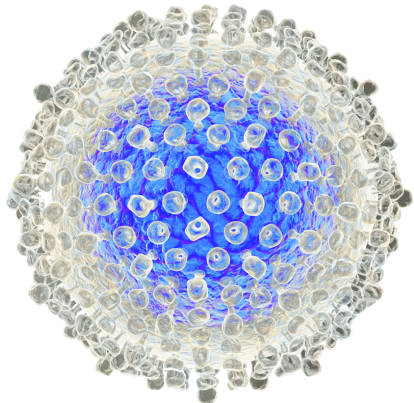
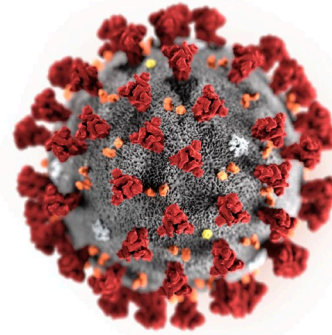


**ALIGOS**  
THERAPEUTICS

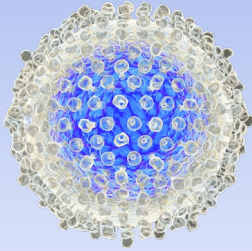


**Lawrence M. Blatt, Ph.D.**  
**CEO & Co-Founder**

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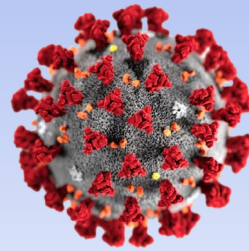
Jefferies Healthcare Conference  
June 4, 2020

# Aligos Therapeutics Mission



## Chronic Hepatitis B Virus (HBV) Infection

- Capsid Assembly Modulator (CAM) IP licensed from Emory University (Schinazi Laboratory)
- Oligonucleotides (STOPS™, ASO)
- Best-in-Class potential



## COVID-19 (Broad Spectrum CoV)

- Oligonucleotide approaches
- Small molecules



## Lipotoxicity - NAFLD, NASH

- THR-β agonist

**“To become a world leader in the development of targeted, antiviral therapies including chronic hepatitis B (CHB) and COVID-19 as well as leveraging expertise in liver diseases to create targeted therapeutics for NASH”**

# Senior Leadership Team



**Lawrence Blatt**  
Chief Executive Officer  
Janssen, Alios, InterMune



**Leonid Beigelman**  
President  
Janssen, Alios, InterMune



**Julian Symons, EVP**  
Chief Scientific Officer  
Janssen, Alios, Roche



**Lucinda Quan, EVP**  
Chief Business Officer  
Merck, Janssen, Alios



**John Fry, EVP**  
Head Clinical Development  
Janssen, Alios, Gilead



**Sushmita Chanda, EVP**  
Head Preclinical Development  
Janssen, Alios, Roche



**Matthew McClure, EVP**  
Chief Medical Officer  
Second Genome,  
Janssen, Alios, Portola



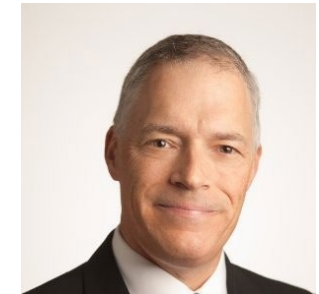
**David B. Smith, VP**  
Head Chemical Operations  
Janssen, Alios, Roche



**Pierre Raboisson, VP**  
Head Small Molecule  
Medicinal Chemistry,  
Head of Belgium Site  
Janssen

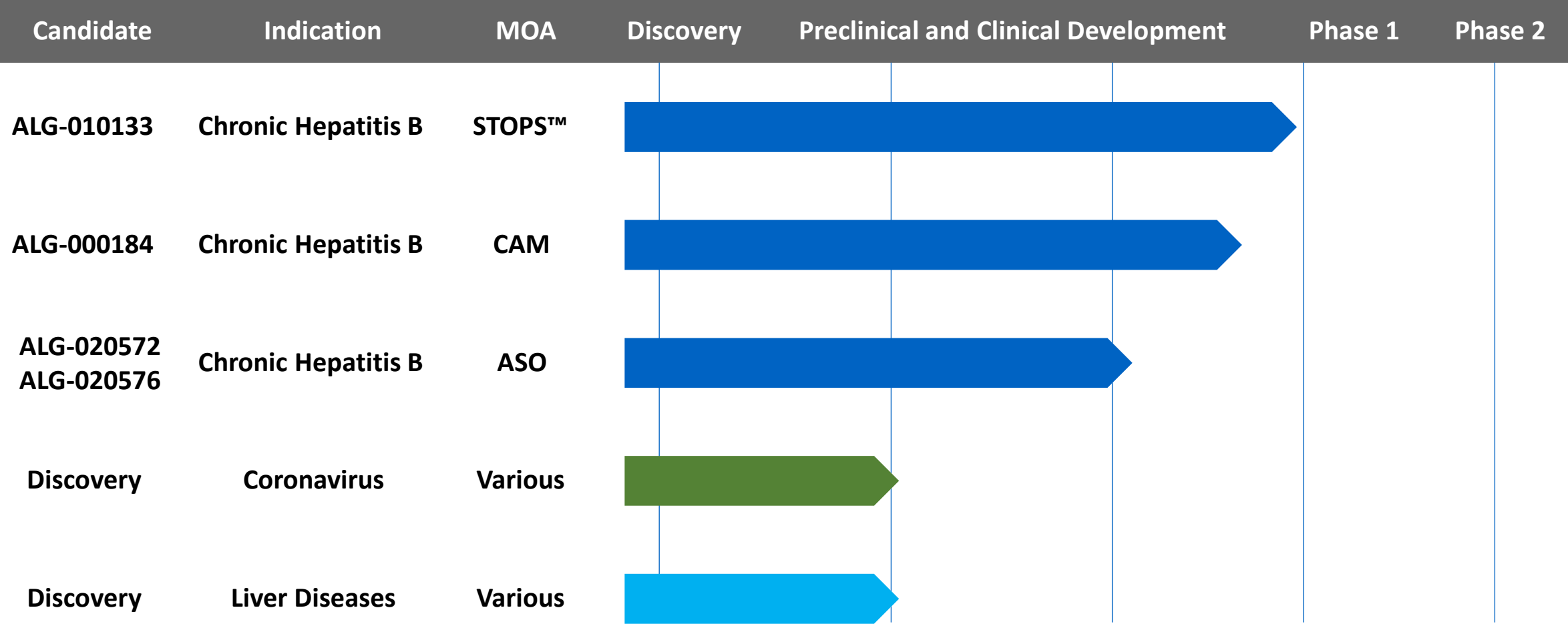


**Lesley Calhoun, EVP**  
CFO  
Global Blood,  
Hyperion, Theravance



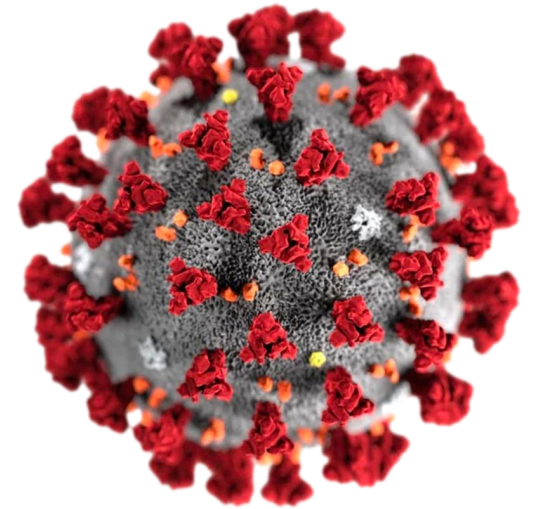
**Brian Dowd, EVP**  
Controller  
Second Genome,  
Janssen, Alios

