Revusiran Program Update

October 5, 2016

Alnylam® PHARMACEUTICALS

Agenda

Welcome

- Christine Lindenboom
  Vice President, Investor Relations and Corporate Communications

Introduction

- John Maraganore, Ph.D.
  Chief Executive Officer

Revusiran Program Update

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

Q&A Session

Alnylam Forward Looking Statements

Various statements in this presentation concerning Alnylam's future expectations, plans and prospects, including without limitation, Alnylam's views with respect to the its discontinuation of development of revusiran, and its ongoing evaluation of the safety data from its revusiran and other clinical trials, its expectations regarding the continued development of patisiran, the safety and tolerability of its products in clinical development, including products utilizing ESC-GalNAc conjugates, and its expectations regarding its STAr pipeline growth strategy and its "Alnylam 2020" guidance, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Actual results and future plans may differ materially from those indicated by these forward-looking statements as a result of various important risks, uncertainties and other factors, including, without limitation, Alnylam's ability to discover and develop novel drug candidates and delivery approaches, successfully demonstrate the efficacy and safety of its product candidates, the pre-clinical and clinical results for its product candidates, which may not be replicated or continue to occur in other subjects or in additional studies or otherwise support further development of product candidates for a specified indication or at all, actions or advice of regulatory agencies, including actions by regulators concerning product candidates in addition to Alnylam's decision to discontinue development of revusiran, which may affect the design, initiation, timing, continuation and/or progress of clinical trials or result in the need for additional pre-clinical and/or clinical testing, delays, interruptions or failures in the manufacture and supply of our product candidates, obtaining, maintaining and protecting intellectual property, Alnylam's ability to enforce its intellectual property rights against third parties and defend its patent portfolio against challenges from third parties, obtaining and maintaining regulatory approval, pricing and reimbursement for products, progress in establishing a commercial and ex-United States infrastructure, competition from others using technology similar to Alnylam's and others developing products for similar uses, Alnylam's ability to manage its growth and operating expenses, obtain additional funding to support its business activities, and establish and maintain strategic business alliances and new business initiatives, Alnylam's dependence on third parties for development, manufacture and distribution of products, the outcome of litigation, the risk of government investigations, and unexpected expenditures, as well as those risks more fully discussed in the "Risk Factors" filed with Alnylam's most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) and in other filings that Alnylam makes with the SEC. In addition, any forward-looking statements represent Alnylam's views only as of today and should not be relied upon as representing its views as of any subsequent date. Alnylam explicitly disclaims any obligation, except to the extent required by law, to update any forward-looking statements.

John Maraganore, Ph.D.
Chief Executive Officer

Introduction

Alnylam ATTR Amyloidosis Portfolio
Committed to Continued Innovation for Patients

patisiran

hATTR-PN

- IV administration
- Phase 2 completed
- Phase 2 Open-Label Extension (OLE) study ongoing
- APOLLO Phase 3 trial ongoing; fully enrolled with top-line results expected in mid-2017
- APOLLO-OLE study ongoing

ALN-TTRsc02

ATTR
hATTR-PN, hATTR-CM & wtATTR

- ESC “second generation” chemistry
- Expect quarterly SC dose regimen
- Phase 1 ongoing; initial data expected in late-2016

