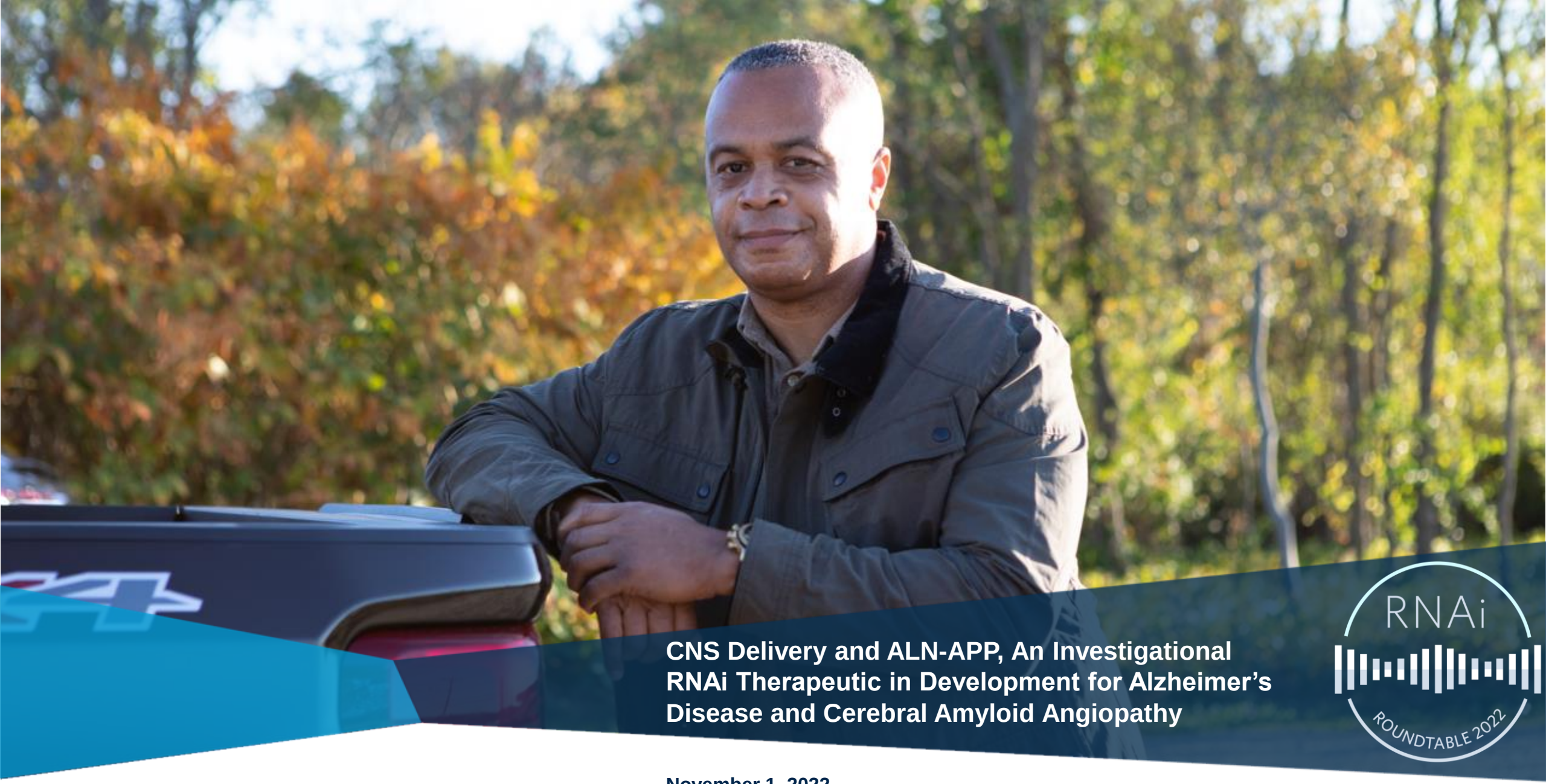

CNS Delivery and ALN-APP, An Investigational RNAi Therapeutic in Development for Alzheimer's Disease and Cerebral Amyloid Angiopathy

RNAi ROUNDTABLE 2022

November 1, 2022

Alnylam@20

Agenda

Welcome
- Josh Brodsky – Senior Director, Investor Relations & Corporate Communications

Introduction
- Eric Green – Senior Vice President, Development Programs

Progress on CNS Delivery for RNAi Therapeutics
- Kirk Brown, Ph.D. – Senior Director, Research, CNS Program

Update on ALN-APP, An Investigational RNAi therapeutic in Development for Alzheimer's Disease and Cerebral Amyloid Angiopathy
- Tim Mooney – Director, Program Leader, ALN-APP Program

Wrap-Up and Q&A Session

Reminders

Event will run for approximately 60 minutes

Q&A session at end of presentation

- Questions may be submitted at any time via the ‘Ask a Question’ field on the webcast interface

Replay, slides and transcript available at https://capella.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, including but not limited to expectations regarding our aspiration to become a top-tier biotech company, the potential of our platform to enable RNAi therapeutics for the treatment of large indications and the extension into extrahepatic tissues, including the CNS, eye and lungs, the potential of RNAi therapeutics to demonstrate superior potency, duration and systemic safety profile versus ASOs, the potential of ALN-APP to treat Alzheimer's disease and other indications, the expected timing of preliminary data from the Phase 1 study of ALN-APP in patients with early-onset AD, and Regeneron's involvement in the research, development and commercialization of ALN-APP. 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: the direct or indirect impact of the COVID-19 global pandemic or any future pandemic on our business, results of operations and financial condition and the effectiveness or timeliness of our efforts to mitigate the impact of the pandemic; the potential impact of the January 2022 leadership transition on our ability to attract and retain talent and to successfully execute on our "Alnylam P5x25" strategy; our ability to discover and develop novel drug candidates and delivery approaches, including using our IKARIA and GEMINI platforms, and successfully demonstrate the efficacy and safety of our product candidates; the pre-clinical and clinical results for our product candidates, including ALN-APP; actions or advice of regulatory agencies and our ability to obtain and maintain regulatory approval for our product candidates, including vutrisiran and patisiran, as well as favorable pricing and reimbursement; successfully launching, marketing and selling our approved products globally; delays, interruptions or failures in the manufacture and supply of our product candidates or our marketed products; obtaining, maintaining and protecting intellectual property; our ability to successfully expand the indication for ONPATTRO, AMVUTTRA and OXLUMO in the future; our ability to manage our growth and operating expenses through disciplined investment in operations and our ability to achieve a self-sustainable financial profile in the future without the need for future equity financing; our ability to maintain strategic business collaborations; our dependence on third parties for the development and commercialization of certain products, including Novartis, Sanofi, Regeneron and Vir; the outcome of litigation; the potential impact of current and risk of future government investigations; and unexpected expenditures; as well as those risks more fully discussed in the "Risk Factors" filed with our most recent Quarterly Report on Form 10-Q filed with the SEC and in our other SEC filings. If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance, timelines 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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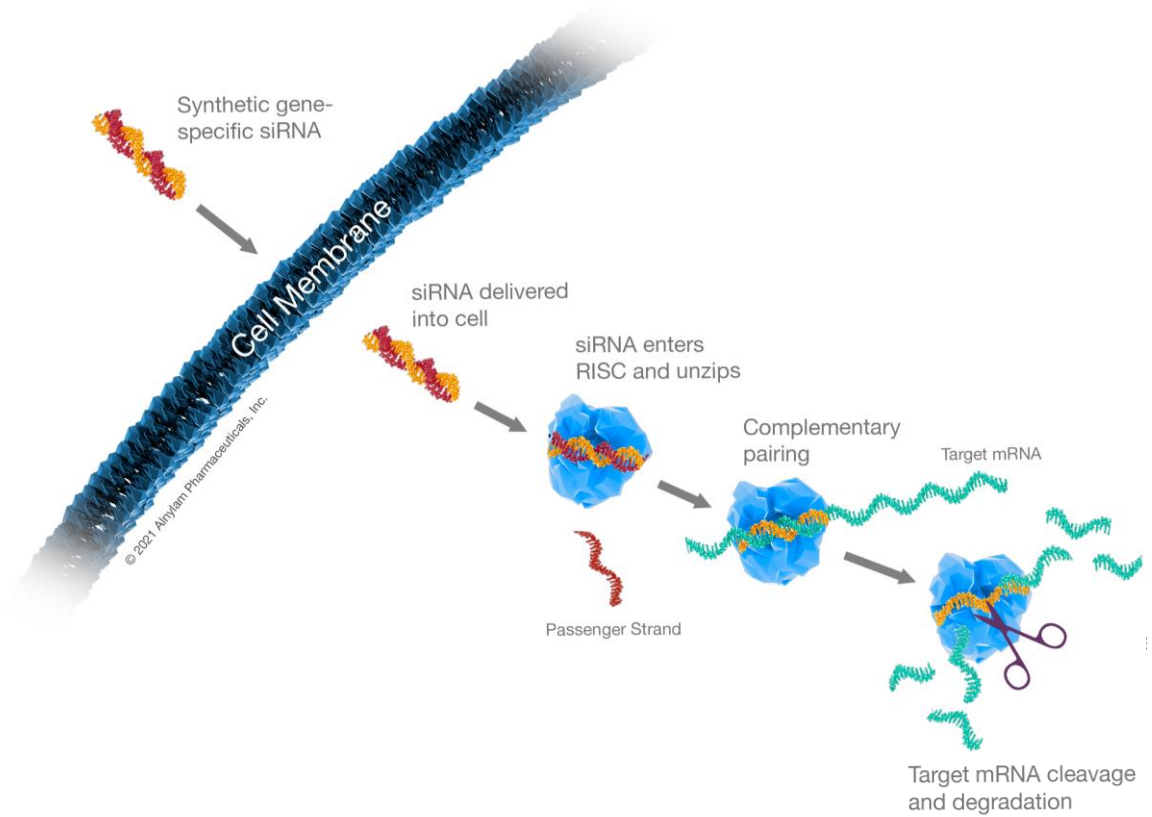
Alnylam Poised to Become a Top-Tier Biotech

Leader in RNAi Therapeutics

- Pioneered **new class of innovative medicines**
- **5** medicines approved in **< 4 years**
- Robust clinical pipeline across rare and prevalent diseases
- **Global footprint** with strong commercial capabilities
- Leading IP estate with fundamental, delivery, and product-specific patent protection
- Strong balance sheet, on path toward financial self-sustainability

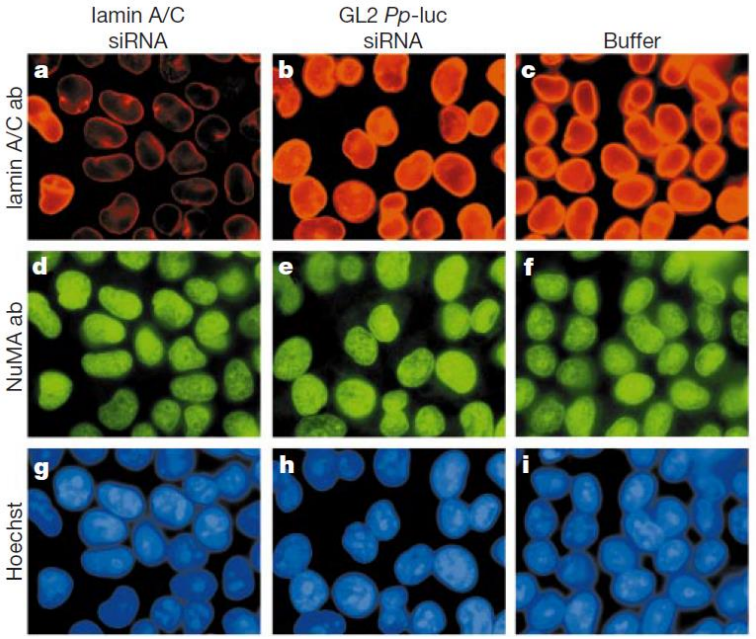
Organic Product Engine Capable of Sustaining Growth Through Innovation

