JP Morgan Week 2018

January 8-10, 2018

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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.

Financial Profile

ARWR - NASDAQ Global Select	
Recent Share Price (1/3/18)	$4.64
Shares Outstanding	~75m
Market Cap	~$348m
Cash (as of 9/30/17)	~$66m

RNAi: Target the Gene, Silence the Disease

Treat intractable medical conditions by silencing the genes that cause them

Now leveraging new TRiM™ platform
Unveiled at Analyst Day in September 2017

Pipeline

Drug	Indication	Pre-clinical	Pre-IND	Phase 1	Phase 2	Phase 3
ARO-AAT	Alpha-1 Antitrypsin Deficiency				CTA filed Q4 2017	
ARO-HBV	Hepatitis B				CTA filed Q4 2017	
ARO-APOC3	Hypertriglyceridemia		CTA planned Q4 2018			
ARO-ANG3	Hypertriglyceridemia		CTA planned Q4 2018			
ARO-Lung1	Undisclosed		CTA planned Q4 2018			
ARO-HIF2	Renal Cell Carcinoma		CTA planned 2019			
ARO-F12	Thrombosis/Hereditary Angioedema		Available for partnering			
ARO-LPA	Cardiovascular Disease		Partnered with Amgen			
ARO-AMG1	Cardiovascular Disease		Partnered with Amgen			

TRiM™ Platform

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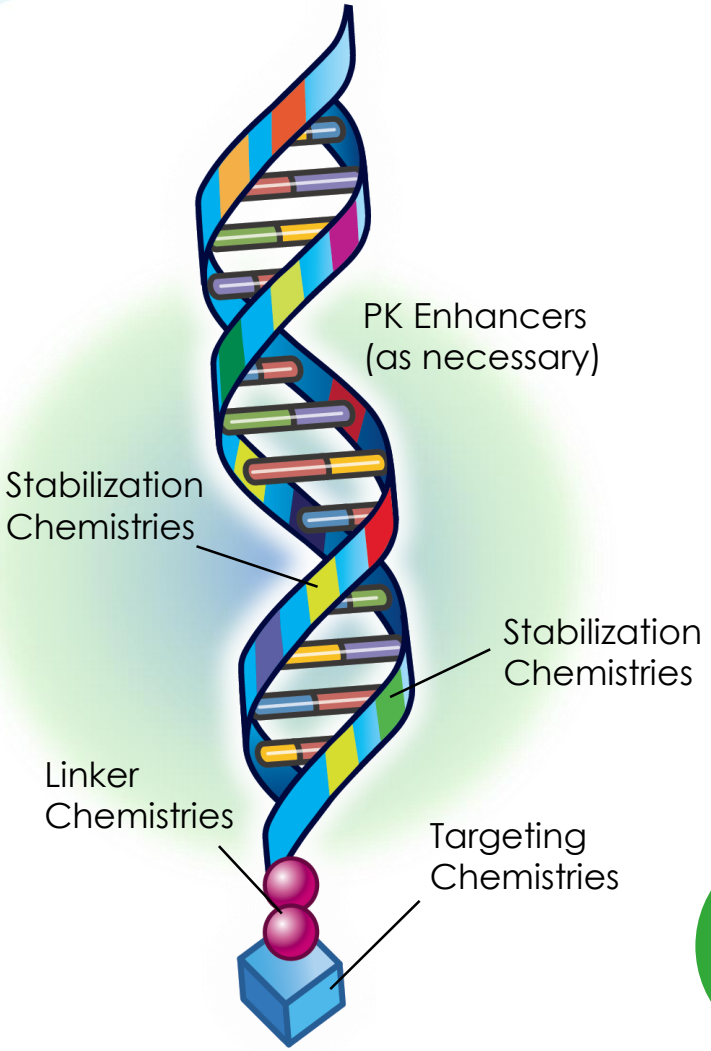
Targeted RNAi Molecules - TRiM™ Platform Simplicity, Specificity, and Activity



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

Now capable of achieving deep KD in diverse tissues using subQ, iv, and inhaled administration routes
Without active endosomal escape

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First Liver-targeted Programs Using TRiM™

ARO-AAT

- For liver disease associated with alpha-1 antitrypsin deficiency
- Estimated 200k people with the ZZ AAT gene mutation in US and Europe
- Restart of clinical program that used prior DPC platform

