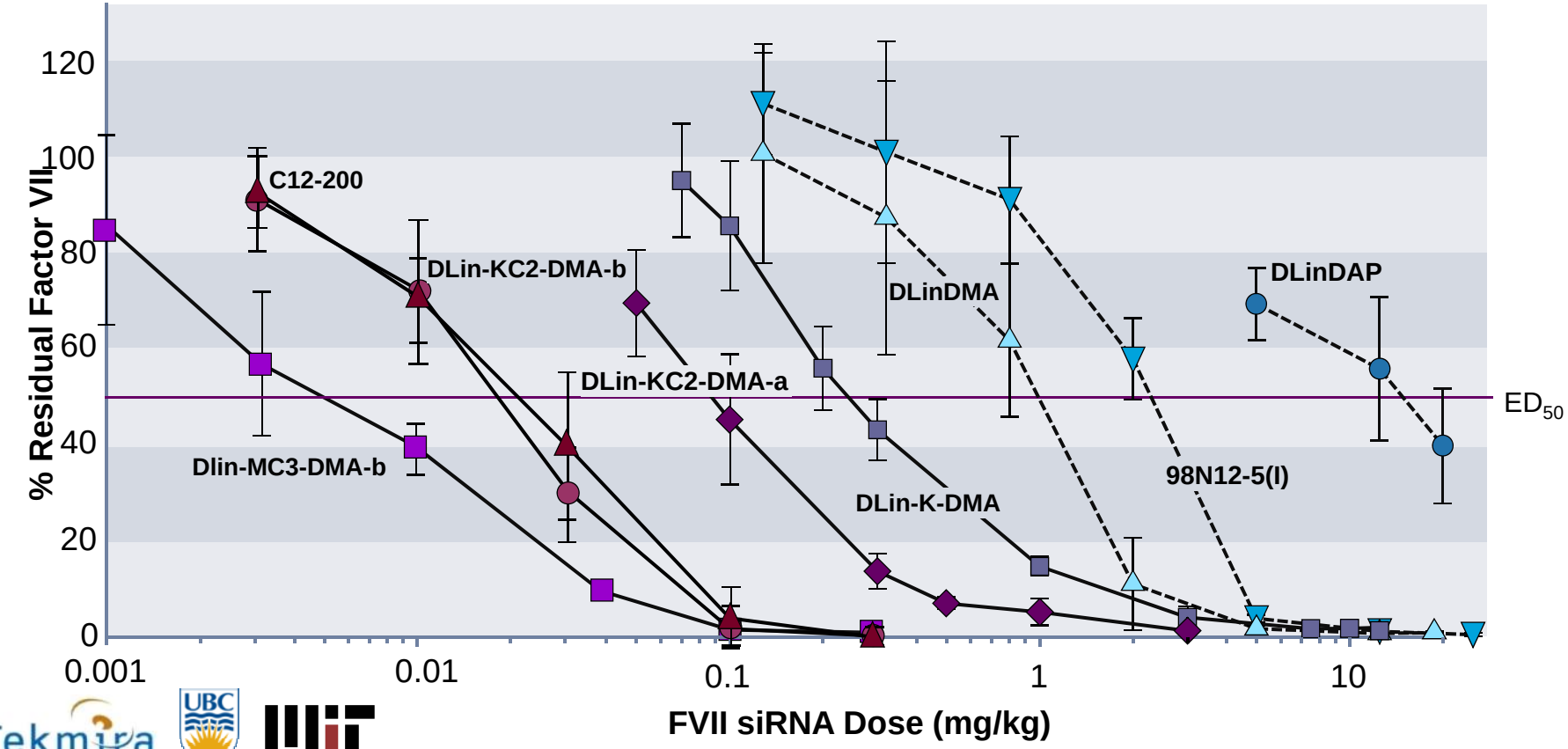
- Including systemic RNAi with formulations and chemistries
- Now enables advancement of products to clinic and market

