Arrowhead Pharmaceuticals

arrowhead
pharmaceuticals

Safe Harbor Statement

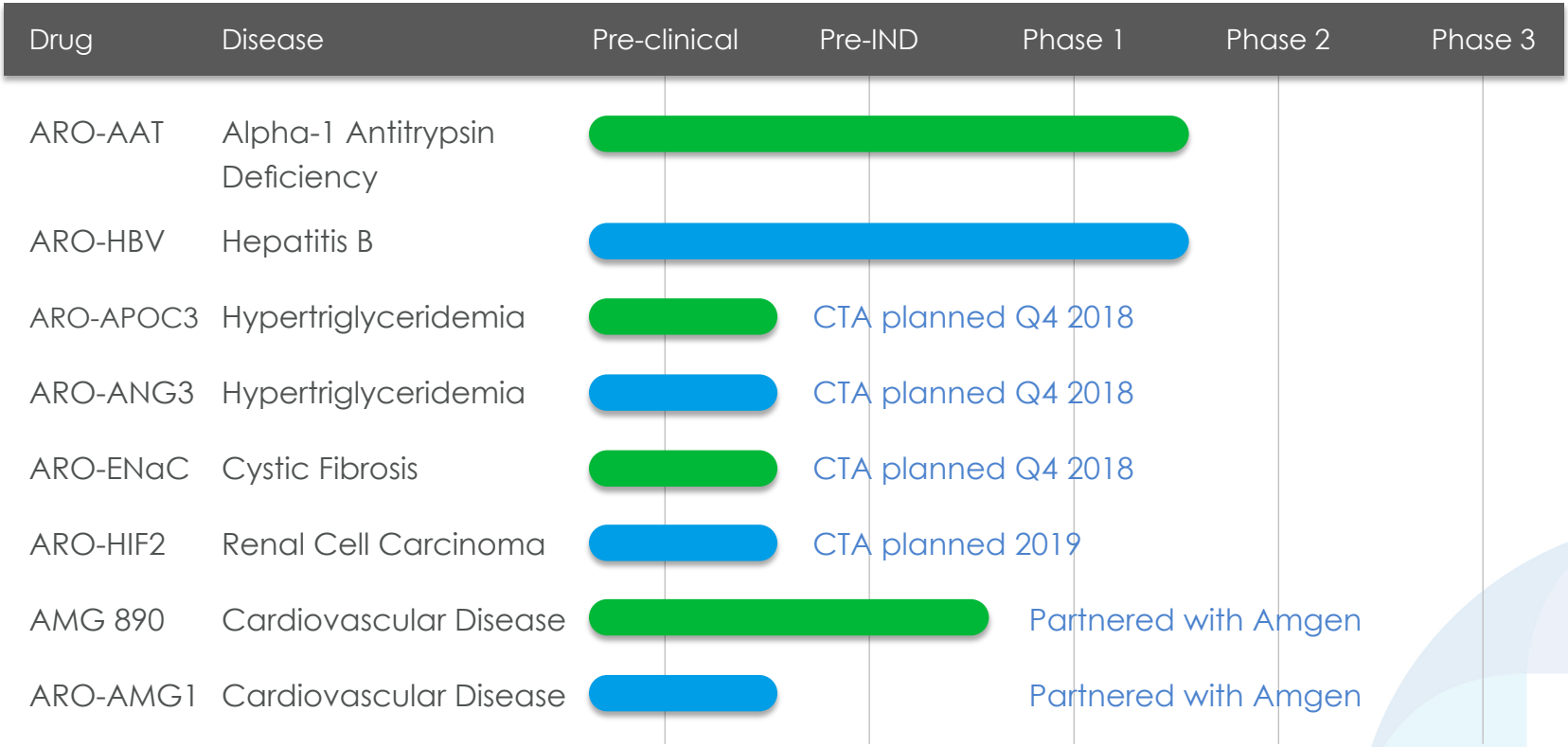
This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These statements are based upon our current expectations and speak only as of the date hereof. Our actual results may differ materially and adversely from those expressed in any forward-looking statements as a result of various factors and uncertainties, including, without limitation, our developmental stage and limited operating history, our ability to successfully and timely develop products, enter into collaborations and achieve other projected milestones, rapid technological change in our markets, demand for our future products, legislative, regulatory and competitive developments and general economic conditions. Our Annual Report on Form 10-K, recent and forthcoming Quarterly Reports on Form 10-Q, recent Current Reports on Forms 8-K, and other SEC filings discuss some of the important risk factors that may affect our ability to achieve the anticipated results, as well as our business, results of operations and financial condition. Readers are cautioned not to place undue reliance on these forward-looking statements. Additionally, Arrowhead disclaims any intent to update these forward-looking statements to reflect subsequent developments.

