The AROAAT1001 Phase 1 Study

June 29, 2018

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Safe Harbor Statement

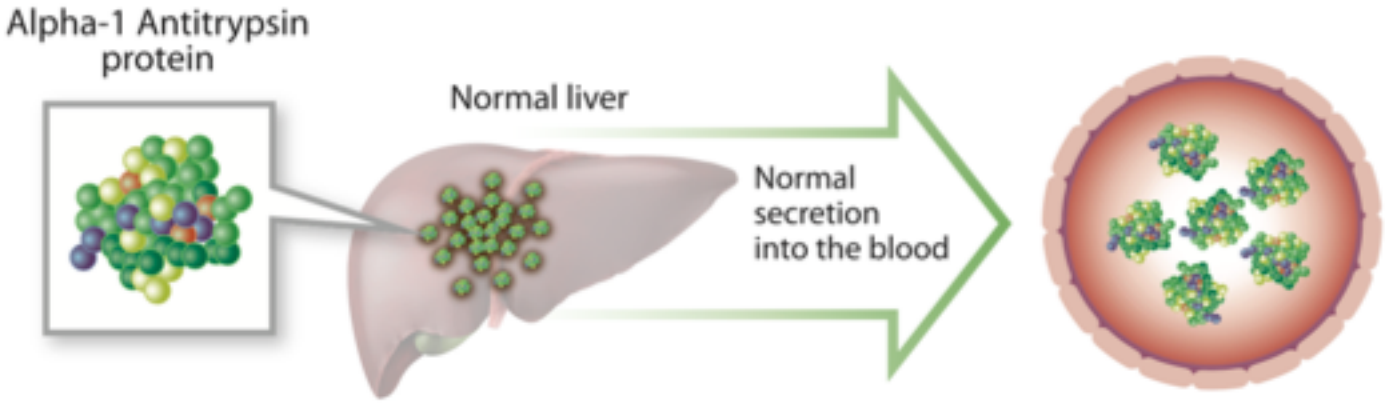
This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. These statements are based upon our current expectations and speak only as of the date hereof. Our actual results may differ materially and 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.

Agenda

- **Introduction**
- ARO-AAT Animal Results
- AROAAT1001 Clinical Study
- Conclusions

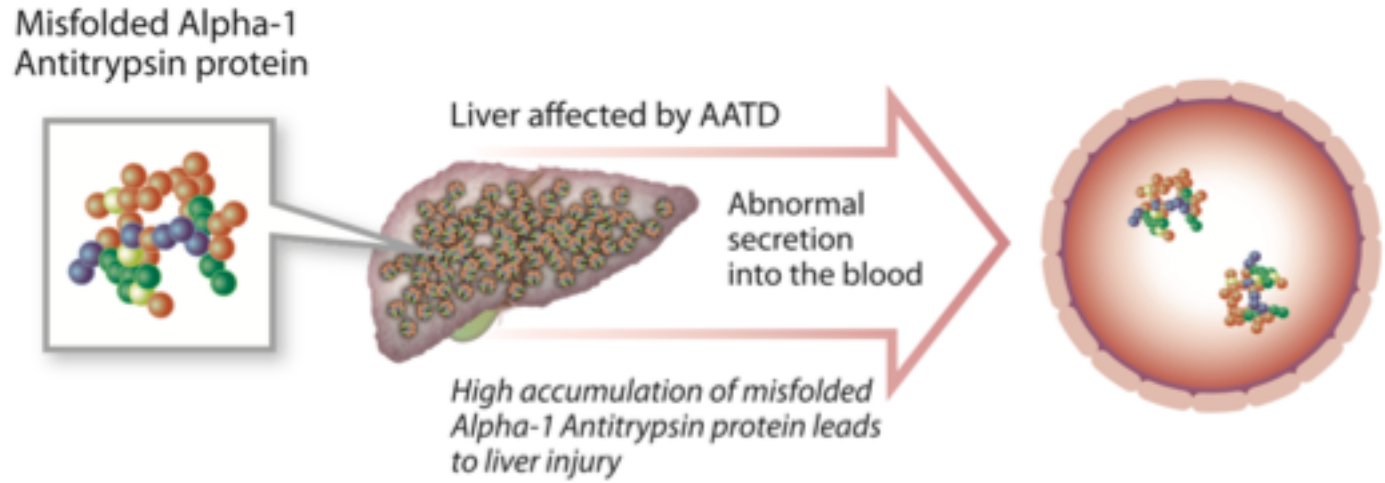
Alpha-1 Antitrypsin Deficiency

Normal AAT



Normal blood levels of normal protein protect lungs

Abnormal AAT (Z-AAT)