Next Generation LNPs

Remarkable Potency Improvements with Novel Lipids

Novel LNPs set new benchmark for systemic RNAi with ~100 fold improved potency

- Efficacy in pre-clinical models following single IV injection
- Each LNP comprised of distinct cationic lipid component
- Improvement in potency has resulted in ED_{50}<0.01 mg/kg

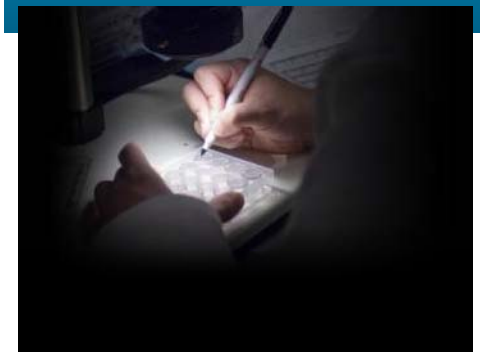


Keystone: Advance in Biopharm., Jan 2010; *Int'l Liposome Research Days*, Aug 2001

Alnylam Strategy

Build a New Top-Tier Biopharmaceutical Company Founded on RNAi

Leadership
Lead translation of science to products



Products
Advance innovative medicines

Intellectual Property
Build value with leading IP estate

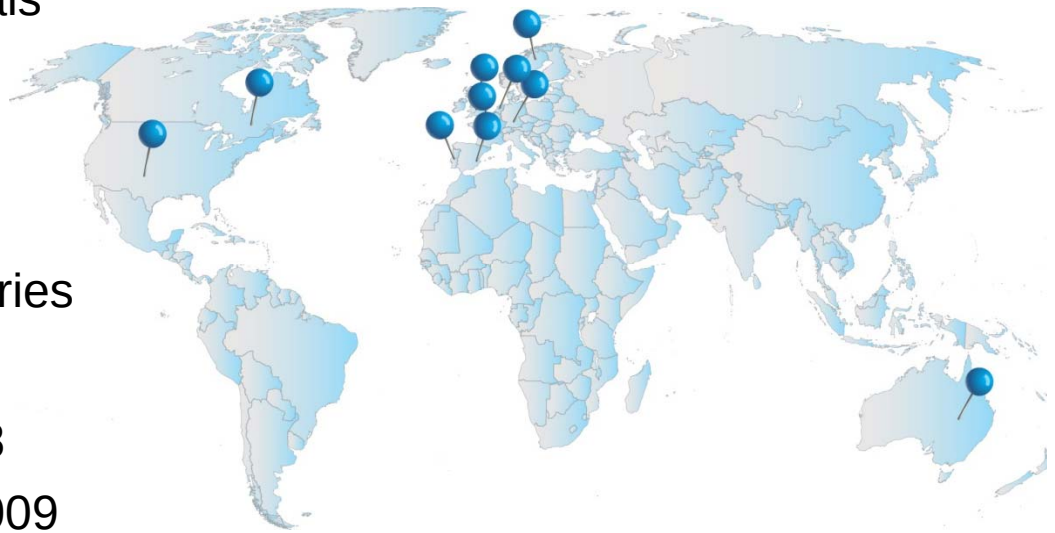
Business
Forge value-creating alliances

Clinical Development of RNAi Therapeutics

Mapping Alnylam's Progress

Clinical Progress

- 8 Completed or ongoing clinical trials
- ~400 Subjects/patients enrolled
- Studies conducted in 10 countries