Arrowhead Pharmaceuticals

Our mission is to treat intractable medical conditions by silencing the genes that cause them

ARWR - NASDAQ Global Select	
Recent Price (June 1, 2018)	$10.91
Shares Outstanding	~87.5m
Market Capitalization	~$955m
Cash Resources (a/o 3/31/18)	~$91.5m

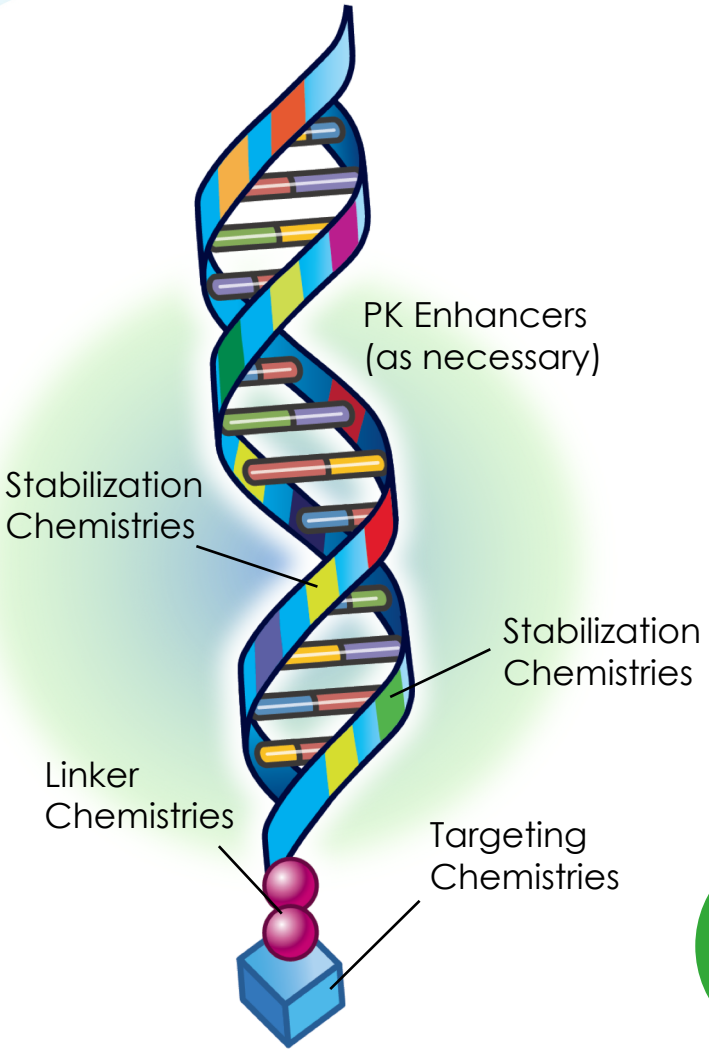
Pipeline


Drug
Disease
Pre-clinical
Pre-IND
Phase 1
Phase 2
Phase 3
ARO-AAT
Alpha-1 Antitrypsin Deficiency
ARO-HBV
Hepatitis B
ARO-APOC3
Hypertriglyceridemia
CTA planned Q4 2018
ARO-ANG3
Hypertriglyceridemia
CTA planned Q4 2018
ARO-ENaC
Cystic Fibrosis
CTA planned Q4 2018
ARO-HIF2
Renal Cell Carcinoma
CTA planned 2019
AMG 890
Cardiovascular Disease
Partnered with Amgen
ARO-AMG1
Cardiovascular Disease
Partnered with Amgen

TRiM™ Platform

arrowhead pharmaceuticals

Targeted RNAi Molecules - TRiM™ Platform Simplicity, Specificity, and Activity



- Proprietary trigger selection technologies
  - Designed to maximize activity and innate stability
- Stabilization chemistries
- pk enhancers as necessary
- Linker chemistries
- Targeting molecules
  - Targeting has always been a core philosophy