# Aligos Pipeline at a Glance



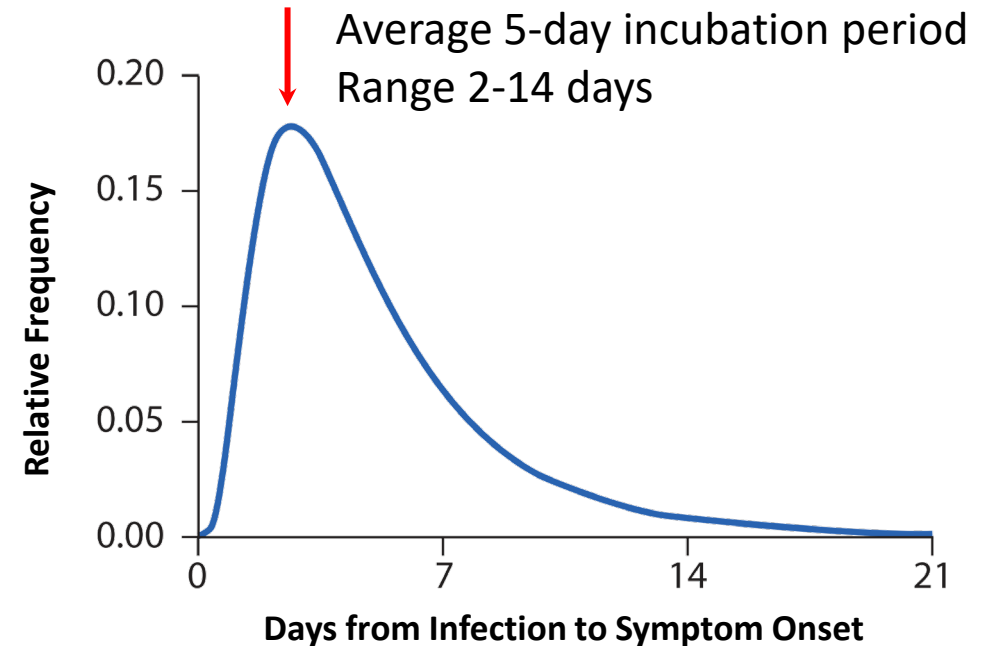
# Coronavirus

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# Preferred Features of Antivirals for Coronavirus

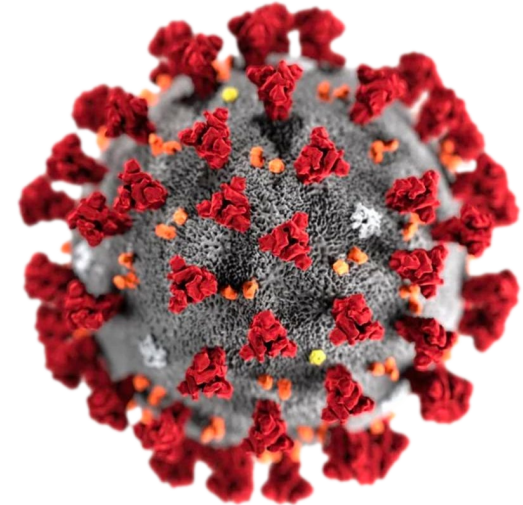
- Broadly active against diverse coronaviruses
- High barrier to resistance
- Extended therapeutic window compatible with prophylaxis and treatment
- Combination therapy preferred to prevent emergence of resistance and provide broader strain coverage



# Approach to Developing a Pan-Coronavirus Treatment

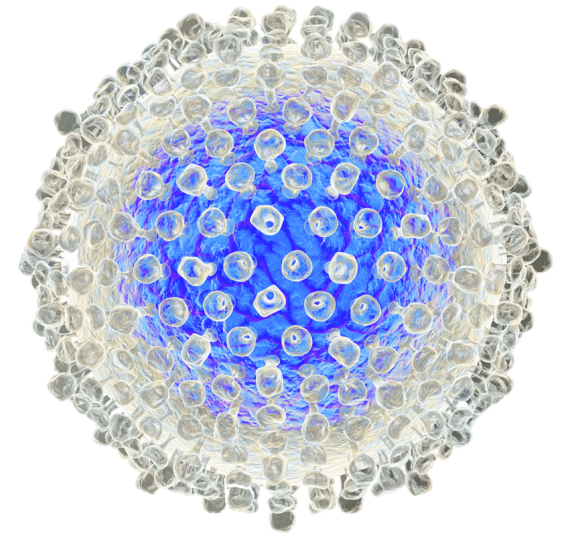
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- Leverage Aligos' virology expertise to develop purpose-built drugs with diverse MOAs
  - Oligonucleotides (ASO, siRNA and aptamers)
    - › Targeting conserved gene sequences
  - Nucleoside and nucleotide analogs
    - › Broadly active against all coronavirus polymerases
  - CoV protease inhibitors
    - › Broadly active against entire family of viruses
- Prioritize regimens with MOAs that may offer therapeutic benefit in potential zoonotic coronavirus transmissions in the future



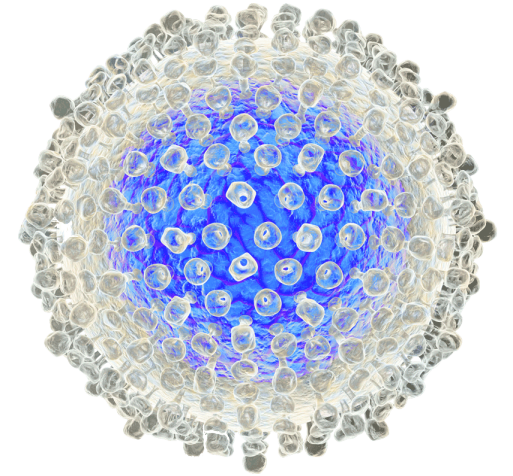
# Chronic Hepatitis B

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# Chronic Hepatitis B Combination Treatment Strategy

- Current nucleos(t)ide analog treatment is lifelong and rarely leads to functional cure
  - Functional cure\*
    - › Sustained, undetectable HBsAg and HBV DNA in serum with or without seroconversion to hepatitis B surface antibody (anti-HBs) after completion of a finite course of treatment
- HBV portfolio is a diverse mix of best-in-class drugs in 3 discrete categories targeting clinically validated MOAs with potential to achieve high rates of functional cure:
  1. S-antigen transport-inhibiting oligonucleotide polymers (STOPS)
  2. Capsid assembly modulators (CAMs)
  3. Antisense oligonucleotides (ASO)