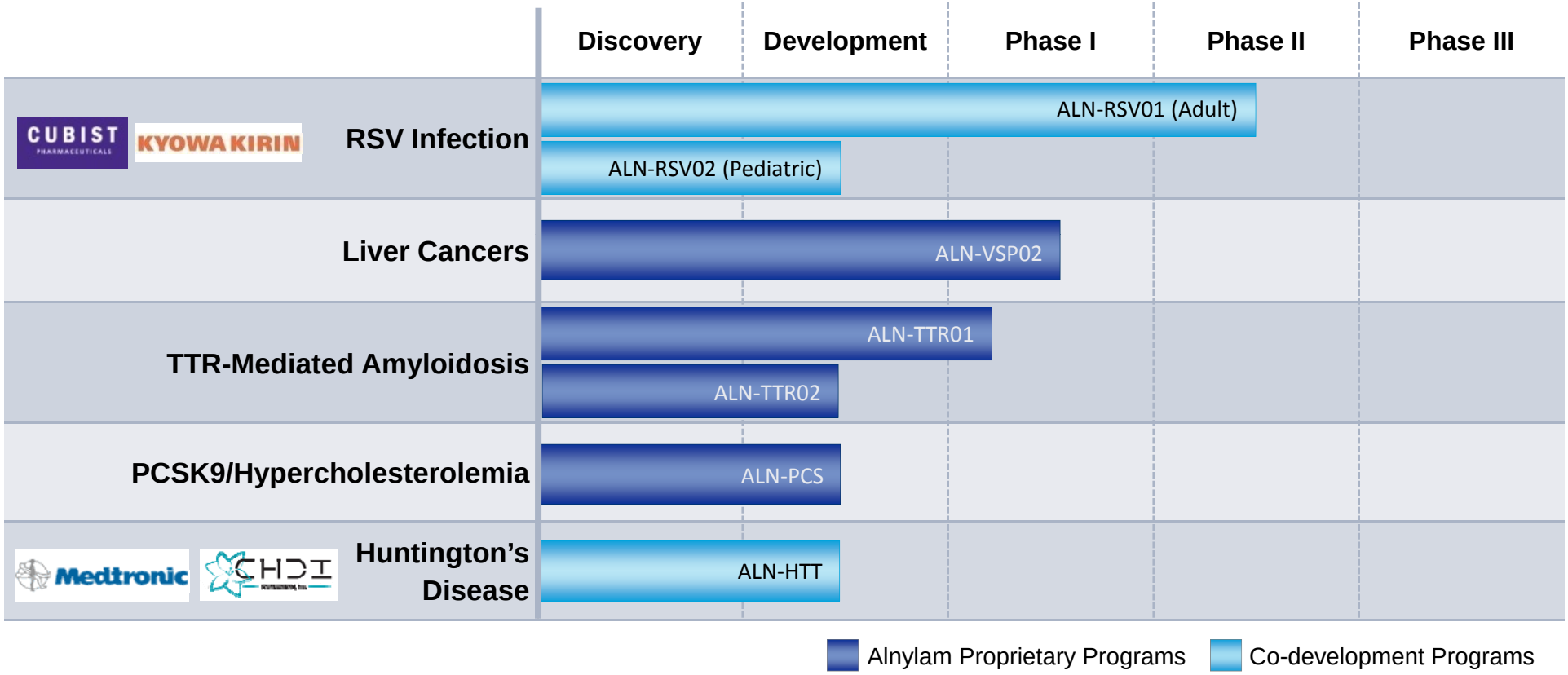
Regulatory Experience

- Regulatory interactions in 10 countries

Key Milestones

- 1st Human proof of concept in 2008
- 1st Systemic delivery program in 2009

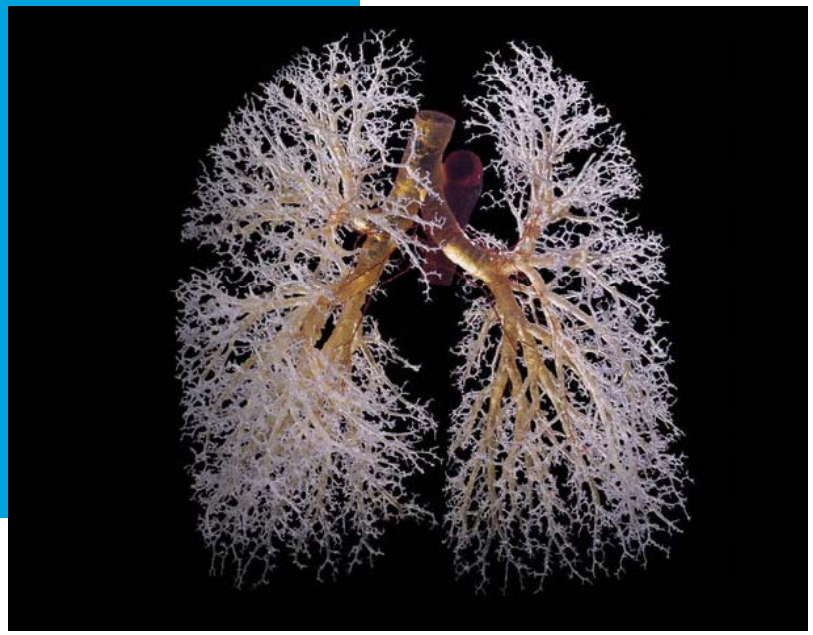
Alnylam Development Pipeline
Key Programs



