Arrowhead Research

CORPORATION

Targeting Innovation

Barclays Healthcare Conference

March 17, 2016

Safe Harbor Statement

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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.

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Comprehensive RNAi Platform Built Around Delivery

RNAi Chemistry

- Broad FTO for Canonical siRNA
- Broad FTO for Dicer siRNA
- Broad FTO for Meroduplex siRNA
- Broad FTO for UNAs
- Novel proprietary RNAi triggers
- Intracellular targeting ligands
  - Activity booster
- ALNY IP license for 30 targets

RNAi Delivery

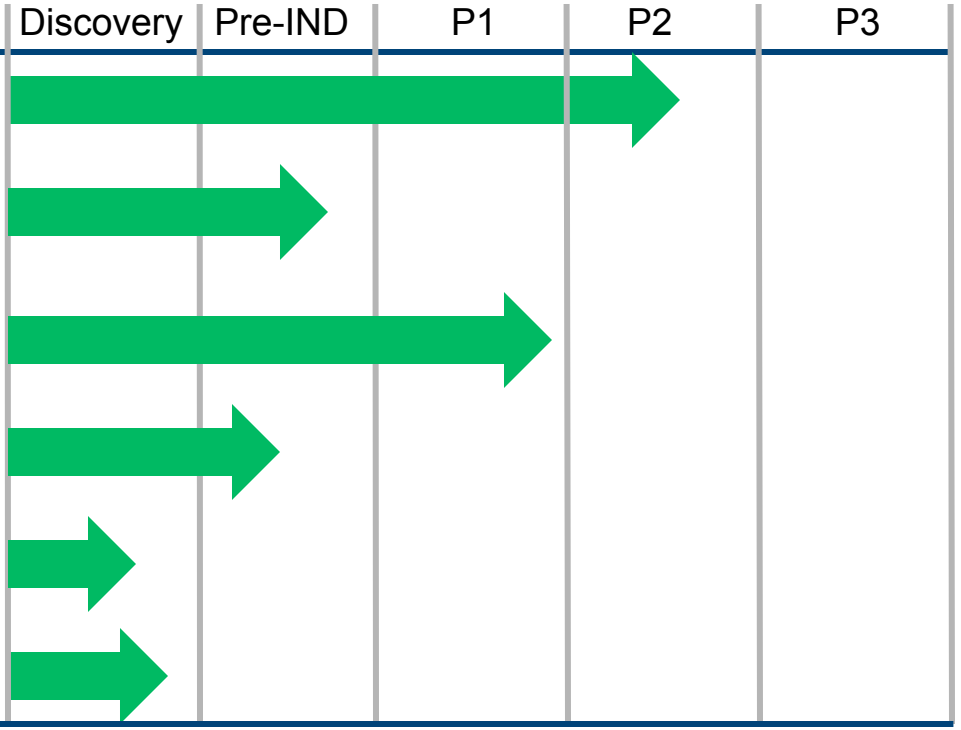
- Highly Efficient / Potent
- Targetable
- Well tolerated

Technology from:
Roche, Novartis, Alnylam, Mirus Bio, City of Hope Cancer Center, Marina

Clinical PoC with HBV and AAT Programs

Pipeline

Program	Indication
ARC-520	Chronic Hepatitis B
ARC-521	Chronic Hepatitis B
ARC-AAT	AATD Liver Disease
ARC-F12	HAE and Thrombosis
ARC-Hif2	ccRCC
ARC-LPa	Cardiovascular Disease



1. RNAi Platform play with attractive clinical candidates
2. Large HBV opportunity with novel first-to-the-clinic approach
   - Clinical data has de-risked ARC-520 ***and*** platform
3. ARC-AAT: dosing P1 in Australia and Europe
4. Deep pipeline

Delivery: Dynamic PolyConjugate (DPCs)

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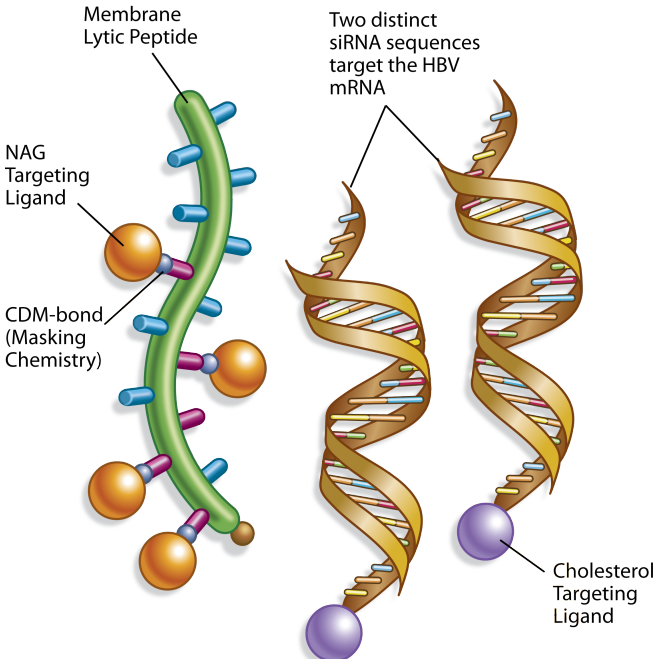
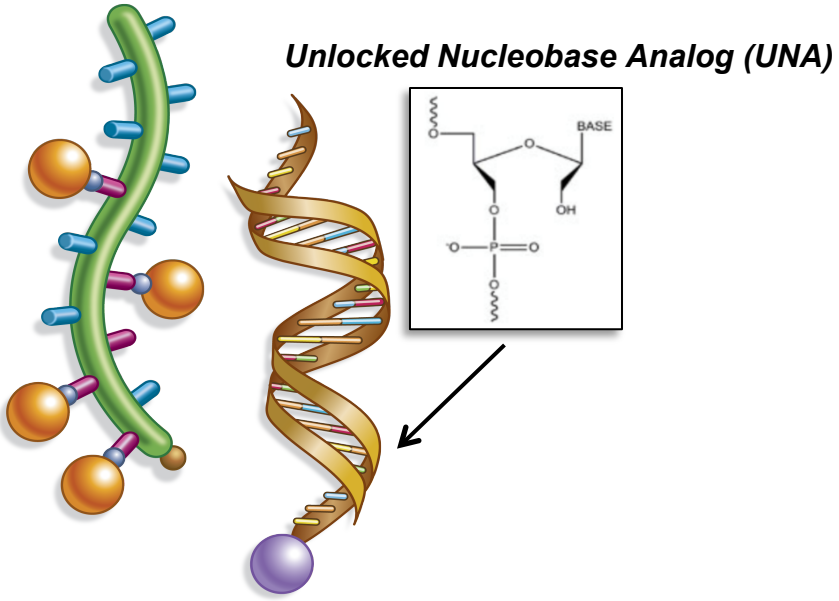
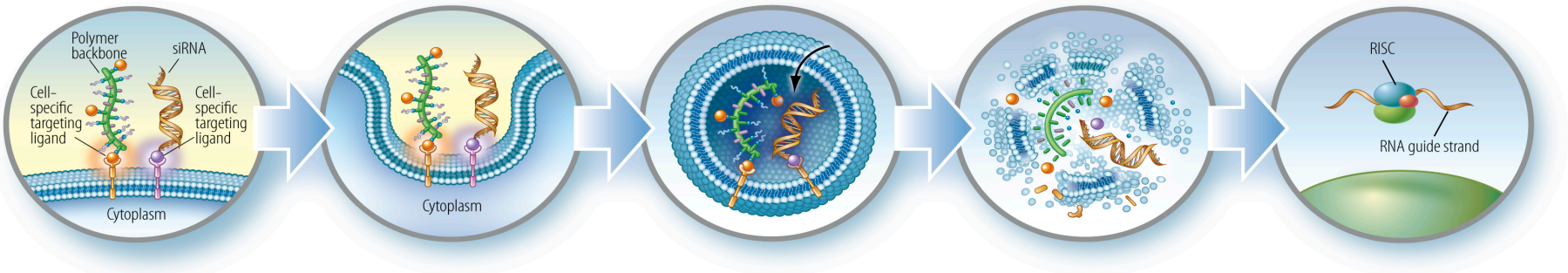
ARC-520 for chronic HBV infection



ARC-AAT for AATD associated liver disease





DPC polymer and siRNA attach to their respective targets on the cell surface.