Deep KD in diverse tissues using subQ, iv, and inhaled administration routes

arrowhead pharmaceuticals

First Liver-targeted Programs Using TRiM™

ARO-AAT

- For liver disease associated with alpha-1 antitrypsin deficiency
- Alpha-1 Foundation estimates >100k people with the ZZ AAT gene mutation in US
- Restart of clinical program that used prior DPC platform

Initial data possible at AASLD in November 2018

ARO-HBV

- For treatment of chronic hepatitis B infection
- CDC estimates 350m chronic infections worldwide
- Restart of clinical program that used prior DPC platform

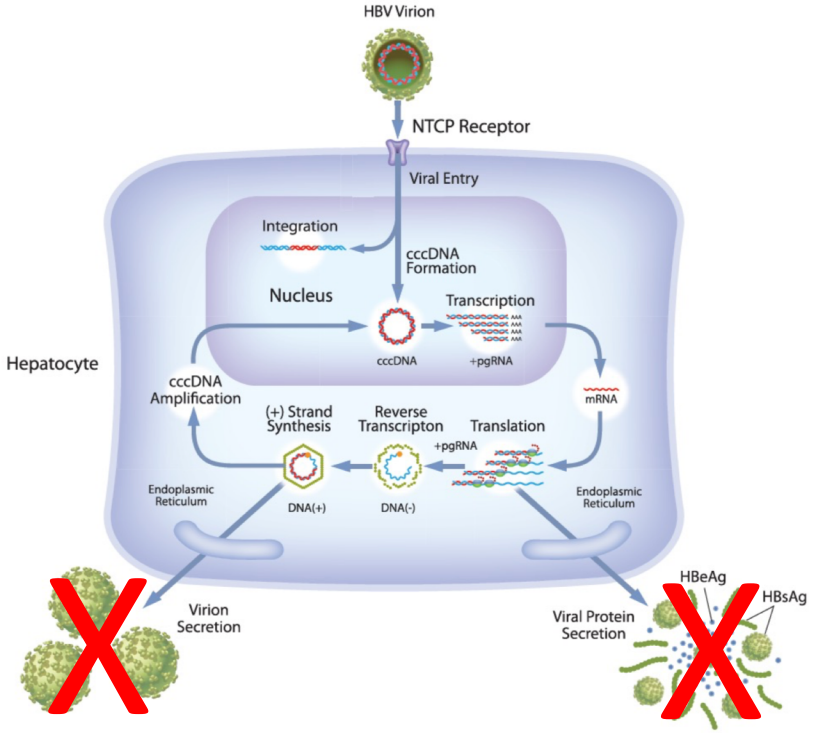
Initial data possible at AASLD in November 2018

Given our knowledge of these diseases and clinical experience with 64 sites in 15 countries, we expect uncommon speed in the clinic

ARO-HBV

arrowhead pharmaceuticals

ARO-HBV and the HBV Life Cycle



- Contagion
- Reinfection

- Immune suppression

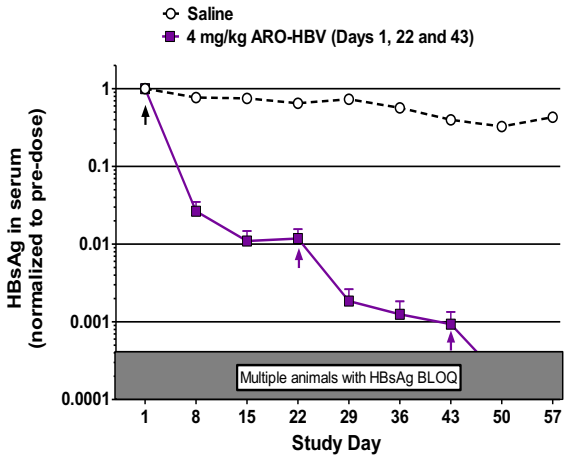
- **Designed to silence the entire transcriptome**
  - Everything from cccDNA
  - HBsAg from integrated DNA
- **Achieve functional cure after finite therapy by:**
  - Silencing immunosuppressive proteins
  - Disrupting HBV life cycle
  - Enabling natural immune control
- **ARC-520 data suggest that immune recovery and control in humans is possible**
- **Monthly (or less frequent) SQ dosing expected**

Lessons from 9 clinical studies of ARC-520/521 inform development path of ARO-HBV