CTA filed in Q4 2017

ARO-HBV

- For treatment of chronic hepatitis B infection
- Estimate 250 – 350m chronic infections worldwide
- Restart of clinical program that used prior DPC platform

CTA filed in Q4 2017

Given our knowledge of these diseases and clinical experience with 64 sites in 15 countries, we expect to *fly* once in the clinic

ARO-AAT

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Alpha-1 Antitrypsin Deficiency

- AATD is a large scale orphan disease
  - Alpha-1 foundation estimates ~100,000 in the US
  - Approximately 100,000+ in Europe
- 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

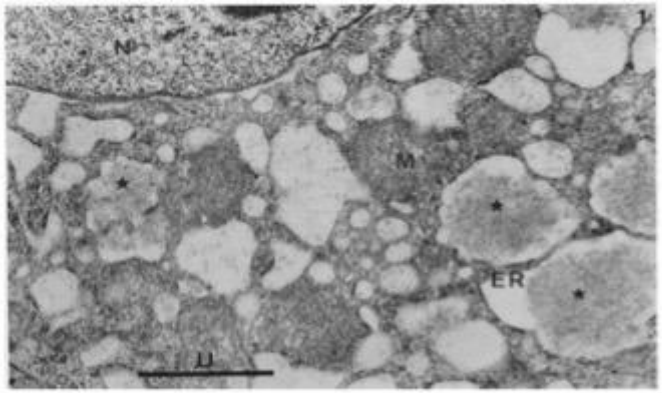
No current treatment

ARO-AAT Mechanism of Action

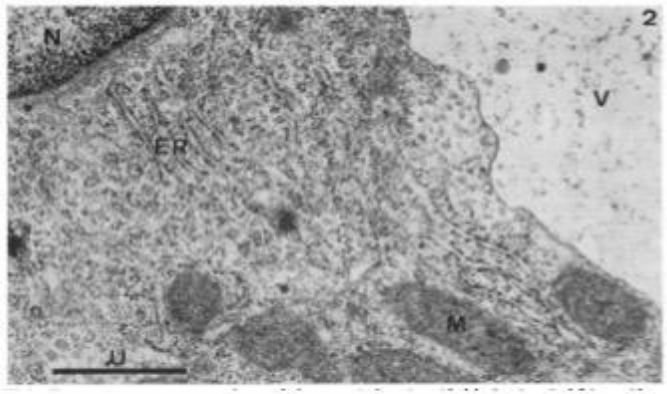
ARO-AAT designed to stop Z-AAT production by silencing AAT gene to:

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

PiZZ phenotype (diseased)



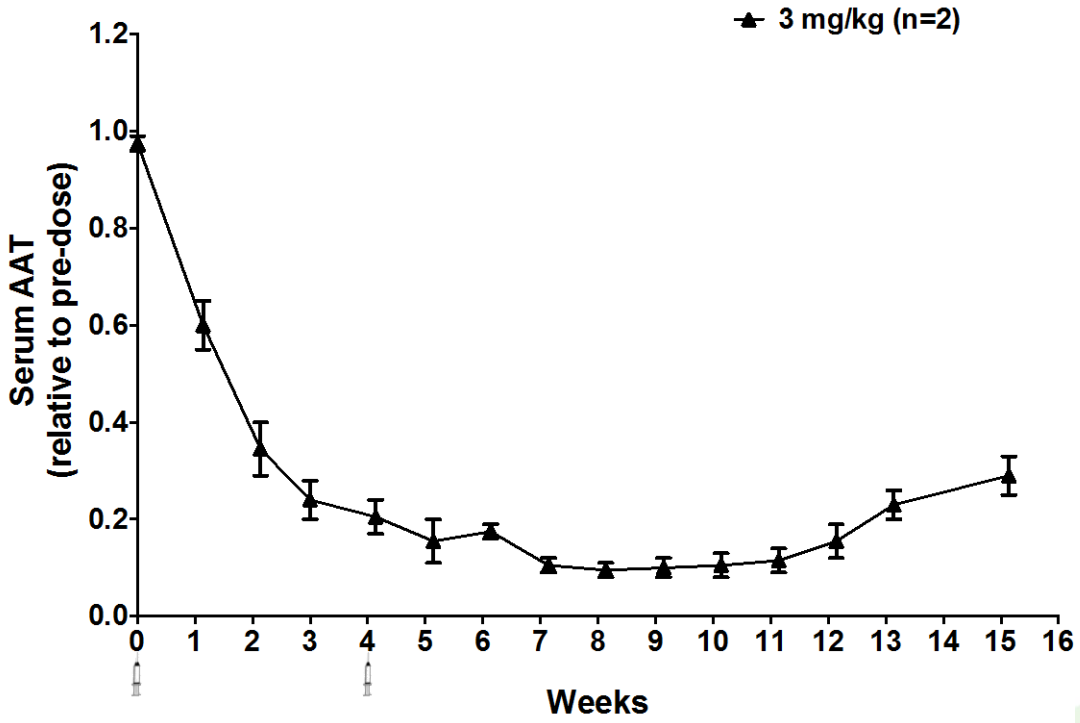
Pi null phenotype (normal)