DPC polymer and siRNA are taken up.

DPC polymer and siRNA are enclosed in an endosome. Low pH results in polymer unmasking.

Polymer induces endosomolysis and release of siRNA payload into the cell cytoplasm.

siRNA engages the cell's interference machinery, resulting in knockdown of target gene expression.

HBV Biology and Current Standards

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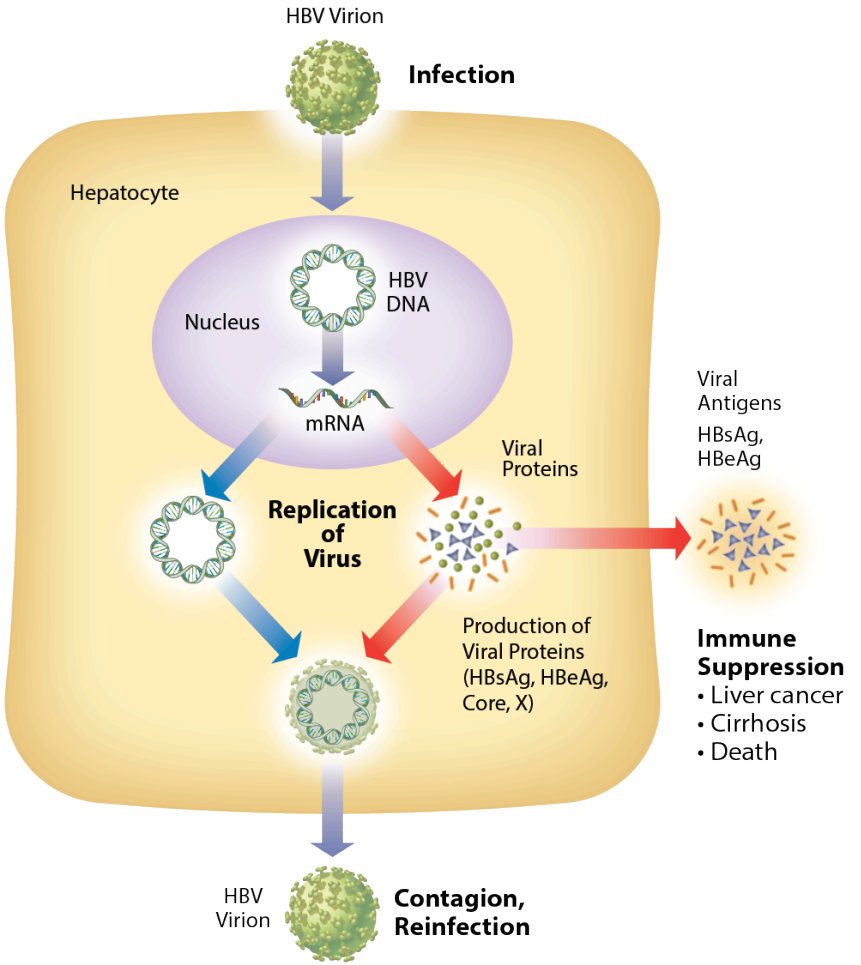
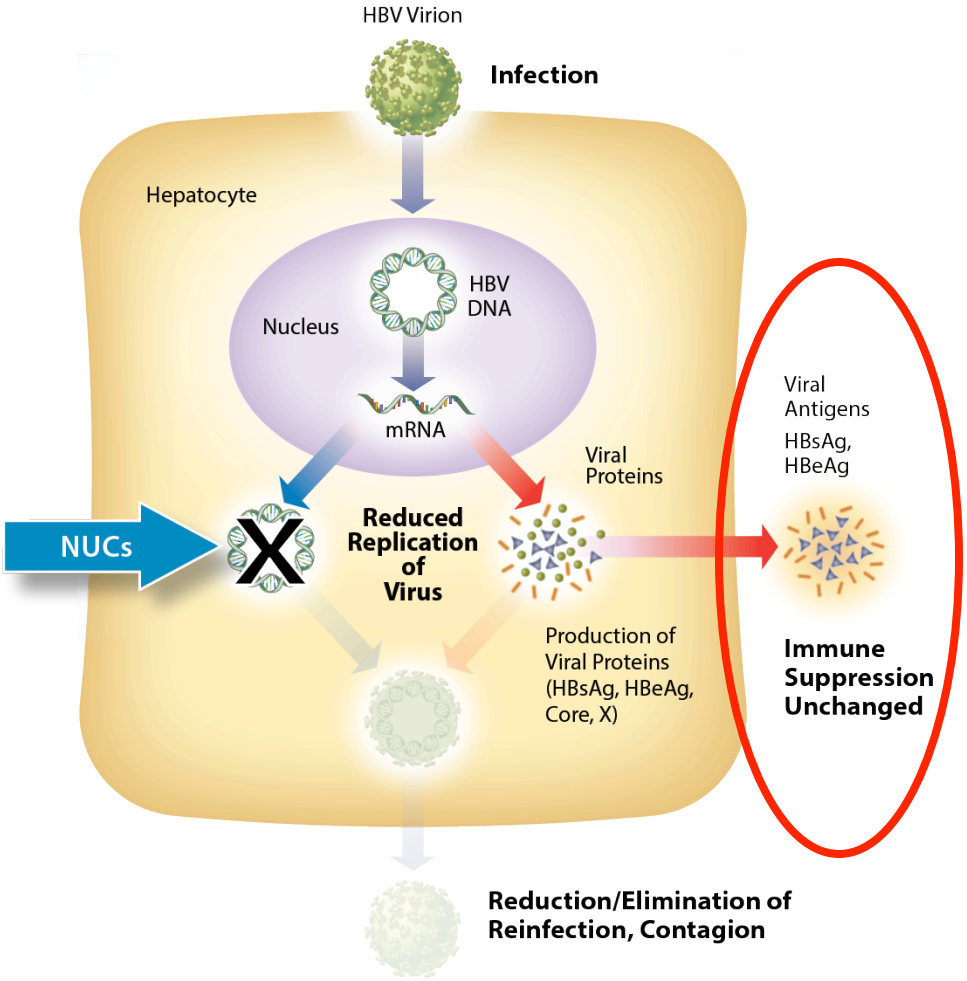
Untreated