Alnylam PHARMACEUTICALS

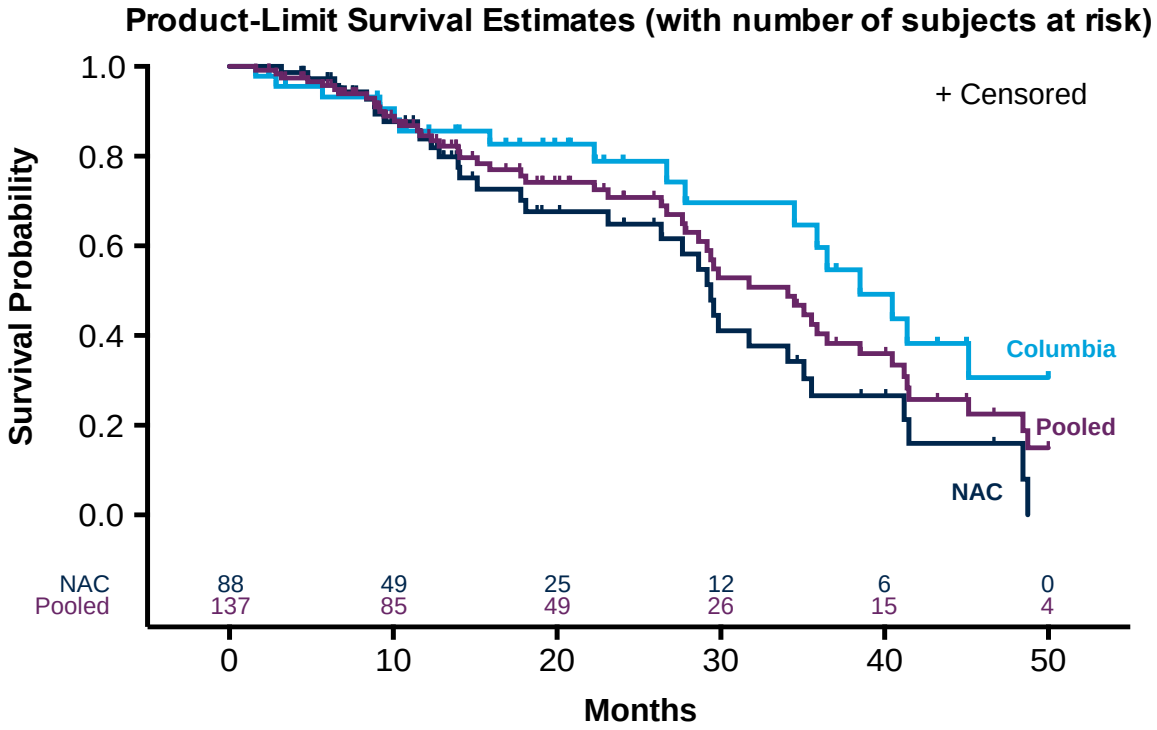
Akshay Vaishnaw, M.D., Ph.D.
Executive Vice President of R&D, Chief Medical Officer

Revusiran Program Update

Natural History of hATTR-CM

Complex disorder with high unmet need

- Significant morbidity and mortality
  - Fatal within 2.5 to 5 years of diagnosis
- Cardiomyopathy
- Peripheral neuropathy, seen in wide range of mutations, including V122I and also in wtATTR



*presented at EC ATTR, November 2015

Revusiran Clinical Studies

Phase 2 OLE Study

- Single-arm, open-label extension study in 25 patients with hATTR-CM or wtATTR

ENDEAVOUR Phase 3 Study

- Placebo-controlled, randomized study in 206 patients with hATTR-CM

Post-OLT Phase 2 Study

- Single-arm, open-label study in 12 patients with hATTR amyloidosis with disease progression following orthotopic liver transplantation

Sequence of Revusiran Safety Findings

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

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

More recently, received new reports of peripheral neuropathy and elevated blood lactate levels