ARO-HBV: potent in rodent studies

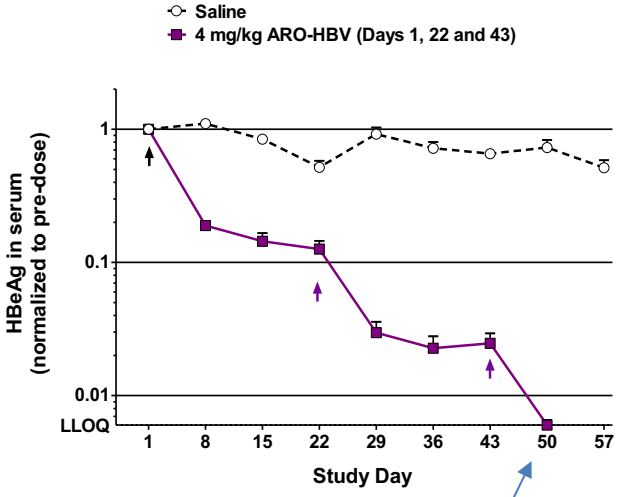
Multiple Dosing in WT pHBV Mice Reduced HBV DNA by 3.44 log10, HBsAg and HBeAg to LOQ

HBsAg



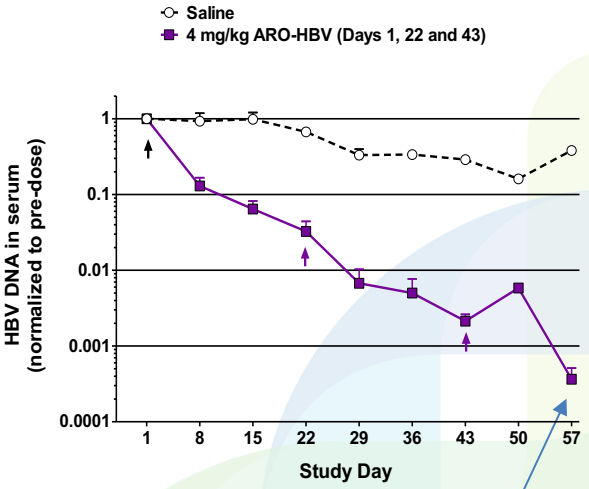
>3 log_{10} reduction after 3 doses

HBeAg



2.2 log10 = 99.4% reduction to LLOQ

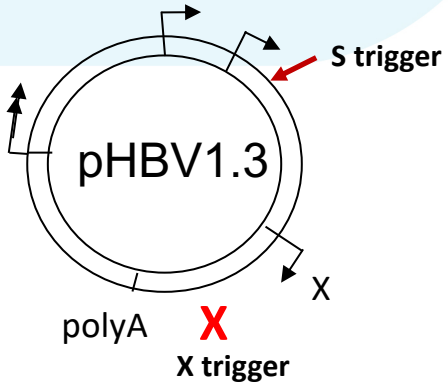
HBV DNA

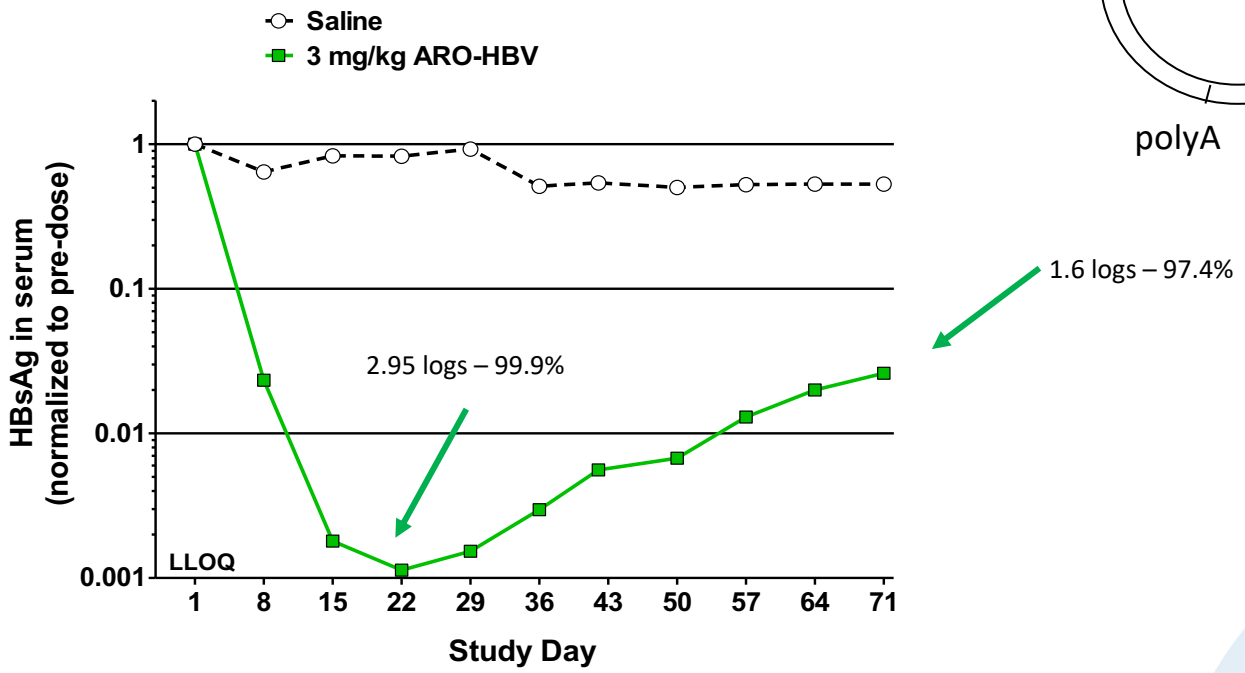


3.44 log10 = >99.9% reduction

arrowhead pharmaceuticals

Integration Modeled in a New, Mutated pHBV Transfected Mouse





HBsAg knockdown is deep and prolonged despite loss of HBx-trigger site

ARO-AAT

arrowhead pharmaceuticals

Alpha-1 Antitrypsin Deficiency

- AATD is a large scale orphan disease
  - Alpha-1 foundation estimates ~100,000 in the US
