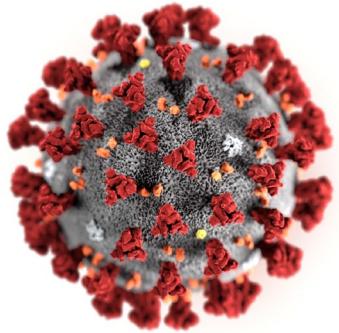
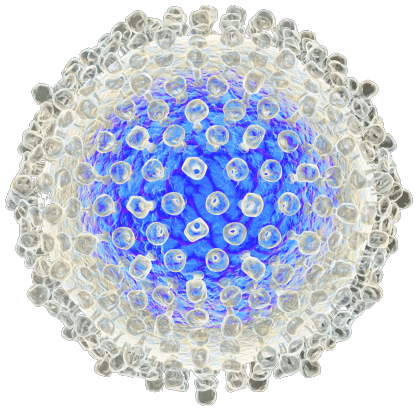
ALIGOS
THERAPEUTICS





Lawrence M. Blatt, Ph.D.
CEO & Co-Founder

Corporate Presentation

June 2021

Disclosures

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This presentation concerns drug candidates, some of which are undergoing nonclinical studies and others of which are under clinical investigation, and all of which have not yet been approved for marketing by the U.S. Food and Drug Administration. These drug candidates are currently limited by federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

Aligos Therapeutics Highlights

OUR MISSION

Develop novel therapeutics to address unmet medical needs in viral and liver diseases

OUR PLATFORM

Oligonucleotides

Small molecules

Leverage complementary modalities to broaden the range of therapeutic targets we can address

OUR STRATEGY

Develop pharmacologically optimized drug candidates against clinically validated targets

Pursue combination regimens designed to achieve improved treatment outcomes

OUR TEAM

Decades of drug discovery and development experience

Proven track record of success in the areas of viral infections and liver diseases

OUR GOAL

Become a world leader in antiviral therapies for CHB and create targeted therapeutics for NASH

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Our Platforms, Capabilities and Collaborations

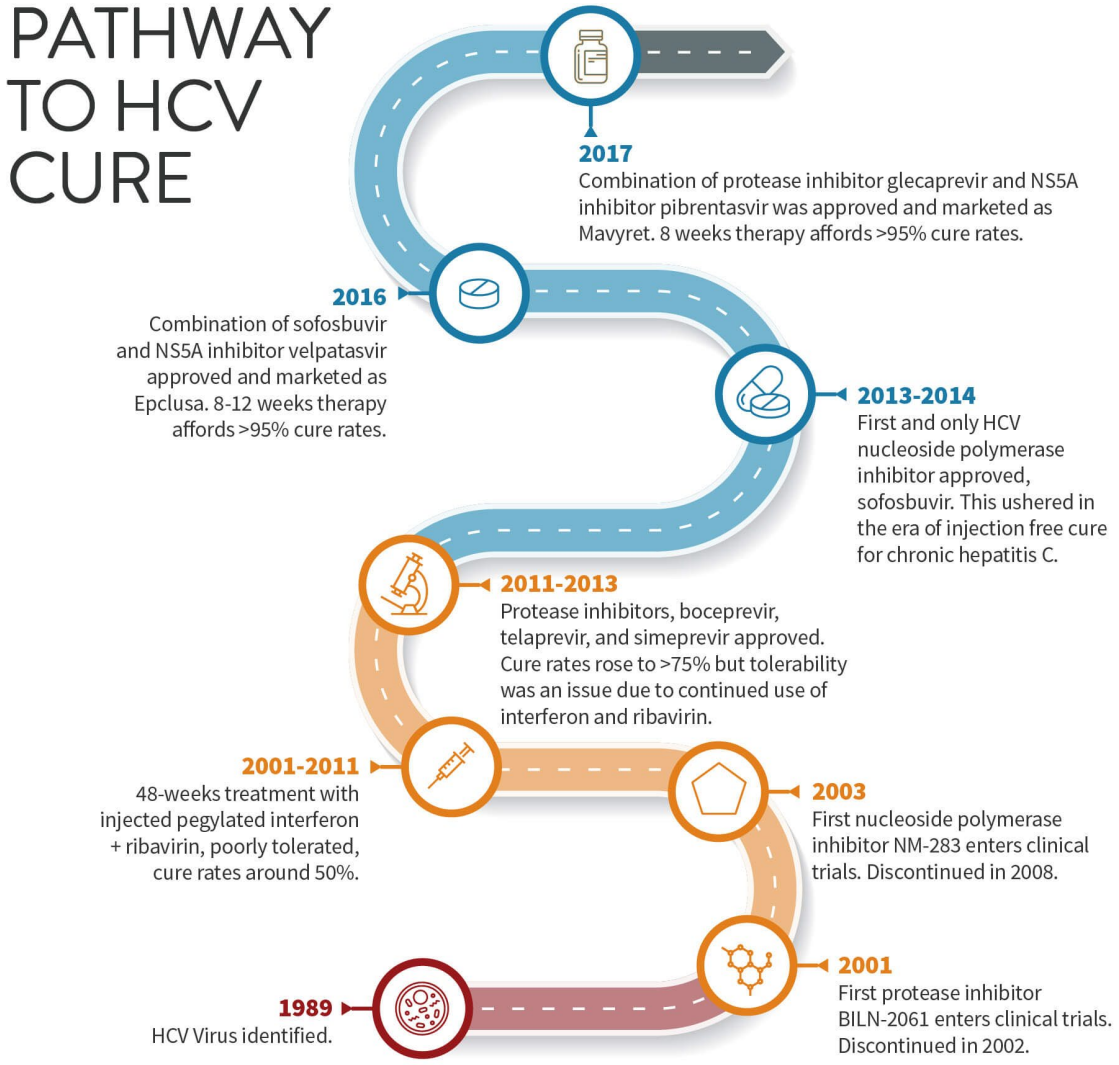
- Oligonucleotide Modalities
- Small Molecule Chemistry
- Intellectual Property
- Chemistry, Manufacturing and Controls
- Biological Sciences
- Translational Safety Sciences
- Clinical Sciences and Operations

- Emory University
  CAM IP & Collaboration
- Luxna Biotech
  3rd Generation XNA Nucleotides
- AM Chemicals
  Proprietary GalNAc
- Merck (MSD) NASH
  Collaboration
- Rega / CD3
  Collaboration COVID Protease
- Agency for Innovation and Entrepreneurship (VLAIO)

Enabling efficient drug discovery in pursuit of optimized combination regimens

A Lesson from Chronic Hepatitis C
From First Movers to Best-in-Class Regimens

- Efficacy → Safety → Convenience
- First in class entrants
  - Demonstrated mechanistic proof of principal
  - Several did not gain approval due to poor pharmacology
- Late entrants with improved pharmacology attained significant market share
- Aligos is pursuing potentially best in class molecules for CHB where clinical validation has been demonstrated



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Our Pipeline

Candidate	Indication	MOA	Discovery	Nonclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
ALG-010133	CHB	STOPS						Initial Phase 1 Data
ALG-000184	CHB	CAM						Initial Phase 1 Data
ALG-020572	CHB	ASO						Phase 1 Start in 2H 2021
ALG-125755	CHB	siRNA						Phase 1 Start in 1H 2022
ALG-055009	NASH	THR-β Agonist						Phase 1 Start in 2H 2021
Discovery	Coronavirus	Multiple						—
Discovery	Liver Diseases	Multiple						—
Discovery	NASH	Undisclosed		MERCK				—

LEGEND Oligonucleotides Small Molecules Multiple Modalities

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ASO = antisense oligonucleotide; CAM = capsid assembly modulator; CHB = Chronic Hepatitis B; MOA = Mechanism of Action; NASH = nonalcoholic steatohepatitis; siRNA = small interfering ribonucleic acid (RNA); STOPS = S-antigen Transport-inhibiting Oligonucleotide Polymers; THR-β = thyroid hormone receptor beta.