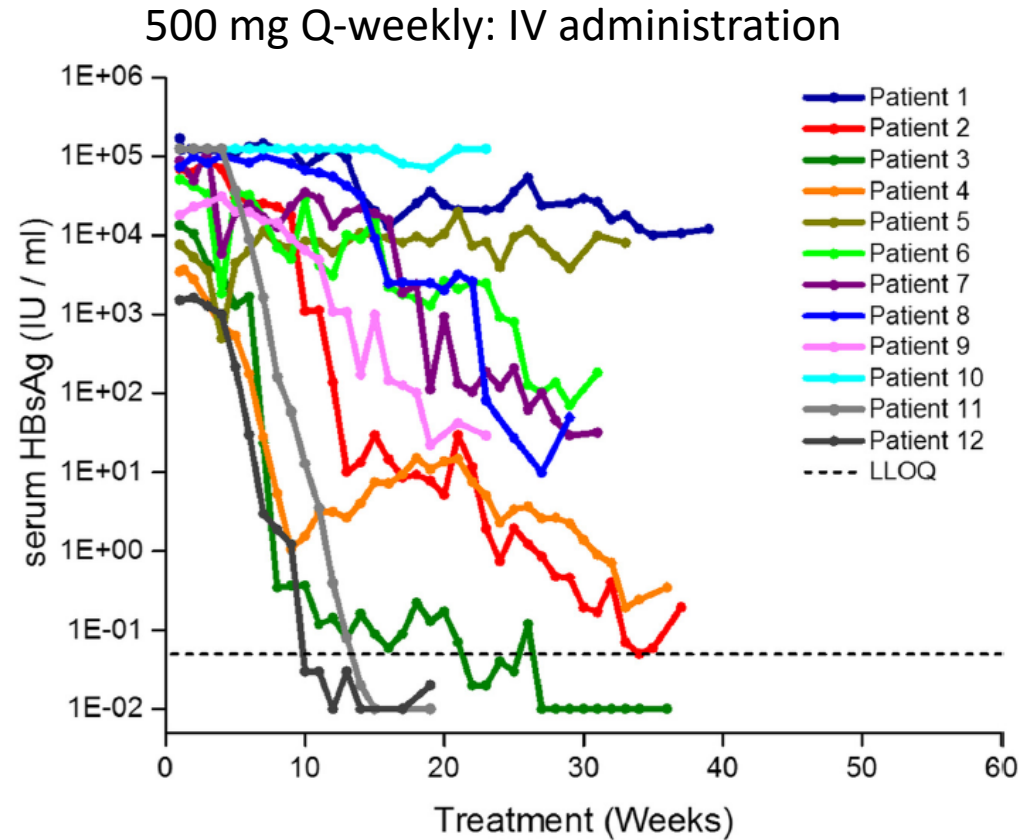


# S-antigen Transport-inhibiting Oligonucleotide Polymers (STOPS™)

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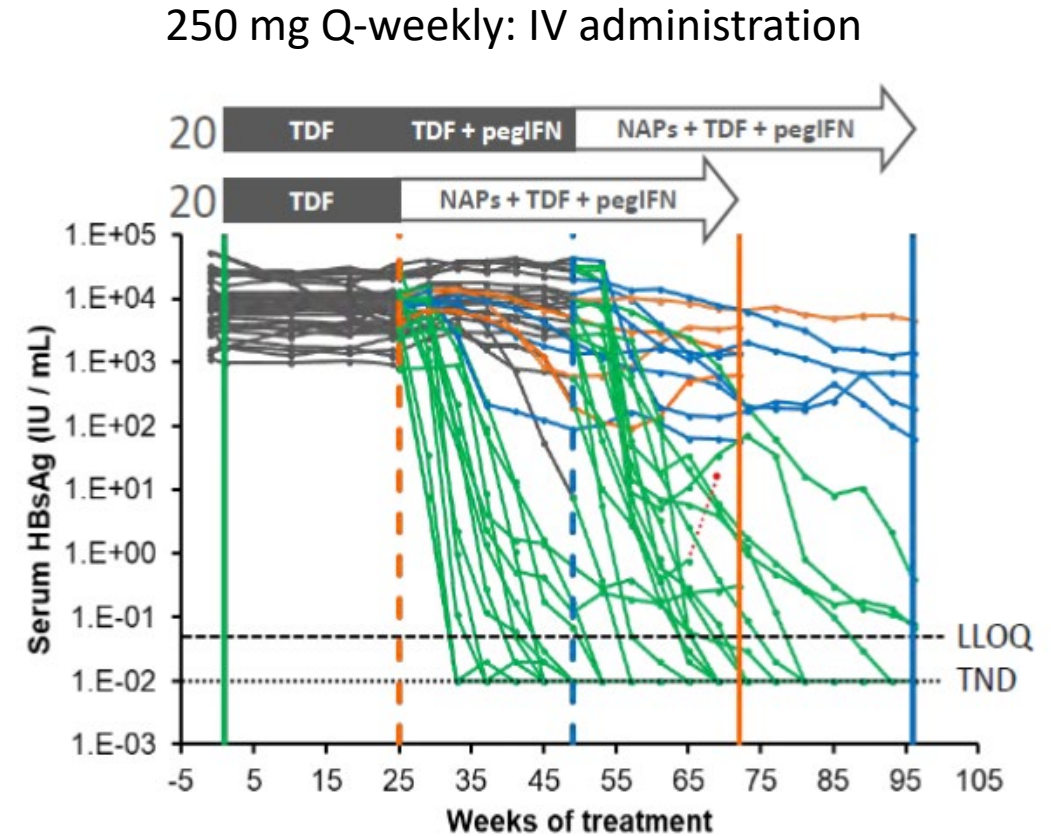
Oligonucleotide aptamers (protein binding),  
comprised of a repeating poly AC sequence

# Poly AC Oligonucleotides Have Clinical Validation: Treatment Results in Multiple $\log_{10}$ Reductions of HBsAg and Functional Cure



*Multiple  $\log_{10}$  reductions*

**REP 102: REP2139 Mono Therapy**  
Al-Mahtab, M. et. al. PLOS ONE June 3, 2016



*Reported a 39% functional cure*

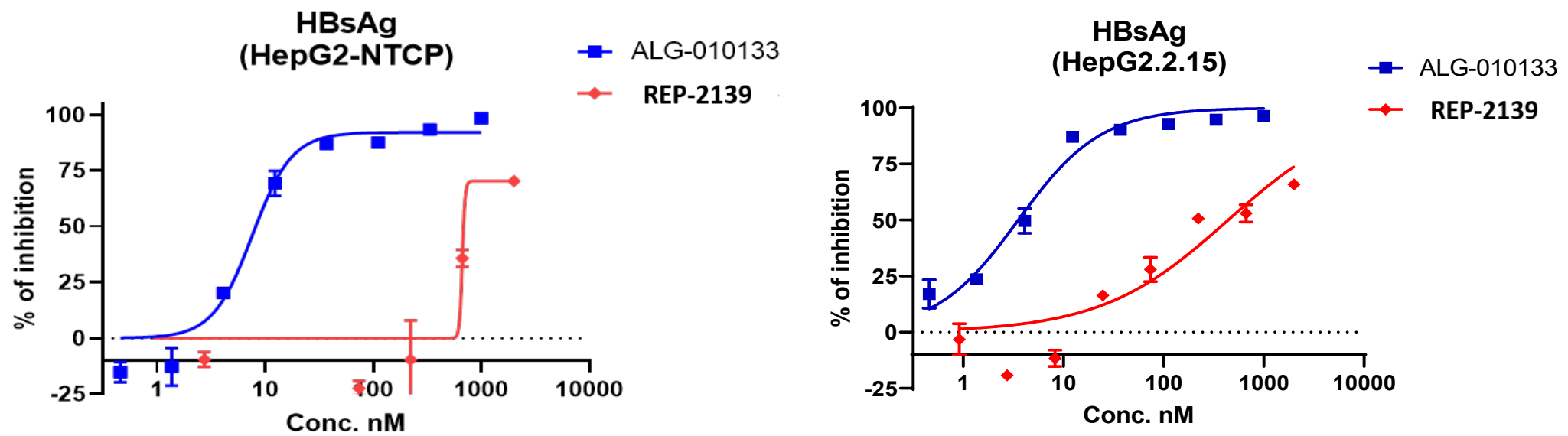
**REP 401: REP2139 Triple Combo**  
Bizinet M. et. al. OP-02 EASL 2019, Vienna Austria

# Aligos Approach to STOPS for Chronic Hepatitis B

- Thoroughly explored chemistry around STOPS structure
  - Optimized for potency, dose frequency and subcutaneous delivery

| <div> <span>★ Aligos Novel</span> <span>■ 2'OME</span> <span>■ Aligos Novel</span> <span>— Traditional Linkage</span> <span>^ Novel Linkage</span> </div> |  | ALG #     | Live Infection      |                     | HepG2.2.15          |                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|--|-----------|---------------------|---------------------|---------------------|---------------------|
|                                                                                                                                                           |  |           | EC <sub>50</sub> nM | CC <sub>50</sub> nM | EC <sub>50</sub> nM | CC <sub>50</sub> nM |
|                                                                                                                                                           |  | REP-2139  | 339                 | >10000              | 343                 | >10000              |
|                                                                                                                                                           |  | ALG-10000 | 4.2                 | >1000               | 3.9                 | 200                 |
|                                                                                                                                                           |  | ALG-10133 | 3.2                 | >1000               | 3.9                 | >1000               |
|                                                                                                                                                           |  | ALG-10093 | 2.1                 | >1000               | 2.5                 | >1000               |
|                                                                                                                                                           |  | ALG-10128 | 37                  | >1000               | 21                  | >1000               |
|                                                                                                                                                           |  | ALG-10129 | 45                  | >1000               | 32                  | >1000               |
|                                                                                                                                                           |  | ALG-10048 | 17                  | >1000               | 23                  | >1000               |
| <span>★</span>                                                                                                                                            |  | ALG-10122 | 23                  | >1000               | 12                  | >1000               |
| <span>★</span>                                                                                                                                            |  | ALG-10125 | 25                  | >1000               | 79                  | >1000               |