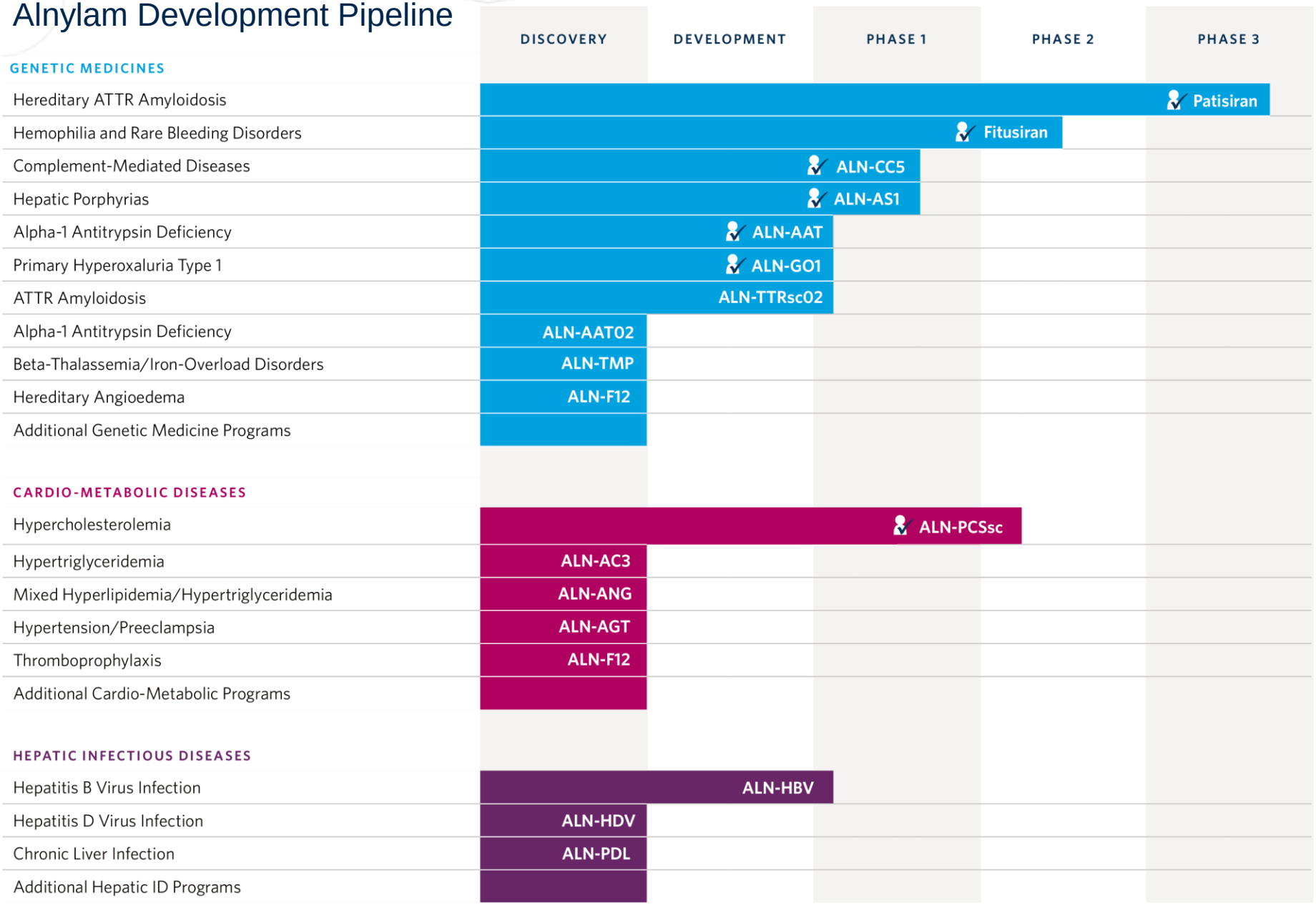
At Company request, ENDEAVOUR DMC met October 4, 2016 to review Phase 3 study data in light of new safety information and to assess overall benefit-risk profile of revusiran

- DMC reported no conclusive evidence of drug-related peripheral neuropathy signal
- However, recommended suspension of dosing based on lack of favorable benefit-risk

Company subsequently reviewed unblinded ENDEAVOUR data which revealed imbalance of mortality in revusiran arm as compared to placebo