- Mutation in AAT gene (Z-AAT) leads to mis-folding of the protein and poor export from hepatocytes: low levels in circulation and accumulation in liver

Pathophysiology

Lung

Tissues susceptible to damage by neutrophil proteases: COPD

Treated with AAT enzyme replacement therapy today

Liver

Accumulation of mutant Z protein causes clinical liver disease

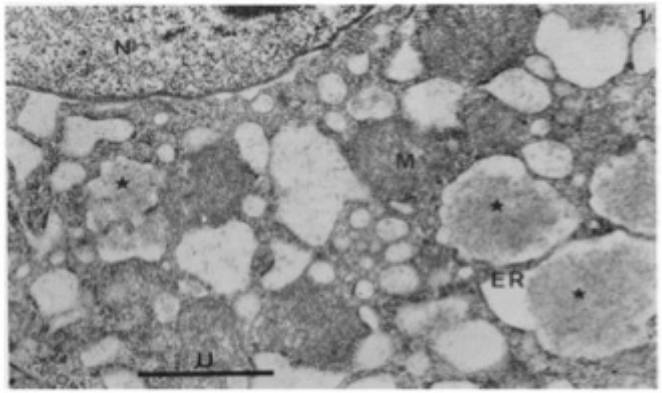
No current treatment

ARO-AAT Mechanism of Action

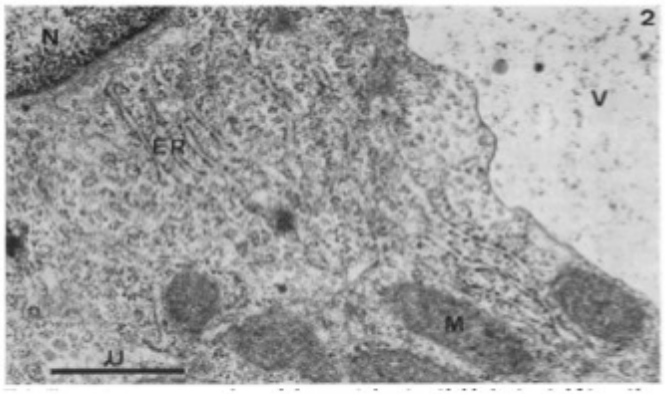
ARO-AAT designed to stop Z-AAT production by silencing AAT gene to:

- Prevent liver accumulation
- Allow clearance of accumulated protein
- Prevent cycles of cellular damage
- Prevent/Reverse progression of liver fibrosis

PiZZ phenotype (diseased)