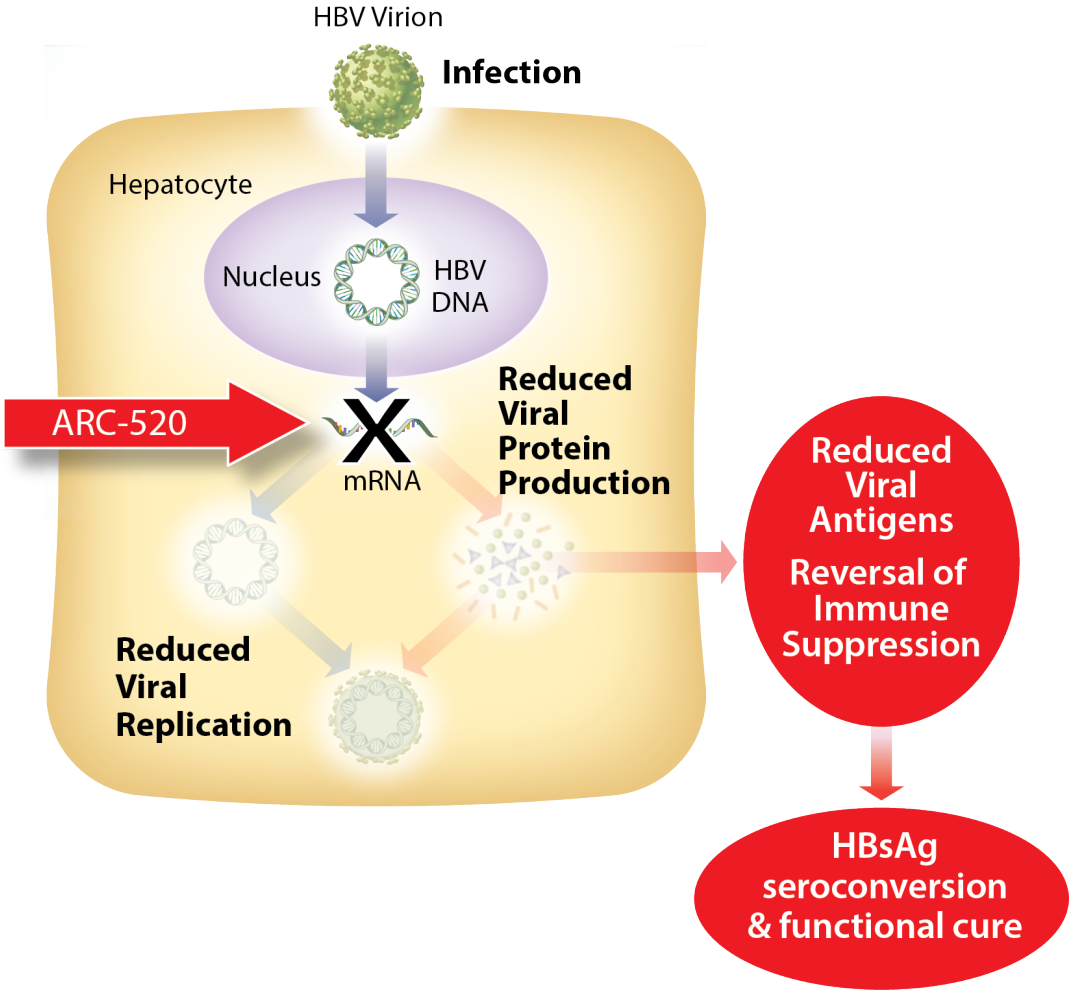


Nucleoside/tide Analogs



NUCs require life-long therapy: not curative

Theory of HBV RNAi Therapeutic



Silence Entire HBV Genome

1. **"HBsAg Theory"**
   - Reducing HBsAg enables host immune system de-repression and long term control of virus
2. **Destabilizing Viral Function**
   - Silencing all antigens could destabilize normal viral function and enable host immune system de-repression and long term control of virus

Enable a Functional Cure

2015: Data-Rich Year for HBV Program

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Long term study in CHB chimps started to read out

Single dose ARC-520 studies in patients read out

Analyst Day: Sept '15
AASLD: Nov '15
HepDart: Dec '15

ARC-520 de-risked
Platform de-risked
Changed the HBV textbooks
Expanded program: additional candidate

Long-term Chimp Study

- ARC-520 leads to deep HBsAg reduction

HBeAg status	HBsAg mean peak KD
HBeAg(+): 4 chimps	99% (2 log)
HBeAg(-): 4 chimps	81% (0.7 log)
HBeAg transitional: 1 chimp	87.4% (0.9 log)

- Well tolerated
  - 6 - 11 monthly doses ARC-520: no signs of any toxicity

- **Evidence of immune reactivation in 7 of the 9 chimps**

Deep KD with ARC-520 and new paradigm for lifecycle of virus

Basis of Difference in HBsAg Responses

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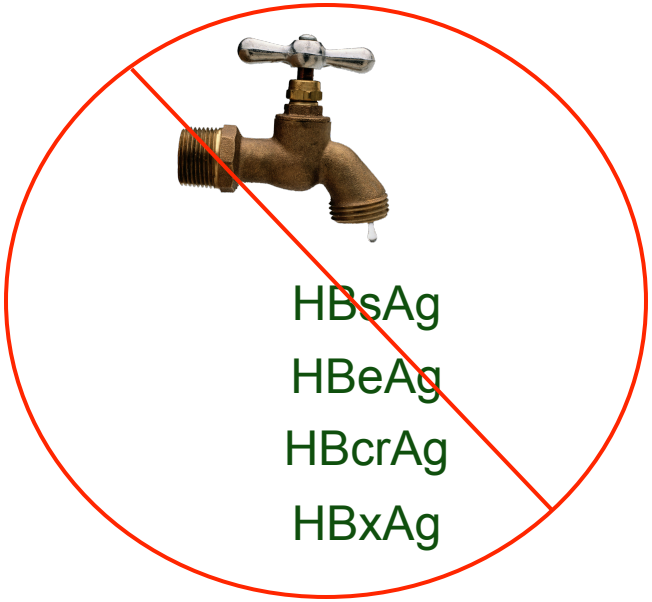
Two Sources of Gene Expression

HBV DNA integrated into host DNA

HBsAg

HBV cccDNA



ARC-520 Silences cccDNA expression;
cccDNA decreases with transition from HBeAg+ to HBeAg-

ARC-520 Safety Profile

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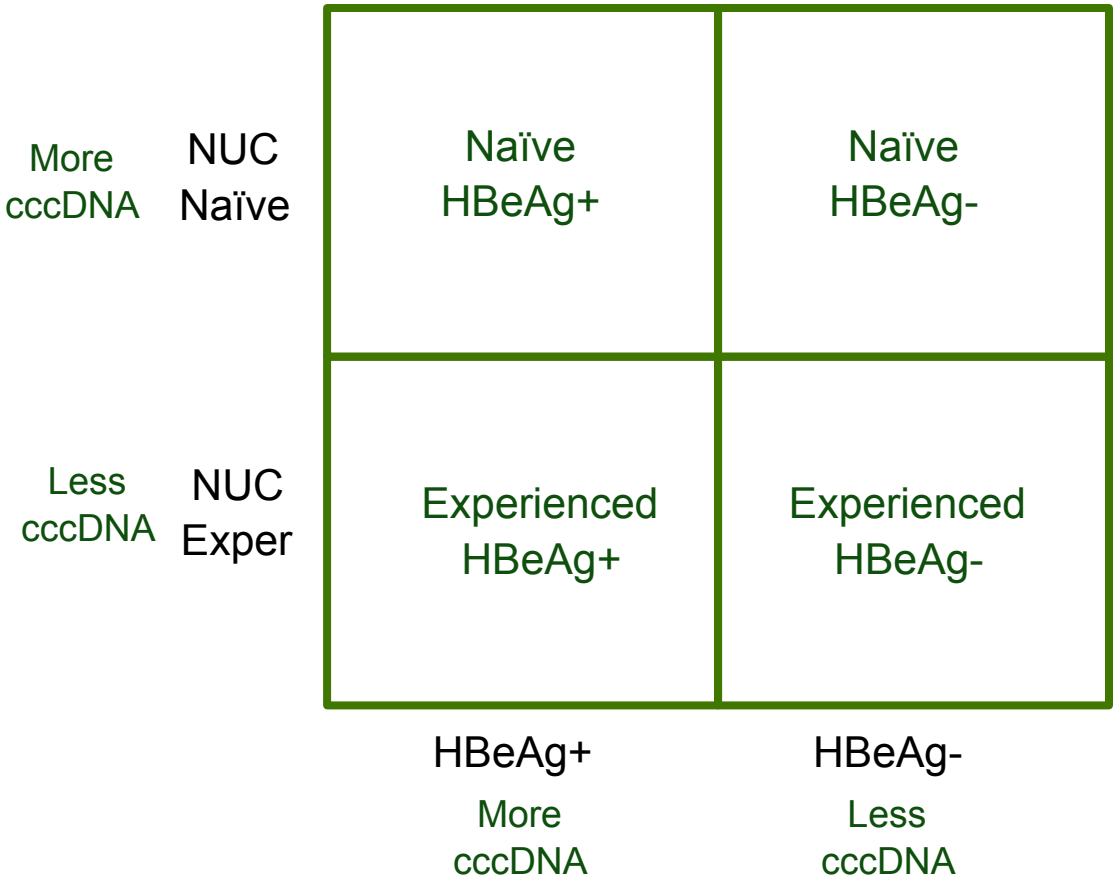
102 humans received ARC-520 between Phase 1 and 2a