# ALG-010133 Demonstrates >100-fold Potency vs. Reference

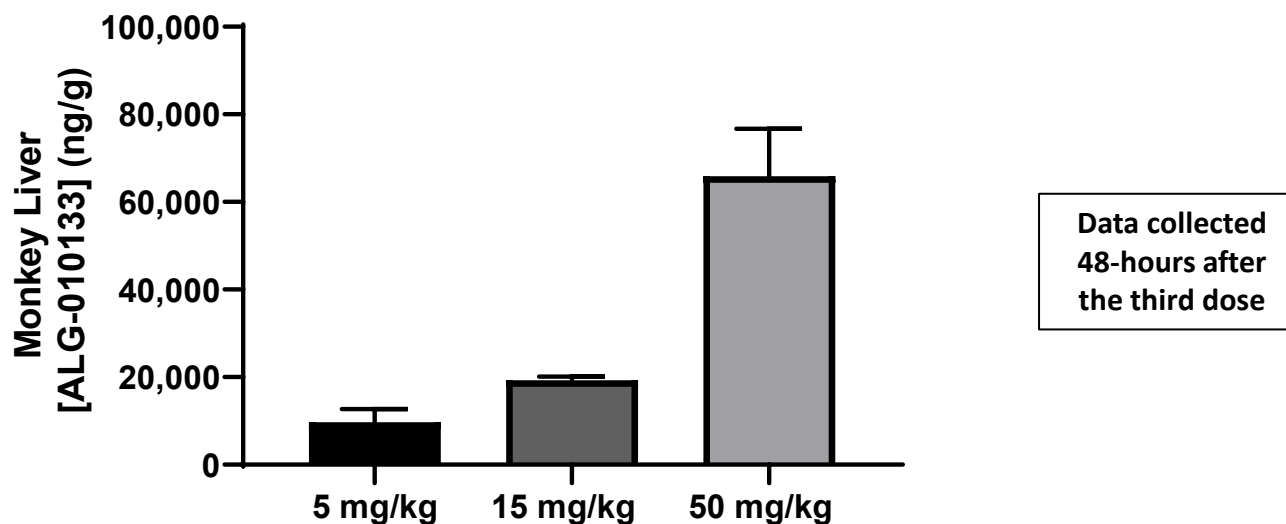


|                          | Structure                                              | PBMC Activation | Live HBV / HepG2-NTCP |                     | HepG2.2.15          |                     |
|--------------------------|--------------------------------------------------------|-----------------|-----------------------|---------------------|---------------------|---------------------|
|                          |                                                        |                 | EC <sub>50</sub> nM   | CC <sub>50</sub> nM | EC <sub>50</sub> nM | CC <sub>50</sub> nM |
| REP 2139<br>(Reference)* | (AC) <sub>20</sub><br>[2'-OMe-A, 2'-OMe-5-MeC, all PS] | +               | 339                   | >10000              | 343                 | >10000              |
| ALG-010133               | Aligos STOP™                                           | -               | 3.2                   | >1000               | 3.9                 | >1000               |

# ALG-010133: NHP Multiple Dose Exposure in Liver

## Supports Weekly Subcutaneous Delivery

- Much higher liver exposure observed for SC compared to IV dosing in NHPs
- High and dose proportional exposure in liver following three weekly SC doses



**Projected human efficacious dose: 30-75 mg delivered SC, weekly**

# Aligos STOPS Summary

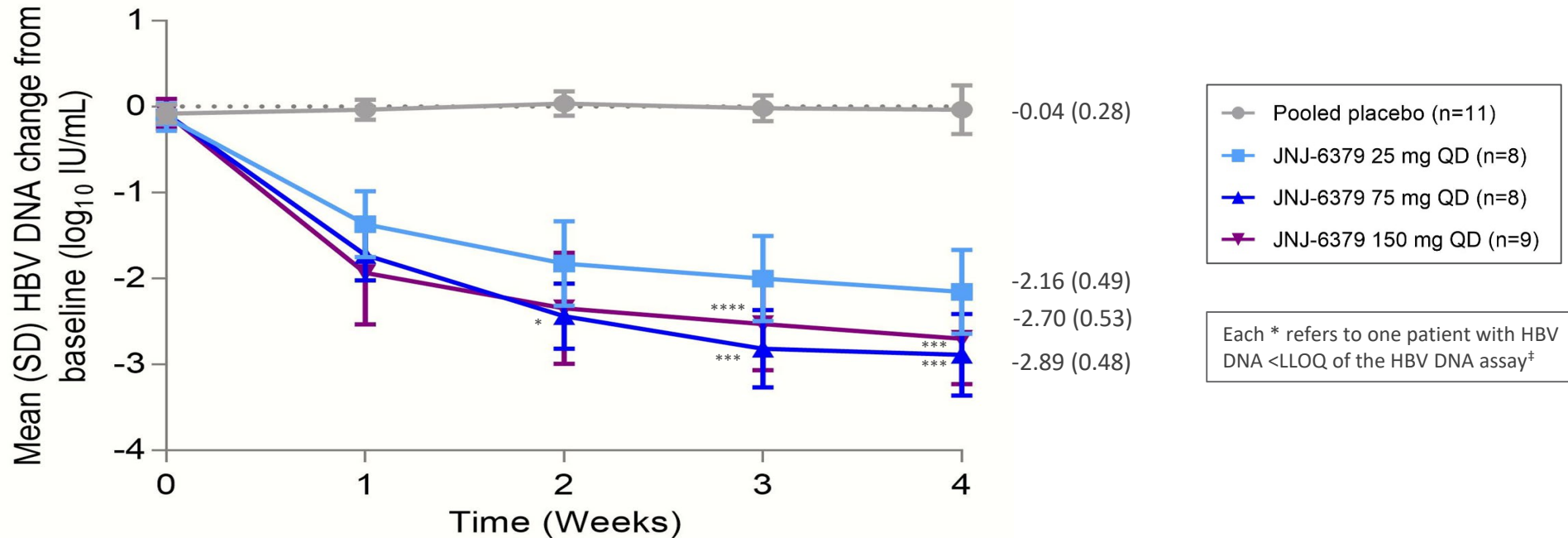
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- Chemistry of STOPS has been thoroughly explored
- Multiple proprietary STOPS with 10-200-fold enhanced *in vitro* potency over REP-2139 in several HBV cell models identified
- ALG-010133 has been selected as the lead candidate
  - Scale-up completed to enable initiation of toxicology studies
  - GLP studies commenced in Q1 2020 enabling mid-2020 clinical start
- Clinical Trial Application (CTA) will be submitted mid-June
  - On target to begin clinical trials in August 2020 – New Zealand

# Capsid Assembly Modulators (CAMs)

# CAMs Have Demonstrated Clinical Anti-HBV Activity

## JNJ-6379 Phase 1b Data in HBV-infected Individuals



- Unlike nucleoside analogues, drops in HBV RNA were also observed
- No relevant changes in HBsAg or HBeAg<sup>§</sup> were observed with any of the doses studied

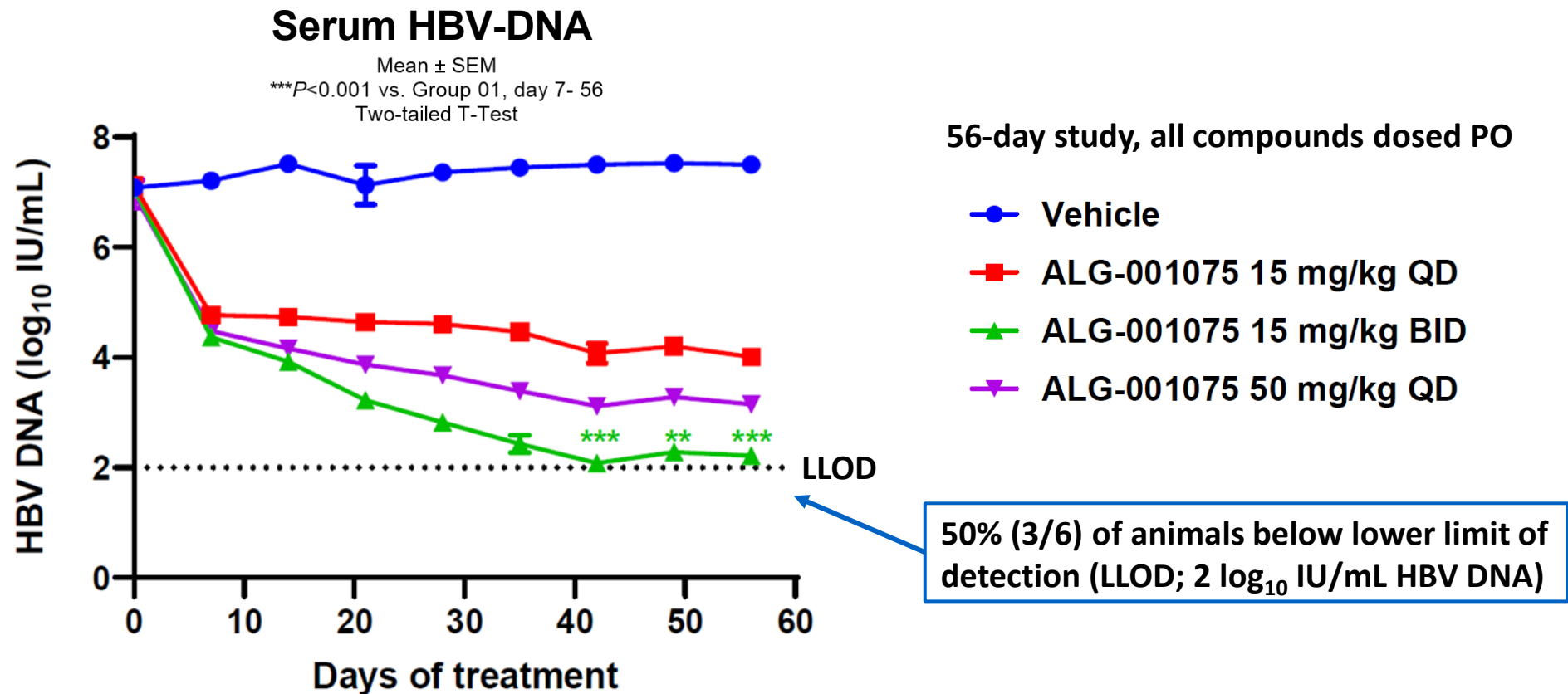
# Aligos Class-II CAMs Demonstrate Best-In-Class Potency