Feldmann G et al., *Gut* 1975

ARO-AAT Provides Durable AAT knockdown:
Multi-dose in NHP, dosed subcutaneously

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



Durable knockdown supports once monthly or less frequent dosing

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ARO-HBV

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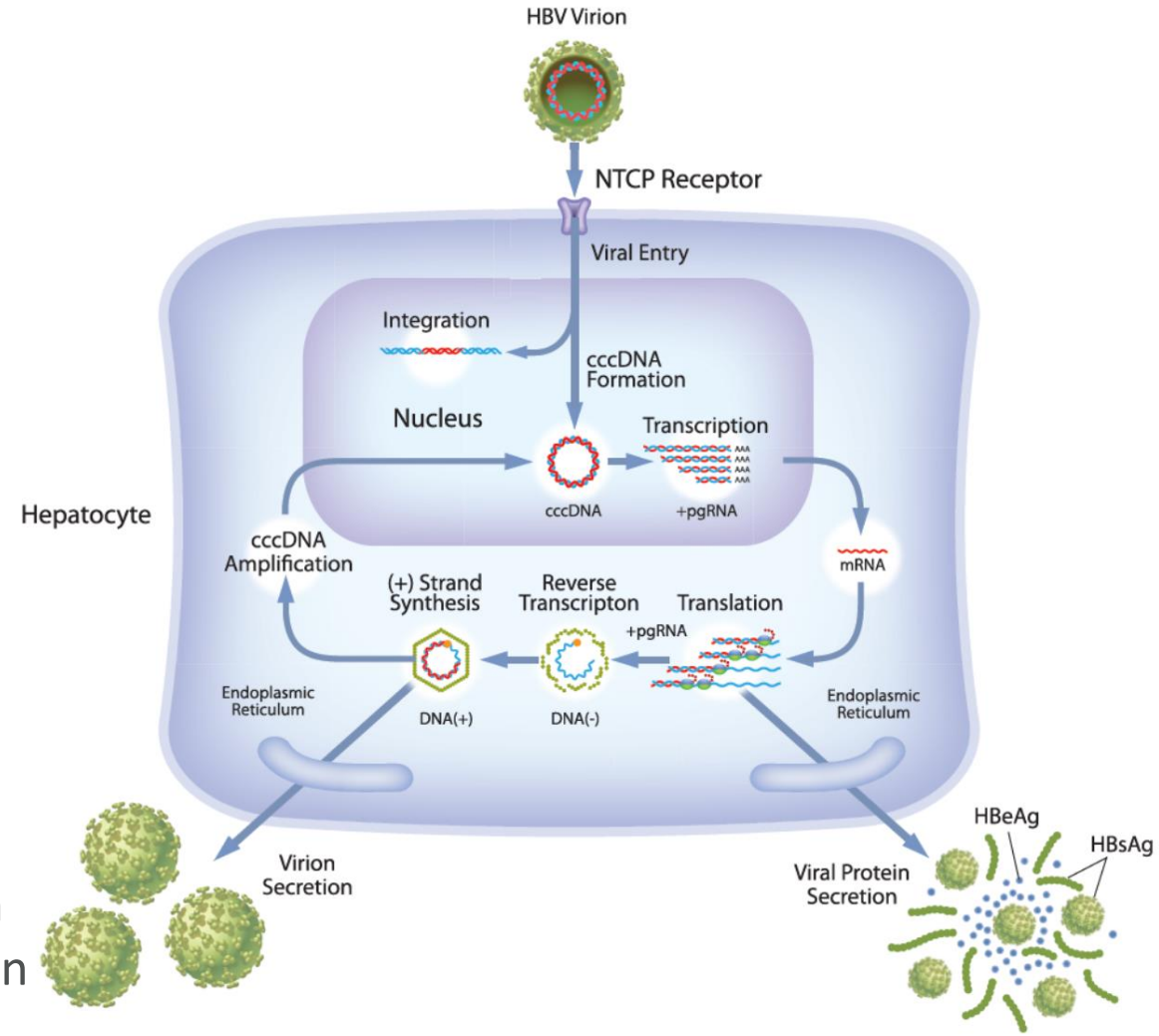
Hepatitis B Virus Life Cycle