- No AEs rated as serious or severe
- No signs of end organ toxicity
- No discontinuations due to AEs

ARC-520 has been very well tolerated

ARC-520 Phase2a explored 4 HBV groups

Think of the groups as quadrants
Defined by HBeAg status and NUC experience



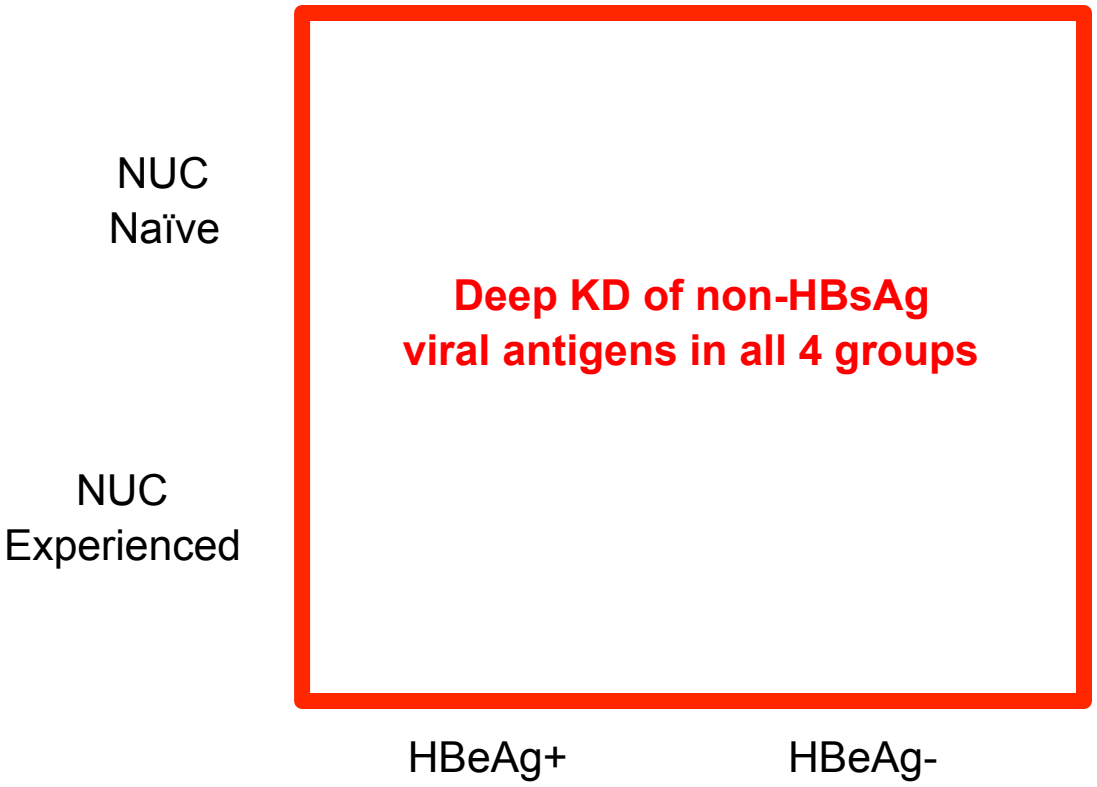
ARC-520 P2a

Cohort	Prior ETV	Pat Type	ARC-520 dose	Active / Placebo	Status
1	Yes	HBeAg neg	1.0 mg/kg	6/2	Complete
2	Yes	HBeAg neg	2.0 mg/kg	6/2	Complete
3	Yes	HBeAg neg	3.0 mg/kg	6/2	Complete
4	Yes	HBeAg neg	4.0 mg/kg	6/2	Complete
5	Yes	HBeAg pos	4.0 mg/kg	6/2	Complete
6	Yes	HBeAg pos	2 x 2.0 mg/kg	6/0	Complete
7	No	HBeAg pos HBeAg neg	4.0 mg/kg	6/0 6/0	Ongoing

Groups distinguished by lifecycle of the virus: cccDNA vs viral DNA integrated into host genome

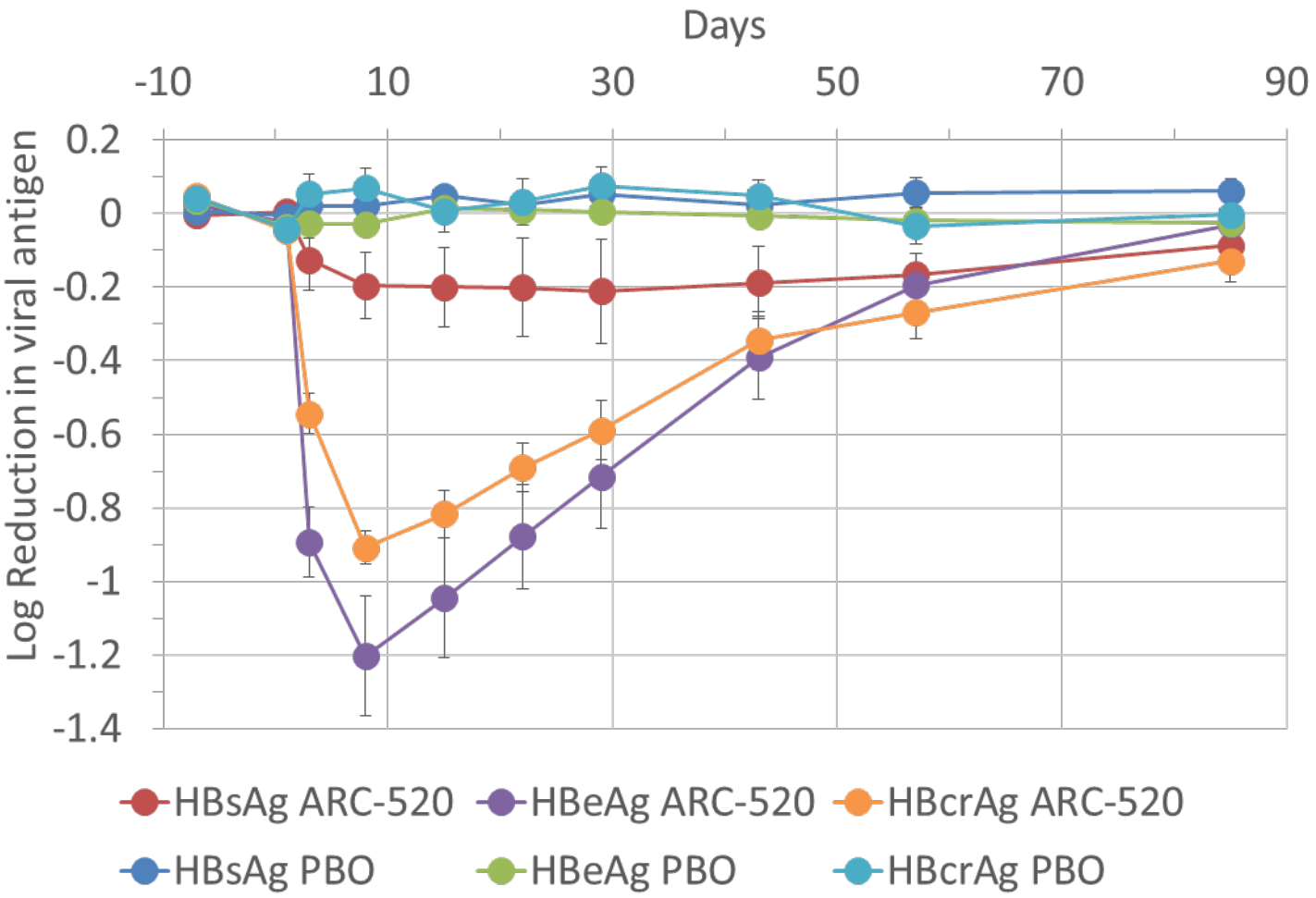
- Long-term NUC therapy decreases amount of viral cccDNA
- cccDNA decreases with transition from HBeAg+ to HBeAg-