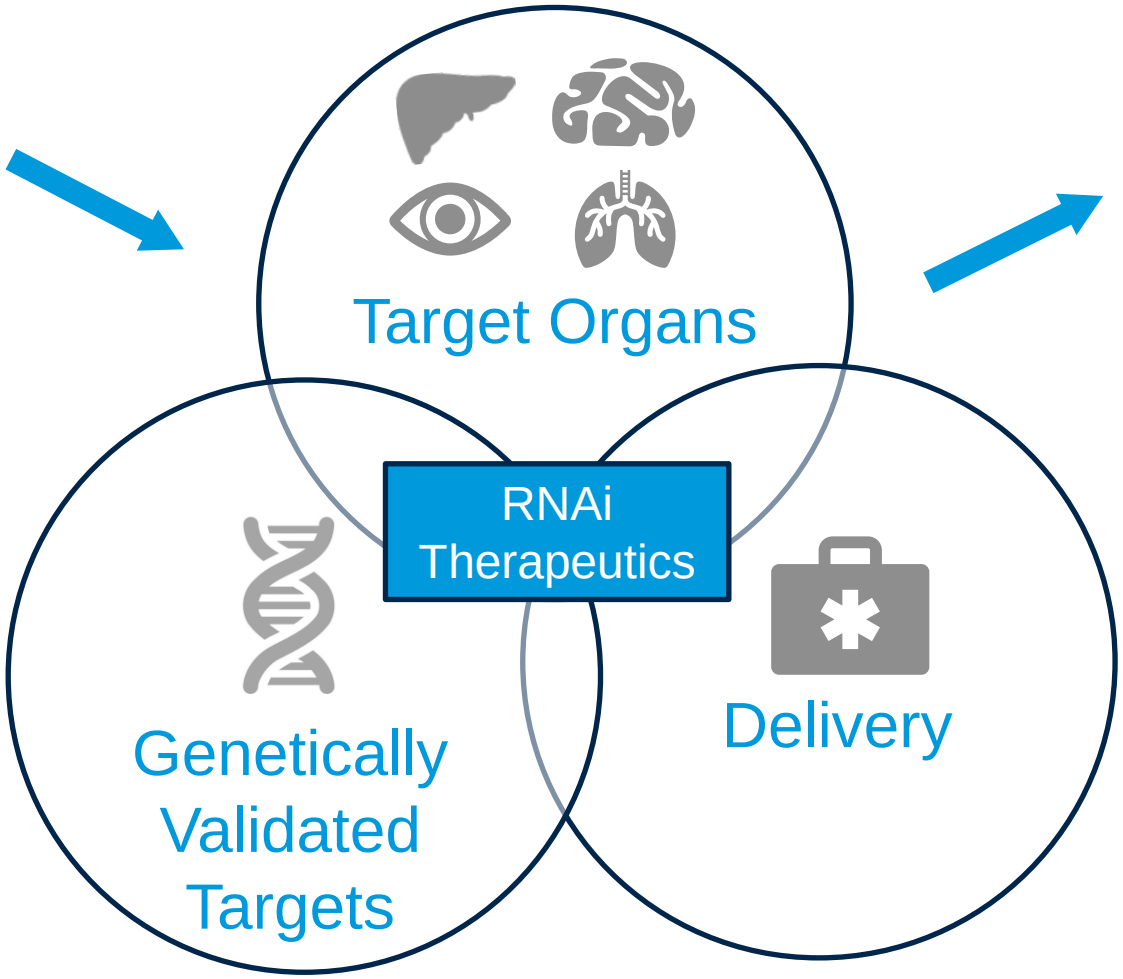
- Targets with **strong genetic validation**
- Platform innovation unlocks opportunities to **bring RNAi therapeutics to new tissue types**
- Building on innovative **IKARIA platform** for potent, safe, and long-duration siRNA design



Focused R&D Strategy

Turning an *In Vitro* Observation into a New Class of Medicines





Alnylam Clinical Development Pipeline

Focused in 4 Strategic Therapeutic Areas (STArs):

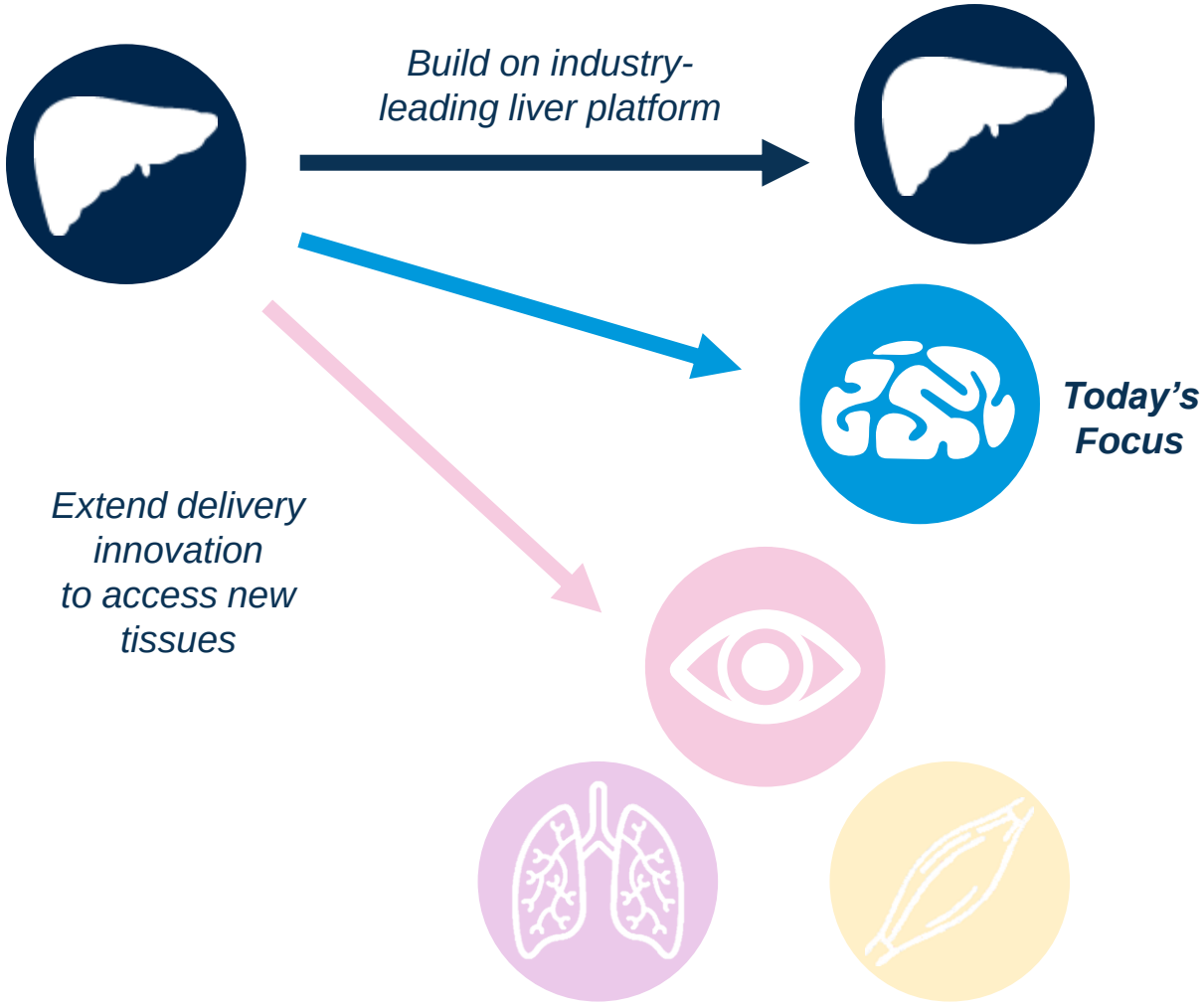
- Genetic Medicines
- Cardio-Metabolic Diseases
- Infectious Diseases
- CNS/Ocular Diseases

		EARLY/MID-STAGE *(IND/CTA Filed-Phase 2)*	LATE STAGE *(Phase 2-Phase 3)*	REGISTRATION/ COMMERCIAL[1] (OLE/Phase 4/IIS/registries)	COMMERCIAL RIGHTS
onpattro (patisiran)	*hATTR Amyloidosis with PN*[2]			●	Global
GIVLAARI (givosiran)	*Acute Hepatic Porphyria*[3]			●	Global
OXLUMO (lumasiran)	*Primary Hyperoxaluria Type 1*[4]			●	Global
LEQVIO (inclisiran)	*Hypercholesterolemia*[5]			●	Milestones & up to 20% Royalties[6]
amvuttra (vutrisiran)	*hATTR Amyloidosis with PN*[7]			●	Global
Patisiran	*ATTR Amyloidosis with CM*		●		Global
Vutrisiran	*ATTR Amyloidosis with CM*		●		Global
TBD*	*Stargardt Disease*		○		Global
ALN-TTRsc04*	*ATTR Amyloidosis*	●			Global
Fitusiran*	*Hemophilia*		●		15-30% Royalties
Lumasiran	*Severe PH1* *Recurrent Renal Stones*	●		●	Global
Cemdisiran (+/- Pozelimab)[9]*	*Complement-Mediated Diseases*		●		50-50; Milestone/Royalty
Belcesiran[10]*	*Alpha-1 Liver Disease*	●			Ex-U.S. option post-Phase 3
ALN-HBV02 (VIR-2218)[11]*	*Hepatitis B Virus Infection*	●			50-50 option post-Phase 2
Zilebesiran (ALN-AGT)*	*Hypertension*	●			Global
ALN-HSD*	*NASH*	●			50-50
ALN-APP*	*Alzheimer's Disease;* *Cerebral Amyloid Angiopathy*	●			50-50
ALN-XDH*	*Gout*	●			Global

[1] Includes marketing application submissions; [2] Approved in the U.S. and Canada for the PN of hATTR amyloidosis in adults, and in the EU, Japan and other countries for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy; [3] Approved in the U.S., Brazil and Canada for the treatment of adults with acute hepatic porphyria (AHP), and in the EU and Japan for the treatment of AHP in adults and adolescents aged 12 years and older; [4] Approved in the U.S., EU and Brazil for the treatment of primary hyperoxaluria type 1 in all age groups; [5] Approved in the U.S. for the treatment of heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD) and in the EU for the treatment of hypercholesterolemia or mixed dyslipidemia; [6] Novartis has obtained global rights to develop, manufacture and commercialize inclisiran; 50% of inclisiran royalty revenue from Novartis will be payable to Blackstone by Alnylam; [7] Approved in the U.S. for the PN of hATTR amyloidosis in adults, and in the EU and Japan for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy; [8] The Company is considering options for the best path forward to bring an RNAi therapeutic to patients with Stargardt Disease; [9] Cemdisiran and pozelimab are each currently in Phase 2 development; Alnylam and Regeneron are evaluating potential combinations of these two investigational therapeutics; [10] Dicerna is leading and funding development of belcesiran; [11] Vir is leading and funding development of ALN-HBV02; * Not approved for any indication and conclusions regarding the safety or efficacy of the drug have not been established.