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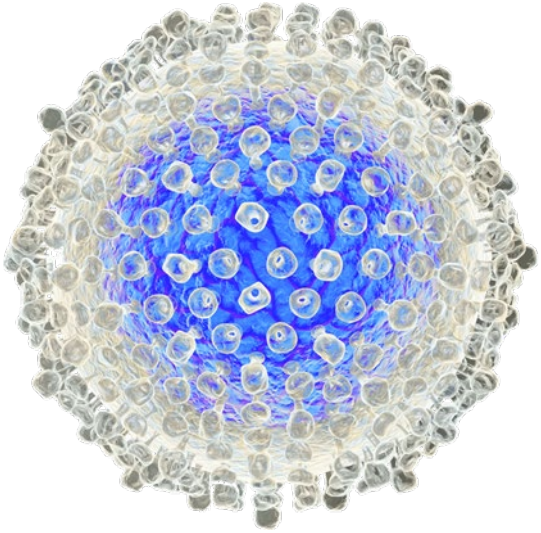
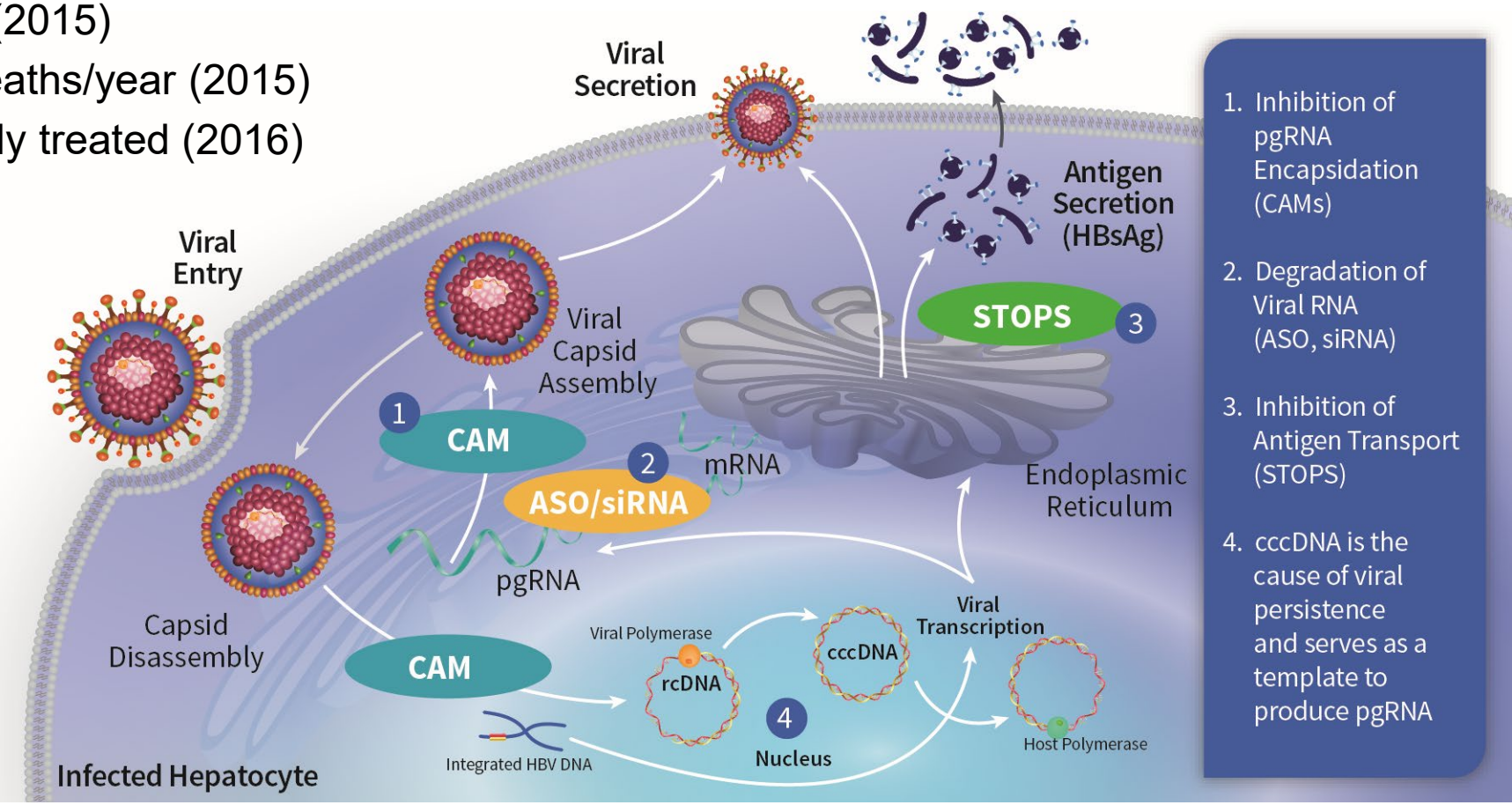
Chronic Hepatitis B



CHB Epidemiology & Our Portfolio

- CHB Epidemiology* - Most common chronic viral infection in world
  - >290 million carriers worldwide (2020)
  - ~8 million in US, EU, Japan (2015)
  - Responsible for ~900,000 deaths/year (2015)
  - Only ~2% of patients currently treated (2016)

- Our Portfolio
  - Potentially best-in-class drug candidates against validated targets with potential for high functional cure rates
    - › CAM
    - › Oligonucleotides
      - STOPS™
      - ASO
      - siRNA

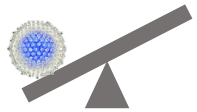


*Hepatitis B Foundation, World Health Organization Global Hepatitis 2017 Report Hepatitis B fact sheet, WHO (2017).

Chronic Hepatitis B and Functional Cure

Outcome Determined by Balance Between Virus and Host Immune Response

Chronic Hepatitis B



Robust Viral Replication
(High HBV DNA & RNA Levels)

+

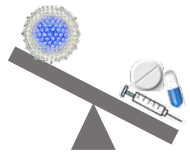
Suppression of HBV-specific immune response
(high HBsAg levels)

Therapeutics Tip the Balance

Direct Acting Antivirals
e.g., NA, CAM

Oligonucleotides
e.g., STOPs, ASO, siRNA

Functional Cure



No viral replication
(undetectable HBV DNA & RNA)

+

Restore HBV-specific immune response
(undetectable HBsAg levels)

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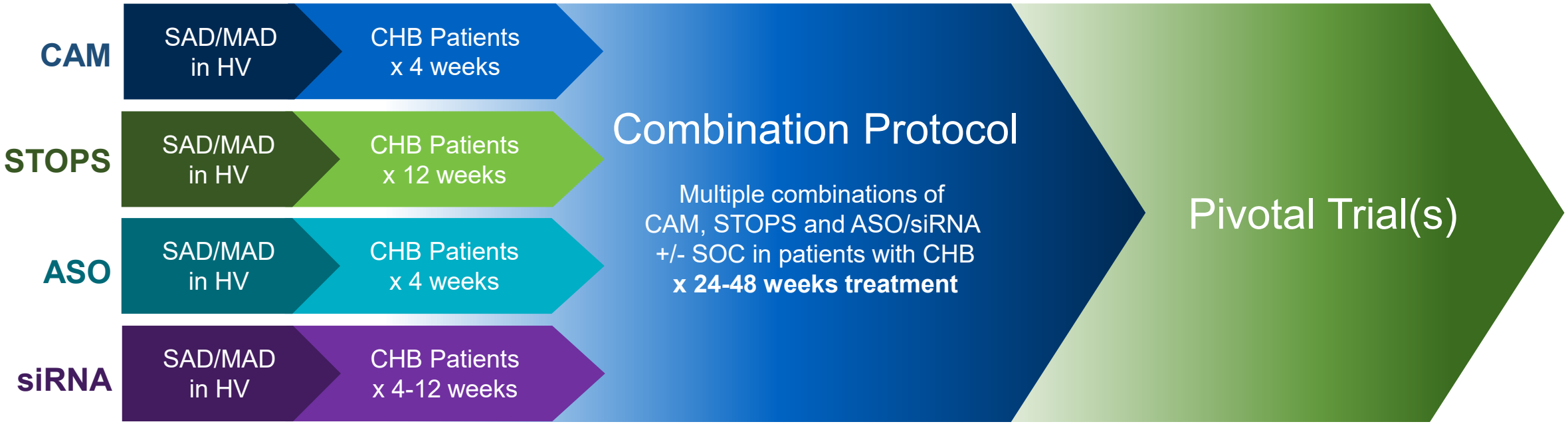
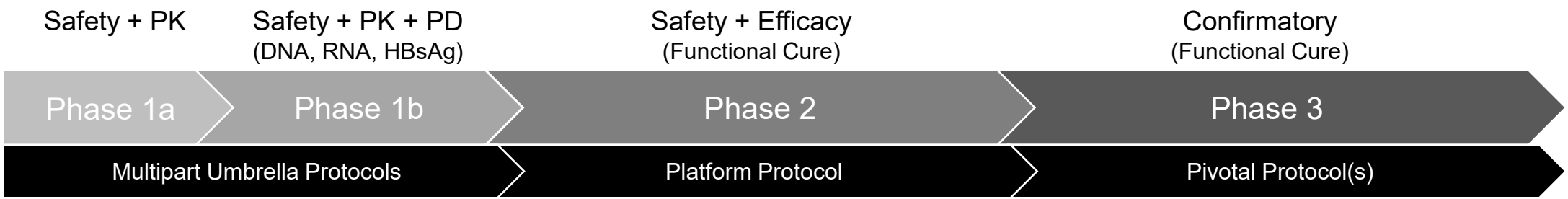
Our CHB Clinical Development Strategy





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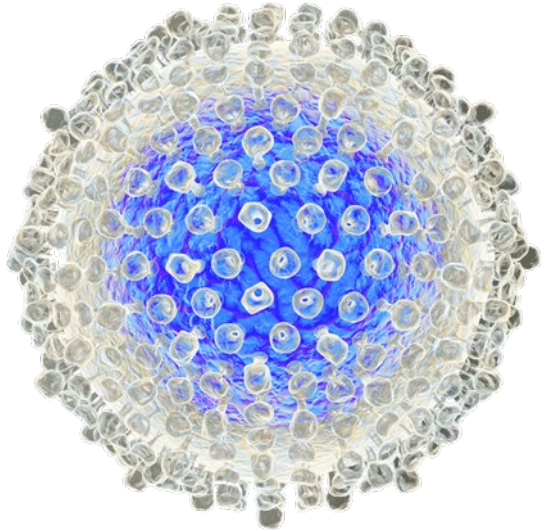
STOPS

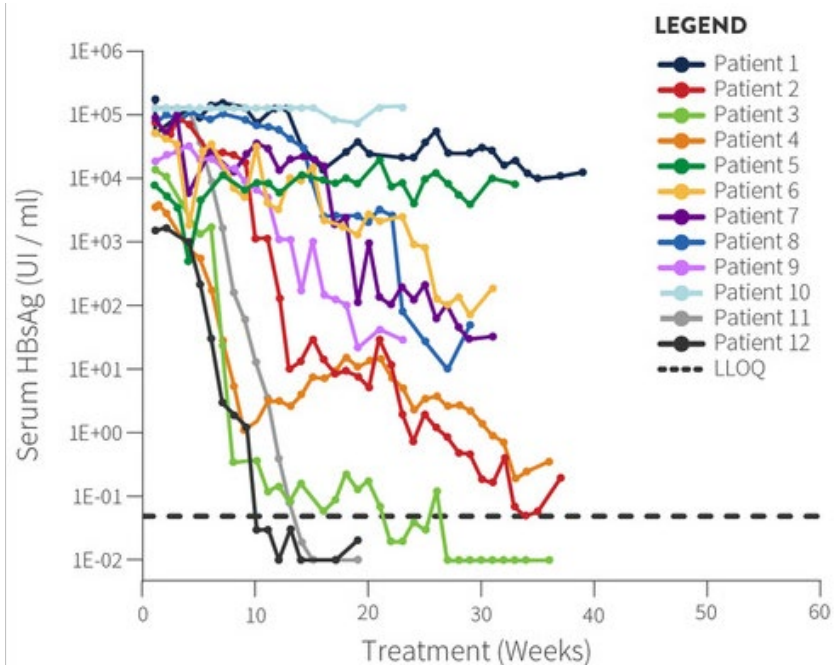
ALG-010133, a novel, chemically optimized poly-AC oligonucleotide analog



