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### ALIGOS

#### Aligos Development Portfolio Multiple Milestones/Data Readouts Anticipated in 2023

THERAPEUTICS



All timelines are approximate and subject to change based on enrollment and operational considerations. Presentations at conferences are subject to abstract approvals.

\*Partly funded by the NIH and NIAID's AVIDD Centers for Pathogens of Pandemic Concern program through the MAVDA consortium.

AASLD = American Association for the Study of Liver Diseases; APASL = Asian Pacific Association for the Study of the Liver; CAM-E = capsid assembly modulator (empty); CHB = chronic hepatitis B; Covid-19 = coronavirus disease of 2019 (SARS-CoV-2); CTA = clinical trial application; EASL = European Association for the Study of the Liver; GLP = good laboratory practice; HV = healthy volunteers; MAD = multiple ascending doses; MOA = mechanism of action; NASH = nonalcoholic steatohepatitis; PK = Pharmacokinetics; SAD = single ascending doses; siRNA = small interfering ribonucleic acid (RNAi); THR-β = thyroid hormone receptor beta.



# NASH

• ALG-055009, small molecule THR-β agonist



#### Thyroid Hormone Receptors Alpha and Beta





Thyroid hormone receptor alpha (THR-α)

Heart, skeletal muscle

#### **Negative effects**

- Increase cardiac work
- Heart rate elevation
- Effects on bone/cartilage

THR-β agonists enhance hepatic metabolic activity, including reducing plasma and liver lipid levels Bone, cartilage and heart toxicity is believed to be THR-α related

### ALIGOS

#### **ALG-055009** More Potent and Selective In Vitro than Resmetirom and VK-2809

#### Relative THR- $\alpha$ and THR- $\beta$ Activity in Cell-Based Assays

	EC <sub>50</sub> α (nM)	EC <sub>50</sub> β (nM)	Relative THR-β Selectivity (α/β)
ALG-055009	191	50	3.8
Resmetirom	5927	2366	2.5
VK-2809 Parent	366	269	1.4
Т3	14.2	11.6	1.2

In vitro, ALG-055009 is ~47x more potent compared to resmetirom and 2-3x more selective for THR-β than VK-2809\*

High  $\beta$  selectivity and potency may improve risk-benefit profile



#### **ALG-055009** Best In Class Potential vs. 1<sup>st</sup> Generation THR-β Agonists

Parameter		ALG-055009	Resmetirom	VK-2809
<b>-ff</b> :	Lipid lowering in DIO mouse model*	$\checkmark$	$\checkmark$	$\checkmark$
Efficacy	>70% of patients with >30% change from baseline in MRI-PDFF in Phase 2	TBD (2024)	X	✓
	Linear PK (Human)	$\checkmark$	X	$\checkmark$
РК	Low risk of DDI (CYP450)*	$\checkmark$	X	X
	Low risk of DDI (Transporters)	$\checkmark$	X	?
	Enhanced selectivity for THR- $\beta$ vs. THR- $\alpha^*$	$\checkmark$	$\checkmark$	X
Safety	Low potential for cardio-safety liability	$\checkmark$	✓	X
	Lack of reactive metabolites/low DILI risk*	$\checkmark$	$\checkmark$	X
	No potential prodrug safety liability	$\checkmark$	$\checkmark$	X

#### Potential for enhanced efficacy vs. resmetirom and enhanced efficacy/safety vs. VK-2809



Abbreviations: CYP = cytochrome P450; DDI = drug drug interaction; DILI = drug induced liver injury; DIO = diet induced obesity; MRI-PDFF = magnetic resonance imaging – proton density fat fraction; PK = pharmacokinetics; TBD = to be determined; THR = thyroid hormone receptor. \*Competitor data derived from in-house studies, except Erion et al., PNAS 2007 for VK-2809 mouse model.