Respiratory Syncytial Virus (RSV)

Harness RNAi for a major infectious disease

- RSV Infection is major unmet medical need
  - » >125,000 Pediatric hospitalizations/yr in US
  - » >170,000 Adult hospitalizations/yr in US
  - » Causes bronchiolitis, pneumonia, and possibly death
- No effective therapies to treat RSV infection
  - » Synagis used for prevention



ALN-RSV01 in clinical trials

- Phase IIb adult lung transplant study ongoing
- 50-50 Partnership with Cubist for US
- Partnered with Kyowa Hakko Kirin in Asia

Liver Cancer

RNAi to treat liver cancers

- Prevalent solid tumor and common site of metastatic disease
  - » ~700,000/yr Incidence of HCC worldwide
  - » ~500,000/yr Patients with liver metastasis
  - » Poor prognosis with ~1-2 years median survival

ALN-VSP in clinical development

- Phase I liver cancer study enrolling
- ASCO 2010/Chemotherapy Foundation Symposium: Encouraging initial data
  - » Dose escalation ongoing
- Targets two key genes involved in liver cancer disease pathway
  - » KSP for proliferation; VEGF for angiogenesis

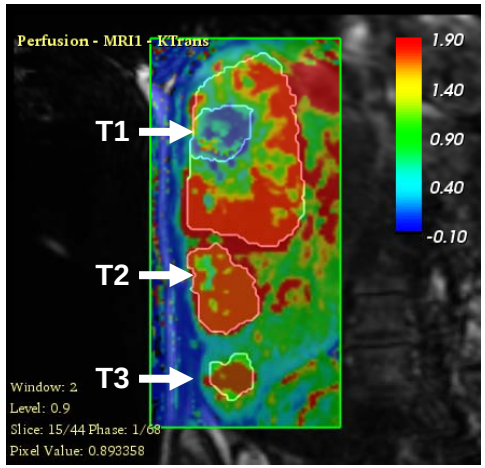
ALN-VSP02 Phase I Study Results

Preliminary Data at ASCO 2010 and Chemotherapy Foundation Symposium

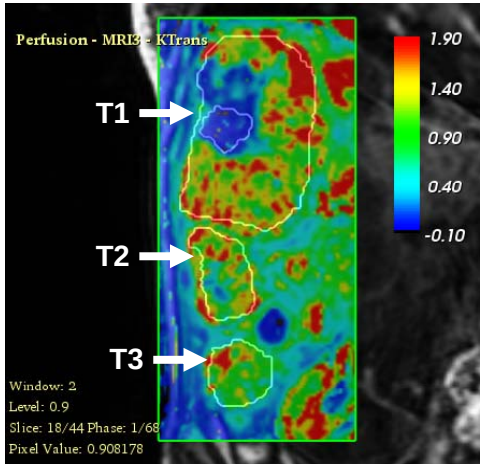
Presented Data Demonstrate Tolerability, PK and PD Effects