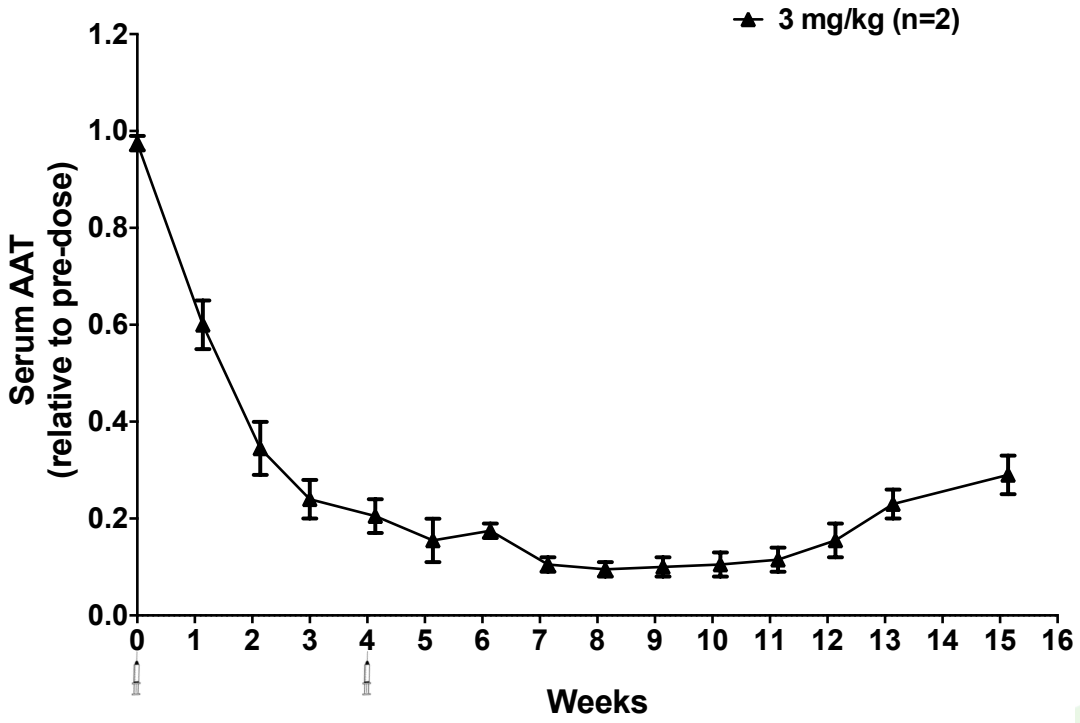
Pi null phenotype (normal)



Feldmann G et al., *Gut* 1975

ARO-AAT: durable AAT knockdown

- 92% maximum serum AAT knockdown achieved
- Knockdown sustained for 7+ weeks following second dose



Durable knockdown may support monthly or less frequent dosing

arrowhead pharmaceuticals

Cardiometabolic

arrowhead pharmaceuticals

Amgen Collaboration

- Cardiovascular collaboration for two RNAi therapeutics
- Amgen received:
  1. Exclusive license to ARO-LPA (now called AMG-890)
  2. Option for an additional candidate against an undisclosed target
- Total deal value of up to $673.5 million
- Arrowhead received $56.5 million upfront
  - $35 million in upfront payments, $21.5 million equity investment
- Up to low double digit royalties for ARO-LPA and single digit royalties for the undisclosed target
- Amgen is wholly responsible for funding and conducting clinical development and commercialization

Building Cardiometabolic Pipeline with TRiM™

ARO-APOC3

- For treatment of hypertriglyceridemia
- Up to 90% KD observed in rodent models (intestines also a source of production)
- SubQ administration
- NHP work and non-GLP tox studies to follow

CTA planned in Q4 2018

ARO-ANG3 (against ANGPTL3)

- For treatment of hypertriglyceridemia
- >90% KD observed in rodent models
- SubQ administration
- Still optimizing chemistries
- NHP work and non-GLP tox studies to follow