# Analysis of Competitor Data



#### PK (Day 14) Data Resmetirom vs. VK-2809

THERAPEUTICS



#### Phase 2 MRI-PDFF Data Resmetirom vs. VK-2809

MRI-PDFF Parameter (Week 12)	Phase 2 Data						
	Resmetirom (80 mg)			VK-2809 (1-10 mg)			
	Placebo (N=38)	Low Exposure (N=34)	High Exposure (N=44)	Resmetirom Overall (N=78)	Placebo (N=62)	2.5 mg QD (N=58)	10 mg QOD (N=56)
% Change from Baseline	-10%	-24%	-40%	-36%	-5%	-48%	-52%
% of Subjects with ≥30% Fat Reductions	18%	41%	75%	60%	14%	78%	85%

Improved PK of VK-2809 associated with enhanced MRI-PDFF reductions vs. resmetirom



#### **Resmetirom Phase 2 Data** Liver Biopsy



MRI-PDFF de-fatting correlates with histologic improvement



#### Hypothetical Impact of PK Variability on Efficacy and Safety



Two drugs with same mean could have different risk-benefit profiles due to different PK profiles



Part 1: Single Ascending Dose (SAD)	Part 2: Multiple Ascending Dose (MAD) – Dosing PO QD X 14 days	Part 3: Relative Bioavailability, Food Effect (Gel Cap)
N = up to 64 Healthy Volunteers	N = up to 80 Subjects with Hyperlipidemia	<u></u>
N = 8 per Cohort, N = 6 ALG-055009 and N = 2 Placebo	N = 10 per Cohort, N = 8 ALG-055009 and N = 2 Placebo	N = 10 Healthy Volunteers





#### Study ALG-055009-301 Part 1: Single Ascending Dose - PK, Safety, Biomarkers

Oral doses evaluated: 0.1, 0.3, 0.9, 2.6, 4.0 mg

- Dose proportional, with low variability
- $t_{1/2} = 20-24$  hours (supports once daily (QD) dosing)
- Safety: well tolerated
  - No serious adverse events (SAEs), Grade ≥3 treatment emergent adverse events (TEAEs), or clinical hyper/hypothyroidism
- Biomarkers
  - Expected thyromimetic effects observed



Single (≤4 mg) ALG-055009 doses well tolerated with favorable PK properties



<sup>•</sup> PK

### Study ALG-055009-301 Part 2: Multiple Ascending Dose - PK, Safety

- Oral doses evaluated: 0.3, 0.5, 0.6, and 1.0 mg QD x 14 days
- PK: favorable profile (dose-proportional, low variability (≤27%), 2x accumulation)
- Safety: well tolerated, no clinical evidence of hypo or hyperthyroidism
  - No SAEs, discontinuations
  - All TEAEs Grade ≤2
  - No concerning labs, ECGs, vital signs, physical examinations



Multiple doses (≤1 mg) well tolerated with favorable PK



#### Multiple Ascending Dose - Biomarkers Part 2: Expected Thyromimetic Effects Observed



Dose proportional increases in SHBG



#### Multiple Ascending Dose - Biomarkers Part 2: Expected Thyromimetic Effects Observed



Dose responsive reductions in lipids (e.g., LDL, Apo-B, Triglycerides)



#### Formulation / Food Effect Part 3: PK Data Comparison in Healthy Volunteers at 0.6 mg



Gel cap vs. liquid formulation: similar PK with low variability, no food effect Phase 2 formulation (gel cap) confirmed



### ALG-055009 Preliminary Phase 2 Study Design



- Population: Adults subjects with NASH and liver fibrosis
- <u>Primary endpoint:</u> Relative change in liver fat content by MRI-PDFF at Week 12

Filing Q4 2023 Topline data Q4 2024



### ALG-055009 Summary

- Discovered by Aligos issued US patent expires 2040
- More  $\beta$ -selective, >50 fold more potent than resmetirom
- Phase 1
  - Safety well tolerated without clinical safety signals
  - PK favorable profile (linear, low variability) that is differentiated vs. resmetirom
    - More uniform exposures may lead to more consistent efficacy and safety
  - Biomarkers generally dose proportional
    - Increases in SHBG
    - Decreases in lipids
  - Formulation gel cap developed
    - > Similar PK to liquid formulation, no food effect noted
- Phase 2 preparation ongoing
  - IND filing Q4 2023
  - Topline data Q4 2024

ALG-055009 is differentiated vs. resmetirom and VK-2809, which may improve risk-benefit profile Ph2 filing planned in Q4 2023





## Coronavirus

• ALG-097558 (CoV Protease Inhibitor)



#### ALG-097558 Aligos' Potent COVID-19 Protease Inhibitor

- Despite the availability of prophylactic vaccines, a need for therapeutics still exists
  - New variants are continuously emerging
  - Large segments of global population lack access to, or are opposed to, vaccination
  - Especially needed to prevent hospitalization in high-risk groups where standard of care is contraindicated
- Current therapeutics lack sufficient efficacy (molnupiravir, Merck), require ritonavir boosting (nirmatrelvir, Pfizer) or are delivered parenterally (remdesivir, Gilead; mAbs)
- In collaboration with KU Leuven/Rega Institute/CD3, we have identified ALG-097558
  - 6-27 times more potent than nirmatrelvir in both biochemical and cell-based assays
  - Can be dosed orally without the need for ritonavir
  - Broadly active against a diverse range of coronaviruses with a high barrier to resistance
  - Can be combined to prevent emergence of resistance and provide broader strain coverage