As of October 2022

Expanding Areas of Therapeutic Focus



Tissues for Extrahepatic Delivery

- Multiple disease areas with high unmet medical need
- Genetically validated targets for disease with established biomarkers
- Leveraging siRNA-conjugate approach for delivery of RNAi therapeutics across multiple organs

Landmark Alliance with Regeneron Accelerating Innovation in CNS

CNS

Alnylam/Regeneron

- ALN-APP
- ALN-SOD
- ALN-HTT
- ALN-REGN-C4
- ALN-REGN-C5
- ALN-REGN-C6
- ALN-REGN-C7
- ALN-REGN-C8
- ALN-REGN-C9
- ALN-REGN-C10
- ALN-REGN-C11

REGENERON®

Landmark alliance with Regeneron focused on CNS & ocular RNAi therapeutics

- Leverages Alnylam R&D expertise and scientific excellence in RNAi therapeutics, in combination with Regeneron's world-leading capabilities in human genetics
- Rapidly expanding portfolio with two development candidates nominated and additional targets rapidly progressing toward development

1st

In 2022, first-ever dose of CNS-targeted investigational RNAi therapeutic in human clinical trials (ALN-APP)

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RNAi Therapeutics for CNS Diseases

REGENERON

No Current Therapies to Prevent or Restore Function in Neurodegenerative Disease

Very high unmet need for new treatments for CNS diseases

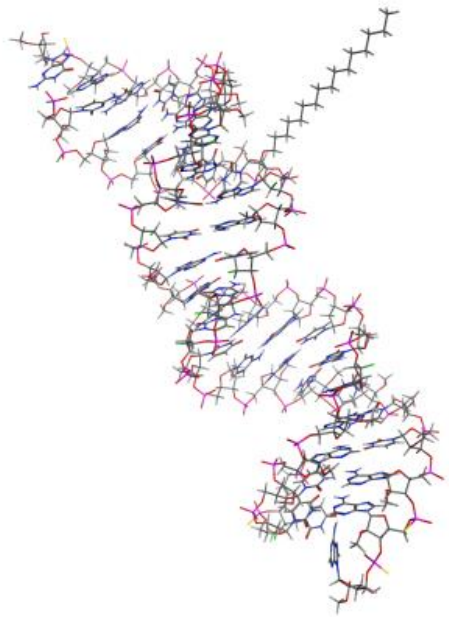
- Genetically defined neurodegenerative diseases include
  - Alzheimer's disease
  - Amyotrophic lateral sclerosis (ALS)
  - Frontotemporal dementia
  - Huntington's disease
  - Parkinson's disease
  - Prion disease
  - Spinocerebellar ataxia
  - Many other orphan genetic diseases with CNS component

- Number of genetically validated targets known but no current disease modifying therapies for these devastating, life-threatening disorders
- Significant opportunity for RNAi therapeutics directed to disease-causing, CNS-expressed genes
- Based on pre-clinical studies, expect potential for differentiated potency, duration and systemic safety profile vs. other therapeutic approaches

CNS Platform Objectives

Potential for Best-in-Class CNS Oligonucleotide Delivery Platform

- **High potency**
- **Wide biodistribution in CNS**
- **Long duration of action**
- **Favorable risk / benefit profile**



C16 Conjugate

RNAi Therapeutics Can Be Delivered to the CNS

Potent, Durable Gene Silencing Achieved in Animals with CNS Conjugates

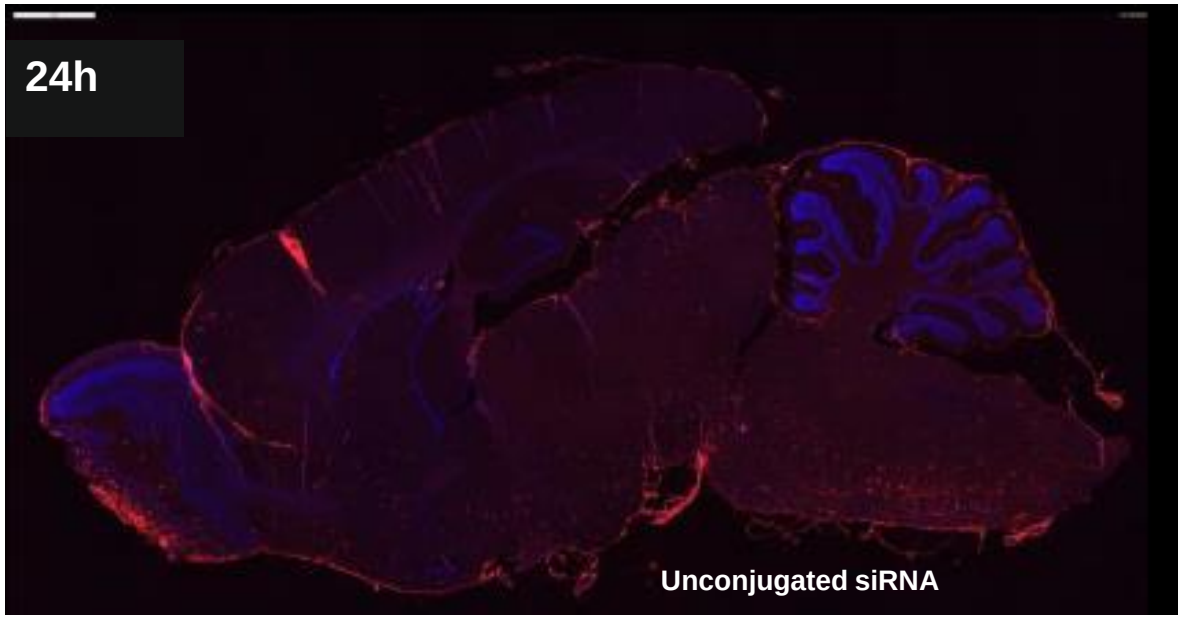
OTS Paper of the Year 2022

Nature Biotechnology

Expanding RNAi therapeutics to extrahepatic tissues with lipophilic conjugates

Brown, et al.

CNS conjugate achieves distribution across brain regions

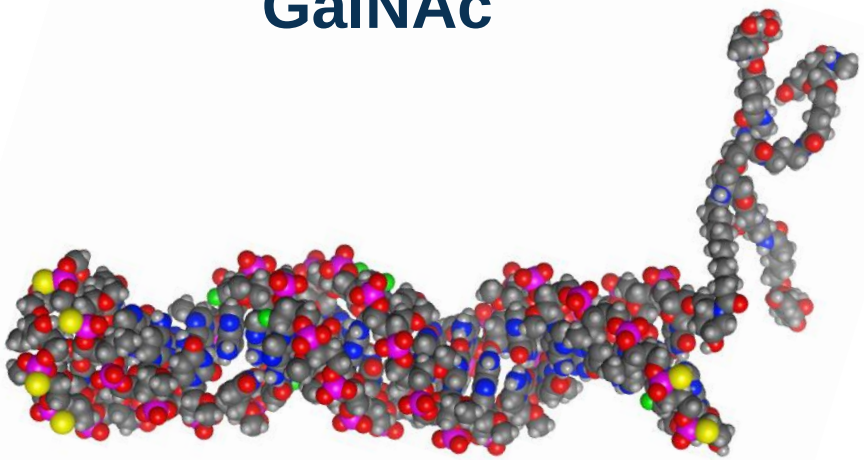


Unconjugated or C16-modified siRNA administered as single IT bolus injection to rats at 0.9 mg. siRNA biodistribution was assessed in whole brain at 24 h post-dose using IHC with anti-siRNA antibody

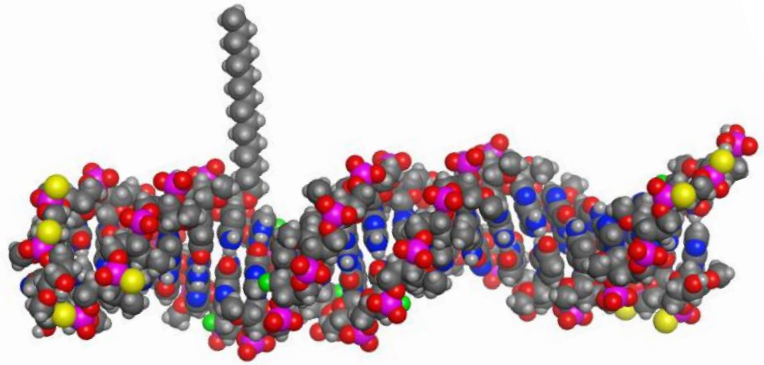
General Properties of siRNA Sense Strand Conjugates

Terminal GalNAc Versus Internal C16

GalNAc



Internal C16



- ASGPR-mediated hepatic uptake

- Backbone chemistry: 2'-O-methyl, 2'-deoxy, 2'-F, GNA, phosphorothioate linkages
- Nuclease-mediated metabolism a major route of elimination
  - Low renal excretion

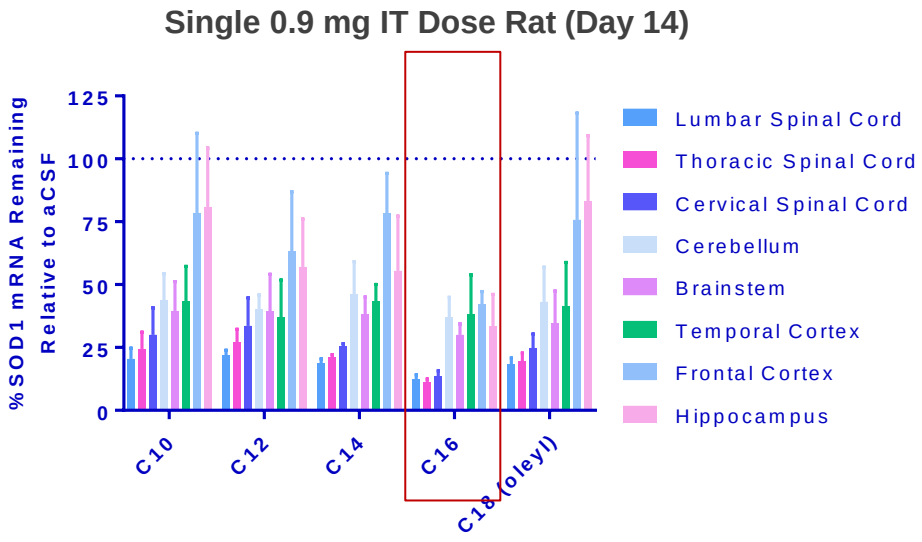
- Lipid-facilitated tissue distribution and/or cell uptake
- VP-mediated RISC loading