- Contagion
- Reinfection

- Immune suppression

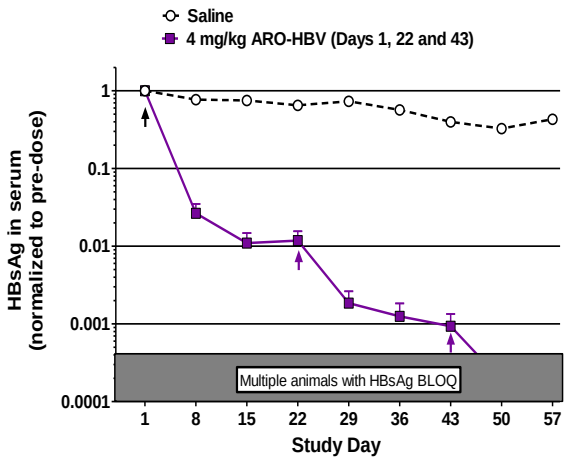
Why We see a Central Role for RNAi in HBV

- Attacks the entire transcriptome
  - Should synergize with **most/all** hepatocyte-active compounds (e.g. NUCs, capsid inhibitors, x protein drugs, RIG-I agonists, etc) by reducing their viral inputs
  - Can reduce HBsAg from integrated DNA, which other mechanisms likely can't
- Monthly (or less frequent) SQ dosing with unusually good tolerability should fit well with oral regimens
- ARC-520 data suggests that immune recovery and control in humans and chimps is possible
  - Creates real excitement that future combination work can build on this

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

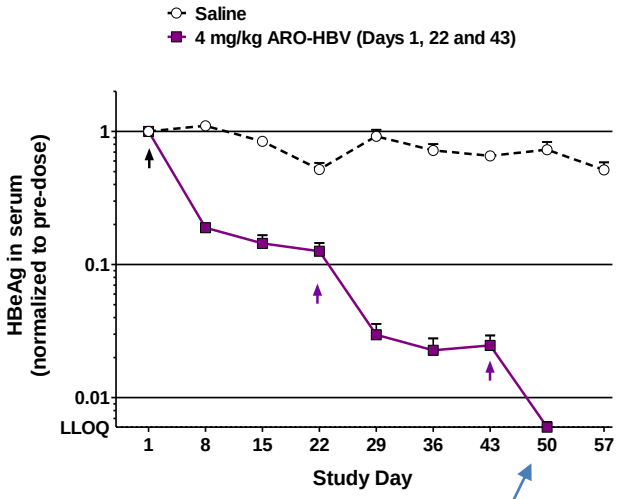
Multiple Dosing in WT pHBV Mice Reduces HBV DNA by 3.44 log10, HBsAg and HBeAg to LOQ