CTA planned in Q4 2018

Extra-hepatic Programs

arrowhead pharmaceuticals

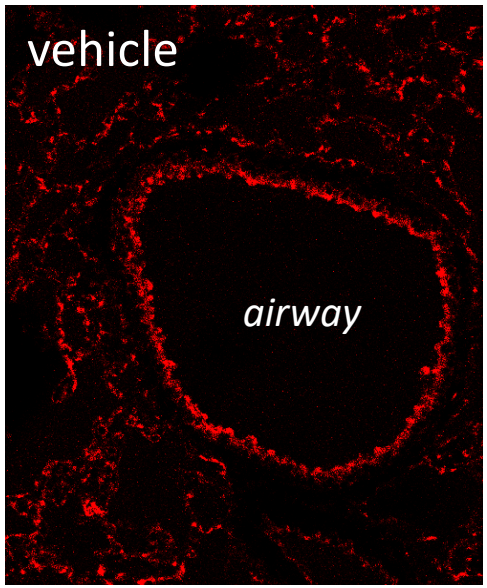
Targeting New Tissues Using TRiM™ Platform

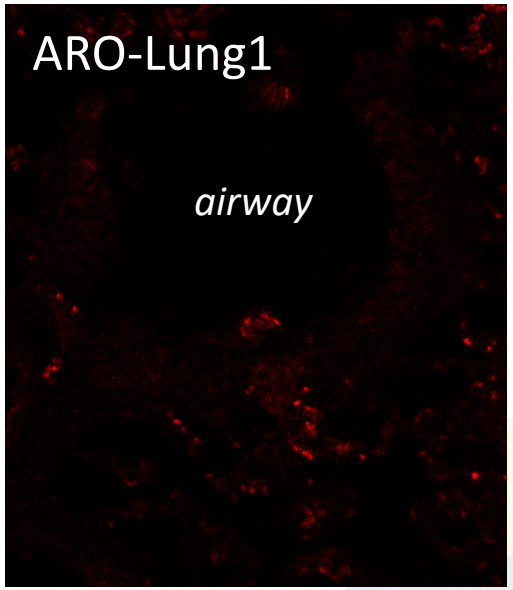
ARO-ENaC

- Almost 90% KD observed in rodent models
- Inhaled administration
- Large animal studies and disease models underway
- Non-GLP tox studies underway

CTA planned for Q4 2018

Red: lung target protein expression by IHC

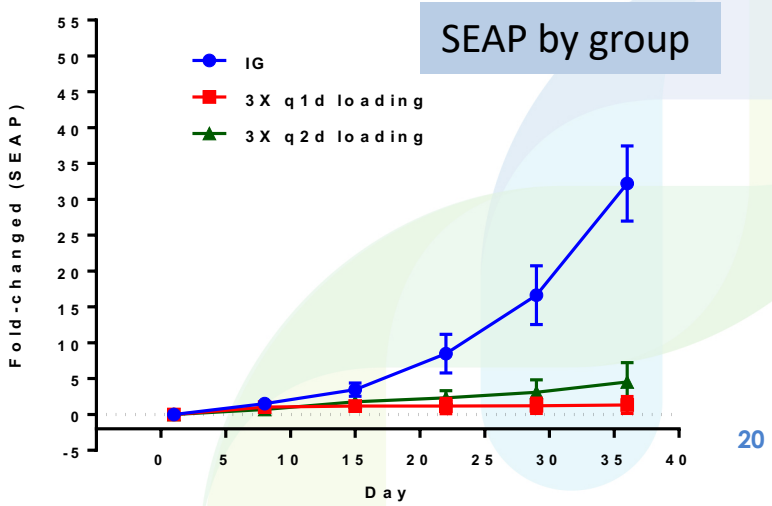




ARO-Hif2 (for renal cell carcinoma)

- Up to 85% KD observed in rodent tumor model
- iv administration
- Solid tumor targeting
- Non-GLP tox studies planned
- Broaden tumor model testing

CTA planned in 2019



arrowhead pharmaceuticals

Investment Thesis

arrowhead pharmaceuticals

Value Proposition

All built on the TRiM™ Platform

- Modular
- Scalable
- Structurally simple
- Widely targetable

- **ARO-AAT and ARO-HBV in clinic now**
  - Potent in animal models
  - Validation from prior clinical programs
  - Potential data at AASLD Nov 2018
- **ARO-APOC3 and ARO-ANG3 are exciting additions to CV portfolio**
  - Orphan and large market opportunities
- **Business development progress**
  - Amgen partnered programs ARO-LPA (AMG 890) and ARO-AMG1 progressing
  - Opportunities for more partnering
- **Using RNAi outside the liver is real now**
  - Tumor targeting has matured
  - Inhaled administration for lung delivery opens interesting new opportunities