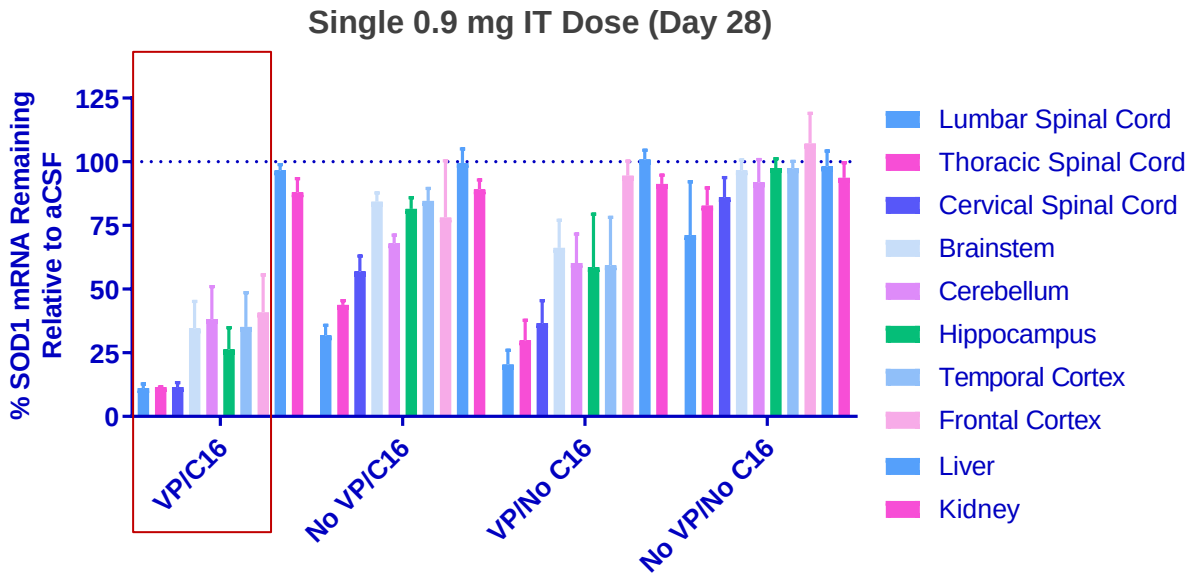
C16 Conjugate Platform

Optimized for CNS Delivery of RNAi Therapeutics

C16 conjugate platform designed to optimize potency, durability, and safety

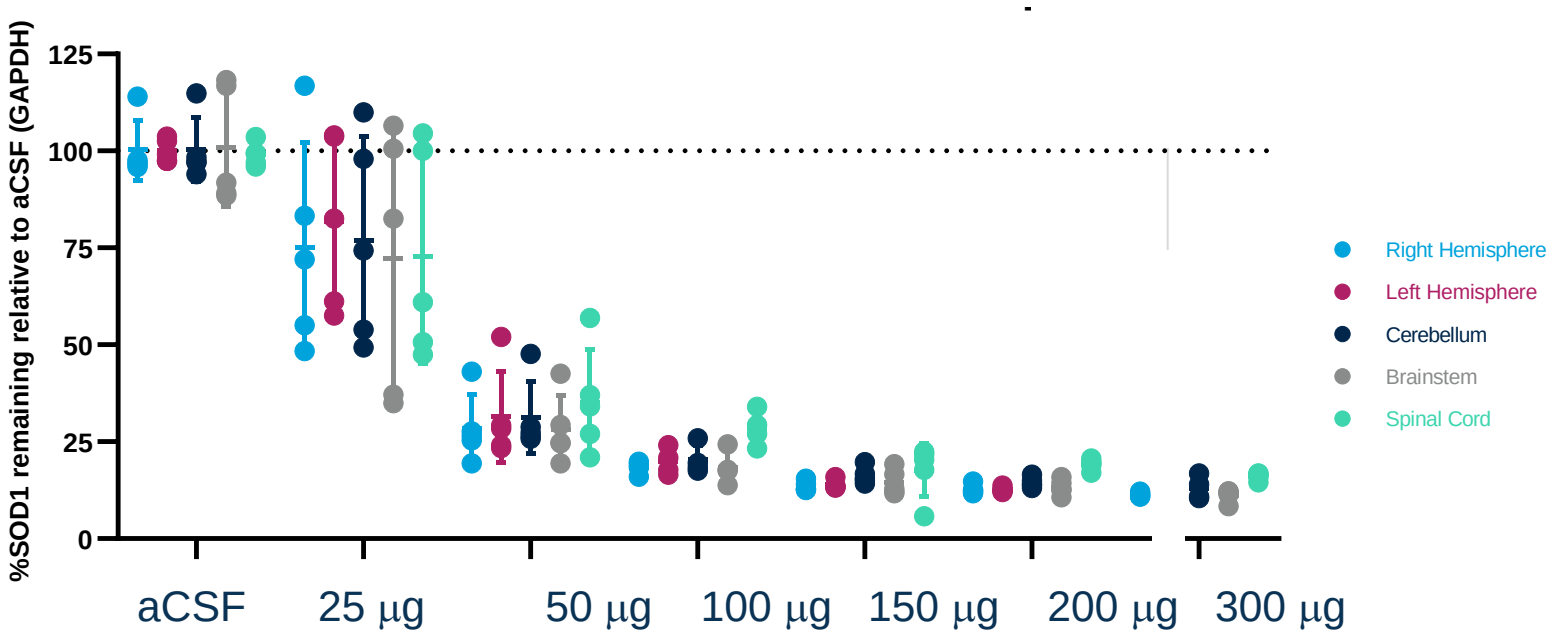
- Exhaustive optimization of siRNA lipophilic moiety, position, and design chemistry
- Backbone modifications to enable similar metabolic stability to liver platform (e.g., ESC+)
- Vinylphosphonate (VP) modification improves potency through enhanced RISC-binding

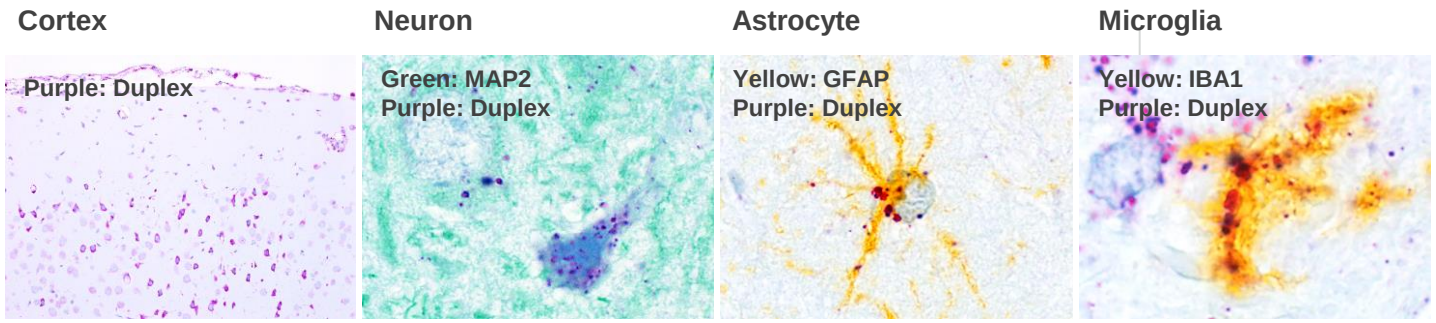




CNS Conjugate Dose Response and Distribution

SOD1 KD at Day 14 in the CNS After Single ICV Injection





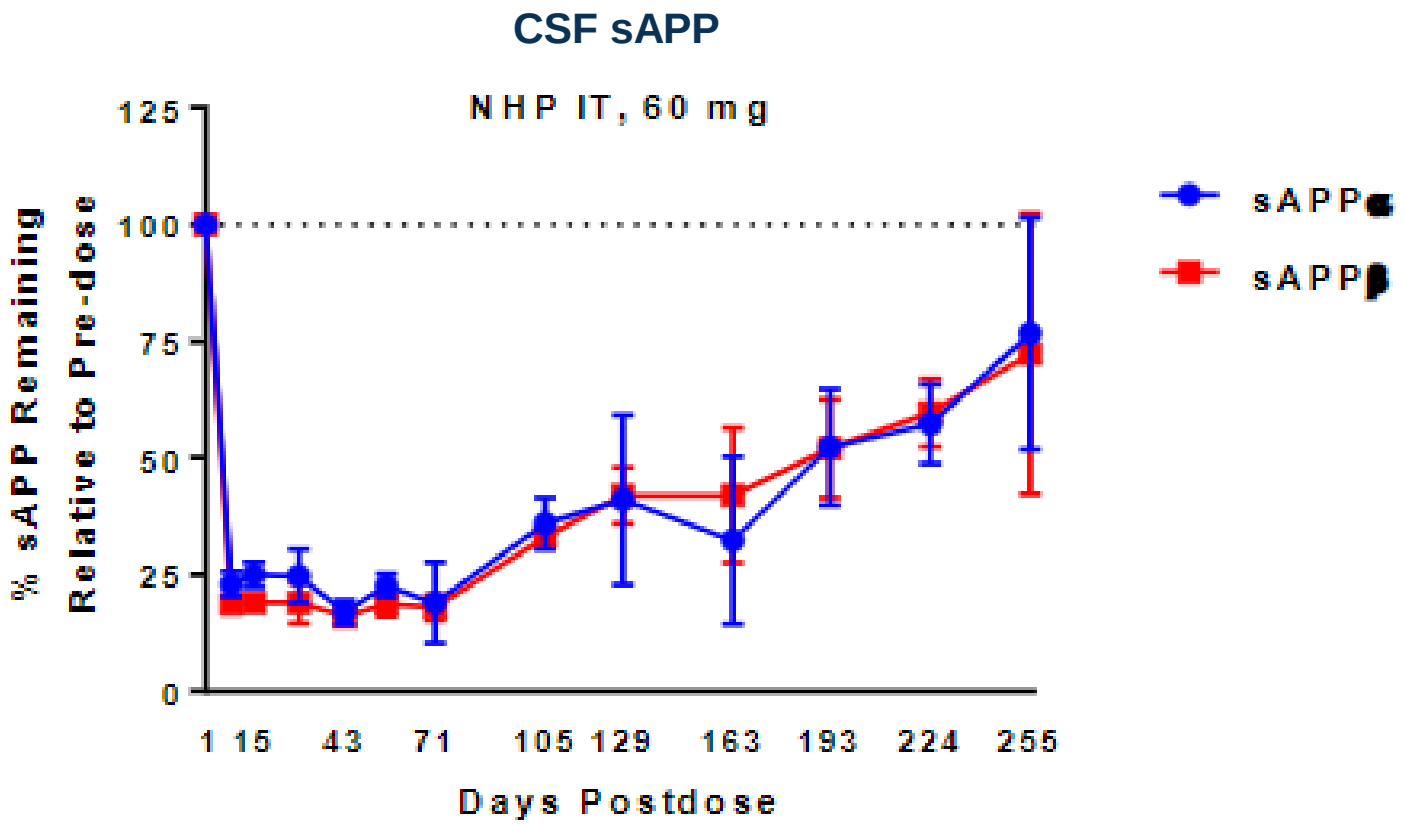
IHC stain after IT dose of 0.9 mg in rats

- ICV dose of 50-300 µg shows consistent and robust KD in the CNS
- ICV dose of 150-300 µg silences SOD1 to its lowest levels across all tissue types
- Robust uptake seen across CNS cell types

Brown et al., Nature Biotechnology, 2022

Long Duration of Action in CNS

Target Knockdown with Single Dose siRNA in NHP



Brown et al., Nature Biotechnology, 2022

CNS RNAi Platform Preclinical Summary

First Program Entered First-in-Human Trial in Early 2022; Additional Pre-Clinical Candidates in Development