Poly AC Oligonucleotides Have Clinical Validation

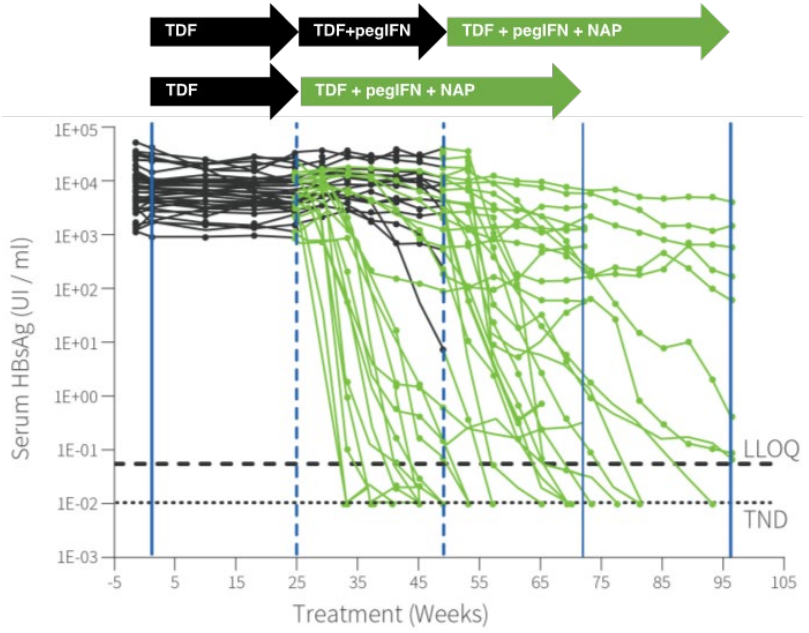
Significant HBsAg reductions observed with NAPs in treatment naïve CHB subjects

REP 102 Study (HBeAg+)*



- Treatment naïve, HBeAg positive
- REP 2139-Ca monotherapy x ≥20 weeks
- 500 mg QW, 2-hr IV administration
- At week 10, HBsAg as estimated from graph
  - Mean $\log_{10}$ reduction of 1.65 ± 1.97
  - Median $\log_{10}$ reduction of 0.4
  - Range of reduction +0.1 to -4.7 $\log_{10}$

REP 401 Study (HBeAg-)**



- Treatment naïve, HBeAg negative
- REP 2139 or 2165 + PEG + NA x 48 weeks
- 250 mg QW, 2-hr IV administration
- Reported a ~39% functional cure rate***

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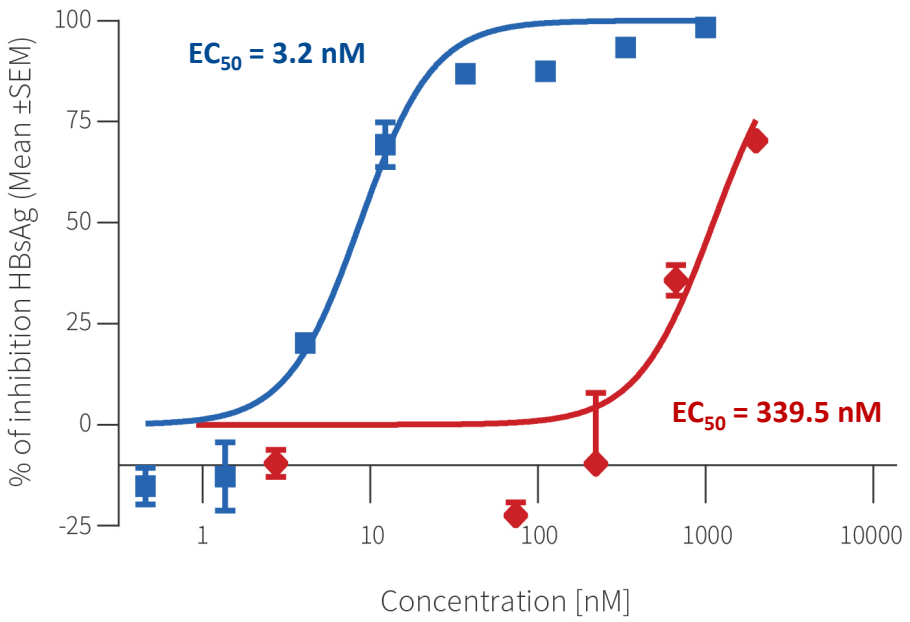
*Figure adapted from REP 102 Study; Al-Mahtab et. al., PLOS One, June 3, 2016.
**Figure adapted from Bazinet M. et. al. OP-02 EASL 2019 and Bazinet M. et. al. EASL 2020, LBP-033.
***Bazinet M., et. al., Gastroenterology 2020 (158) 2180.

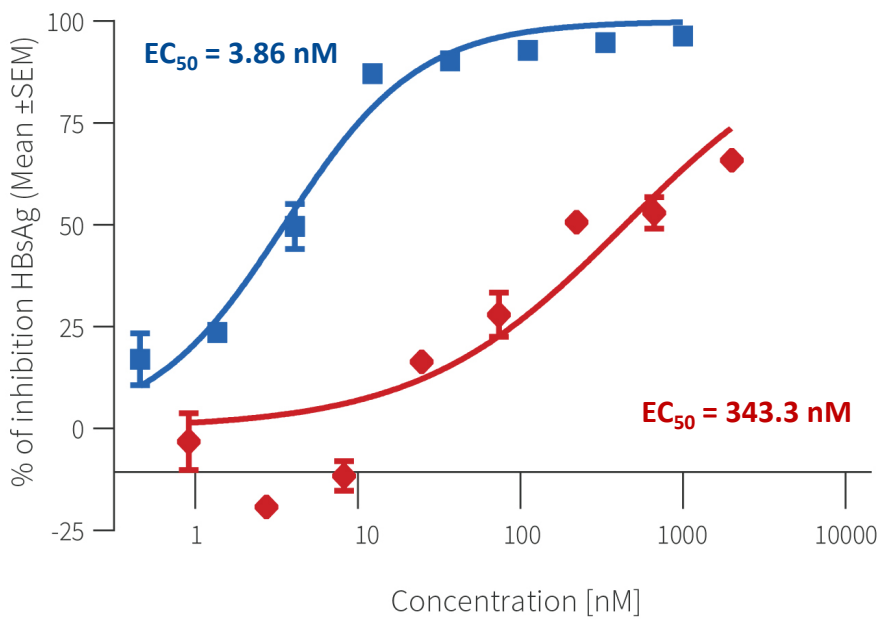
ALG-010133
Our Lead STOPS Molecule

Significantly greater potency* vs. reference Poly-AC oligonucleotide**

Dose-response curves for ALG-010133 and ALG-010004 induced inhibition of HBsAg in HepG2-NTCP



Dose-response curves for ALG-010133 and ALG-010004 induced inhibition of HBsAg in HepG2.2.15



LEGEND ALG-010133 ALG-010004

~100-Fold improvement in potency enables efficient subcutaneous administration

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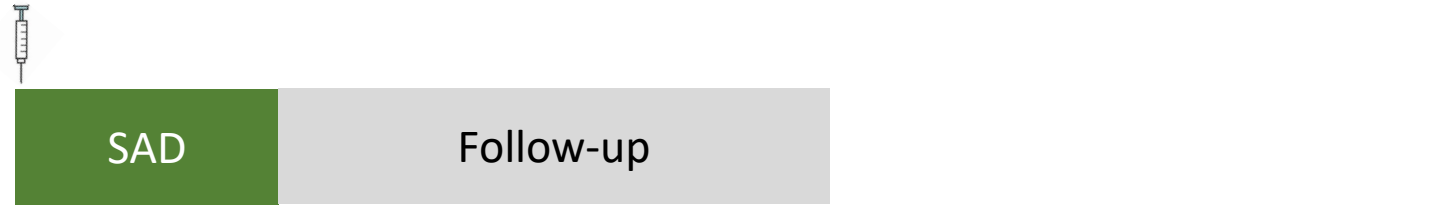
*Hong et. al., AASLD (2019), poster #0689.
**ALG-010004 has an identical oligonucleotide sequence as REP 2139. A. Vaillant, Antiviral Research 133 (2016) 32.

ALG-010133
Phase 1 Study Data In Healthy Volunteers

Single/Multiple Ascending Dose (SAD/MAD) study in HV

N=72; n=8 per Cohort, n=6 ALG-010133, n=2 Placebo

Single (SAD) or Three weekly subcutaneous (SC) doses (MAD)



Safety and PK of single doses of 20, 50, 75, 125, 160 and 200 mg

Safety and PK of 3 doses of 120 and 180 mg

Dosing in HV complete
PK and safety data identified doses that are projected to have antiviral activity in CHB patients

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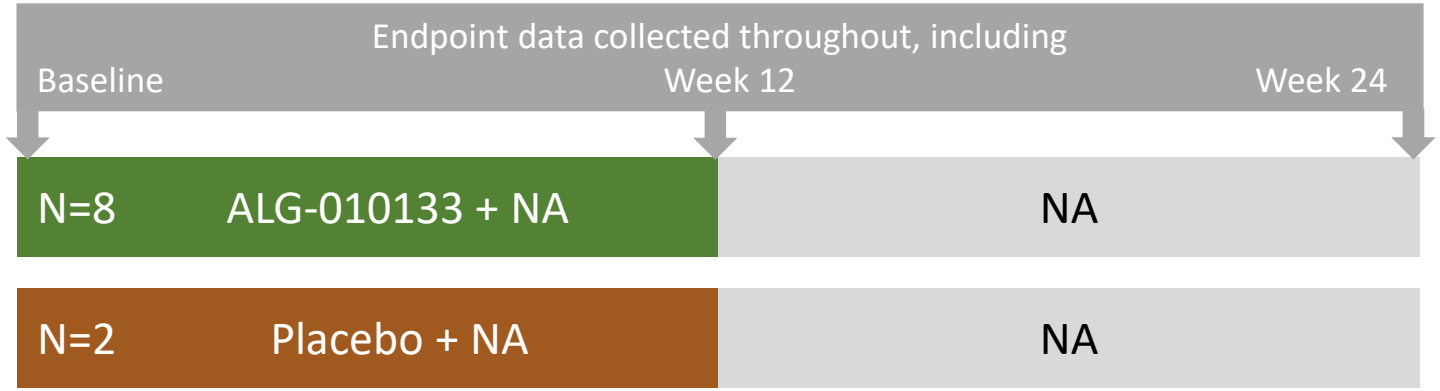
clinicaltrials.gov: NCT04485663