| Compound                                                          | Janssen<br>JNJ-6379 | Assembly<br>ABI-H0731 | Arbutus*<br>AB-423 | Janssen<br>JNJ-0440 | Assembly<br>ABI-H2158 | Arbutus*<br>AB-506 | Enanta<br>EDP-514 | Assembly<br>ABI-H3733 | ALG-001075<br>(Advancing<br>as prodrug<br>ALG-000184) |
|-------------------------------------------------------------------|---------------------|-----------------------|--------------------|---------------------|-----------------------|--------------------|-------------------|-----------------------|-------------------------------------------------------|
| Current Status                                                    | Phase 2a            | Phase 2a              | Completed Phase 1  | Completed Phase 1   | Phase 1               | Phase 1            | Phase 1           | Phase 1               | Preclinical                                           |
| **EC <sub>50</sub> for HBV DNA reduction in Cell Based Assay (nM) | 54                  | 172                   | 146                | 12                  | 22                    | 40                 | 18                | 5                     | 0.63***                                               |
| Cell Type                                                         | HepG2.117           | AD38                  | HepG2.117          | HepG2.117           | AD38                  | HepG2.2.15         | HepG2.2.15        | AD38                  | HepG2.117                                             |

Balancing Superior Potency with DMPK Properties to Deliver a Best in Class Candidate Development

# ALG-001075

## 5-Log<sub>10</sub> IU/mL Drop in HBV DNA in the AAV-HBV Mouse Model



- Dose dependent reduction in HBV DNA observed in all treatment groups
- No changes in HBsAg levels noted
- No significant changes in body weight

# Aligos Capsid Assembly Modulator Summary

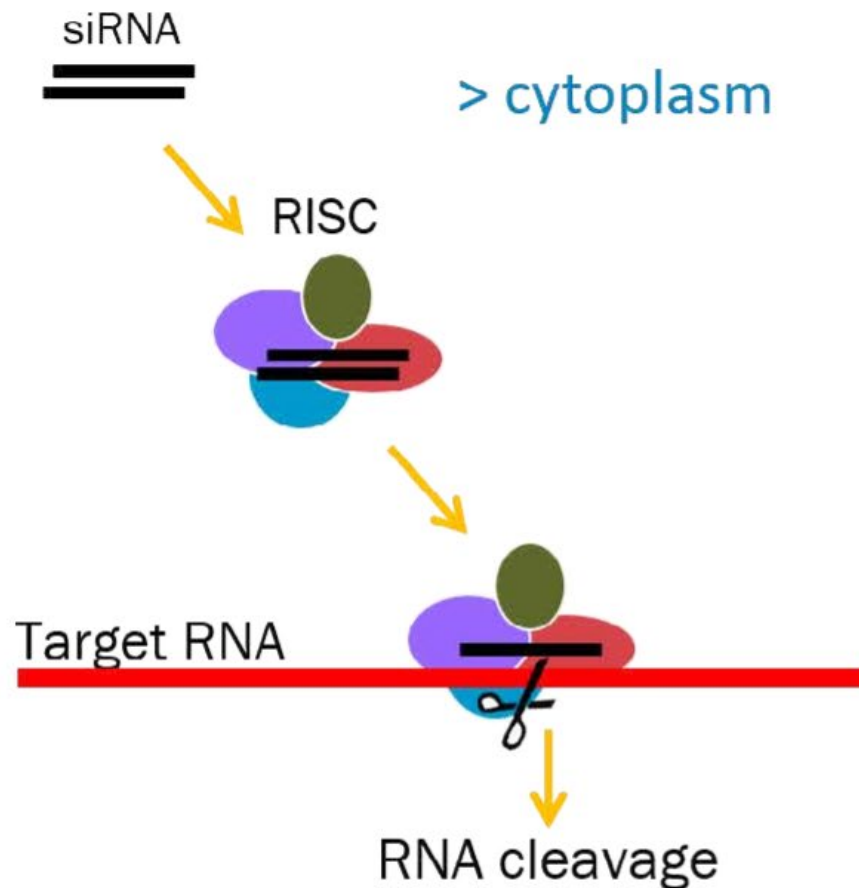
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- ALG-000184, a prodrug of ALG-001075, selected as lead candidate
  - Dose range finding studies completed in rat and dog with ALG-000184
  - GLP toxicology studies to support first in human studies are ongoing
  - Regulatory filing planned Q3 2020
    - › On-track to begin clinical studies October 2020 in New Zealand
- Additional novel series are in lead optimization

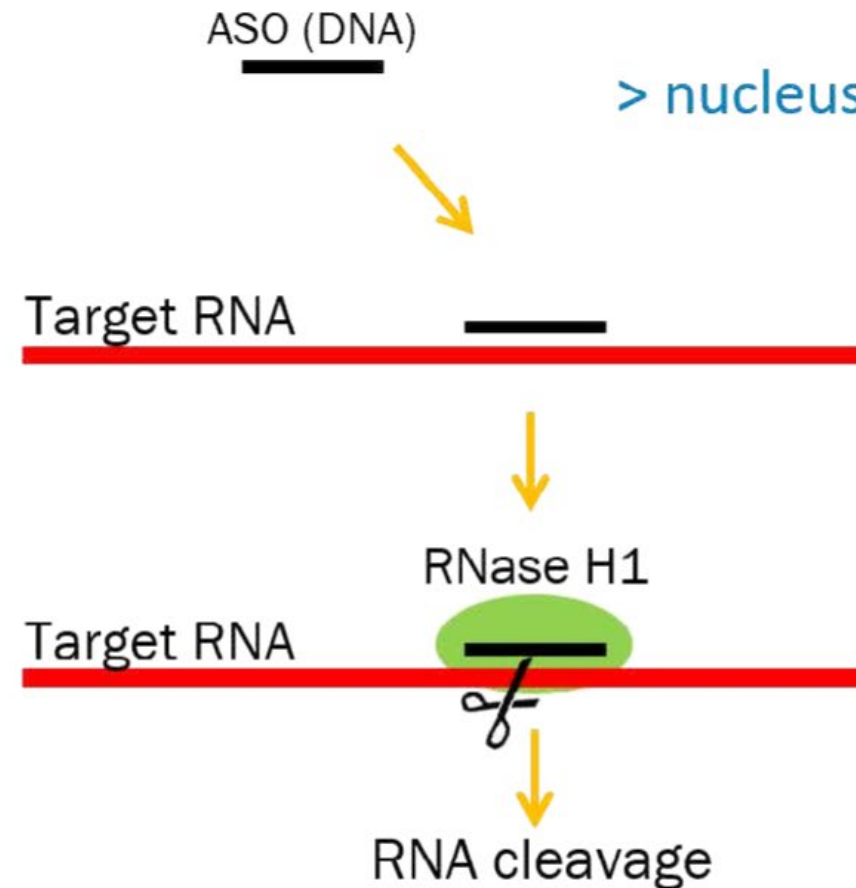
# Antisense Oligonucleotides (ASO)