C16 conjugates provide potent, durable silencing with distribution throughout the CNS

- C16 conjugate designed to optimize potency, durability, and safety of CNS platform
  - Lipophilic moiety provides for robust cellular uptake
  - VP modification enhances potency through enhanced engagement of RISC
  - “Walks” conducted to optimize potency and durability of construct design
- Robust silencing achieved throughout the brain and spinal cord at low doses
- Extended pharmacodynamic profile suggests possibility for infrequent dosing; single IT dose provides robust knockdown for 6+ months in NHP
- Platform and ALN-APP CTA-enabling toxicology studies support further development of C16 conjugates; ALN-APP Phase 1 ongoing

Alnylam CNS Pipeline Strategy

Expanding Pipeline of Potentially Transformative Medicines

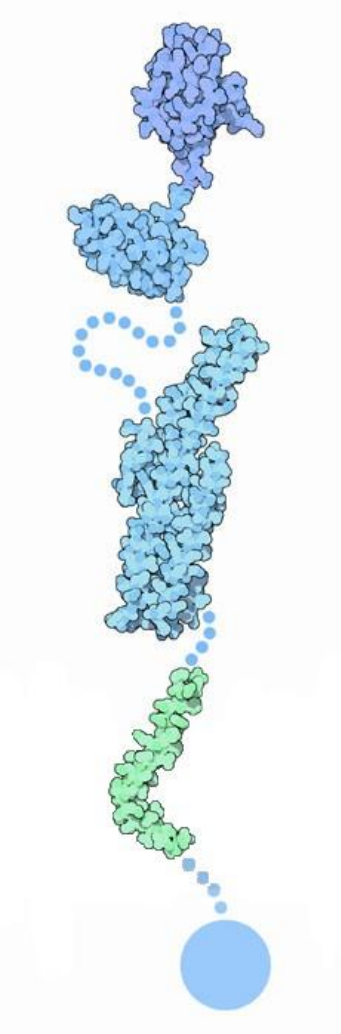
Genetically validated target gene

Biomarker for POC in Phase 1

Definable path to approval and patient access

Amyloid Precursor Protein (APP)

Target for Alzheimer's Disease and Cerebral Amyloid Angiopathy



APP: One target, two distinct pathological processes

- 87 kDA membrane-associated protein produced in many tissues, but with the highest expression in the nervous system
- Processed via serial cleavage by various enzymes include (α-, β-, and γ-secretase) to produce a variety of peptides, including Aβ
- Genetically validated target for both Alzheimer's Disease and Cerebral Amyloid Angiopathy

Alzheimer's Disease (AD)

- APP mutations and duplications cause Early Onset AD
- Amyloid deposits in brain tissue, tau tangles in neurons, neurodegeneration

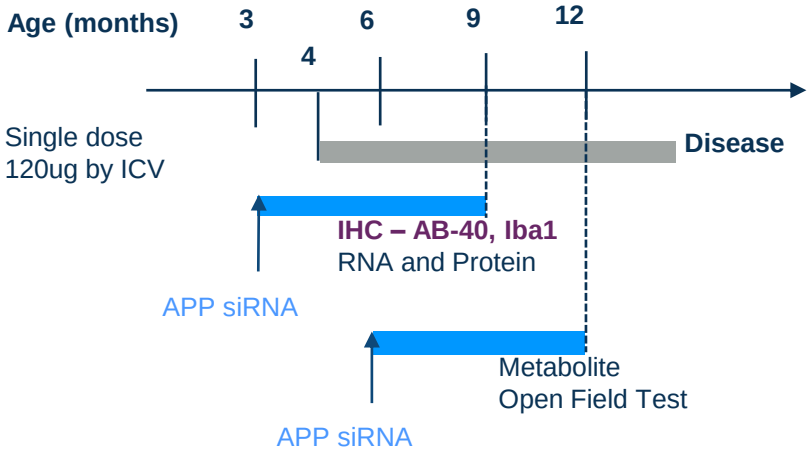
Cerebral Amyloid Angiopathy (CAA)

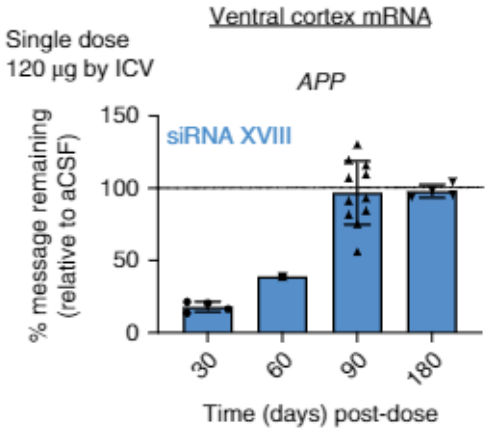
- APP mutations cause hereditary CAA
- Amyloid deposits in walls of vessels in CNS and causes cerebral hemorrhages and cognitive impairment

APP Protein Structure courtesy of David S. Goodsell and the RCSB Protein Data Bank

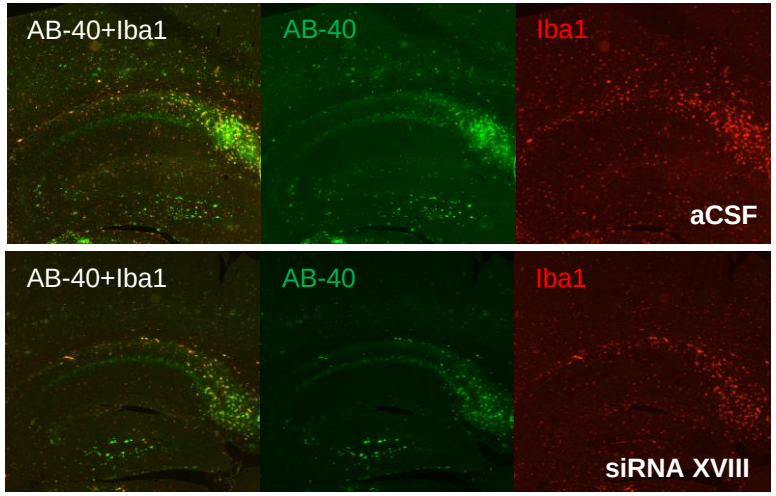
APP-Lowering with siRNA Reduces Amyloid in AD Mouse Model

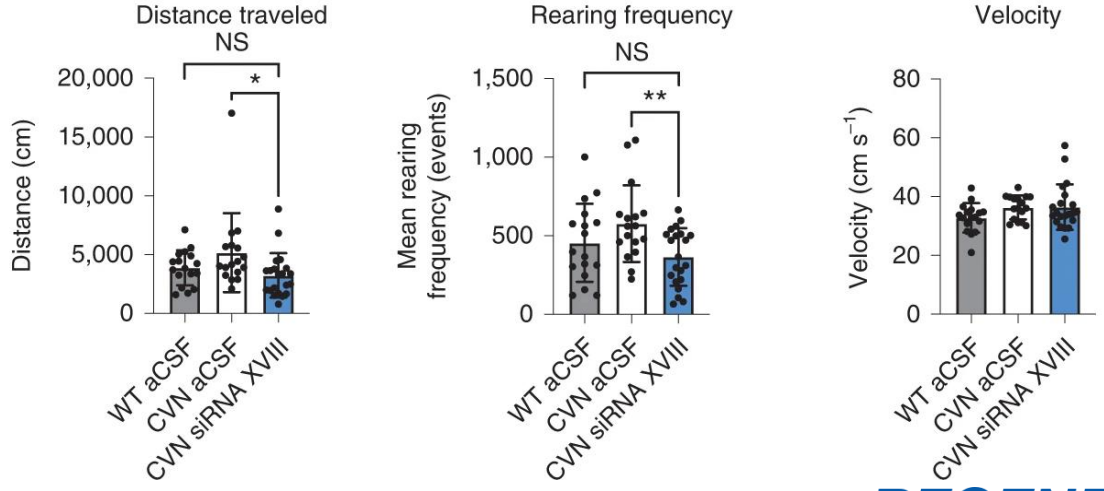
Single Dose of APP siRNA Reduced $A\beta_{40}$ Deposits, Modestly Reduced Inflammation and Corrected Behavior Deficits in CVN Mice





9 months

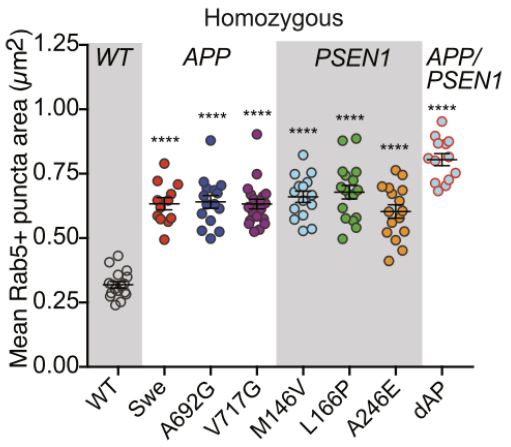




Brown et al., Nature Biotechnology (2022)

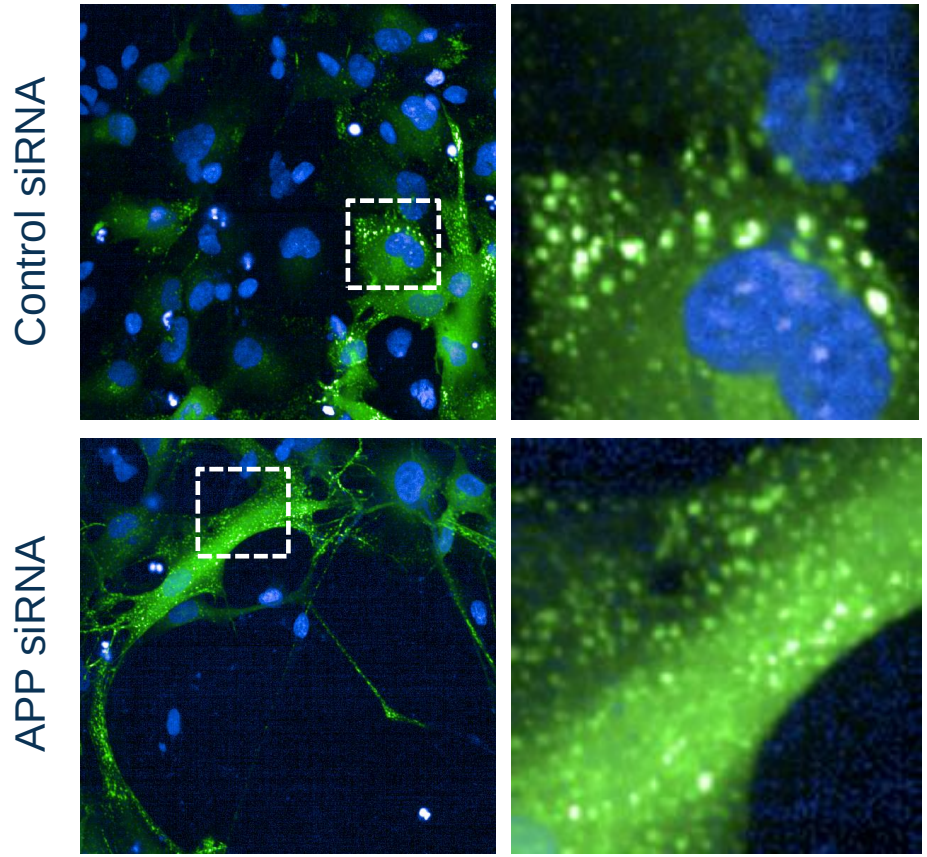
APP siRNA Corrects Intracellular ADAD Endosomal Phenotype