- Trial continuing in dose escalation
  - » 28 Patients enrolled; 127 Total doses administered; Range of 2-13 doses/patient
  - » MTD not yet achieved
- ALN-VSP02 well tolerated in most patients
  - » No dose-dependent trends in clinical/laboratory adverse effects, including changes in LFTs
- Plasma PK dose-proportional with no evidence of drug accumulation
- 17 Biopsy samples obtained for molecular analysis; Ongoing
- While preliminary, some encouraging pharmacodynamic data
  - » >40% decline in Ktrans in 62% of evaluable liver tumors
- Several patients at higher dose groups with stable disease, enrolled in extension study

Baseline (BL) Pre-Dose



Day 7 Post-Dose 1

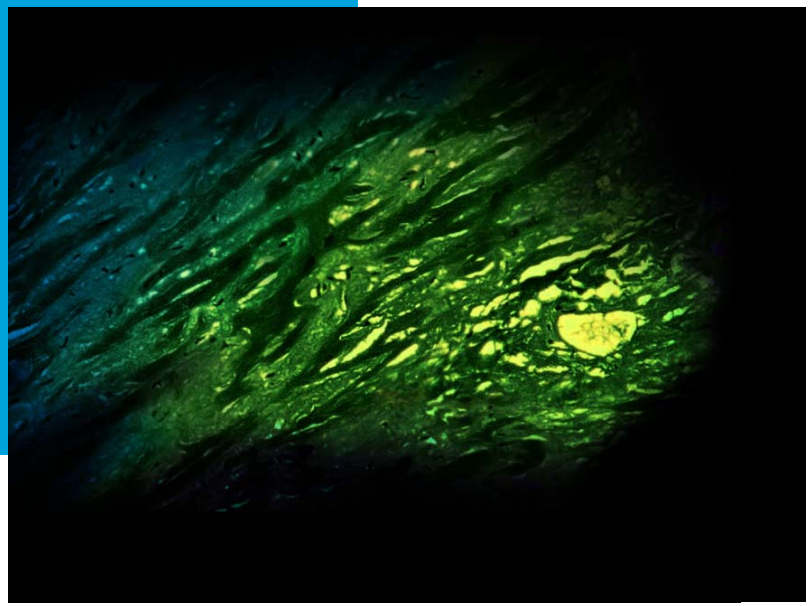


ASCO, June 2010; *Chemotherapy Foundation Symposium*, November 2010

Transthyretin-Mediated Amyloidosis (ATTR)

RNAi to treat an orphan genetic disease

- ATTR is well defined orphan disease
  - » Caused by transthyretin (TTR) gene mutations
  - » Amyloid deposits in nerves and heart
  - » ~50,000 patients worldwide
- Clinical pathology
  - » Onset ~30 to >60 years
  - » Fatal within 5-15 years
- Liver transplant current standard of care



ALN-TTR01 in clinical development

- Initiated Phase I in ATTR patients, July 2010
- Additional second generation program (ALN-TTR02)