# Small-Interfering RNAs vs. Antisense Oligonucleotides

## RNA interference (RNAi)



## Antisense oligonucleotides (ASOs)



# Aligos' Unique Two-Trigger ASO Strategy for CHB

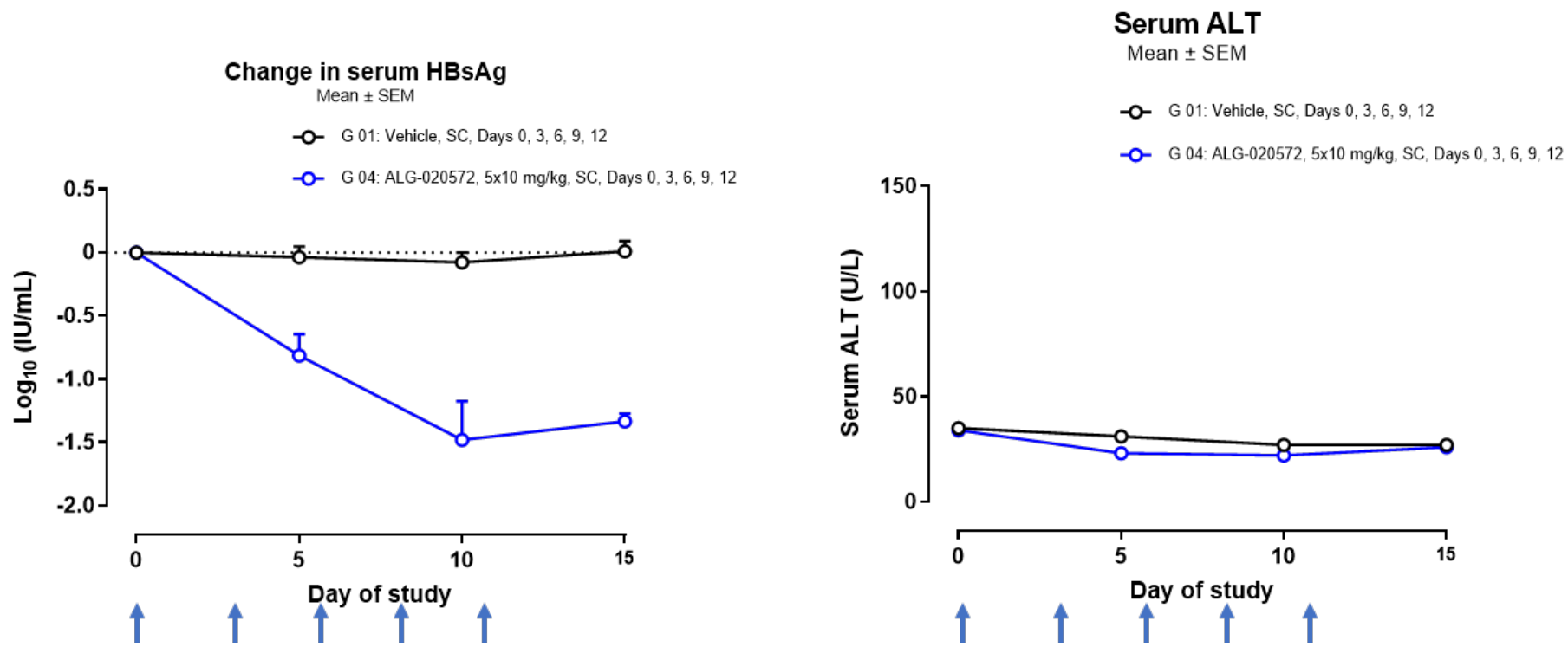
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- **Single-trigger:** Roche, GSK (Ionis), Dicerna, Vir (Alnylam), Arbutus
- **Two-trigger:** Aligos' ASO strategy uses both S and X triggers
  - Benefits of the two-trigger strategy
    - › Increased resistance barrier, better coverage of genotypes & integrated genomes
    - › X trigger: High homology, more potent, close to high integration region
    - › S trigger: Good sites for targeting integrated HBV
    - › Potential for synergy using the two-triggers in combination
  - Bioinformatics conducted using latest available data (>8,000 sequences)

# ALG-020572 Selected as S-trigger Candidate

## AAV-HBV Mouse Model: Excellent Efficacy without ALT Elevation

| Genotype   | A   | B    | C   | D    | E    | F    | G    | H    | I    | J    |
|------------|-----|------|-----|------|------|------|------|------|------|------|
| % Homology | 98% | 100% | 99% | 100% | 100% | 100% | 100% | 100% | 100% | 100% |

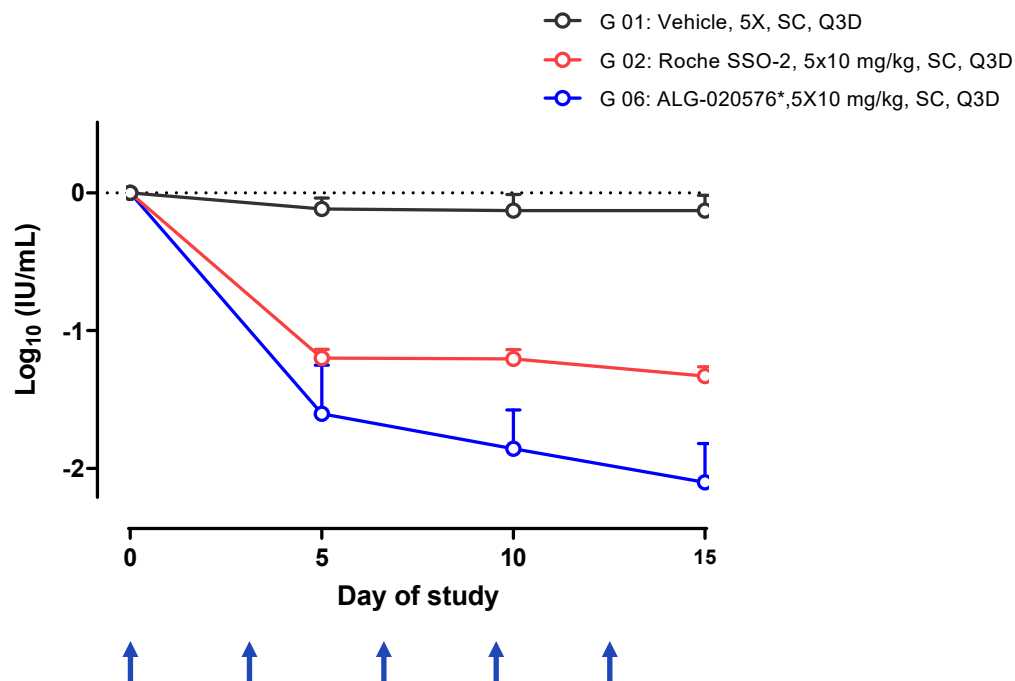


# ALG-020576 Selected as X-trigger Candidate

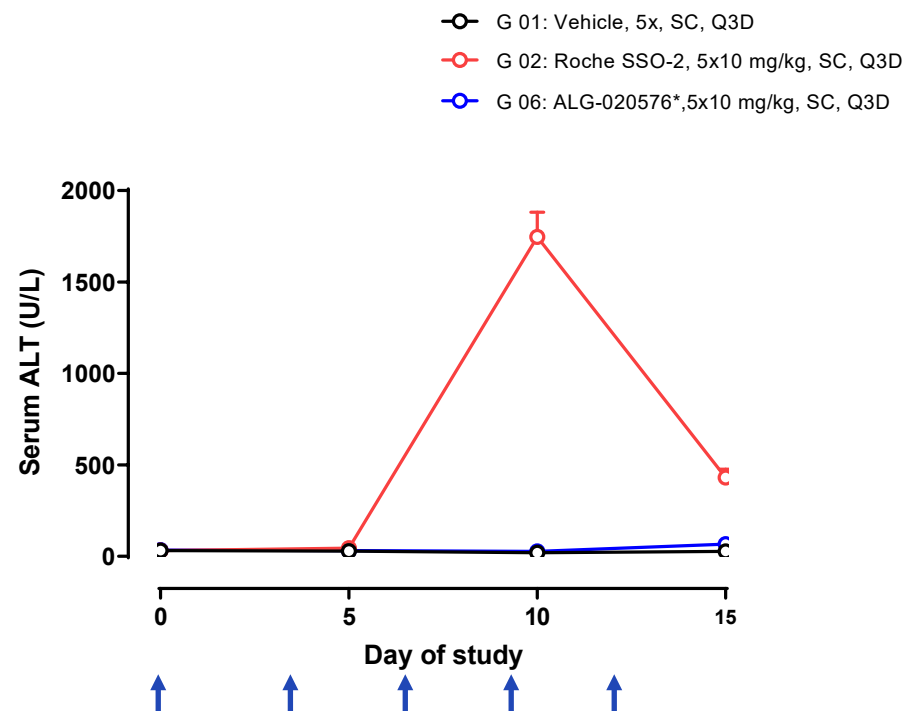
## AAV-HBV Mouse Model: Excellent Efficacy without ALT Elevation

| Genotype   | A   | B    | C   | D    | E   | F    | G   | H    | I    | J   |
|------------|-----|------|-----|------|-----|------|-----|------|------|-----|
| % Homology | 99% | 100% | 99% | 100% | 96% | 100% | 99% | 100% | 100% | 97% |