ALG-010133
Phase 1 Study Data In CHB

Multiple Doses in CHB Subjects

NA Suppressed (DNA < LLOQ), HBeAg Negative, HBsAg >1000 IU/mL
N≤60 Subjects; n=10 per Cohort, n=8 ALG-010133, n=2 Placebo
Up to 12 weekly doses
Endpoints: PK, safety, antiviral activity (e.g., HBsAg)



1st cohort (120 mg) currently dosing
Safety, antiviral activity data from 1st cohort(s) in H2 2021
Target HBsAg reduction: ≥1 $\log_{10}$ IU/mL

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clinicaltrials.gov: NCT04485663

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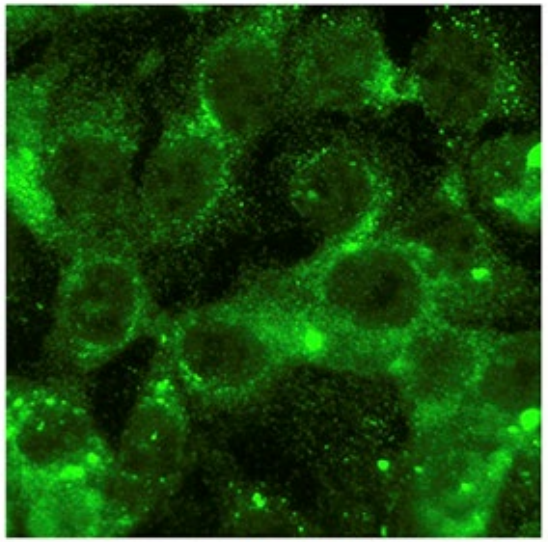
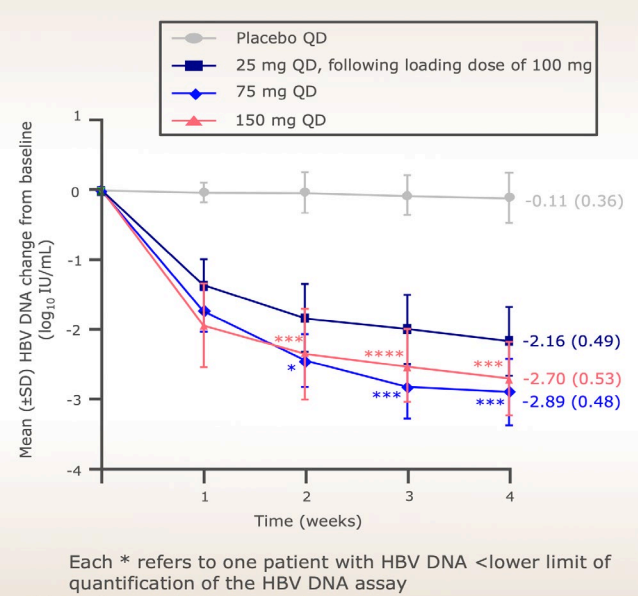
CAM

ALG-000184, a prodrug of ALG-001075

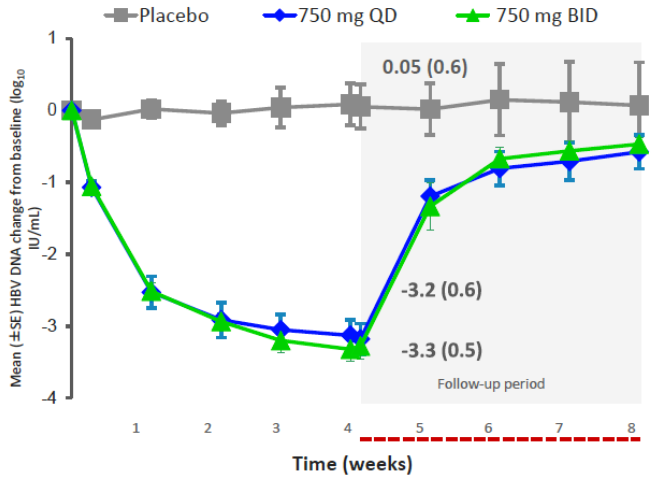


Class-II CAMs Have Clinical Validation

JNJ-6379*



JNJ-440*



ABI-731

	Change from Baseline Log_{10} HBV DNA (IU/mL) At Day 28			
Patients	HBeAg Pos		HBeAg Neg	
Dose (mg)	N	Mean (Range)	N	Mean (Range)
100 mg	6	1.3 (0.8 - 1.7)	4	2.2 (0.7 - 3.6)
200 mg	5	1.9 (1.0 - 2.6)	5	2.4 (1.5 - 3.8)
300 mg	6	2.9 (1.8 - 3.9)	3*	2.5* (0.8 – 4.1)

*Excludes subject with known resistance at baseline

Class-II CAMs result in ~2.5-3 log_{10} reductions in DNA at Day 28 in treatment naïve HBeAg negative CHB

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*~75% of subjects are HBeAg negative

Zoulim et al., Gastroenterology 2020
Gane et al., AASLD 2019
Yuen, AASLD 2018

ALG-000184 Demonstrates ~10 to 300-Fold Improvement in In Vitro Potency vs. Other Known CAMs in Clinical Development

Compound	Current Status	HBV DNA reduction (EC_{50} nM)	Cell Type
Assembly ABI-H0731	Phase 2	172	AD38
Assembly ABI-H2158	Phase 2	22	AD38
Assembly ABI-H3733	Phase 1	5	AD38
Janssen JNJ-6379	Phase 2	54	HepG2.117
Janssen JNJ-0440	Completed Phase 1	12	HepG2.117
Enanta EDP-514	Phase 1	17	HepG2.2.15
Aligos ALG-000184	**Phase 1**	**0.63**	**HepG2.117**
		0.53	**HepG2.2.15**

With the exception of ALG-000184, data was sourced from publicly available literature, posters and presentations.
ALG-000184 data was generated by Aligos on the parent compound ALG-001075.

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Study ALG-000184-201
SAD and MAD Completed

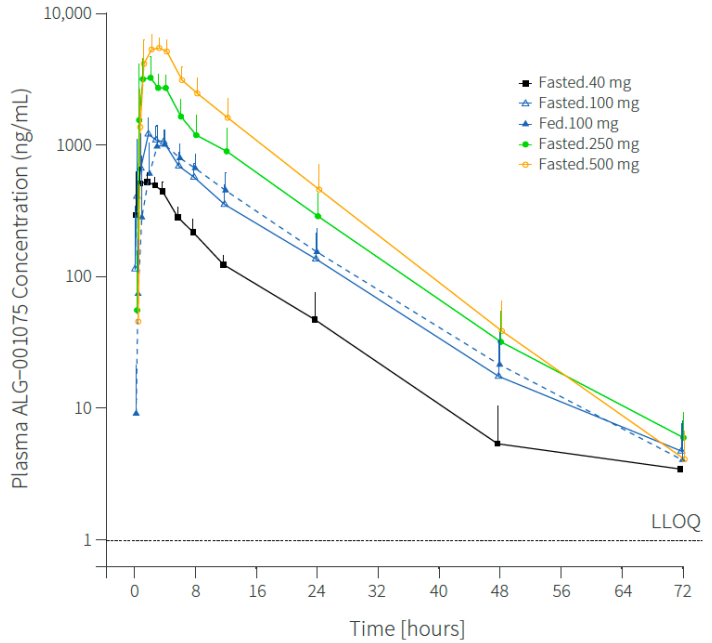
Parts 1 and 2: Single and Multiple Ascending Doses in Healthy Volunteers.
N=48; n=8 per Cohort, n=6 ALG-000184, n=2 Placebo
Up to 7 oral daily doses

SAD | Follow-up

Safety and PK of single doses of 40, 100, 250 and 500 mg

MAD | Follow-up

Safety and PK of 7 doses of 150 and 250 mg



All doses well tolerated; Linear PK; No food effect; No differences between Asian and non-Asian subjects
Identified doses projected to have antiviral activity

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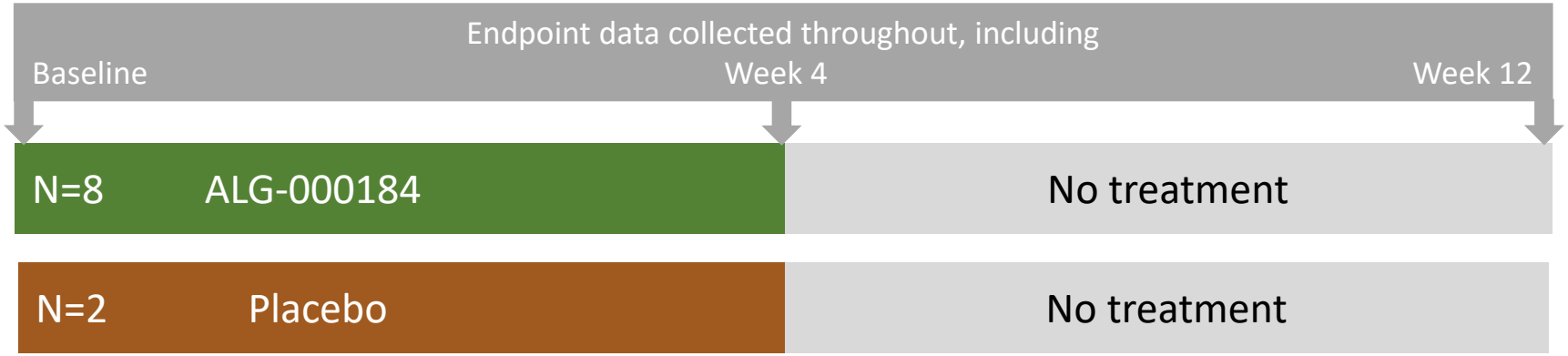
clinicaltrials.gov: NCT04536337
Gane et al., APASL 2021

ALG-000184
Phase 1 Study Data In CHB

Multiple Doses in Currently Not Treated/Treatment Naive CHB Subjects

HBV DNA > 2000 IU/mL, HBeAg Negative
N≤60 Subjects; n=10 per Cohort, n=8 ALG-000184, n=2 Placebo
28 daily oral doses
Endpoints: PK, safety, antiviral activity (e.g., DNA, RNA)



1st cohort (100 mg) currently dosing
Safety, antiviral activity data from 1st cohort(s) expected H2 2021
Target HBV DNA reduction: ≥2 $\log_{10}$ IU/mL