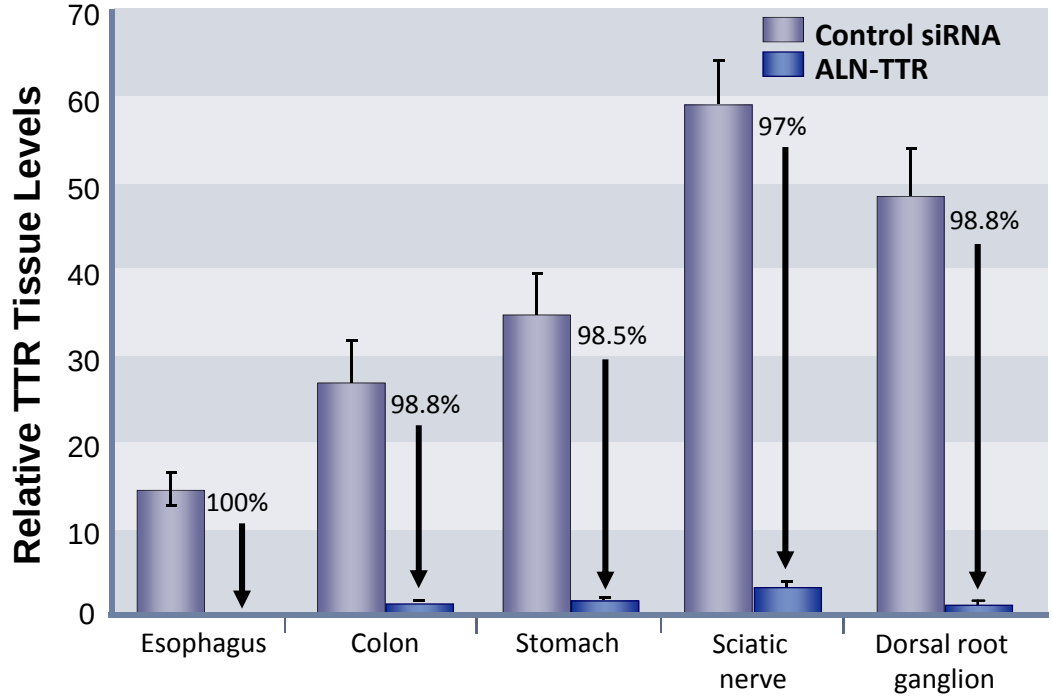
Alnylam PHARMACEUTICALS

ALN-TTR Therapeutic Efficacy

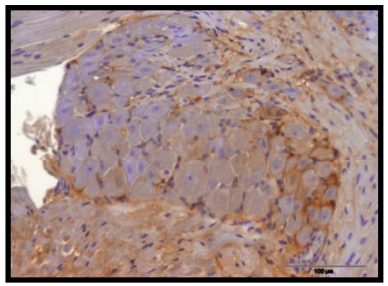
V30M TTR Transgenic Model

ALN-TTR promotes regression of pathogenic mutant human TTR deposits in peripheral tissues in pre-clinical models

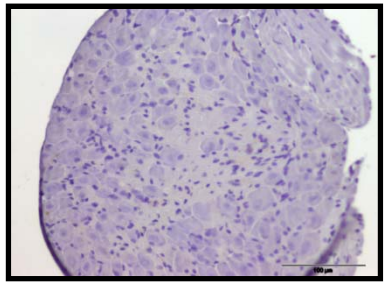
- >90% Regression of existing V30M hTTR tissue deposits
- Multi-dose IV bolus of ALN-TTR01 or control siRNA, 3 mg/kg (week 0, 2, 4, 6, 8, 10)
- Quantitation of TTR deposition by immunohistochemistry (week 11)



Dorsal Root Ganglion



Control siRNA



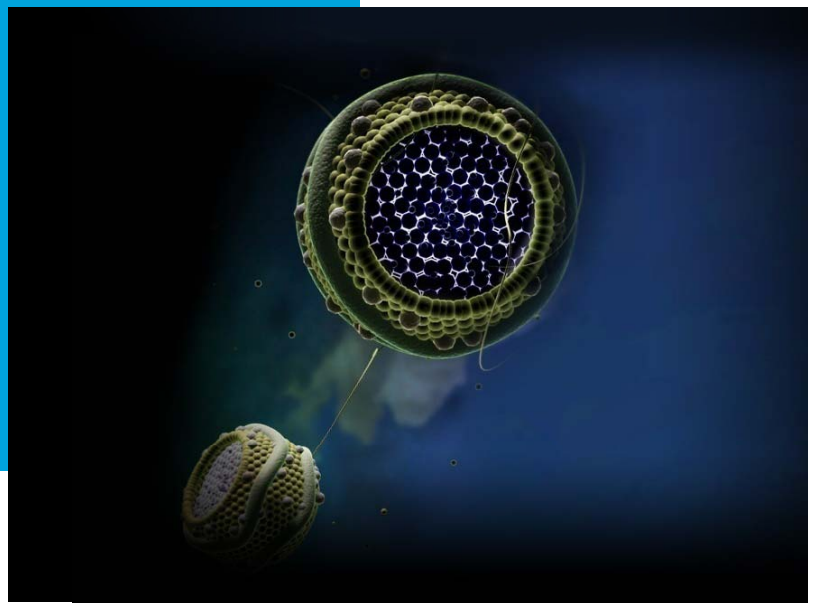
ALN-TTR01

Int'l Amyloidosis Symp., April 2010

Severe Hypercholesterolemia

RNAi to treat severe hypercholesterolemia

- Significant unmet medical need
  - » >500,000 Patients with severe hypercholesterolemia
    - – Inadequately managed by statins and other drugs
  - » Associated with risk of coronary artery disease and myocardial infarction