Low blood levels of abnormal protein leaves lung susceptible to damage from inflammation caused by inhaled irritants or infection

No current treatment

Treated with AAT protein replacement therapy today

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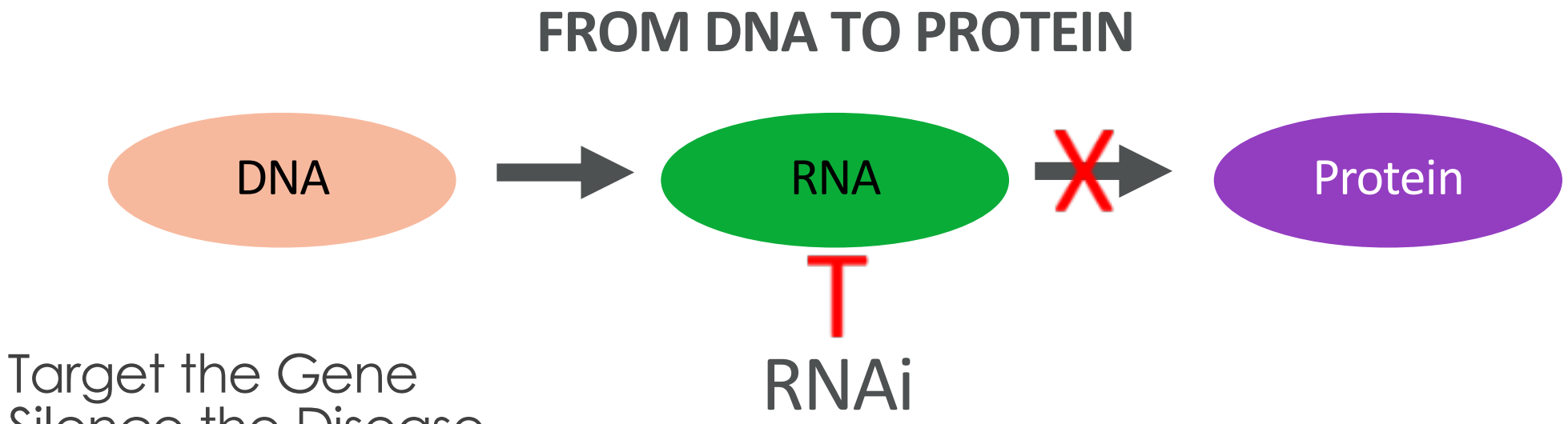
RNAi-based Therapeutics: *What is RNAi?*



RNAi = RNA interference

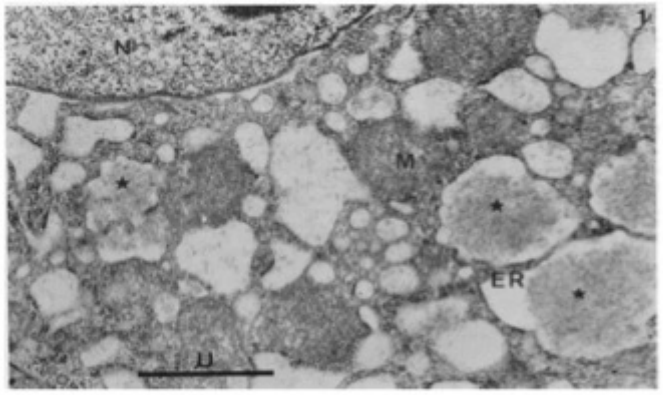
- A normal cellular process that regulates production of proteins
- RNAi silences gene expression so specific protein is not produced
- RNAi triggers can be designed and synthesized to target a specific protein