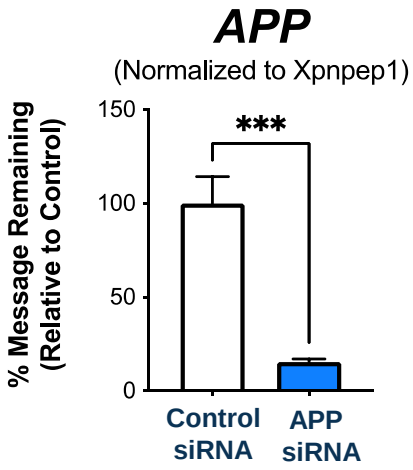
PSEN1 ^{A246E} Patient iPSC-Derived Neurons Treated with APP siRNA Show a Reduction in Rab5+ Early Endosome Size

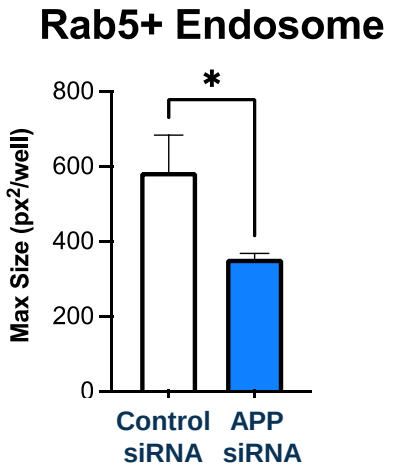


Mutations in APP and PSEN1 cause enlargement of Rab5+ Early Endosomes in human iPSC derived Neurons

Kwart et al., Neuron 2019







- Phenix High Content Imaging, 63X, analysis on Harmony
- Rab5+ endosome Alexa 488 for live imaging

REGENERON®

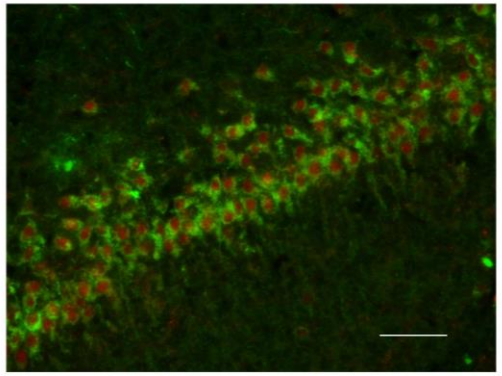
Robust Reduction of Human APP Protein in Rat hCAA Model

Single IT Dose of 0.9 mg in rTg-DI Rat

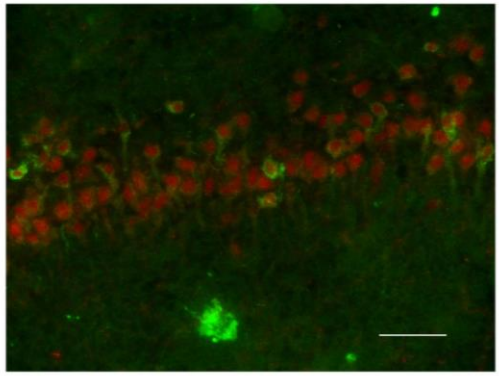
Detection Antibodies

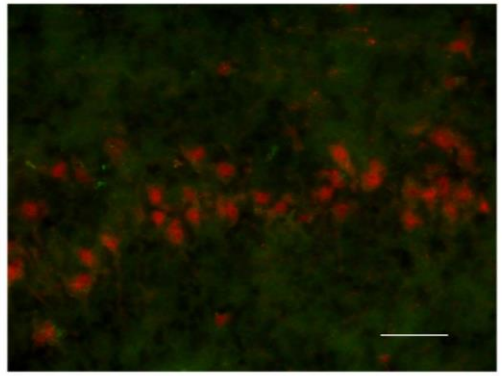
- NeuN (red)
- hAPP (green)

ACSF-CTRL



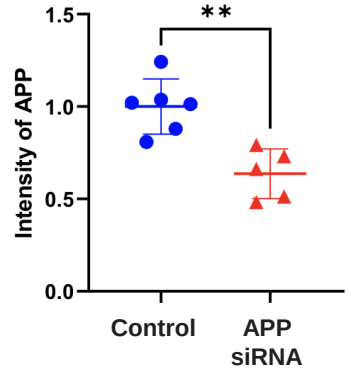
siRNA Treatment

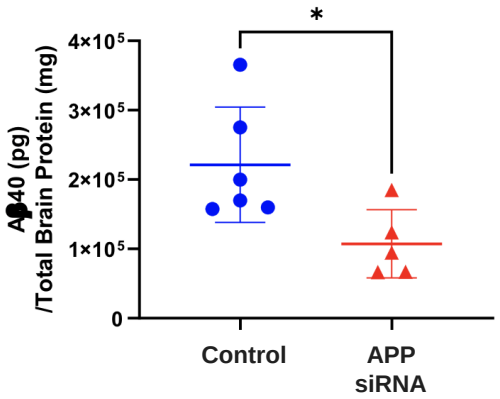




Single IT Dose APP siRNA of 0.9 mg in rTg-DI Rat – Day 28 in Hippocampus

Single IT Dose of 0.9 mg APP siRNA in rTg-DI Rat 2 months post-dose





Van Nostrand lab, URI

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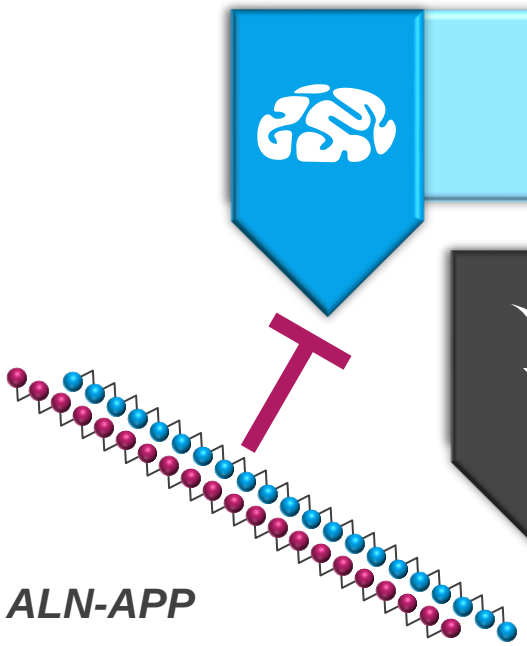
Wrap-Up and Q&A Session

Building on Success of RNAi Therapeutics for Other Types of Amyloidosis

ALN-APP is Designed to Reduce APP Protein Production Upstream of Amyloidogenic Process

Therapeutic hypothesis



Production of APP in CNS

Reduce
Amyloidogenic protein fragments (Aβ)

Reduce
Amyloid deposition in tissues

Stabilize or Improve
Clinical manifestations of AD and CAA

Targeting APP for Alzheimer's Disease (AD)

Most Common Cause of Dementia Worldwide

High prevalence and high unmet need for new therapies

- Over 5M people affected by AD in the US (over 30M worldwide); population continues to grow as the population ages
- Significant driver of disability and mortality in older adults
- Early-onset and genetic forms impact cognition earlier in life
- Current therapies have not been shown to halt or reverse disease progression

Genetically Validated Target	✓	• Mutations that increase APP production or alter APP metabolism cause early-onset AD; Mutations decreasing APP metabolism to Aβ are protective
Biomarker In Phase 1	✓	• Target engagement: sAPPα, sAPPβ in CSF, Aβ • Disease progression: Fluid biomarkers (tTau, pTau, NfL, etc.), neuroimaging
Definable Path to Approval	✓	• Multiple populations for potential development • Established development and regulatory path • High unmet need for disease modifying therapy

Multiple Development Opportunities

- **Early Onset AD (<65 yo) (EOAD)**
  - Autosomal Dominant AD(ADAD)
  - Non-familial early onset AD (nf-EoAD)
  - Down Syndrome AD
- **Late Onset AD (>65 yo) (LOAD)**

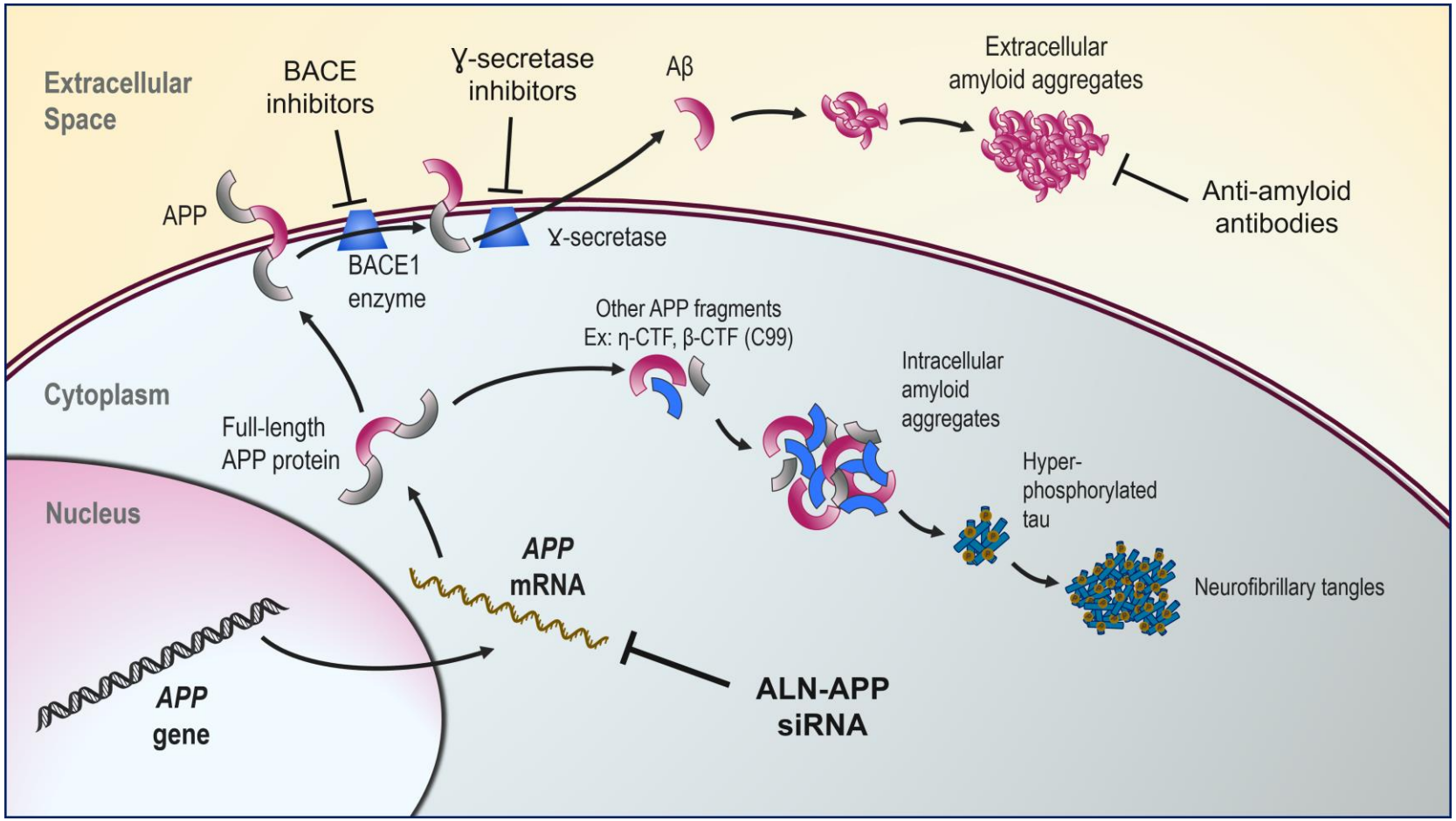
2020 AD Facts and Figures, *Alzheimer's Dementia* (2020); WHO Dementia Fact Sheet (2021); Tom SE, et al., Am J Public Health (2015)