HBsAg



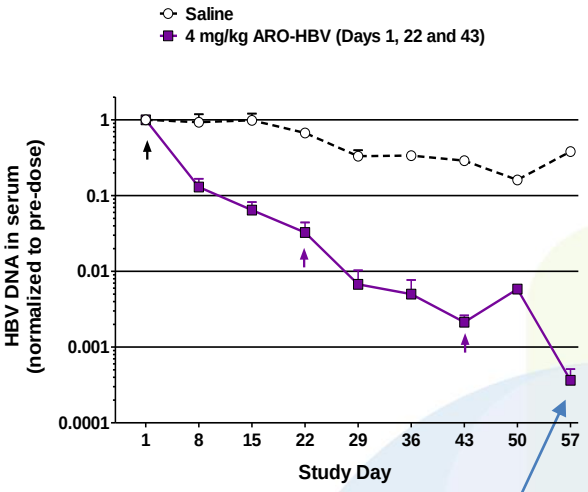
>3 log_{10} reduction after 3 doses

HBeAg



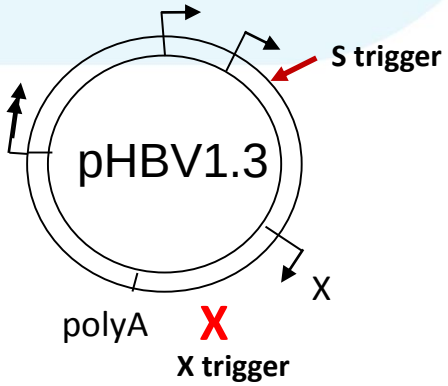
2.2 log10 = 99.4% reduction to LLOQ

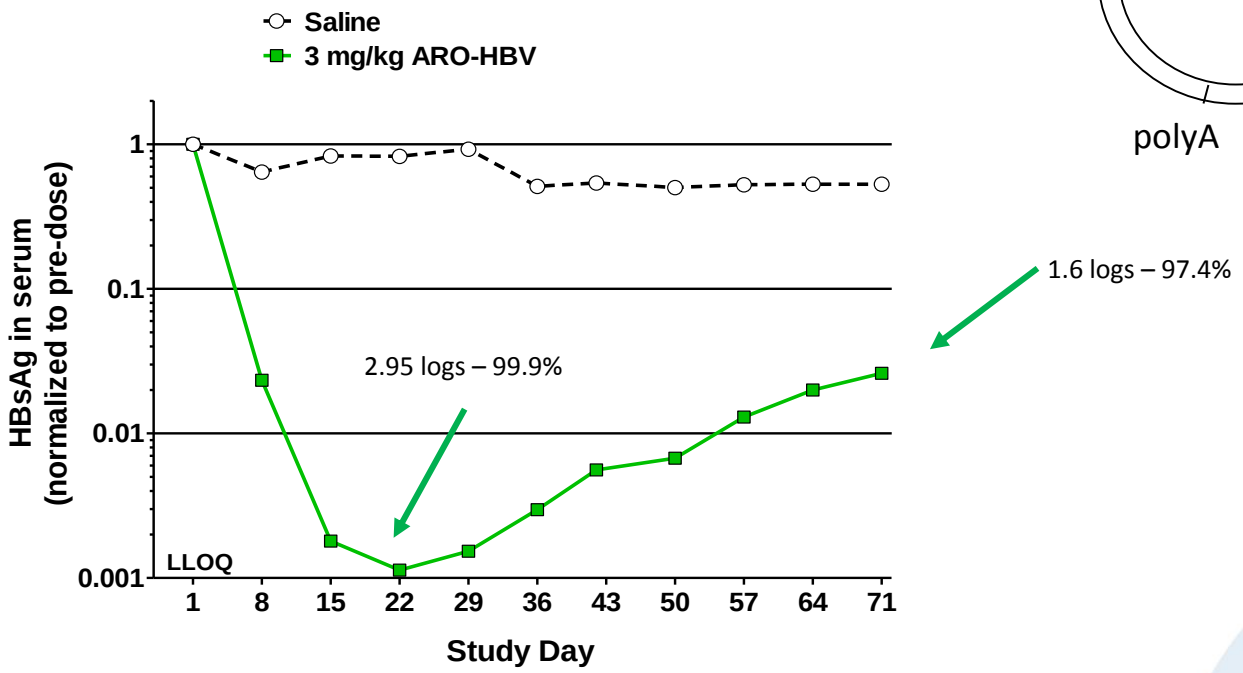
HBV DNA



3.44 log10 = >99.9% reduction

Integration Modeled in a New, Mutated pHBV Transfected Mouse





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

Cardiovascular Disease

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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 Out CV Portfolio Using TRiM™ platform

Already building candidates for Lp(a) and Gene X with Amgen,
Now adding as wholly-owned assets:

ARO-APOC3

- For treatment of hypertriglyceridemia
- Up to 90% KD 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 in rodent models with several good triggers
- SubQ administration
- Still optimizing chemistries
- NHP work and non-GLP tox studies to follow