ALN-PCS in development

- Goal: Initiate Phase I, 2011
- ALN-PCS targets the PCSK9 gene, a key regulator of LDL metabolism
  - » Controls expression of LDL receptor
  - » RNAi targets *both* intracellular and extracellular PCSK9
  - » Validated in human genetics

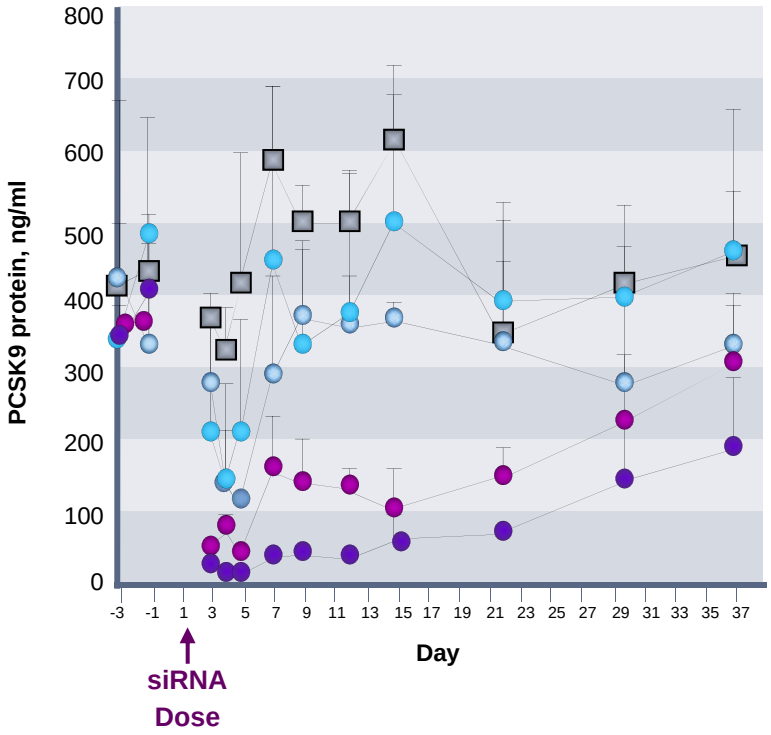
Alnylam PHARMACEUTICALS

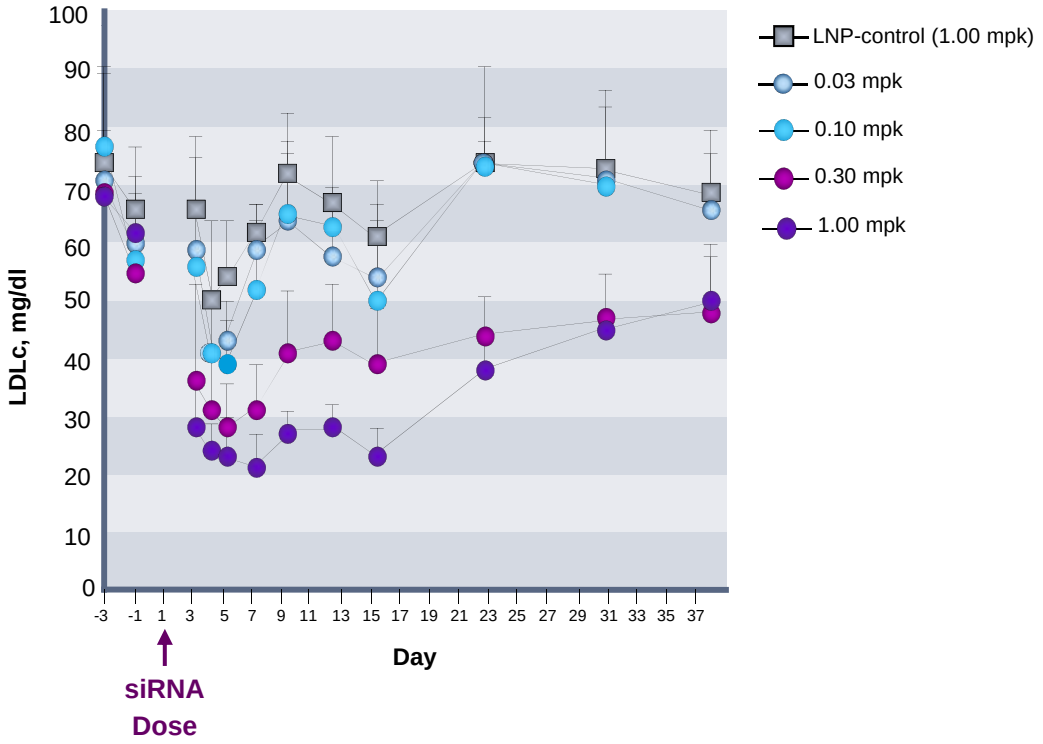
ALN-PCS Pre-Clinical Efficacy

Potent Silencing of PCSK9 and Reductions in LDLc

ALN-PCS demonstrates potent efficacy in pre-clinical models >30 days after single dose

- Employs 2nd generation LNPs
- Rapid and durable dose-dependent reduction in PCSK9 protein
- PCSK9 silencing results in >50% reductions in LDLc
- No decrease in HDL levels





PCSK9 Conference: From Gene to Therapeutic, Mar 2010

Huntington's Disease

RNAi to treat Huntington's Disease

- Significant inherited neurodegenerative disease
  - » Caused by mutant huntingtin protein
  - » ~30,000 US patients;
    - – ~150,000 with 50% risk of disease
- Clinical pathology
  - » Onset at ~35-44 yr
  - » Symptoms: Involuntary movement, dementia, behavioral changes
  - » Fatal disease

CHDI FOUNDATION, Inc.

Medtronic

ALN-HTT in pre-clinical development

- Drug-Device Collaboration with CHDI and Medtronic
  - » CHDI to initially fund 50% of IND application-enabling activities