ALG-097558 is a potent pan-coronavirus protease inhibitor that does not require ritonavir boosting



#### ALG-097558 Best In Class Potential vs. other Oral Protease Inhibitors

	Parameters	Aligos ALG-097558 (preclinical)	Pfizer Nirmatrelvir/RTV (authorized – global)	Shionogi Ensitrelvir (authorized – Japan)	Sorrento Olgotrelvir (Phase 3)	Enanta EDP-235 (Phase 2)
	SARS-CoV-2 variants/subvariants*	✓	✓	✓	✓	✓
Antiviral Activity	Pan-coronavirus <sup>*</sup>	✓	✓	X	?	✓
	Favorable resistance profile vs nirmaltrevir*	✓		X	?	?
PK	No need for ritonavir (RTV)	✓	X	✓	$\checkmark$	✓
	Favorable DDI profile (CYP450) vs nirmaltrevir/RTV <sup>^</sup>	✓		X	?	X
	Favorable DDI profile (Transporters) vs nirmaltrevir/RTV <sup>^</sup>	✓		X	?	X
	No food effect	TBD	✓	✓	X	X
Safety	No teratogenicity	TBD	✓	X	?	?
	Low DILI risk	✓	$\checkmark$	$\checkmark$	<b>X</b> #	<b>X</b> #

#### Potential for enhanced antiviral activity and less DDI, DILI risk vs. frontrunner PIs



\*Competitor data in-house except for EDP-235 and olgotrelvir (per report). ^DDI data for competitors based on ct.gov (EDP-235), PMDA review report (ensitrelvir), EMA assessment report (nirmatrelvir). #Grade 3 (EDP-235) and Grade 2 (Olgotrelvir) ALT elevations noted in Ph1 studies.

#### ALG-097558 Superior Cell-Based Potency Against SARS-CoV-2 and Variants

Viruo	Variant/Cell line	EC <sub>50</sub> (μΜ)				
VIIUS		PBI-0451	Ensitrelvir	Nirmatrelvir	ALG-097558	
	03021/2020 <sup>1</sup>	n.d.	n.d.	0.114	0.012	
	B.1.1.7 (alpha) <sup>2</sup>	0.038	0.022	0.106	0.011	
SARS-CoV-2	B.1.617.2 (delta) <sup>2</sup>	0.126	0.141	0.217	0.013	
	B.1.1.529 (omicron) <sup>1</sup>	0.152	0.123	0.069	0.008	
	BA.2 <sup>1</sup>	0.137	0.035	0.045	0.007	
	BA.5 <sup>1</sup>	0.215	0.119	0.089	0.013	
SARS-CoV-1 <sup>1</sup>		0.323	0.154	0.173	0.022	
MERS-CoV <sup>1</sup>		>0.1	0.1	0.025	0.005	
OC43 (β-hCoV) <sup>3</sup>		0.168	0.135	0.047	0.009	
229E (α-hCoV) <sup>4</sup>		0.281	6.30	0.476	0.017	

Bioinformatics predicts retained activity against BA.2.12.1, BA.3, BA.4, BQ.1, BQ1.1, BF.1

ALG-097558 demonstrates pan-coronavirus antiviral activity ALG-097558 is more active than nirmatrelvir, PBI-0451 and ensitrelvir across all CoV's tested



#### ALG-097558 Phase 1 Safety, PK Study in HVs



Topline data anticipated H1 2024



### ALG-097558 Coronavirus Protease Inhibitor Drug Candidate

- Potent pan-coronavirus protease inhibitor drug candidate
  - Additional candidates from the series advancing as backup compounds
- Superior preclinical profile versus nirmatrelvir (Pfizer)
  - 6-27 fold more potent in biochemical and cell-based assays vs. SARS-CoV-2
    - > 7-fold more potent vs. the omicron variant (cell-based assay)
  - Greater cellular potency across other coronavirus strains
  - Retains activity against resistant variants
  - Excellent efficacy in the SARS-CoV-2 hamster model
- Potential for more convenient, less complex treatment regimen
  - Preclinical PK profile predicts a projected human efficacious dose of 240-380 mg BID without ritonavir
  - DDI risk appears lower vs. competitor protease inhibitors
- Phase 1 HV dosing anticipated H2 2023 with topline data expected in H1 2024