Therapeutic Hypothesis: Alzheimer's Disease

A New Approach: Targeting the APP Protein

Lower APP production *at its source*, upstream of the pathogenic process

- Reduce ***both intracellular and extracellular*** drivers of disease pathology
- ***Reduce all APP cleavage products*** including all species of Aβ
- Removing substrate for amyloid deposit formation and ***enable natural clearance***

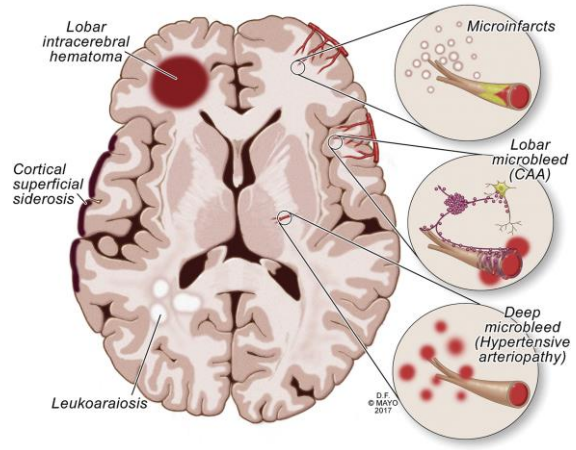


Targeting APP for Cerebral Amyloid Angiopathy

Currently no Targeted Therapies Available and Little Ongoing Development

High unmet need for new treatments to address CAA

- APP metabolism results in the Aβ protein fragments that aggregate into amyloid deposits in the vessels of the brain
- No specific treatments available to target CAA disease progression
- Little activity in the development landscape; targeting vascular amyloid with antibodies has been unsuccessful



Genetically Validated Target	✓	• Mutations that alter APP cleavage and Aβ aggregation cause hereditary CAA
Biomarkers in Early Development	✓	• Target engagement: sAPPα, sAPPβ, $Aβ_{40}$ • Disease progression: Measures of vascular reactivity (BOLD fMRI), cerebrovascular imaging abnormalities
Definable Path to Approval	✓	• High unmet need for disease modifying therapy • High recurrence risk in patients with previous stroke • Well-defined and measurable clinical endpoint

Multiple Development Opportunities

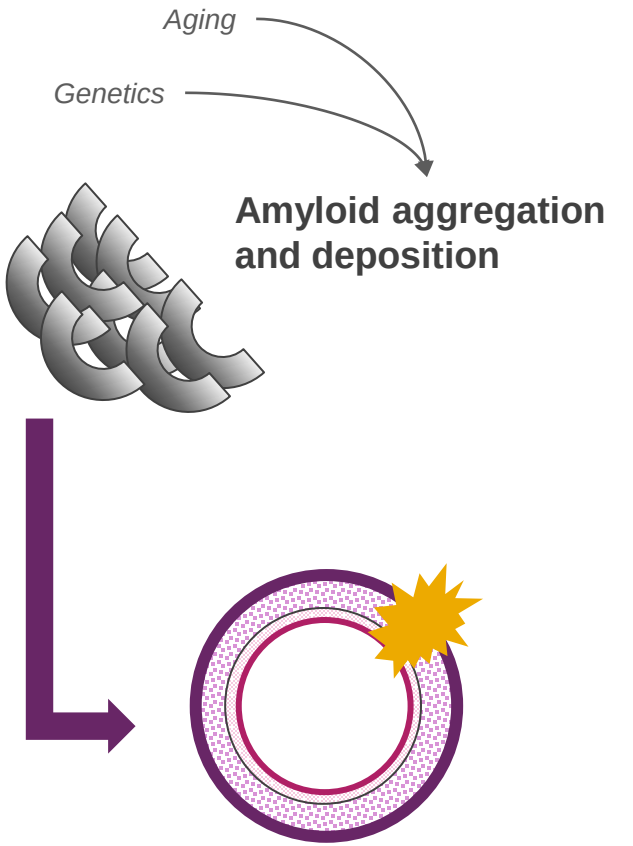
Hereditary CAA: Ultra-orphan genetically defined population found primarily in the Netherlands and Australia; onset in 40s/50s

Sporadic CAA: More common cause of ICH that increases with age. Onset typically after age 60

Jäkel L, et al., Alzheimer's Dement (2021); Aguilar MI, et al., Neurohospitalist (2012); Kozberg MG et al., Int J Stroke (2020).
Figure republished with permission of the American College of Cardiology from DeSimone CV, et al., J Am Coll Cardiol (2017)

Cerebral Amyloid Angiopathy: Disease Overview

Amyloid Accumulation in Vessels of the Brain Results in Progressive Cerebrovascular Disease

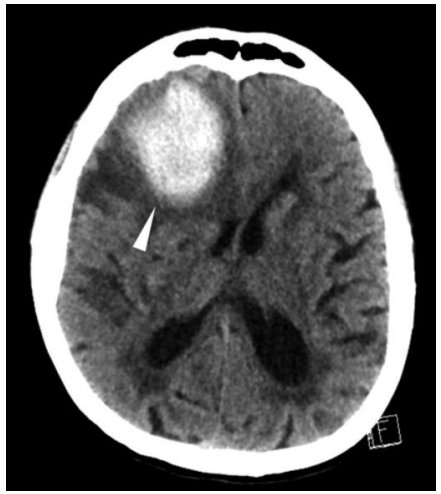


- Vascular disease caused by deposition of Aβ in arteries, arterioles, and capillaries in the brain
  - Deposits made up primarily $Aβ_{40}$, APP protein fragment produced in the CNS when APP is cleaved by β- and γ-secretases
  - Deposition driven by age-related changes to Aβ clearance mechanisms or genetic mutations which alter APP cleavage, Aβ fibrillogenic potential, or Aβ affinity for vascular smooth muscle cells
  - Amyloid deposition results in disruption of vascular architecture and loss of vascular reactivity
- CAA progresses over time: amyloid deposits spread, and vascular damage becomes more severe
- The most common clinical manifestation of CAA is spontaneous lobar hemorrhage (i.e., hemorrhagic stroke)

Kumar-Singh, Genes Brain Behav (2008); Dumas, Ann Neuol (2012); van Dijk, Stroke (2022); Biffi, J Clin Neurol (2011)

Cerebral Amyloid Angiopathy: Unmet Need

Common Cause of Intracerebral Hemorrhage (ICH), the Most Severe Type of Stroke



ICH: Most severe and life-threatening clinical manifestation of CAA

2nd most common cause of ICH (after hypertension)

3x more likely to recur than other causes of ICH

major driver of disability and mortality

CAA may also be an independent driver of cognitive deficits

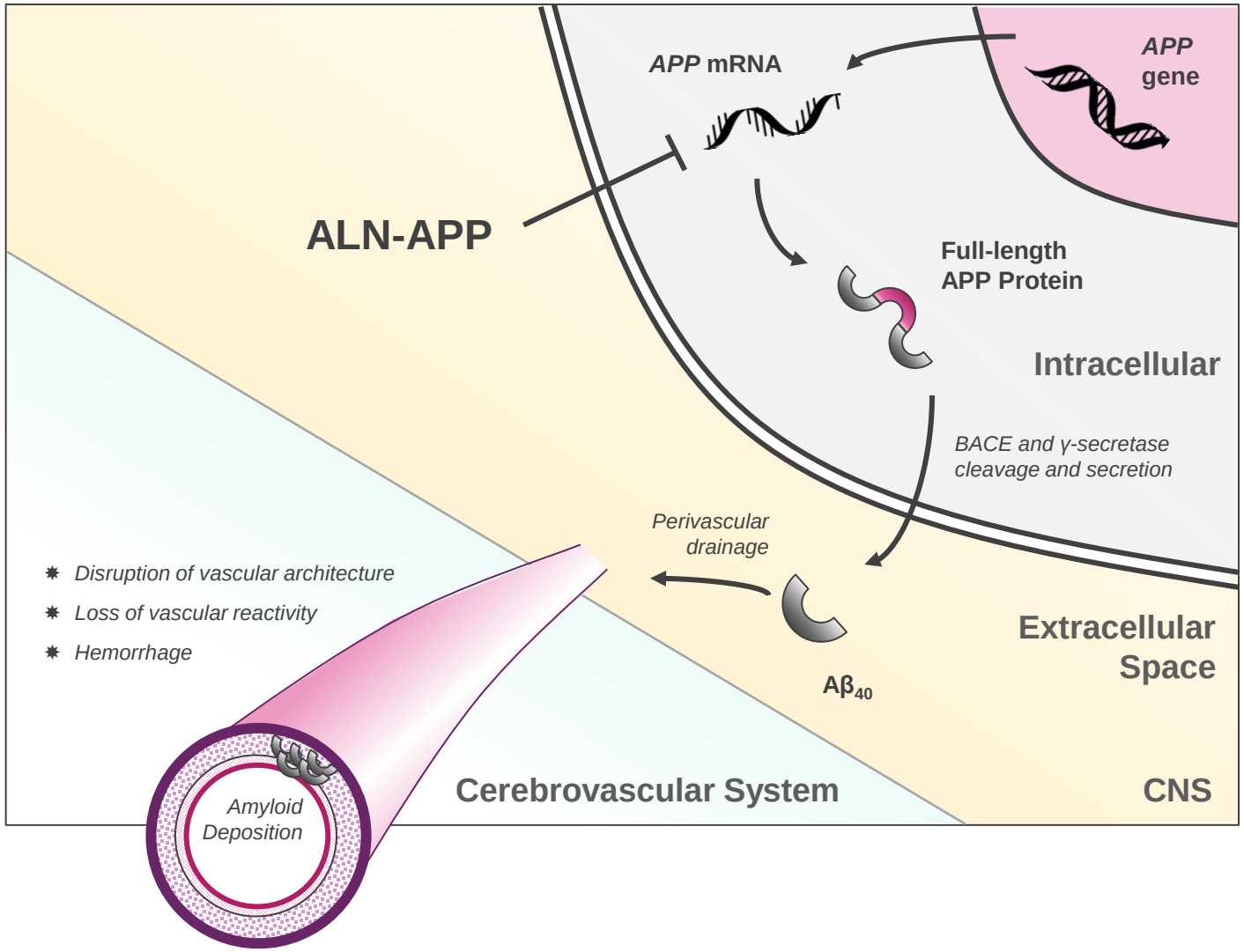
- More severe CAA pathology is associated with faster rate of cognitive decline, independent of other common comorbid neuropathologies