KD profiles in the 4 HBV groups



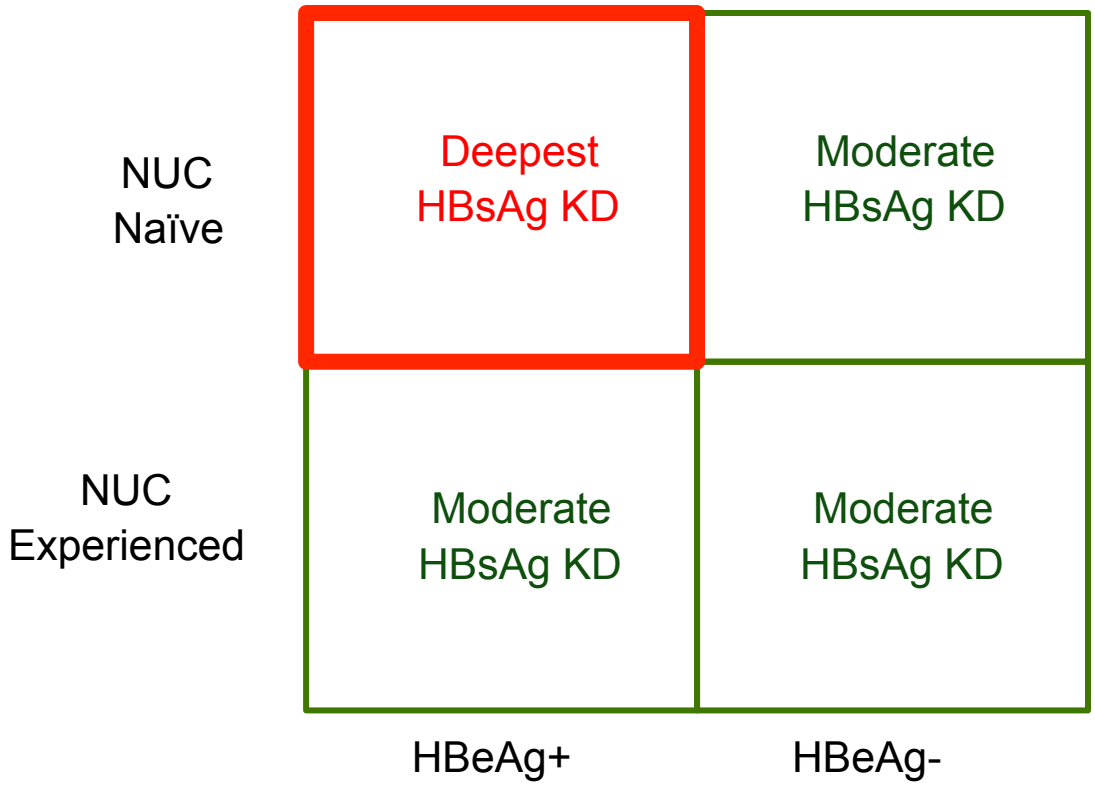
ARC-520 targets cccDNA; all non-HBsAg antigens are ***only*** expressed by cccDNA

Deep HBeAg and HBcrAg KD: Cohort 5



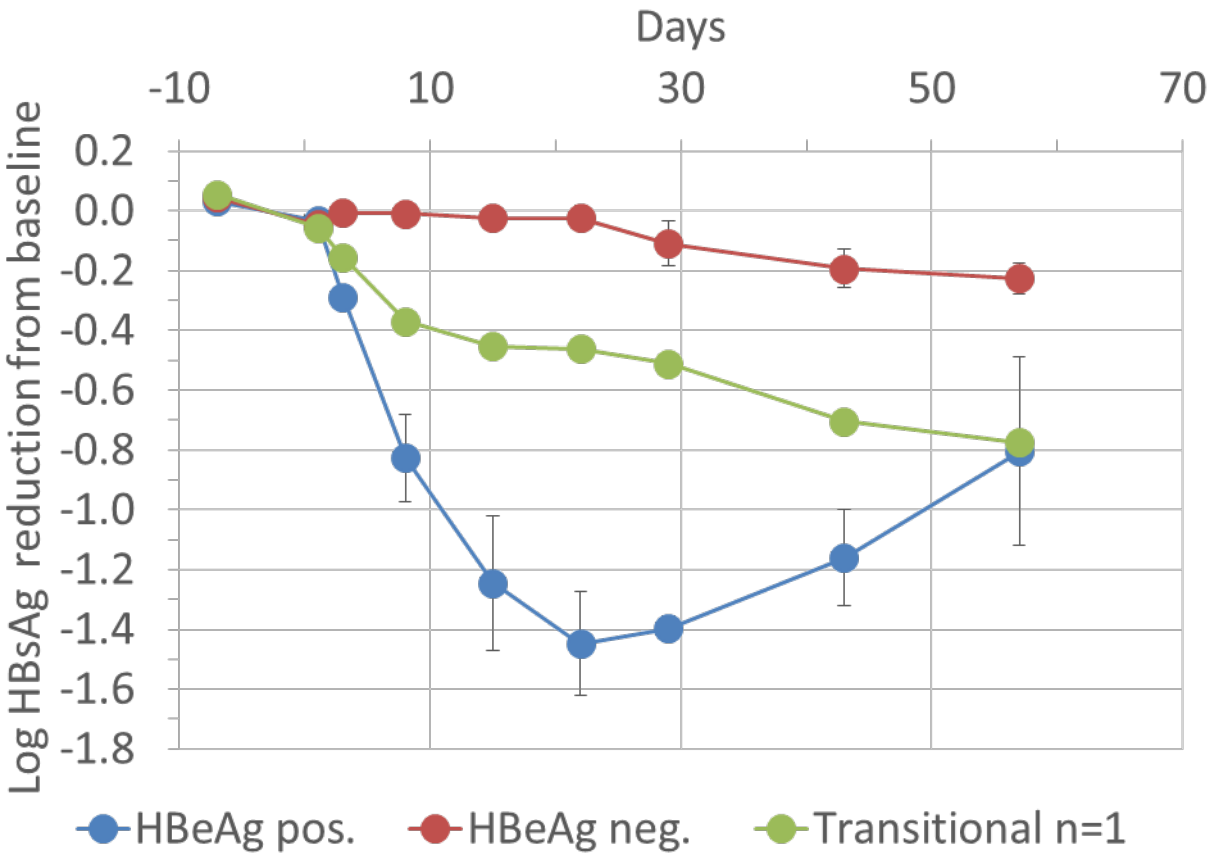
Platform and drug validation

KD profiles in the 4 HBV groups



HBsAg is expressed by ***both*** cccDNA ***and*** integrated DNA: NUC-naïve HBeAg+ patients are richest in cccDNA so demonstrate deepest HBsAg KD

Deep and Durable HBsAg KD: Naïve patients



Transitional patient was HBeAg-pos. at baseline and HBeAg negative at days 3 to 43

More validation: deepest single dose KD ever demonstrated in humans with RNAi

ARC-520 Key Points

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- Well tolerated
- Deep HBsAg KD in treatment-naïve HBeAg+ patients
  - Max 99% HBsAg KD (1.9 log); mean nadir 97% (1.5 logs)
  - Speaks to “HBsAg theory” of achieving functional cure
- Clearly disrupts virus in NUC-experienced and HBeAg- patients
  - >1 log KD of HBeAg, HBcrAg, and presumably others
  - ARC-520 intended for multi-dose therapy: sustained measurable HBsAg KD and very deep KD of **all** other antigens could be important to reaching functional cure
  - Could be important beyond “HBsAg theory”

ARC-520 is very potent at silencing cccDNA: could be key component in achieving functional cure

What if the "HBsAg Theory" is Dominant?