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clinicaltrials.gov: NCT04485663

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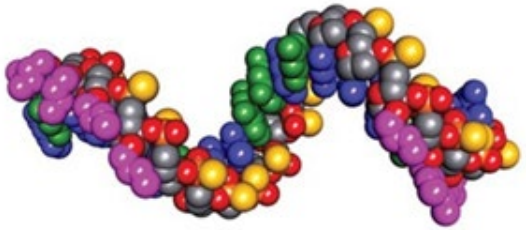
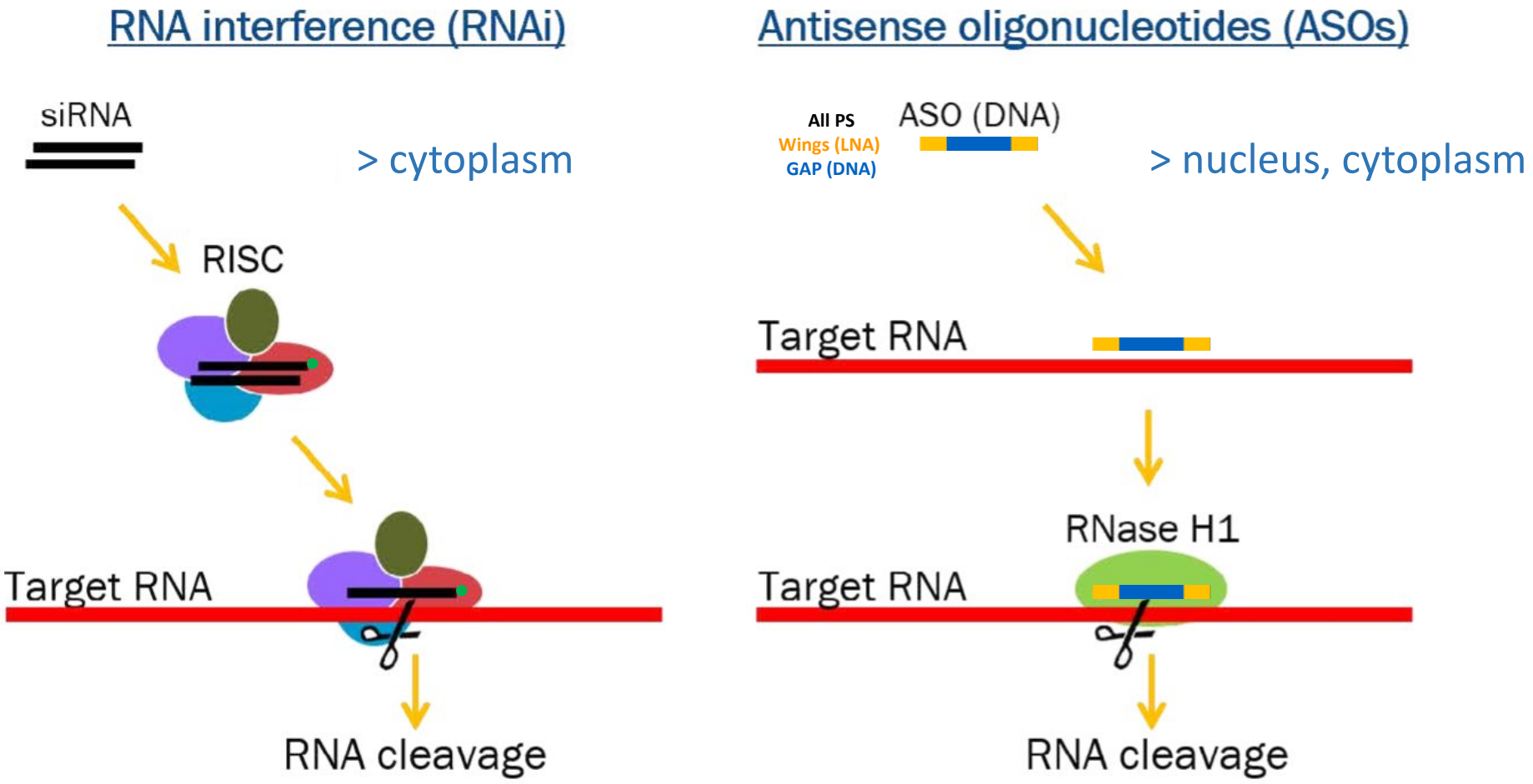
Additional Oligonucleotide Approaches

- ALG-020572 (ASO)
- ALG-125755 (siRNA)



Antisense Oligonucleotides and Small-Interfering RNAs



The Aligos team is agnostic to oligonucleotide modality

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Antisense Oligonucleotide ALG-020572
Discovery and Advancement of a Differentiated ASO

- Antisense oligonucleotides have demonstrated clinical validation in CHB infected patients

- We have optimized our sequences using our proprietary Luxna Biotech 3rd generation XNA nucleotides to enhance potency, stability and, potentially, safety
  - Our ASO has been conjugated to our proprietary GalNAc ligands for targeted liver delivery

- ALG-020572 demonstrates potent suppression of HBsAg in vivo in the AAV-HBV mouse model of HBV infection

- We have completed first-in-human enabling GLP studies with ALG-020572

ALG-020572 is differentiated from potential competitors and is progressing towards clinic entry in 2H 2021

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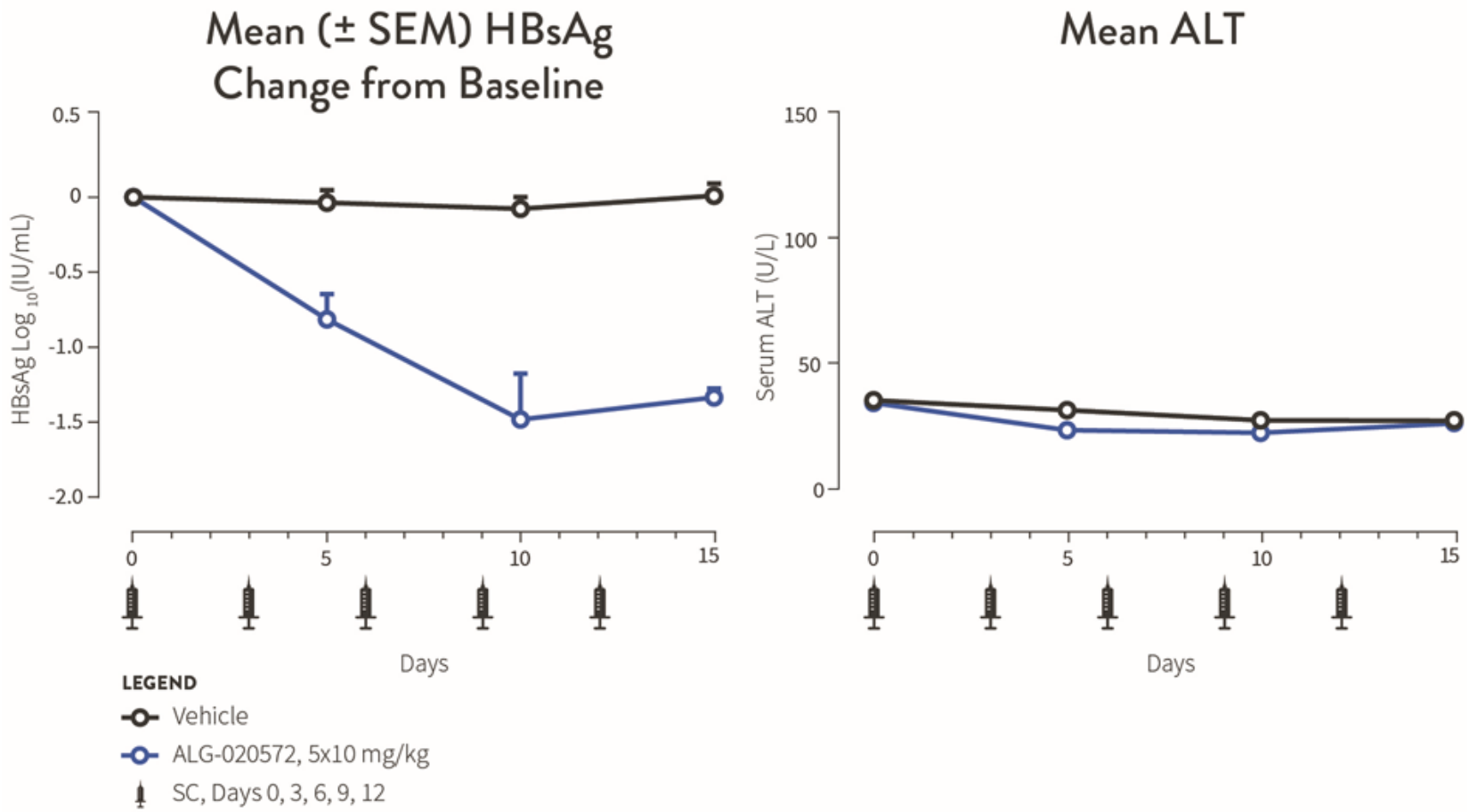
ALG-020572
Our ASO Drug Candidate in the Mouse AAV-HBV Model



Potent in vivo activity of ALG-020572 in the AAV-HBV mouse model without ALT elevation