ARO-AAT, An Investigation Drug for AATD Liver Disease:
Mechanism of Action

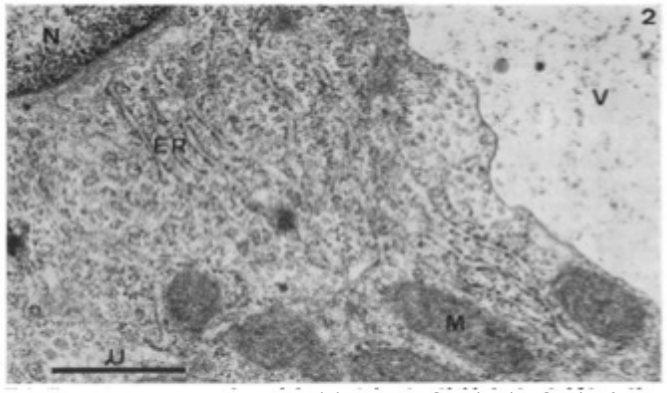
ARO-AAT designed to stop Z-AAT production by silencing AAT gene expression to:

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

PiZZ phenotype (diseased)



Pi null phenotype (normal liver)



Feldmann G et al., *Gut* 1975

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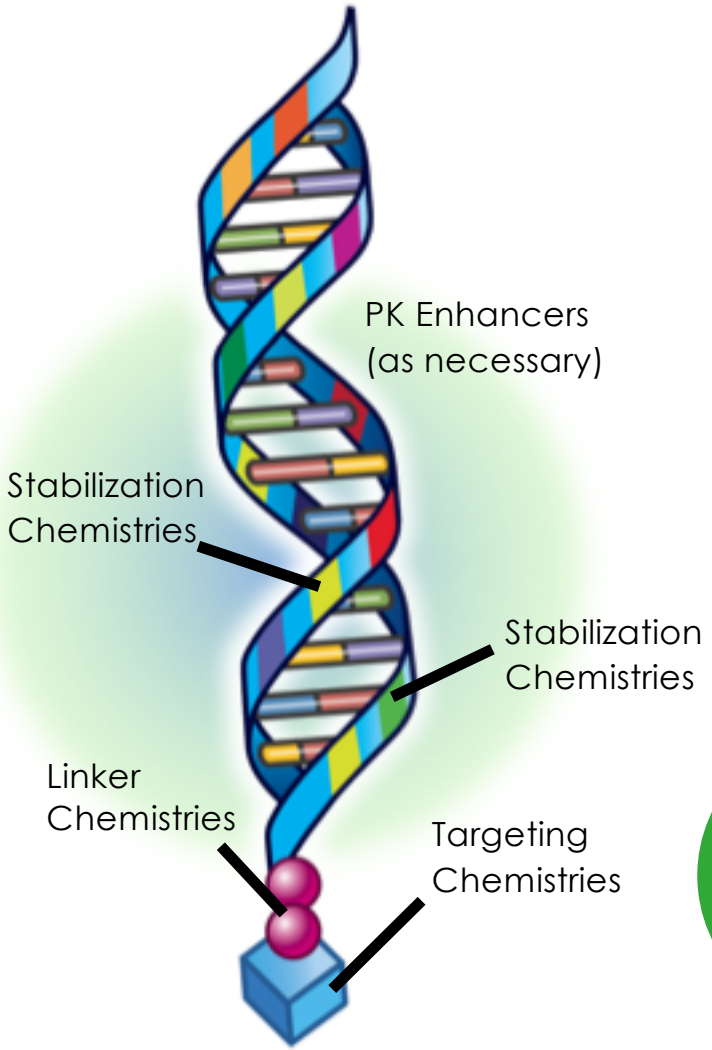
Arrowhead RNAi Platform: TRiM™: Simplicity, Specificity, and Activity



Components:

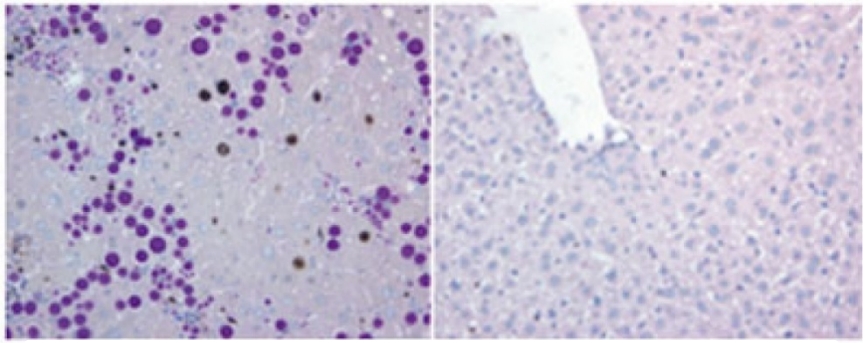
- Stabilization chemistries
- Linker chemistries
- Targeting ligands

Now capable of achieving deep Knockdown in diverse tissues using subQ, iv, and inhaled administration routes

PiZ Mouse Model of AATD Liver Disease

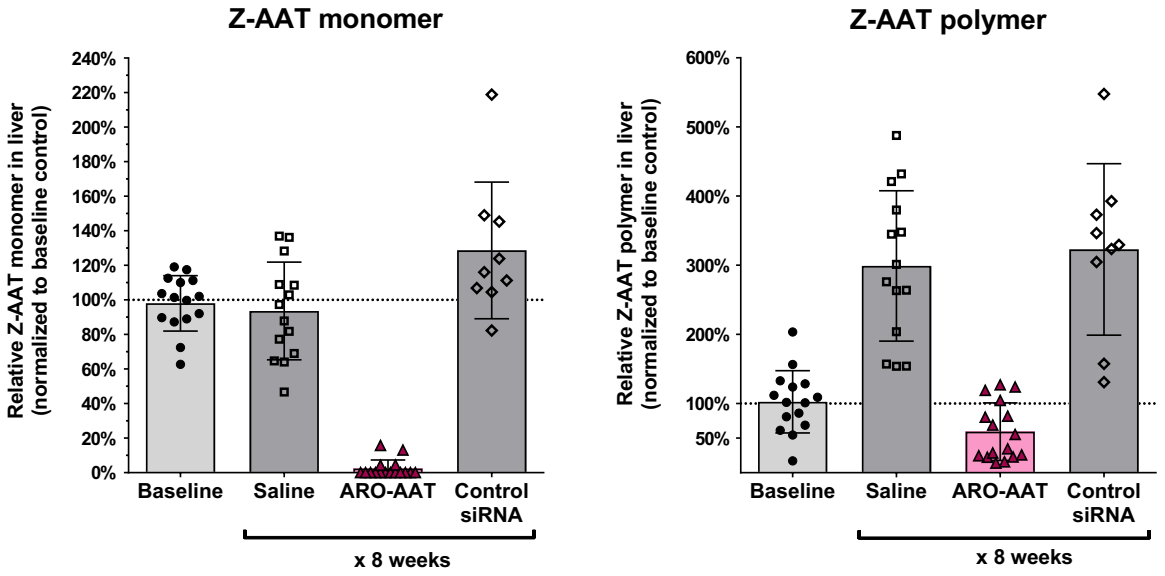
The PiZ mouse model expresses the human Z-mutant AAT gene (Z-AAT) and recapitulates the human AATD-associated liver phenotype:

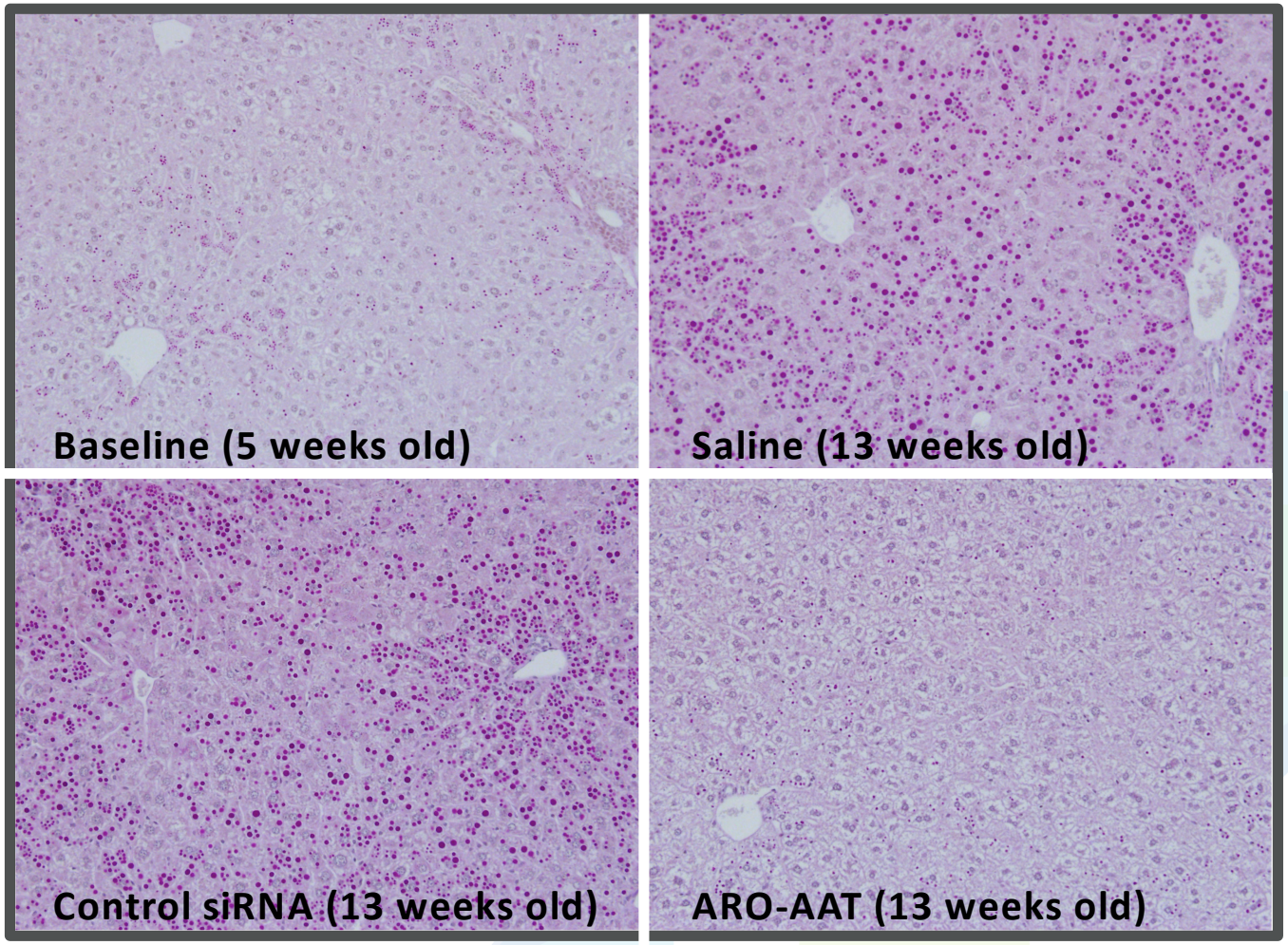
- Hepatocytes (liver cells) produce high levels of human Z-AAT
- Hepatocytes are not able to efficiently process and secrete the Z-AAT
- Z-AAT forms polymers that accumulate in large "globules"
- These globules stress the hepatocytes, leading to fibrosis
- Globules are visualized with Periodic Acid Schiff (PAS) staining + diastase (dark purple stain)



PiZZ **Wild Type**

ARO-AAT Reduces Monomer and Polymer and Prevents Globule Accumulation in Young PiZ Mice