NUC-naïve HBeAg(+) patients
will experience greatest HBsAg KD:

Large segment of the chronic HBV population

In U.S.
95% of estimated CHB are naïve

~50% estimated to be HBeAg(+)

In W. Europe
90% of estimated CHB are naïve

~33% estimated to be HBeAg(+)

Proprietary data from Clarion Healthcare, LLC

What about the rest of the market?

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We have developed an additional candidate to:

(1) Ensure broader coverage of entire market;
(2) Provide 2 shots on goal

ARC-520

- Optimized for cccDNA KD
  - Clarity on KD and safety
- >1log KD in all antigens studied
- Began multi-dose studies
- Combo studies ongoing

ARC-521

- Safety expected = ARC-520
- Optimized to include integrant KD
- Validated in chimps
  - Multi-log KD
- Complement to ARC-520
- IND or equivalent by June 2016

De-risked program with safety/activity of ARC-520, increased exposure to additional patient populations

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HBV Program Next Steps

- **ARC-520 multiple dose P2b studies underway**
  - 2002: ARC-520 + NUCS in e- NUC-experienced patients (Europe/Asia)
    - Expected enrollment completion: 2016
  - 2003: ARC-520 + NUCS in e+ NUC-experienced patients (Europe/Asia)
    - Expected enrollment completion: 2016
  - 2004: ARC-520 + NUCS in e+ NUC-experienced patients (US only)
    - Expected completion: 2016
  - 2001 extension: ARC-520 + NUCS in e-/e+ NUC-experienced/naïve patients (open label)
    - Expected enrollment completion: 2016
  - Monarch combination studies: ARC-520 alone; ARC-520 + NUCS + other agents in NUC-naïve patients (open label)
    - Monotherapy and with interferon actively enrolling now
    - Expect additional arms with new combinations this year and beyond
- **ARC-521 in clinic in mid-2016**
  - Expect IND or equivalent by June 2016

Alpha-1 antitrypsin deficiency

- AATD is a large scale orphan disease
  - Alpha-1 foundation estimates 100,000 in the US
- Mutation in AAT gene 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

↓

Controlled with enzyme replacement therapy

Liver

Accumulation of mutant Z protein causes clinical liver disease

↓

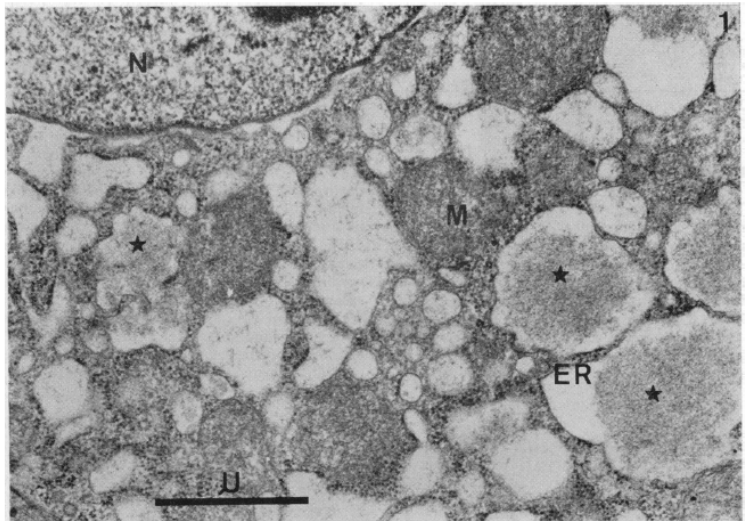
No current treatment

ARC-AAT MOA

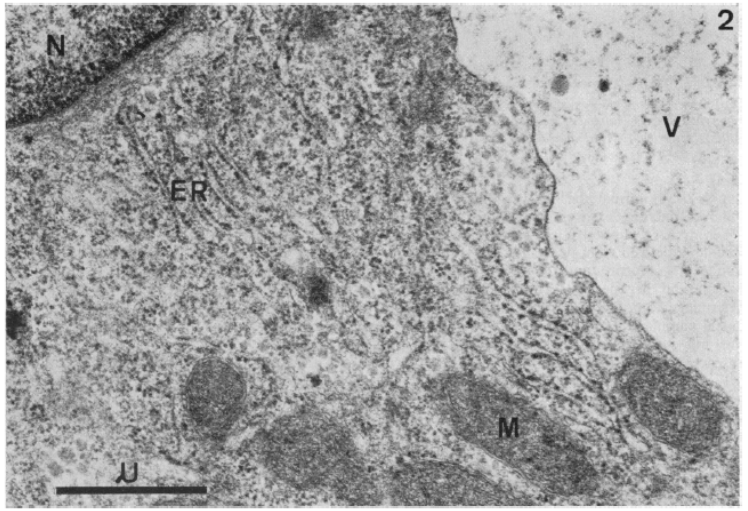
ARC-AAT designed to stop Z-AAT production by silencing AAT gene to:

- Prevent accumulation of disease causing protein
- ***Allow*** clearance of accumulated protein
- ***Prevent*** repeated cycles of cellular damage and tissue repair.
- ***Reverse*** fibrosis associated with prior damage by allowing repair

PiZZ phenotype (diseased)



Pi null phenotype (normal)

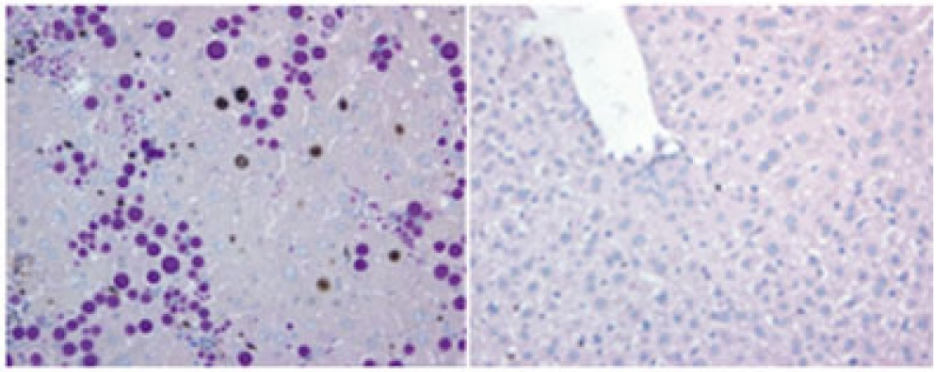


Feldmann G etal., *Gut 1975*

PiZ Model Mirrors Human Adult Disease

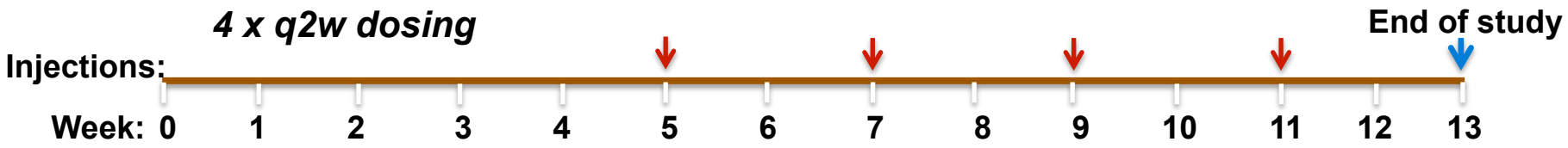
The transgenic PiZ mouse model expresses the human Z-mutant AAT gene (Z-AAT) and recapitulates the human AATD-associated liver phenotype:

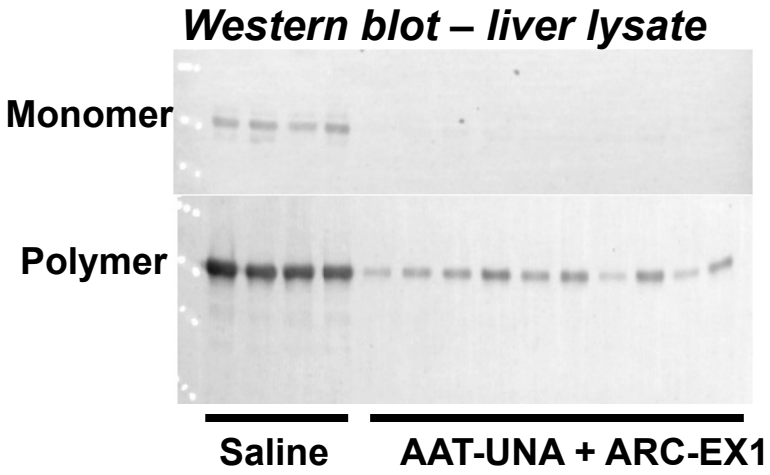
- Hepatocytes produce high levels of human Z-AAT
- Hepatocytes are unable to efficiently process and secrete the Z-AAT
- Z-AAT forms polymers that accumulate in large “globules” within the hepatocytes.
- These globules stress the hepatocytes, eventually leading to fibrosis and hepato-cellular carcinoma.