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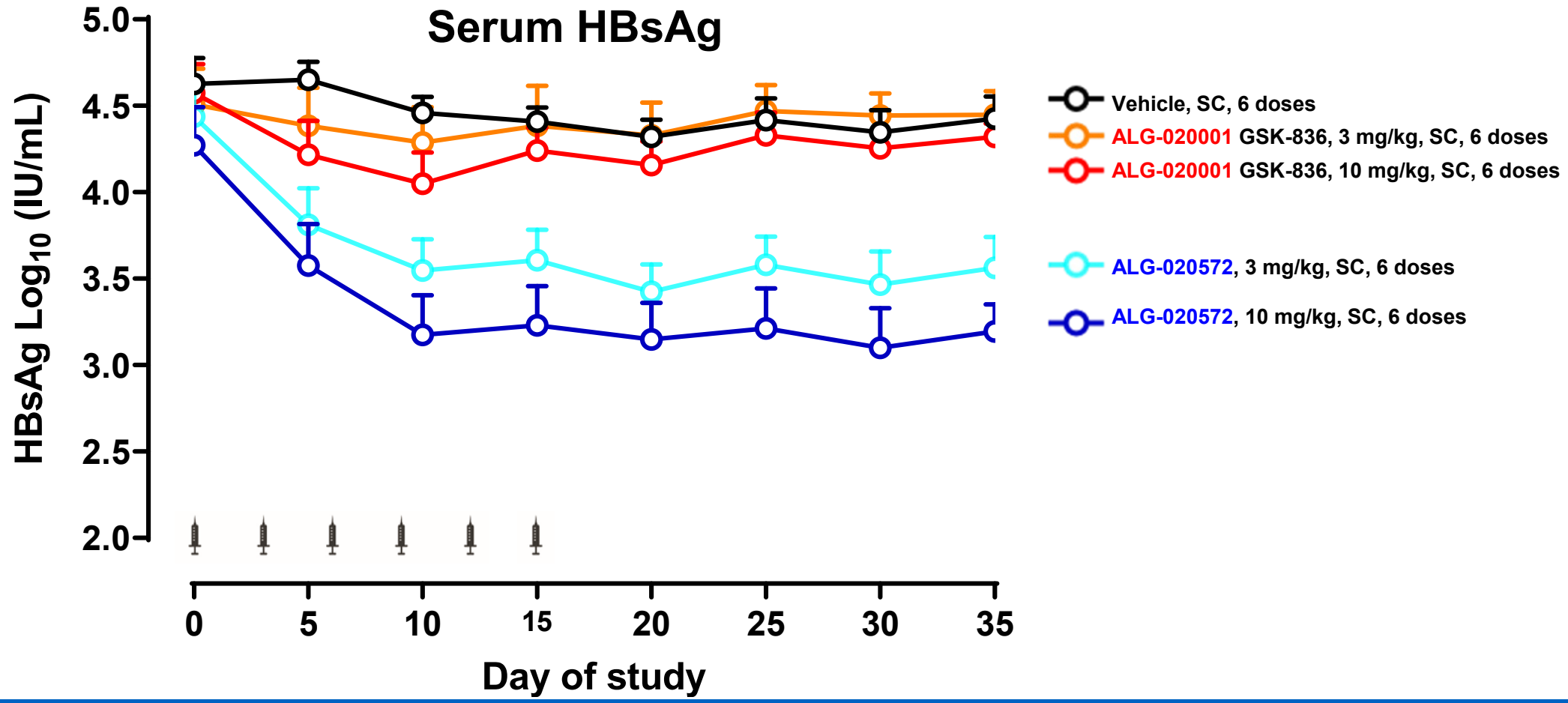
ALG-020572
Our ASO vs. GSK-836 ASO in the Mouse AAV-HBV Model



ALG-020572 demonstrates significantly improved efficacy in vivo vs. a competitor ASO

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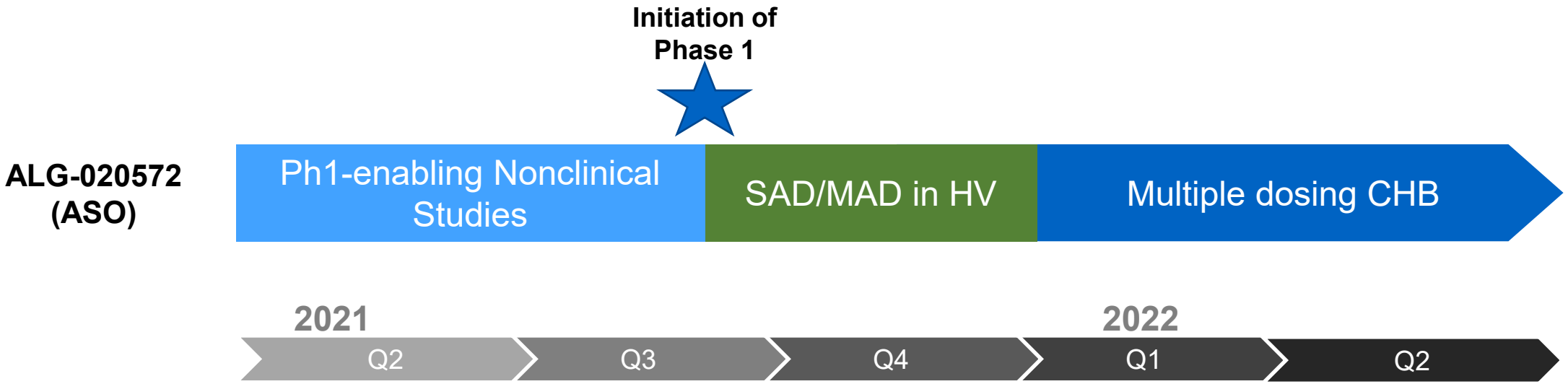
ALG-020572
Development Timelines*



Ph 1 target HBsAg reduction: ≥1 $\log_{10}$ IU/mL

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SAD – Single ascending doses; MAD- Multiple ascending doses; HV – Healthy volunteers; CHB – Chronic hepatitis B
*Timelines are approximate and subject to change based on regulatory approvals.

Short Interfering Nucleic Acid ALG-125755
Discovery and Advancement of a Differentiated siRNA

- siRNAs have demonstrated clinical validation in CHB infected patients
- We have optimized our siRNA sequences using our proprietary technology and liver targeting conjugation to maximize in vitro and in vivo potency
  - Novel monomers to stabilize antisense strand in the RISC complex
  - Proprietary patterns discovered to increase potency and stability / duration of action
  - Exclusive license to GalNAc technology applicable for liver targeting across oligo modalities
- Our approach to developing siRNAs may have safety, stability and potency advantages over other siRNAs
- We have initiated dose-range-finding studies with our siRNA ALG-125755
  - First-in-human enabling GLP studies are planned for 2H 2021

ALG-125755 is differentiated from potential competitors and is progressing towards clinic entry in 1H 2022

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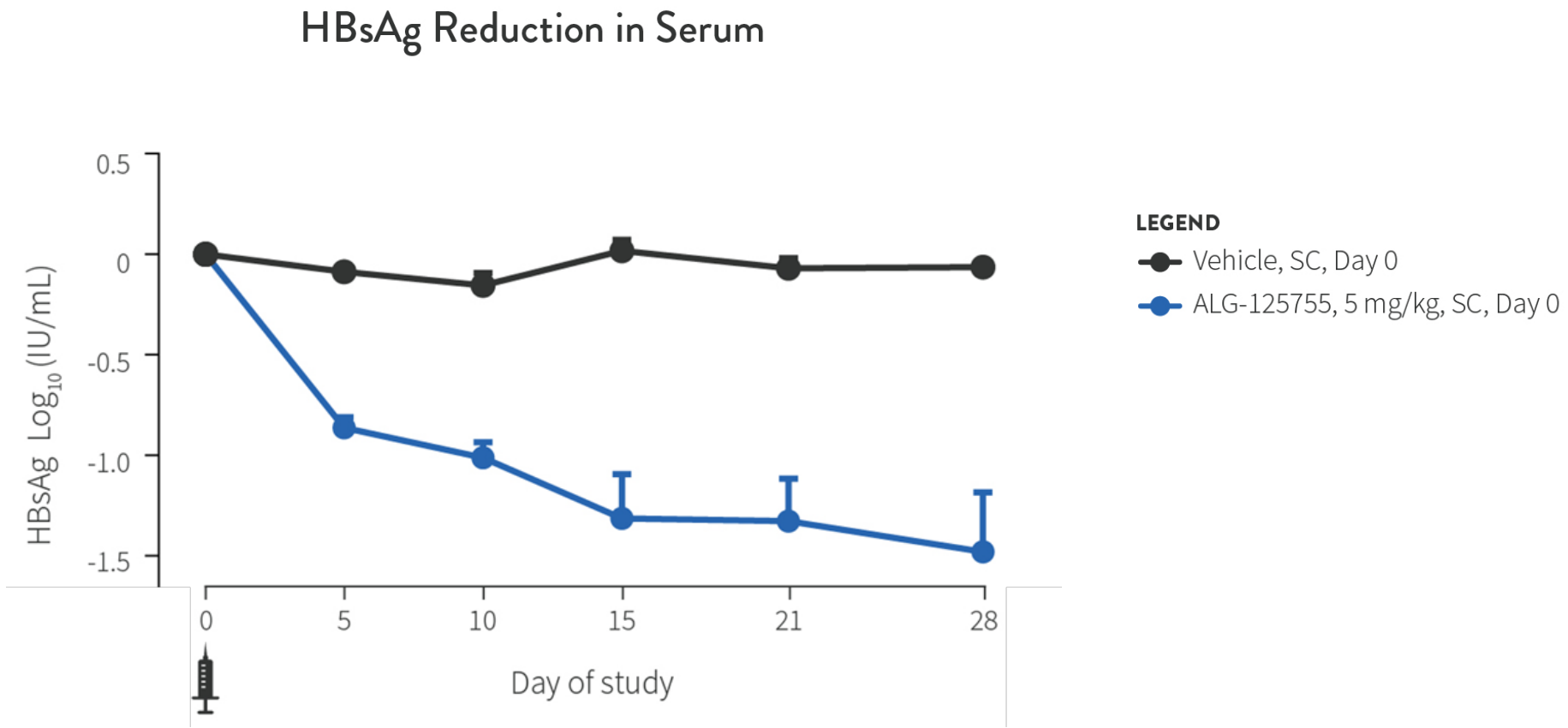
ALG-125755
siRNA Drug Candidate in the Mouse AAV-HBV Model



Potent and sustained antiviral activity following a single dose through 28-days of monitoring