- Decision to discontinue development of revusiran

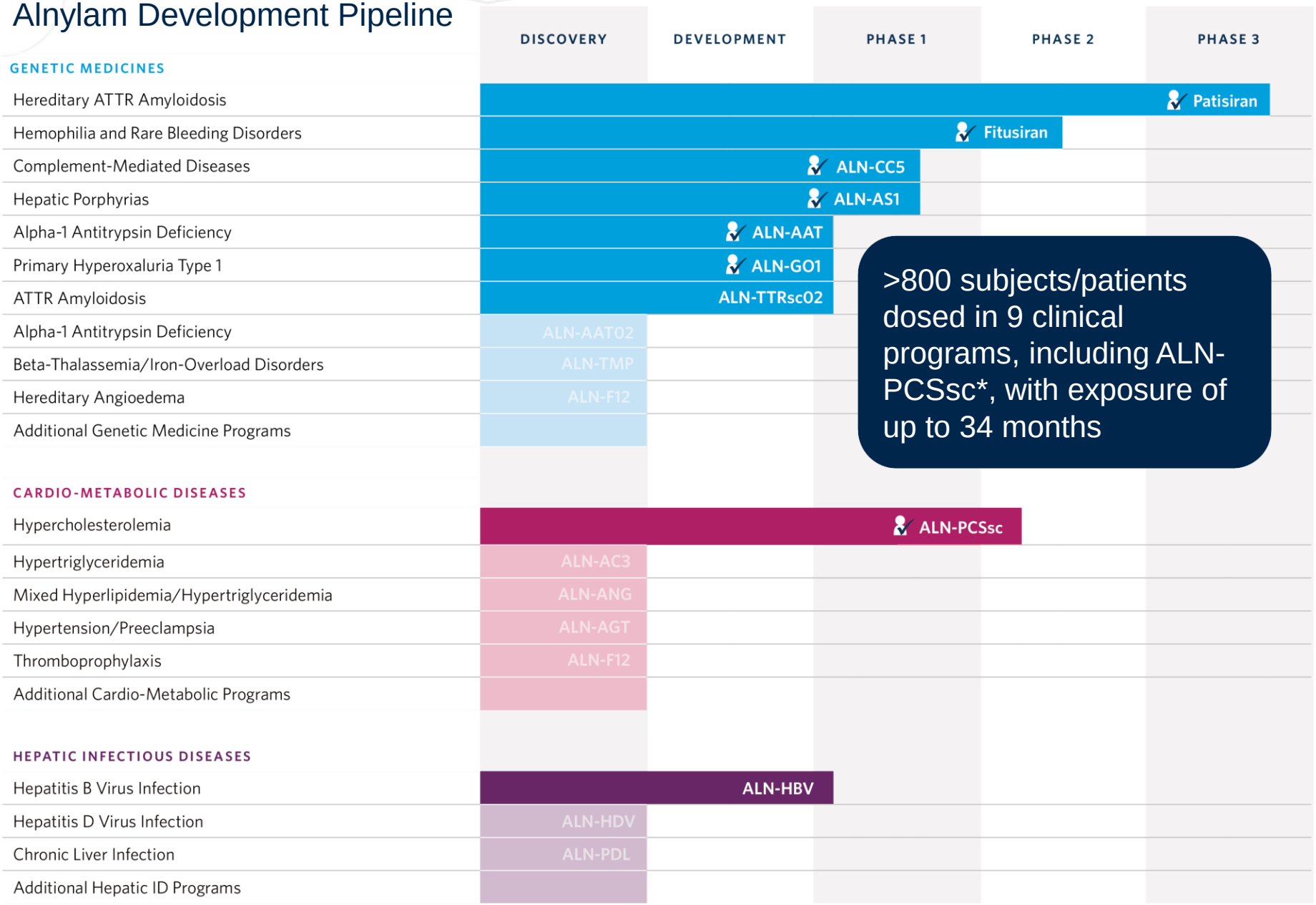
Alnylam Development Pipeline



Updated October 4, 2016

Human Proof of Concept Achieved

Alnylam Development Pipeline



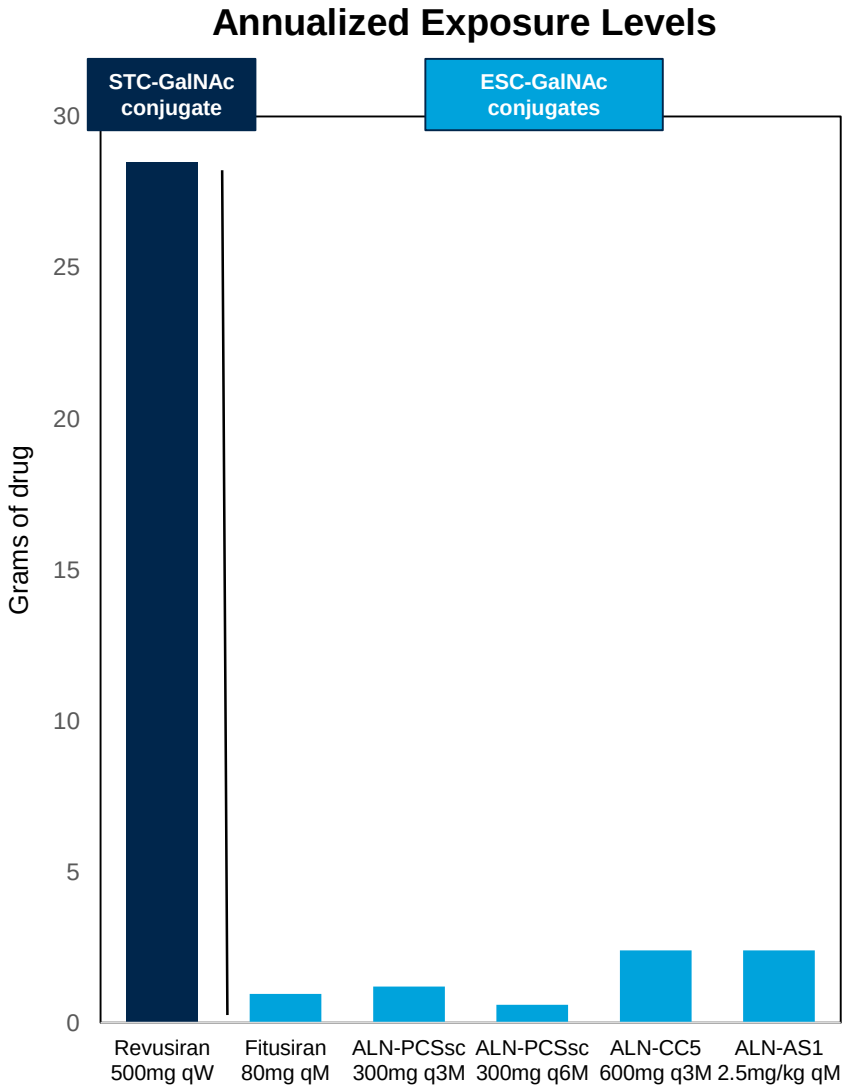
>800 subjects/patients dosed in 9 clinical programs, including ALN-PCSsc*, with exposure of up to 34 months