ALG-097558 is a ritonavir-free, highly differentiated, pan-coronavirus protease inhibitor





# **Chronic Hepatitis B**



### ALG-000184 In Vitro Potency vs. Competitor Class-II CAMs

Compound	Current Status	HBV DNA reduction (EC <sub>50</sub> nM)	Cell Type
	Dhace 1	0.63	HepG2.117
Aligos ALG-000184	PlidSe I	0.53	HepG2.2.15
Vebicorvir	Discontinued	172	AD38
Assembly ABI-H3733	Discontinued	5	AD38
Janssen JNJ-6379	Discontinued	54	HepG2.117
Enanta EDP-514	Phase 1	17	HepG2.115
Arbutus AB-836	Discontinued	10	HepDE19

ALG-000184 has ~10 to 300-fold enhanced potency vs. other known CAMs Optimal liver exposures via pro-drug strategy



#### ALG-000184-201 Part 4 Cohort 2 (300 mg ALG-000184 + ETV x 48 Weeks)



Prior Cohort Data

Single, multiple doses in HV well tolerated with linear PK

Multiple doses (≤24 weeks) in CHB well tolerated with linear PK and dose responsive reductions in HBsAg, DNA, RNA



#### **300 mg ALG-000184 + ETV x 48 weeks, HBeAg+** HBV DNA Declines in Subjects Receiving ALG-000184 x ≥12 Weeks



N=7 dosed with 300 mg ALG-000184 + ETV x  $\geq$ 12 weeks At Week 24: subjects had  $\geq$ 6 log<sub>10</sub> IU/mL HBV DNA decline, 2 subjects were undetectable



#### **300 mg ALG-000184 + ETV x 48 weeks, HBeAg+** HBsAg Declines in Subjects Receiving ALG-000184 x ≥12 Weeks



#### <u>300 mg ALG-000184 + ETV</u>

Dosed ≥12 weeks (N=7): 6 of 7 subjects had decline of at least ~0.4 log<sub>10</sub> IU/mL Dosed ≥24 weeks (N=5): 4 of 5 subjects had decline of ≥1 log<sub>10</sub> IU/mL **Maximum observed decline: 1.65 log<sub>10</sub> IU/mL at Week 28** 



#### ALG-000184-201 - Part 4 Interim Data Superior Antiviral Activity with a Favorable Safety Profile

- Safety well tolerated
- Significant antiviral activity in HBeAg+ subjects in combination with ETV
  - Significant antiviral activity for ALG-000184 + ETV compared with ETV alone
  - 4/5 of subjects dosed x ≥24 weeks had HBsAg reductions of ≥1.0  $\log_{10}$  IU/mL
  - Maximum HBsAg reduction observed to date is 1.65 log<sub>10</sub> IU/mL in a subject dosed with 300 mg ALG-000184 + ETV x 28 weeks
- Longer dosing continues, and other cohorts (BID dosing) will further define the safety, PK, and antiviral activity of ALG-000184 ± ETV
- ALG-000184 appears to have best in class properties and may contribute to enhanced rates of functional cure in combination with
  - Novel antivirals and immunomodulators, including other oral drugs (e.g., oral PD-L1)

Additional available data will be presented at scientific conferences (EASL, AASLD) throughout 2023



#### **Executive Summary** Aligos Advancing Multiple Promising Drugs in Areas of Unmet Need

NASH

- ALG-055009, our THR-β small molecule agonist more uniform exposure vs. competitor THR-β drugs may lead to more consistent efficacy and safety
  - > Phase 2 filing planned Q4 2023 with topline data expected Q4 2024
- Additional oligonucleotide efforts (including Merck collaboration) are progressing
- Coronavirus Protease Inhibitor (ALG-097558)
  - Ph1 CTA filed, anticipate dosing in HV throughout H2 2023 with topline data in H1 2024
- CAM-E (ALG-000184) best in class reductions for HBsAg, HBV DNA and RNA
  - Phase 1b cohorts (≤48 weeks) are ongoing
- March 31, 2023: cash balance \$103.5M\*; fully diluted common shares: 53,834,551
- The Company continues to believe our cash balance provides sufficient cash to fund planned operations through the end of 2024

# ALIGOS THERAPEUTICS