Charidimou, Neurol (2017); Meretoja, Stroke (2012); Goeldlin, J Stroke (2022); Garg, Neurol (2022); Boyle, Neurol (2015)

Therapeutic Hypothesis: Cerebral Amyloid Angiopathy

Reducing Production of Amyloidogenic Protein Fragment

- Target pathogenic protein production at its source ***upstream of amyloid production and deposition***
- Lower ***all Aβ isoforms*** including AB_{40}, the primary component of vascular amyloid deposits
- Enable **natural clearance mechanisms** and reversal of vascular damage



ALN-APP Phase 1 Overview

Randomized, Double-Blind Study in Patients with Early-Onset Alzheimer's Disease (EOAD)

Part A: Single Ascending Dose ***(Ongoing)*** → **Part B**: Multiple Dose *(expected to begin 2023)*

- **Population**: Patients with Early Onset Alzheimer's Disease
- **Primary Objective**: Safety and tolerability of ALN-APP
- **Secondary Objective**: Pharmacology of ALN-APP
- **Exploratory Objective**: Impact of ALN-APP on disease
  - Fluid biomarkers for amyloid, tau, and neurodegeneration
  - Measures of synaptic health
  - Neuroimaging
  - Exploratory cognitive and functional clinical measures

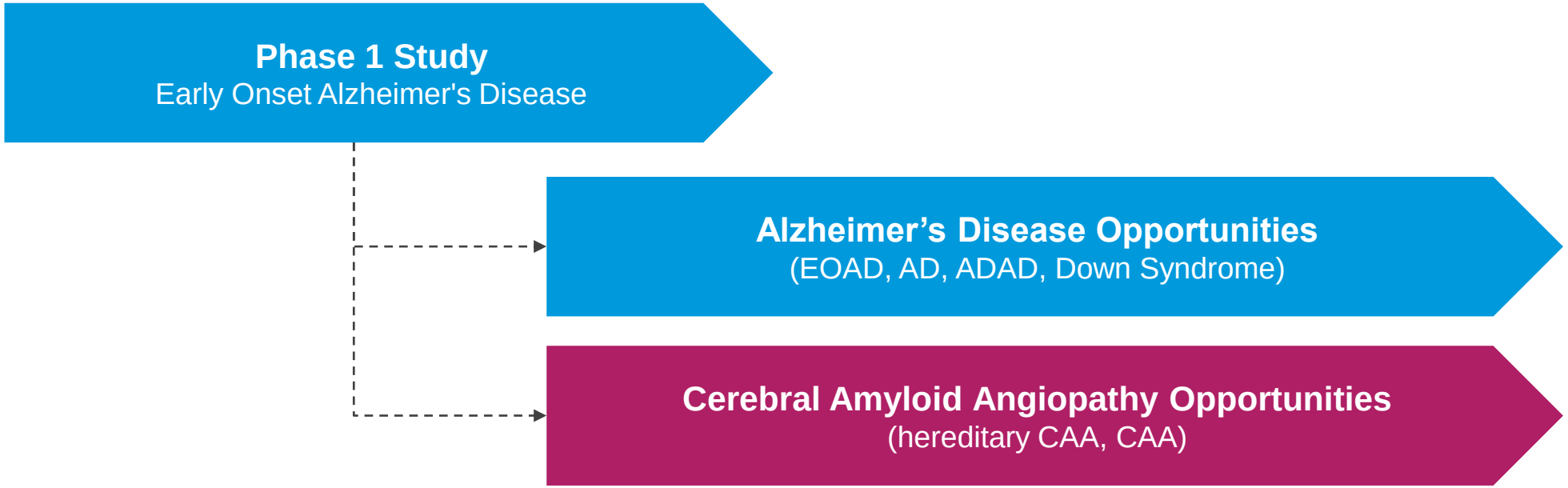
Progress Update

Dose escalation continuing in Part A

Preliminary data expected early 2023

Multiple Disease Populations with High Unmet Need

Phase 1 Data will Potentially Unlock Development Opportunities in Both AD and CAA



Multiple options for development and commercialization for ALN-APP

- Multiple genetically validated diseases with large populations and high unmet need
- Opportunities to adapt based on program learnings and evolving disease landscape

Potential to Make History with ALN-APP

Anticipating Many Future Firsts for Investigational RNAi Therapeutic

- ***First siRNA delivered to the human brain***

- First therapeutic **targeting *APP* mRNA**, sole precursor of all APP cleavage products, including Aβ, and genetically validated target for AD and CAA

- First therapeutic to comprehensively lower ***intracellular and extracellular*** amyloid proteins, including isoforms that aggregate in AD and CAA

- First therapeutic preventing synthesis of other potential **non-Aβ drivers of Alzheimer's Disease**: β-CTF (C99), η-CTF

Leading RNAi Therapeutics to New Frontier

Potential to Open New Opportunities Beyond Liver

ALN-APP: First of robust portfolio of CNS targets

- Phase 1 data with ALN-APP is expected to establish pharmacologic profile for CNS conjugates in humans
  - Target knockdown
  - Safety profile
  - Durability

- Modular and reproducible platform may enable rapid generation of additional therapeutic candidates for other high unmet need disease of the CNS

- Platform innovation continues and may enable further improvement for CNS conjugates, and further expansion to other extrahepatic tissues

Additional targets in pre-clinical development

ALN-SOD: SOD1-Specific ALS

Fatal progressive neurodegenerative disease characterized by motor neuron loss in the spinal cord and brain.

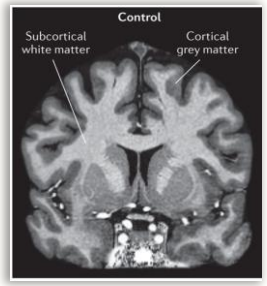
Healthy Motor Neuron

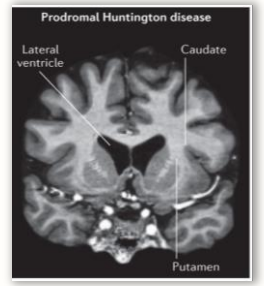
ALS Motor Neuron

ALN-HTT: Huntington's Disease

Fatal progressive neurodegenerative disease characterized by motor, cognitive, and psychiatric decline

Control Brain





HD Brain

Agenda

Welcome
- Josh Brodsky – Senior Director, Investor Relations & Corporate Communications

Introduction
- Eric Green – Senior Vice President, Development Programs

Progress on CNS Delivery for RNAi Therapeutics
- Kirk Brown, Ph.D. – Senior Director, Research, CNS Program

Update on ALN-APP, an Investigational RNAi Therapeutic in Development for Alzheimer's Disease and Cerebral Amyloid Angiopathy
- Tim Mooney – Director, Program Leader, ALN-APP Program

Wrap-Up and Q&A Session

Summary

Success with CNS delivery could result in significant expansion of Alnylam product engine driving sustainable growth through innovation

- CNS platform enables conjugate-based delivery of RNAi therapeutics that provide potent and durable target engagement with good distribution across CNS tissues
- Multiple genetically validated targets for diseases with high unmet need progressing toward development

Continued progress with first CNS program, ALN-APP

- Dose escalation in phase 1 trial in EOAD ongoing; topline results expected early 2023
- Significant opportunity to expand development to Alzheimer's Disease and Cerebral Amyloid Angiopathy, a major cause of hemorrhagic stroke

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Wrap-Up and Q&A Session

Save the date!

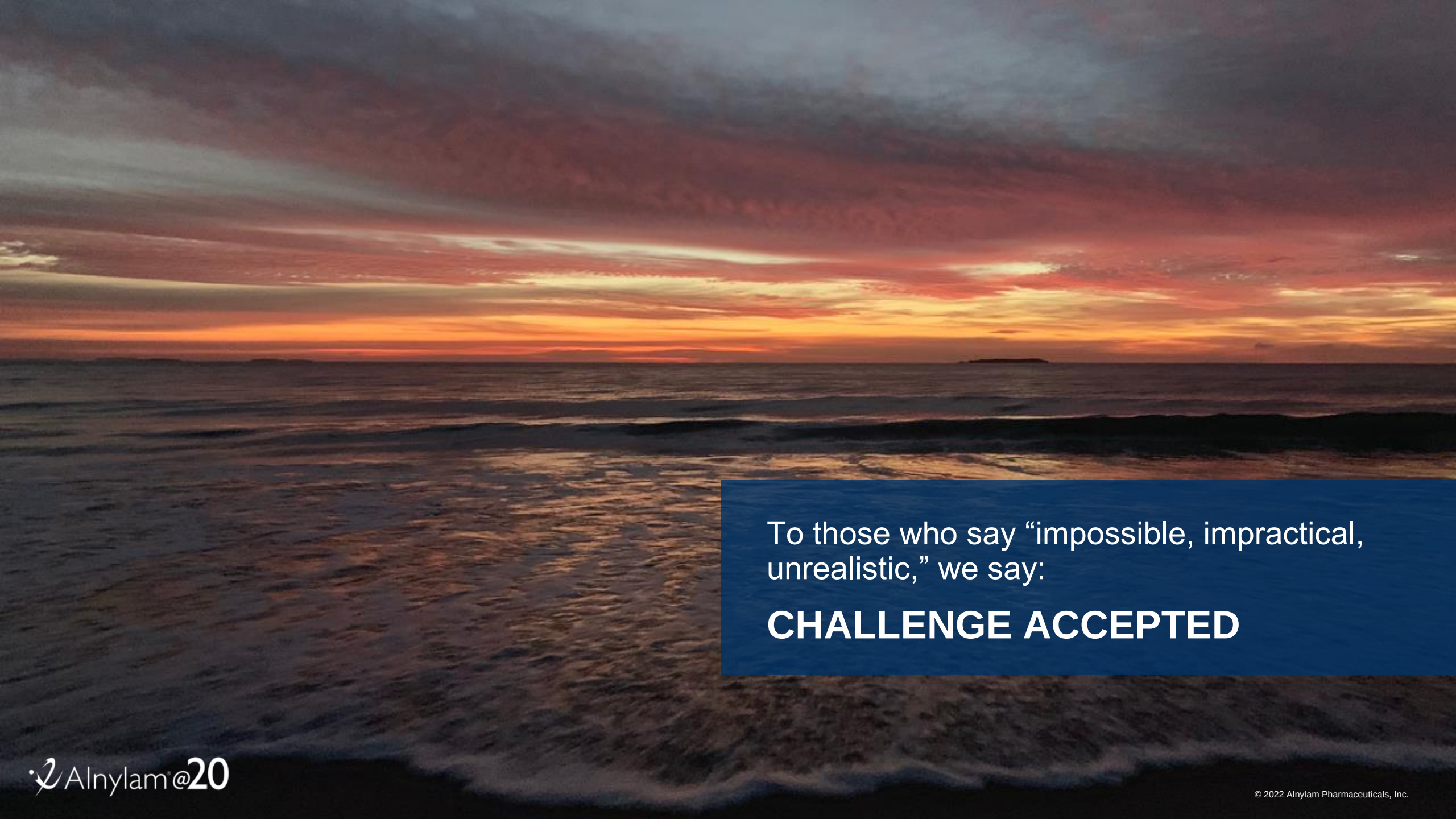
Alnylam®

R&D Day

December 15, 2022

A VIRTUAL EVENT

Registration information
coming soon.



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