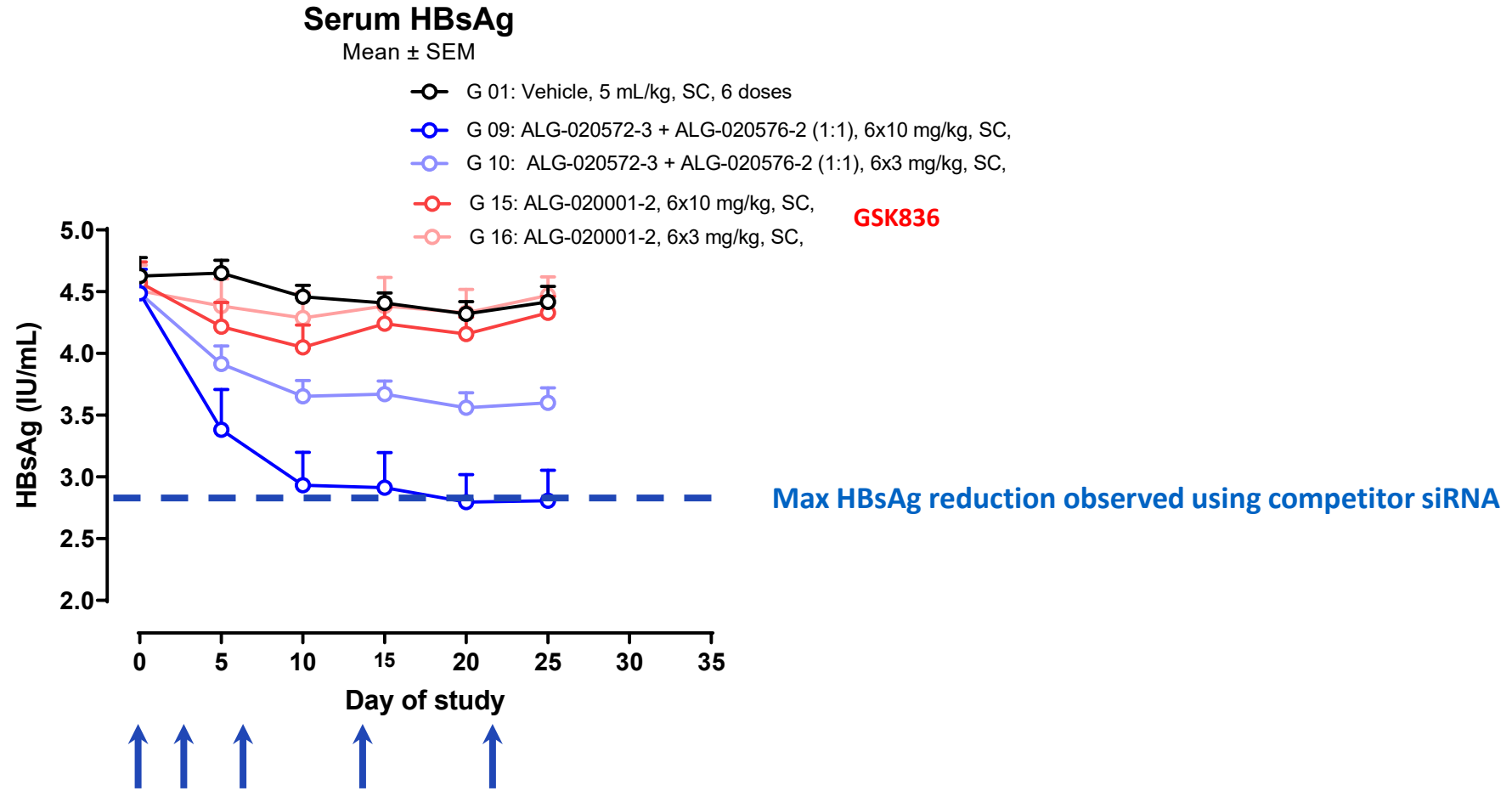
**Change in HBsAg**  
Mean ± SEM



**Serum ALT**  
Mean ± SEM



# ALG-020572 (S) and ALG-020576 (X) in 1:1 Combination Demonstrated Enhanced Potency over GSK836



# Aligos Antisense Oligonucleotide Summary

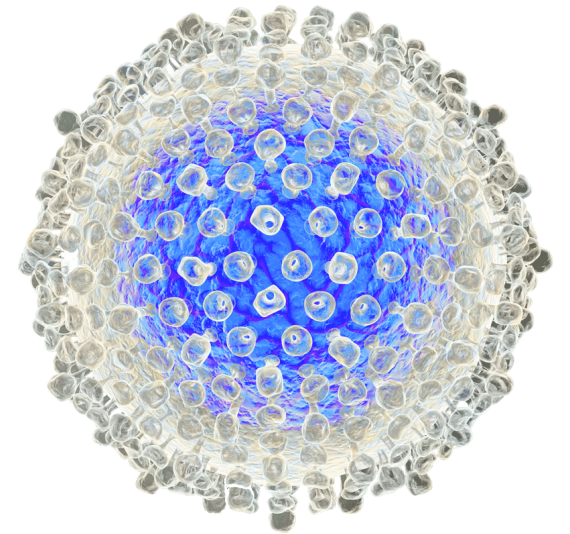
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- Aligos is pursuing a two-trigger ASO strategy
  - Bioinformatics applied using >8000 available HBV sequences
  - Two triggers provide a higher resistance barrier and better genome coverage
- X and S triggers selected, ALG-020572 and ALG-020576
  - These incorporate proprietary chemistries for IP, safety and liver targeting
  - 1:1 combination demonstrates best-in-class potency with no ALT elevation
- Currently advancing through dose range finding toxicology studies
  - GLP toxicology studies scheduled for Q3 2020
  - Planned GMP synthesis will enable Q2 2021 clinical entry

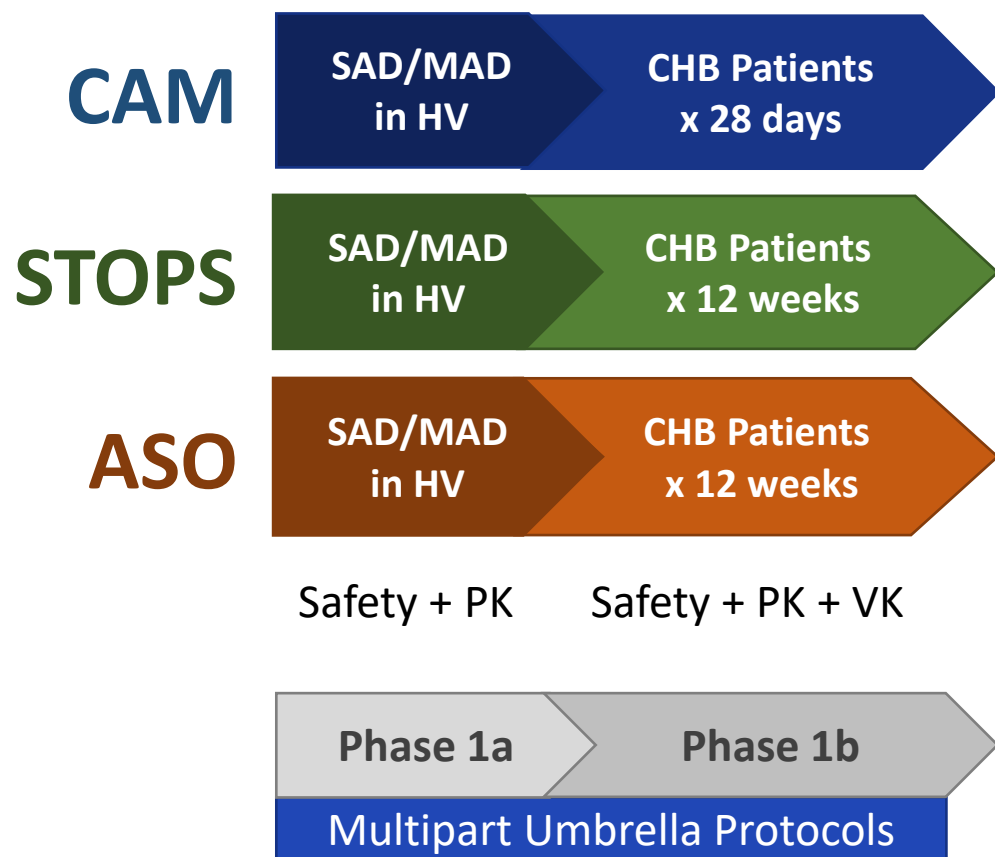
# Hepatitis B Virus

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Clinical Development Combination Strategy