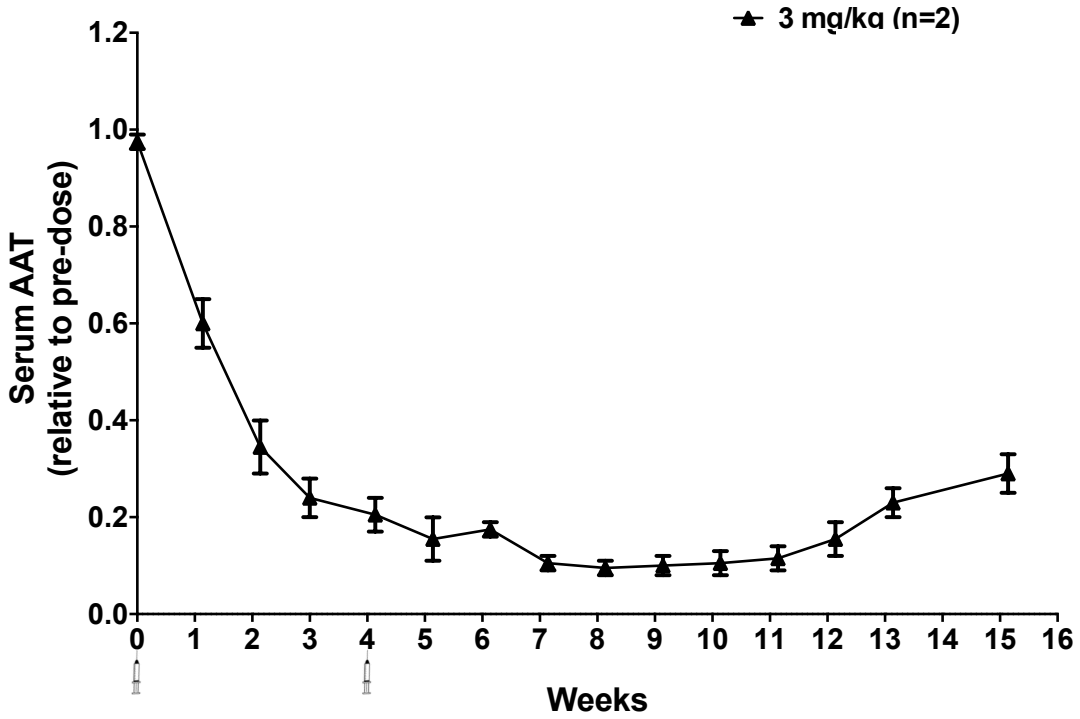




In collaboration with SLU (Jeff Teckman, M.D.)

ARO-AAT Provides Durable AAT Knockdown

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



Durable knockdown supports once monthly or less frequent dosing

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AROAAT1001 Clinical Study in Healthy Volunteers has 2 Parts

DOUBLE BLIND PART

- 4 treatment arms
  - 35, 100, 200 and 300 mg
  - 100, 200, 300 mg receive ***3 monthly doses***
  - 4 active, 4 placebo
- Assessments of safety, tolerability, plasma levels of ARO-AAT, plasma AAT changes