  - » Alnylam/Medtronic 50/50 in U.S

Alnylam PHARMACEUTICALS

Alnylam Key Goals
Next 12-18 Months

Advance clinical pipeline to human proof of concept

- ☑ ALN-RSV01: Initiate Phase IIb
  - » *Initiated in February 2010*
- ☑ ALN-VSP: Preliminary data mid-2010
  - » *Preliminary data, ASCO June 2010; Interim data, Chemotherapy Foundation Symposium November 2010*
- ☑ ALN-TTR01: Initiate Phase I, 1H'10, *Initiated in July 2010*
  - » Advance ALN-TTR02 with 2nd generation LNP program
- ALN-PCS: Initiate Phase I, 2011
- Advance additional pre-clinical programs
  - » ALN-RSV02, ALN-HTT, other

Continued scientific and delivery leadership

- ☑ Publish 15+ major scientific publications
  - » *31 Papers published YTD*
- ☑ Continue major progress in delivery
  - » *In vivo silencing at single digit μg/kg; extra-hepatic tumors, immune cells, vascular endothelium, hepatic stellate cells*

Continued leadership on business execution

- ☑ Continue IP dominance with 30+ new patent grants
  - » *42 New patent grants YTD*
- Form new partnerships
  - » *GSK/Regulus miR-122 alliance, Feb 2010; sanofi-aventis/Regulus microRNA therapeutic alliance, June 2010; CHDI/Medtronic collaboration, Nov 2010*

Maintain solid financial performance

- >$325M in year-end '10 cash

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www.Alnylam.com