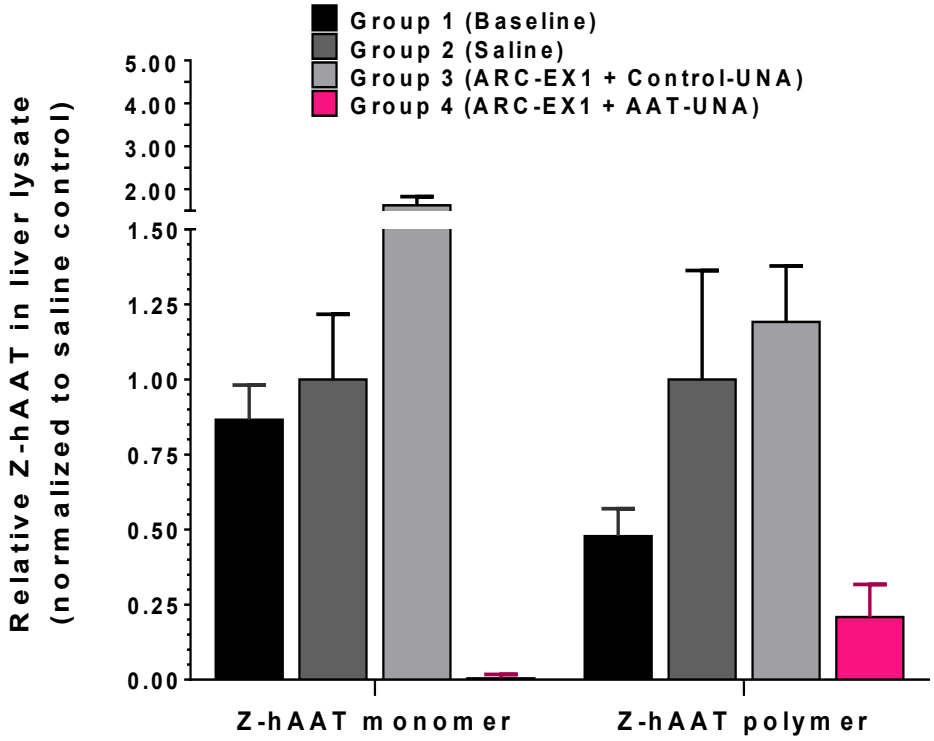


Rudnick DA et al., *Hepatology. 2004*

Reduction of Z-hAAT aggregates







99% less soluble (monomer) Z-hAAT
79% less insoluble (polymer) Z-hAAT

Male and female PiZ mice

Reduction in Z-AAT Liver Globules

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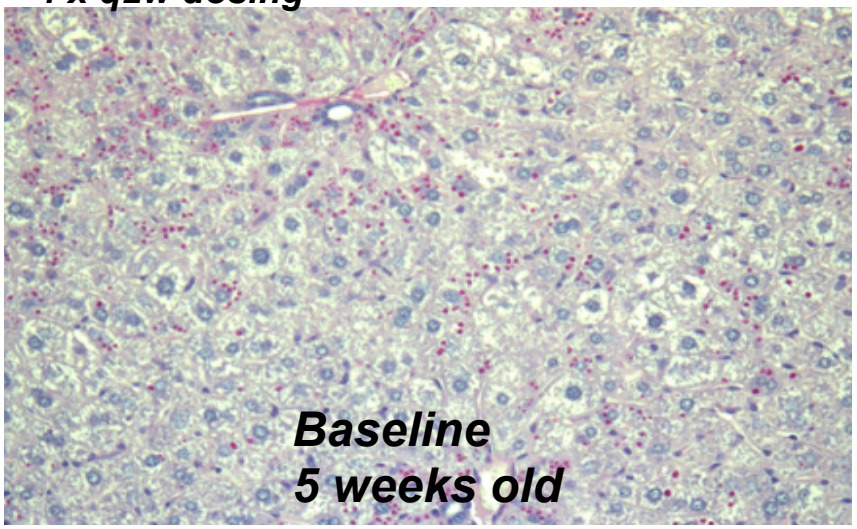
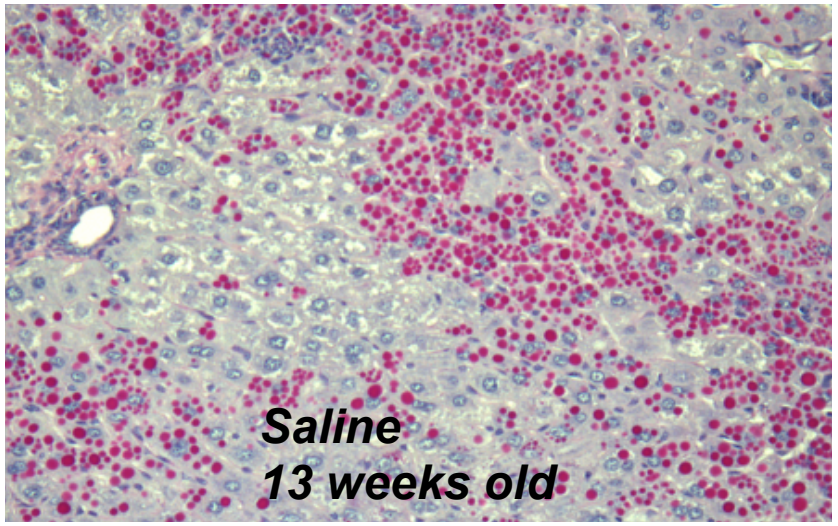
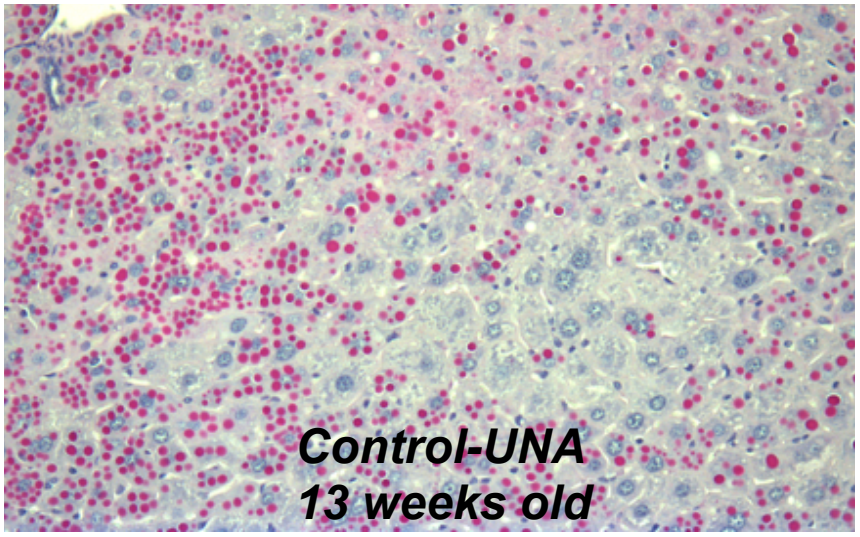
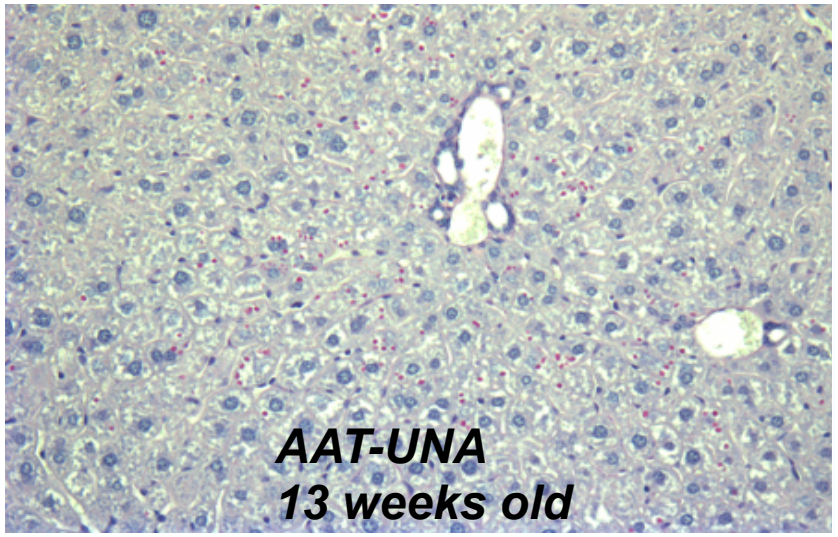
4 x q2w dosing



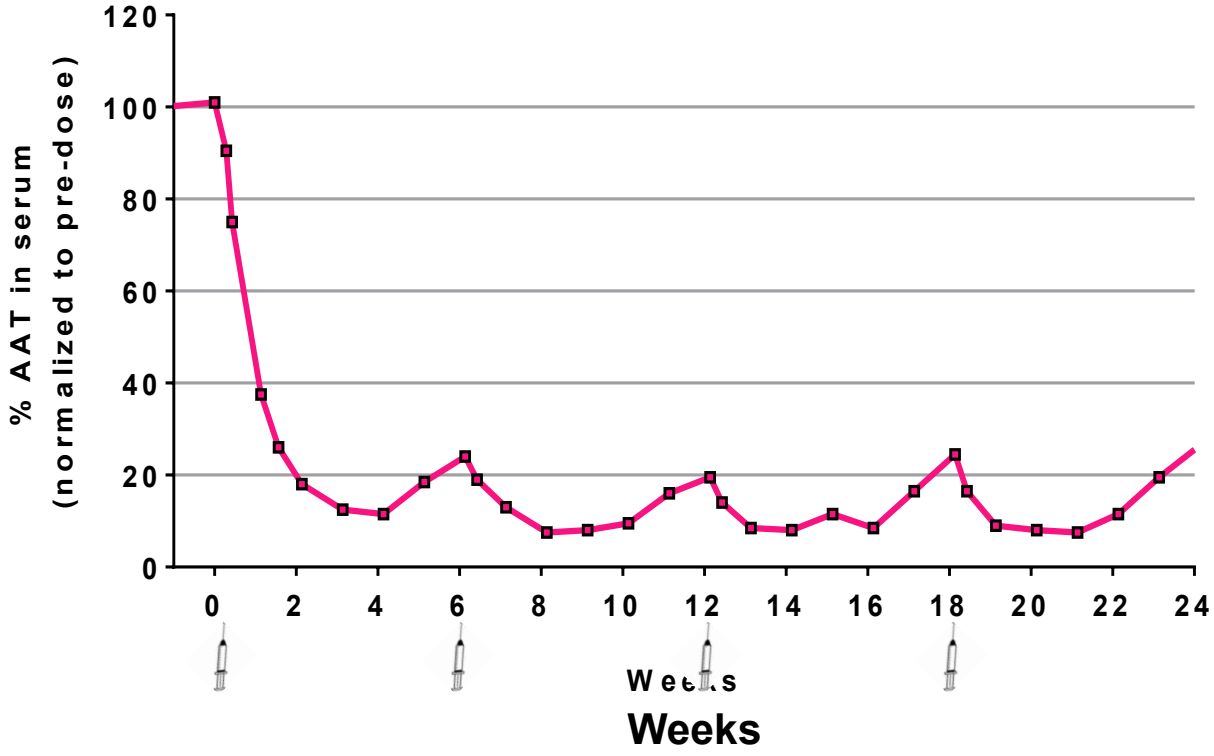






Liver globule burden is reduced after just two months of ARC-AAT treatment

Repeat dosing in NHPs



6 mg/kg AAT-UNA
3 mg/kg ARC-EX1
N=2

~90% reduction of serum AAT after first injection of ARC-AAT
Long duration of effect: ~80% reduction at 6 weeks
Sustained reduction of AAT with q6w dosing
Safety: no changes in clinical chemistry (ALT, AST, BUN, Creatinine)

ARC-AAT: Phase I clinical plan

- Single ascending dose P1 study ongoing in Australia and Europe
- Healthy volunteers and AATD patients
- **Primary Objectives:**
  - Determine the safety and tolerability of escalating doses of ARC-AAT
  - Evaluate the pharmacokinetics of different doses
- **Secondary Objectives:**
  - Evaluate the depth and duration of decline in serum total alpha-1 antitrypsin levels
  - Time for serum alpha-1 antitrypsin levels to return to baseline

- **Milestone-rich 2016**
  - P2b ARC-520 studies
    - Complete enrolling 2002
    - Complete enrolling 2003
    - Complete enrolling 2004
    - Complete enrolling 2001 extension (open label, so reporting flexibility)
    - Complete enrolling initial MONARCH cohorts (open label, so reporting flexibility)
  - Complete ARC-AAT P1 in healthy volunteers and patients
  - Launch ARC-AAT P2 studies
  - ARC-521 IND or equivalent
- **Pipeline**
  - ARC-F12 in the clinic in 2017
  - ARC-LPa in the clinic in 2017
  - ARC-Hif2 in the clinic in 2017
  - Additional candidates coming

Financial and Market Data

NASDAQ: ARWR	
Recent price (March 16, 2016)	$4.21
Shares outstanding (including preferred as converted)	62m
Market cap	$ 261m
Cash (12/31/15)	$77m