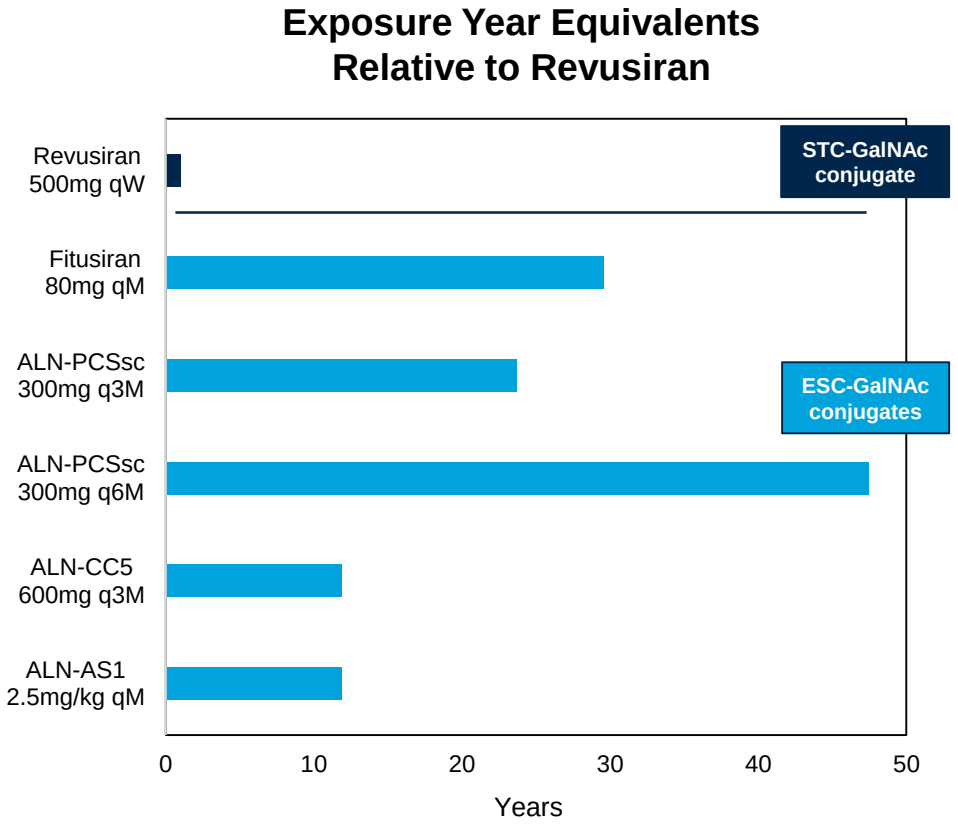
Updated October 4, 2016

*partnered with The Medicines Company, also referred to as PCSK9si

Human Proof of Concept Achieved

Exposure Levels with Revusiran Significantly Higher than other GalNAc Conjugate Programs





Q&A Session

Thank You

Alnylam® PHARMACEUTICALS