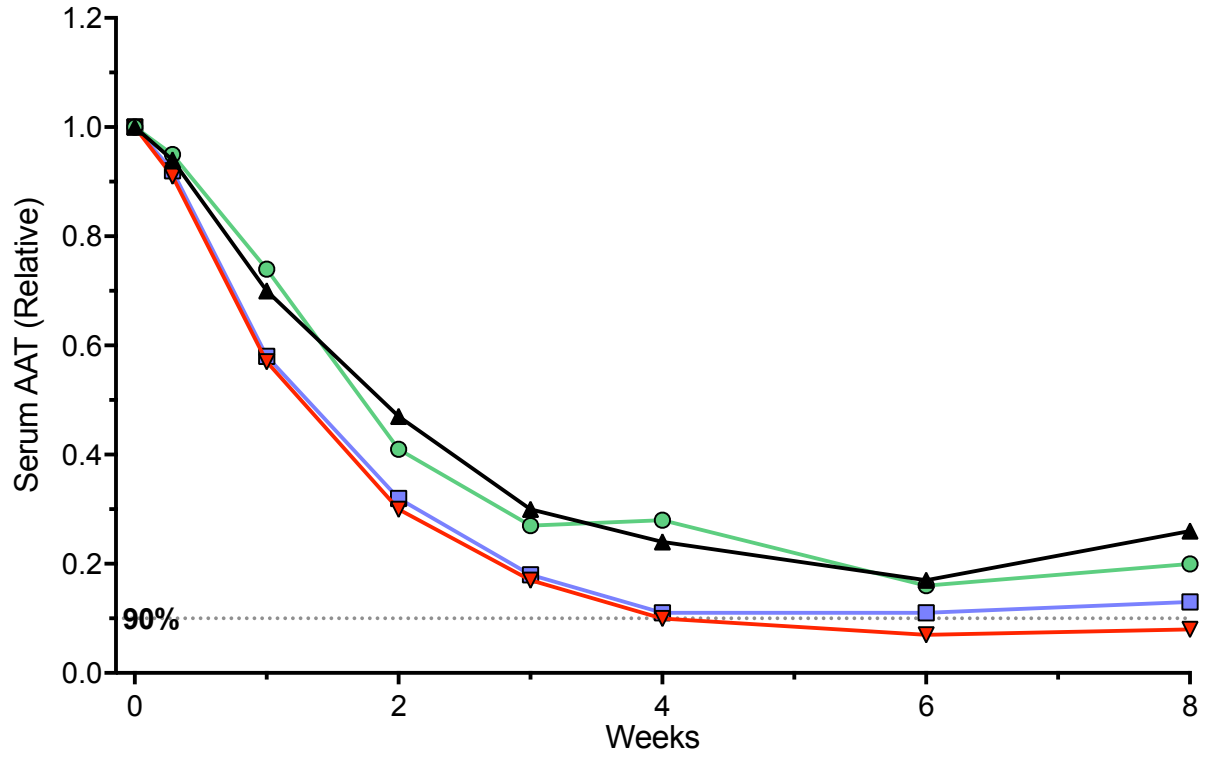
UNBLINDED PART

- No placebo
- 3 groups
  - ***Single doses*** of 100, 200 and 300 mg of ARO-AAT
  - 4 per cohort
- Assessments of safety, tolerability, depth and duration of AAT reductions after a single dose

AROAAT1001 - Results to Date

- Enrollment complete
- 44 total subjects enrolled (28 active, 16 placebo) and have received at least one dose
- Multi-dose cohorts – dosing ongoing and still blinded
- Single-dose cohorts to be followed until plasma AAT normal or within 20% of baseline

Open Label AAT Plasma Data at 100 mg:
Single Dose, Healthy Volunteers



93%: Maximum Serum AAT Reduction achieved 6-weeks following a single dose
87%: Mean maximum serum AAT reduction achieved 6-weeks following a single dose

AROAAT1001 Safety Summary

- Safety data cutoff as of 6/11/18
- No SAEs, No Severe AEs
- Most AEs reported as mild (one moderate gastroenteritis)
- 2 cases of mild injection site erythema at 100 mg after 1st dose.
  - Both mild, both resolved within 48 hours
- No clinically meaningful adverse changes in BUN, creatinine, ALT, AST or total bilirubin
  - No pattern of adverse laboratory changes seen

AEs Reported in More Than One Subject

AROAAT1001 AE Reported Terms (> 1 occurrence)	35 mg Blinded n = 8	100 mg Blinded n = 8	100 mg Open Label n = 4	200 mg Blinded n = 8	200 mg Open Label n = 4	Total AEs
Headache	4	1		2	1	8
Sore throat, Throat irritation	2		1			3
Rhinorrhoea, Runny nose	1	1	1			3
Sinus congestion, Nasal congestion		1		1		2
Upper Respiratory Tract Infection, Viral Upper Respiratory Infection		1			2	3
Nausea	2			2		4
Emesis, Vomiting			1	1		2
Lightheadedness, Dizziness	1	1		1		3
Back pain, Lower back pain		2				2
Venipuncture bruise, hematoma antecubital fossa		2			1	3
Pain at cannulation site, Tenderness antecubital fossa	2		1		1	4
Injection site erythema			2			2

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Conclusions

- AATD - related liver disease is not well recognized
- As smoking declines and pulmonary disease is better treated, AATD – related liver disease is set to gain in importance
- RNA inhibition is well suited for treating the liver disease at its source – mutant protein production
- ARO-AAT is a RNAi drug designed to halt liver production of AAT with infrequent, subcutaneous injection
- Early clinical data indicates that ARO-AAT may prove to be well tolerated and should only require injection monthly or less frequently
- We hope to initiate longer term studies in AATD patients in US and EU next