# Value Creation in Phase 1 - Establish POC in Monotherapy



- Phase 1 studies (monotherapy)
  - Establish safety
  - Determine dose and schedule

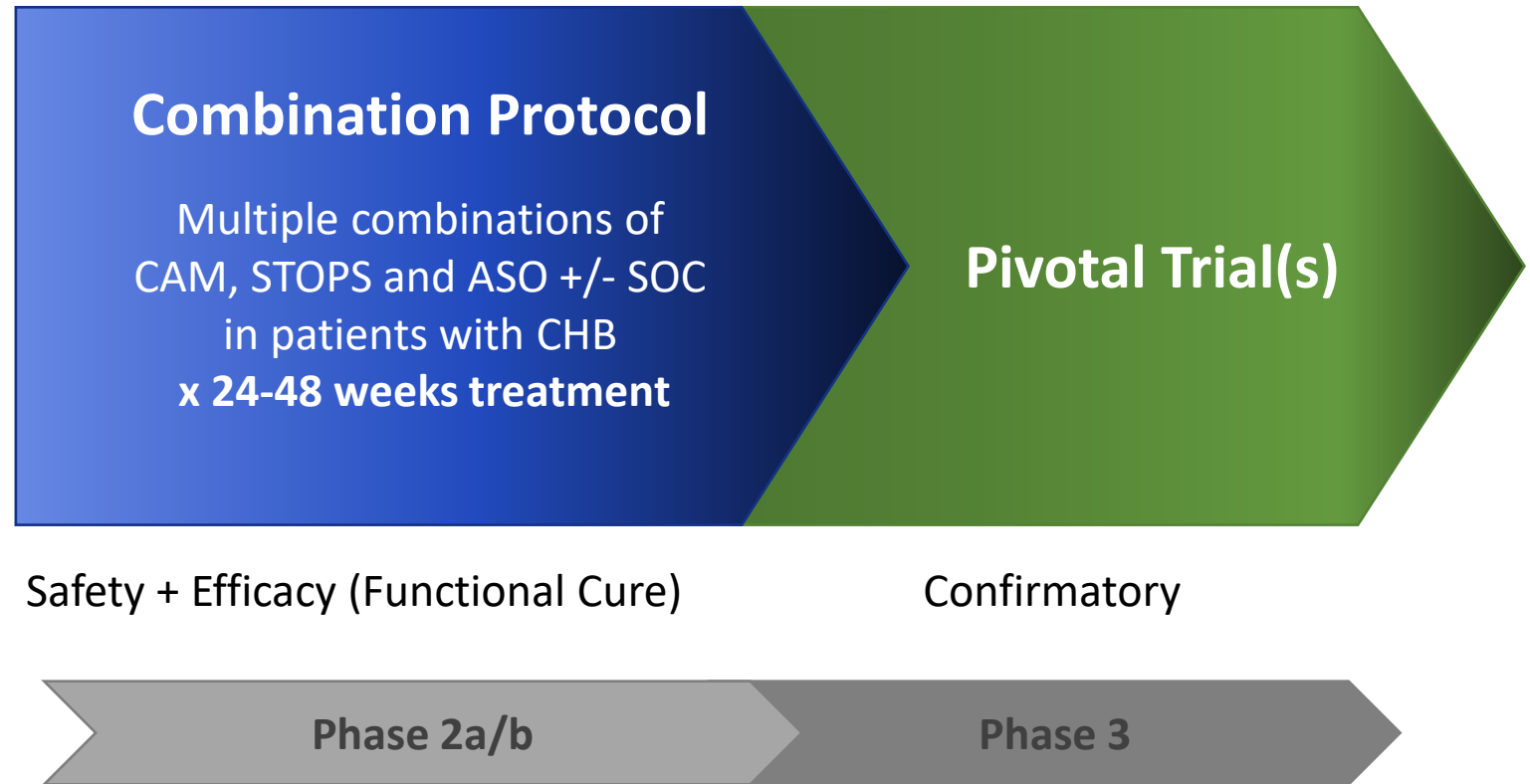
- CAM
  - HBV DNA and RNA reductions

- STOPS
  - HBsAg and DNA reductions emergence of anti-HBsAg antibodies

- ASO
  - HBV DNA, HBV RNA and HBsAg reductions

# Phase 2 and Phase 3 - Establish Value of Combinations

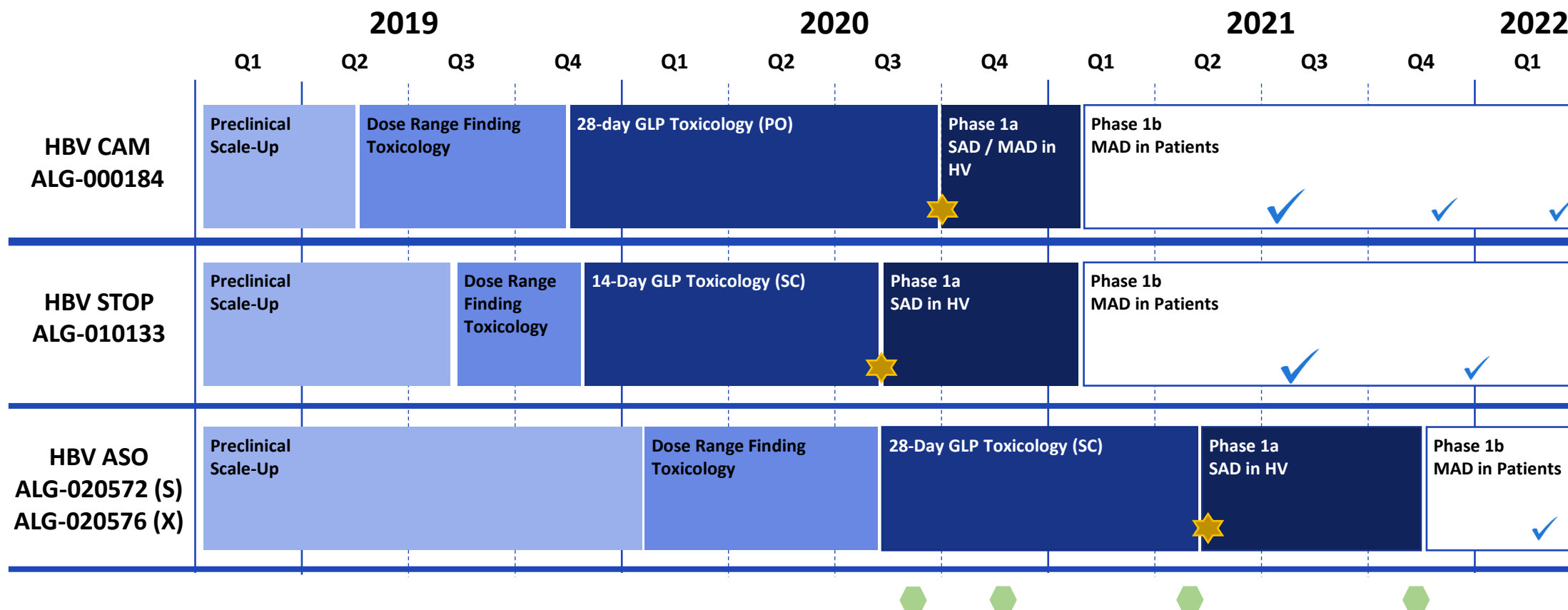
- Unique ability to explore multiple validated agents in combination therapy
- Achievement of functional cure
- Establishment of a best-in-class therapy



Combination therapy proven essential for establishing efficacious antiviral treatments – lessons from HIV, HCV

# Aligos Clinical Development Pipeline

-  CTA Approval
-  POE & POC Data Readouts
-  Conference Presentations



## Notes:

April Conference – EASL (moved 2020 to August)

November Conference – AASLD

# Aligos Therapeutics Summary

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- Assembled a world-class team with a proven track record of success
- Substantial Angel, Series A and B funding completed
- License agreement with Emory University for HBV lead asset executed
- License agreement executed for 3rd generation oligonucleotide chemistry
- Research programs in HBV, Coronavirus, NASH and Oncology ongoing
- 3 lead clinical candidates selected, GLP toxicology programs advancing
- 2 HBV compounds with clinically-validated MOAs to be advanced into clinical development in 2020
  - Enabling the development of a fully-owned combination therapy
  - 3rd compound to advance in early 2021

# ALIGOS

THERAPEUTICS

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