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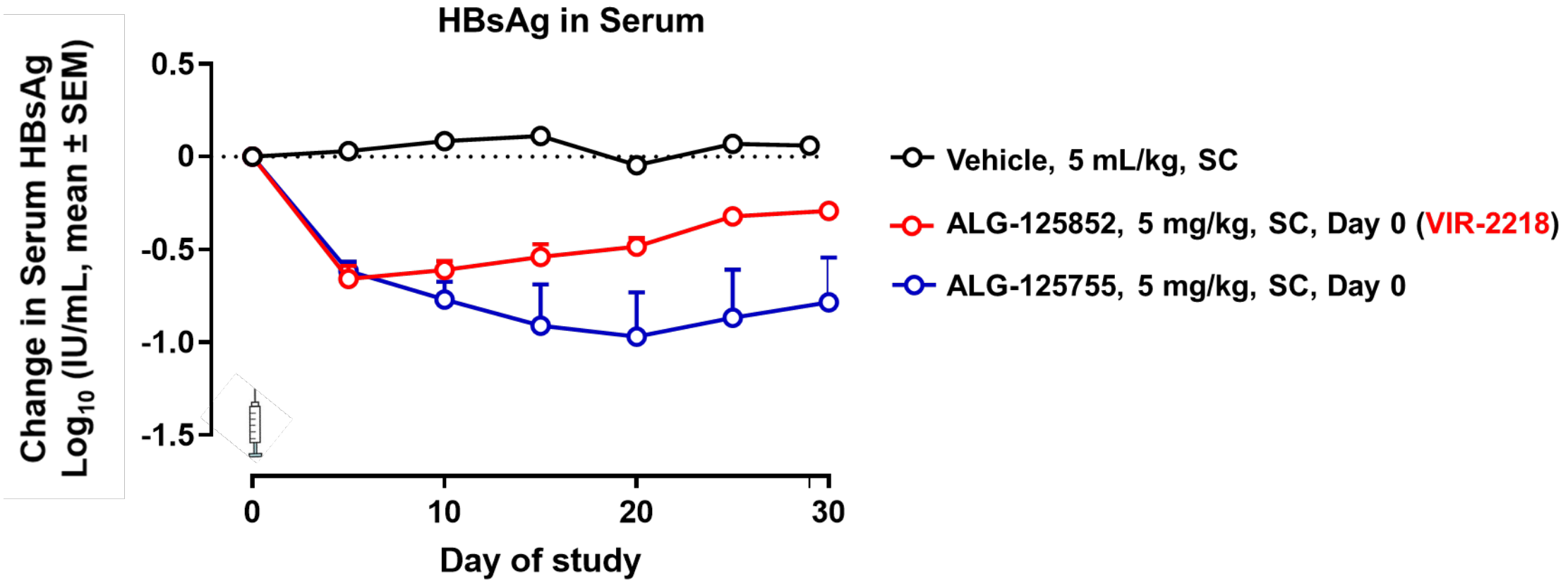
ALG-125755
Our siRNA vs. VIR-2218 siRNA in the Mouse AAV-HBV Model



ALG-125755 demonstrates significantly improved efficacy in vivo vs. a competitor siRNA

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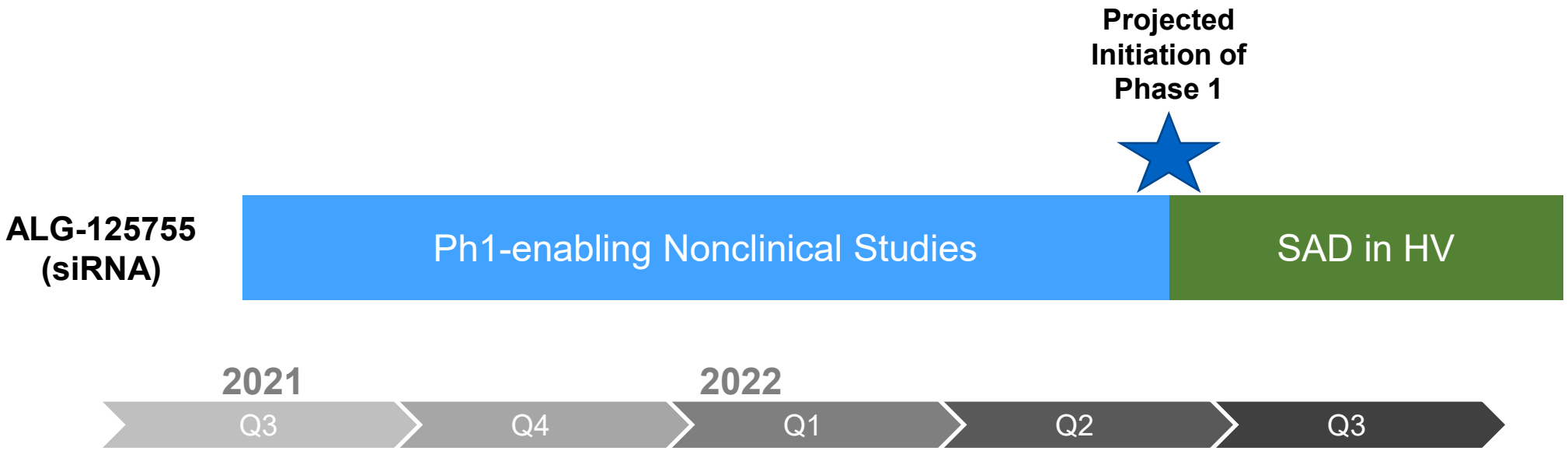
ALG-125755
Development Timelines*



Ph1 target HBsAg reduction: ≥1 log_{10} IU/mL

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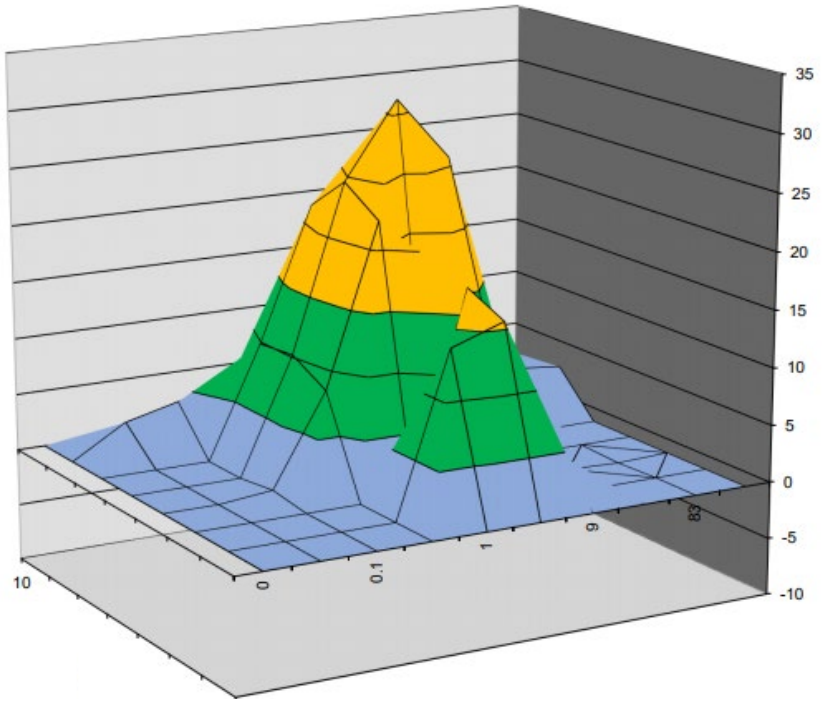
SAD – Single ascending doses; MAD- Multiple ascending doses; HV – Healthy volunteers; CHB – Chronic hepatitis B
*Timelines are approximate and subject to change based on regulatory approvals.

Aligos' Advancing CHB Portfolio
Excellent Performance in Combination Studies

- STOPS ALG-010133 + ASO ALG-020572 (Unconjugated form)
  - Strong synergy (HBsAg)
- STOPS ALG-010133 + CAM ALG-000184 (ALG-001075)
  - Minor synergy (HBV DNA)
- siRNA ALG-125755 + ASO ALG-020572 (Unconjugated versions)
  - Minor synergy (HBsAg)



Aligos' CHB development compounds are synergistic with each other in combination studies

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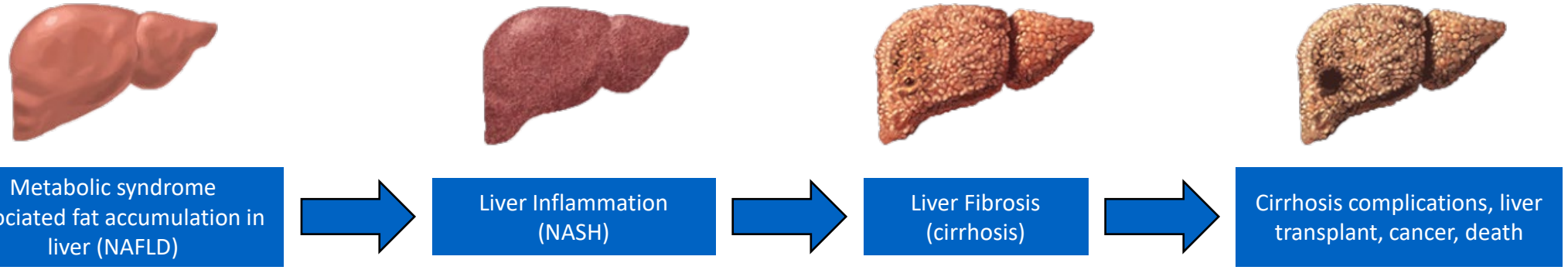
NASH

ALG-055009, small molecule THR-β agonist

NAFLD and NASH*
High Prevalence + No Approved Therapy: Large Unmet Need

- Disease Progression



- Incidence
  - NAFLD – 25% worldwide
  - NASH – 1.5-6.5% (~450 million people) worldwide
    - Projected to affect 27 million Americans by 2030**
- Impact
  - Causes significant morbidity and mortality
- Treatment
  - Diet and exercise – effective but difficult to achieve at population level
  - Drugs – no approved therapy

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* NASH: nonalcoholic steatohepatitis
NAFLD: nonalcoholic fatty liver disease
Younossi et al. Hepatology 2016.
**Estes et al., Hepatology 2018.

THR-β Agonists are Clinically Validated

THR-β Drug^	Serum LDL Lowering*	Liver Fat Reduction at 12 Weeks* (MRI-PDFF)	NASH Resolution Without Fibrosis Worsening* at 36 weeks (Liver Biopsy)
Resmetirom**	17.3% (30 weeks)	22.5%	18.2%
VK-2809***	21.8% (12 weeks)	49.2%	—

THR-β agonists have demonstrated beneficial effects on serum lipid levels and liver histology

^All dose levels pooled.
*Placebo corrected values.
** In patients with NASH, Harrison, Lancet, 2019. Resmetirom = MGL-3196.
*** In patient with NAFLD, hyperlipidemia, Loomba, AASLD, 2018.
LDL: Low Density Lipoprotein, MRI-PDFF: magnetic resonance imaging proton density fat fractionation.