CTA planned in Q4 2018

Extra-hepatic Programs

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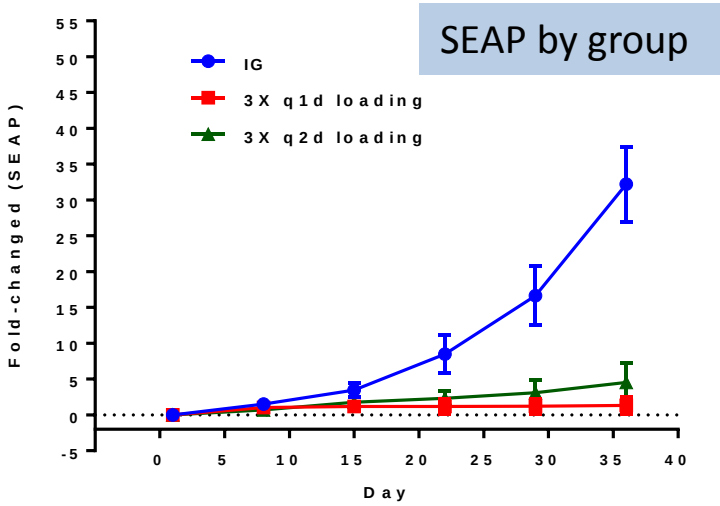
Targeting New Tissues Using TRiM™ Platform

ARO-Hif2 (for renal cell carcinoma)

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

CTA planned in 2019

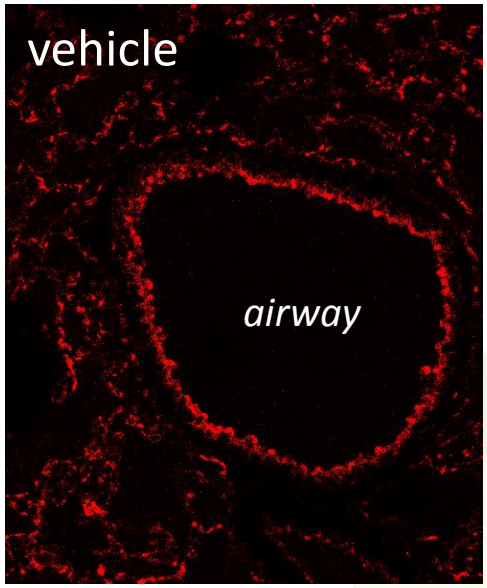


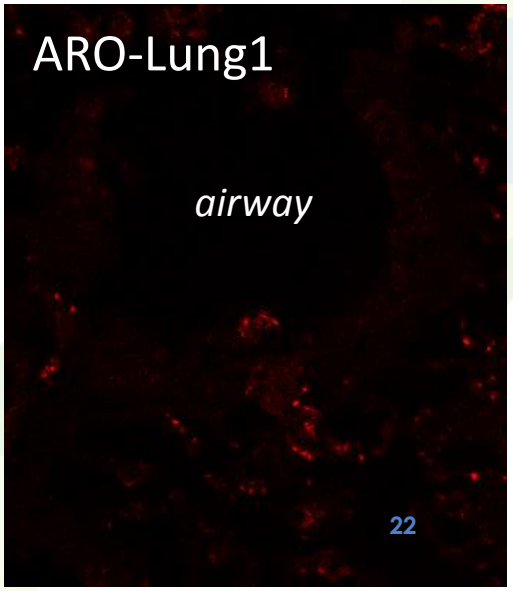
ARO-Lung1

- Almost 90% KD 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





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Extra-hepatic Delivery is upon Us

Treat intractable medical conditions, wherever they are, by silencing the genes that cause them

Targeting lung and tumors with the TRiM™ platform

- Demonstrates flexibility of the TRiM™ platform
- Expands opportunities into new markets/indications
  - Once RNAi activity is validated in a new organ, allows expansion into other disease areas within that organ
  - Potential to develop into new franchise
  - Powerful engine of growth
- Fundamentally changes RNAi competitive landscape
- Expands partnership opportunities

Investment Thesis

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Value Proposition

All built on the TRiM™ Platform

- Modular
- Scalable
- Structurally simple
- Widely targetable

- **ARO-AAT and ARO-HBV in the clinic shortly**
  - Potent in animal models
  - Validation from prior clinical programs
- **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