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ALG-055009
More Potent and Selective In Vitro than MGL-3196 and VK-2809

Relative THR-α and THR-β Activity in Cell-Based Assays

	EC_{50} α (nM)	EC_{50} β (nM)	Relative THR-β Selectivity (α/β)
T3	14.2	11.6	1.2
MGL-3196	5927	2366	2.5
VK-2809 parent	366	269	1.4
ALG-055009	**191**	**50**	**3.8**

In vitro, ALG-055009 is 5-47x more potent compared to resmetirom (MGL-3196) and 2-3x more selective for THR-β than VK-2809*

High β selectivity and potency may improve risk-benefit profile

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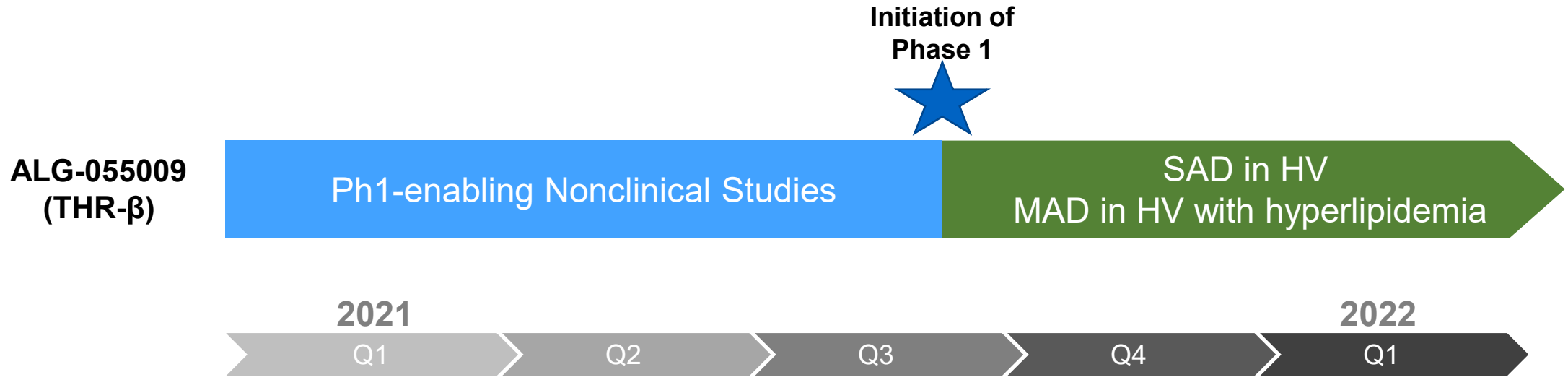
*Data collected in HEK293T cells.

ALG-055009
Development Timelines*



Lipid Reduction Target

Exceed Madrigal/Viking Ph1 results at Ph2b/3 dose levels

Placebo-corrected LDL-C reduction ≥27%

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SAD – Single ascending doses; MAD- Multiple ascending doses; HV – Healthy volunteers
*Timelines are approximate and subject to change based on regulatory approvals.

Our NASH Strategy

- Advance ALG-055009 through Phase 1 proof of concept study
  - Benchmark safety, PK, anti-lipid data vs. resmetirom & VK2809 Phase 1 data
  - Data expected 2H 2022
- Resmetirom Phase 3 Phase 2b readouts are expected in 2H 2022
- Aligos NASH ALG-055009 program has strong optionality in 2022
  - Continue to advance program on our own into Phase 2
  - If enthusiasm for resmetirom and/or VK-2809 is high and ALG-055009 compares favorably in Phase 1, we will seek partnership with a company that is advancing a NASH asset with a complimentary MOA

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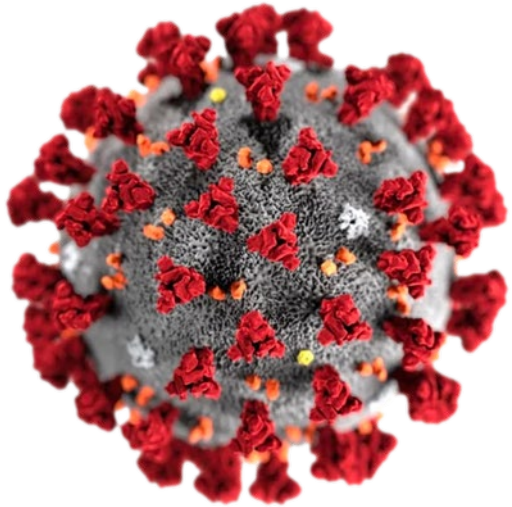
Coronavirus

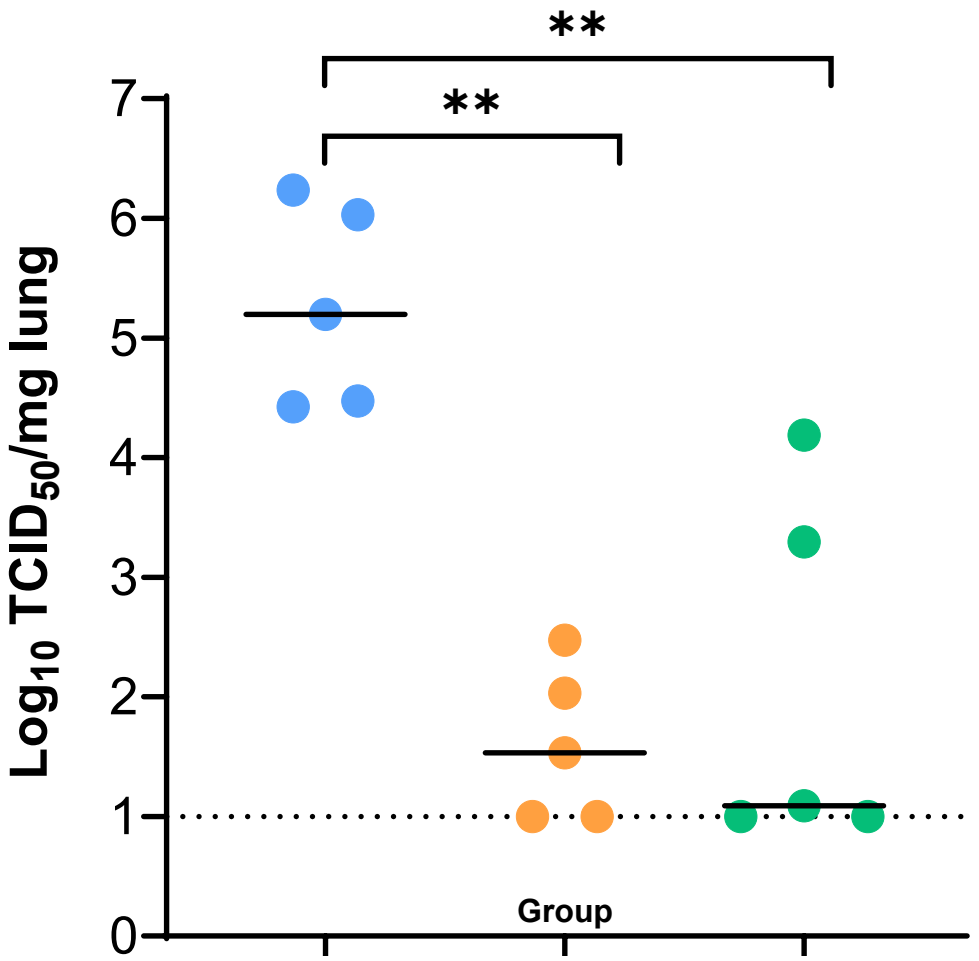


Our Approach to Developing a Broad Coronavirus Treatment

- Despite the recent availability of prophylactic vaccines, a need for therapeutics still exists
  - Resistant variants are emerging and may become dominant
  - Large segments of global population lack access to, or are opposed to vaccination
  - Especially needed in the hospitalized patient population
- Leveraging our virology / chemistry expertise to develop purpose-built drugs with distinct MOAs
  - Protease inhibitors (collaboration with KU Leuven / Rega Institute / CD3)
- We are aiming to develop drug candidates that
  - Are broadly active against a diverse range of coronaviruses with a high barrier to resistance
  - Have a therapeutic window compatible with prophylaxis and treatment
  - Can be combined to prevent emergence of resistance and provide broader strain coverage
- We are prioritizing therapeutics with MOAs that may have activity against potential zoonotic coronavirus transmissions in the future
  - Need for drugs with broad pan-coronavirus activity is essential for the management of future pandemics

ALG-097111
Efficacy in SARS-CoV-2 Hamster Model

Infectious viral loads *in the lungs of SARS-CoV-2 infected hamsters at day 2 post-infection after 5 doses with either vehicle or study drugs*



ALG-097111 SARS-CoV-2 In Vitro

Biochemical IC_{50} = 7 nM
Cell-based EC_{50} =200 nM (A549)

- **RTV + Vehicle**
  60% PEG400 in water, subcutaneous[SC]) + ritonavir (50 mg/kg/dose, BID oral gavage)
- **RTV + ALG-097111**
  (200 mg/kg/dose, BID, SC) + ritonavir (50 mg/kg/dose, BID, oral gavage)
- **EIDD-2801**
  (200 mg/kg/dose, BID, oral gavage)

ALG-097111 efficiently inhibits viral replication in the lungs of infected hamsters

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Biochemical and Biophysical Research Communications (2021), v555, p134-9

TCID = Tissue culture infectious dose
EIDD-2801 = Nucleoside analog, RTV = Ritonavir

Aligos Therapeutics Summary

- We are advancing multiple drug candidates with clinically-validated MOAs with the goal of rapidly developing optimized combination regimens
  - CHB
    - STOPS molecule (ALG-010133) Phase 1 clinical trial ongoing, dosing in CHB patients
    - CAM (ALG-000184) Phase 1 clinical trial ongoing, dosing in CHB patients
    - ASO and siRNA oligonucleotide compounds are planned to advance into the clinic (2H 2021 / 1H 2022)
  - NASH
    - We are advancing our small molecule THR-β agonist, ALG-055009, into clinical development 2H 2021
    - We have an exclusive oligonucleotide-based License and Research collaboration with Merck
  - Coronavirus
    - We have identified multiple nM potent coronavirus protease inhibitors

- As of March 31, 2021, our cash balance was $213.4M*
- As of May 7, 2021, common stock shares outstanding, 38,153,690

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*Reflects unrestricted cash, cash equivalents and investments.

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