

## FORWARD-LOOKING STATEMENTS

#### Safe-Harbor Statement

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# **COMPANY HIGHLIGHTS**



Proprietary intranasal vaccine platform ideally suited for rapid response to pandemics, including COVID-19



Developing next generation peptide therapeutics for liver disease



Near-term value-driving catalysts with sufficient cash and investments on hand



# STRONG EXECUTIVE MANAGEMENT TEAM



Vipin K. Garg, PhD President & CEO



Will Brown, CPA, MBA Chief Financial Officer



**Scott Harris, MD Chief Medical Officer** 



Scot Roberts, PhD Chief Scientific Officer



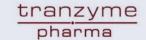
**Bertrand Georges, PhD** Chief Technology Officer



José Ochoa, JD **Chief Business Officer** 



























# ADVANCING STRONG DEVELOPMENT PIPELINE

PROGRAM	PRODUCT NAME	PRECLINICAL	PHASE 1	PHASE II	PHASE III	STATUS
INTRANASAL VACCINES	$AdCOVID^TM$	COVID-19				In Phase 1, data readout expected Q2 2021
	NasoShield <sup>TM</sup>	Anthrax		Funded by \$133.7M Pot		Phase 1b completed; ready for Phase 2
	NasoVAX <sup>TM</sup>	Seasonal & Pan	demic Influenza			Ready for Phase 2b
INTRANASAL THERAPEUTIC	T-COVID™	COVID-19			2 Trial Funded y DoD	In Phase 1/2, data readout expected Q2 2021
LIVER DISEASES	ALT-801	NASH				In Phase 1, data readout expected Q2 2021
	HepTcell <sup>TM</sup>	Chronic Hepatiti	s B			In Phase 2, data readout expected H1 2022



# ALTIMMUNE IS WELL POSITIONED TO ADVANCE MULTIPLE PRODUCT CANDIDATES





# STRONG INTELLECTUAL PROPERTY PORTFOLIO

SIGNIFICANT PATENT TERM REMAINING IN ALL FAMILIES

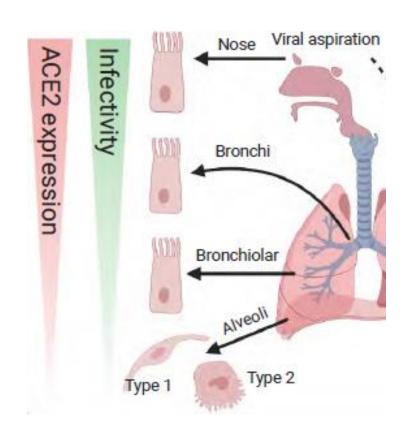
AdCOVID	Issued claims in EP, Prioritized review of pending US claims
NasoShield	Granted US, EP, JP patent Expiry ≥ 2032
NasoVAX	Granted US, EP, JP patent   Patent applications other territories Expiry $\geq 2032$
T-COVID	Prioritized review of pending US claims
ALT-801	2 Granted US patents   Patent applications other territories Expiry ≥ 2035
HepTcell	Granted US patent   Patent applications other territories Expiry ≥ 2033

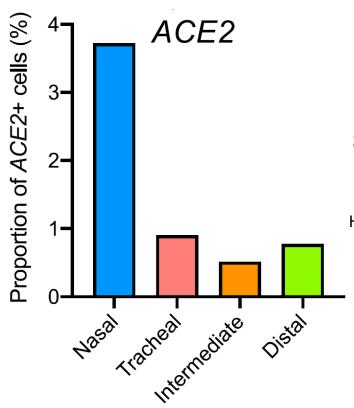




# AdCOVID: SINGLE-DOSE INTRANASAL VACCINE FOR COVID-19

#### MUCOSAL IMMUNITY TO BLOCK INFECTION AND TRANSMISSION IN NASAL CAVITY







"highest ACE2 expression in the nose...high SARS-CoV-2 infection in proximal airways vs distal airways"

Hou YJ, Cell 182, 429-446, 23 July 2020



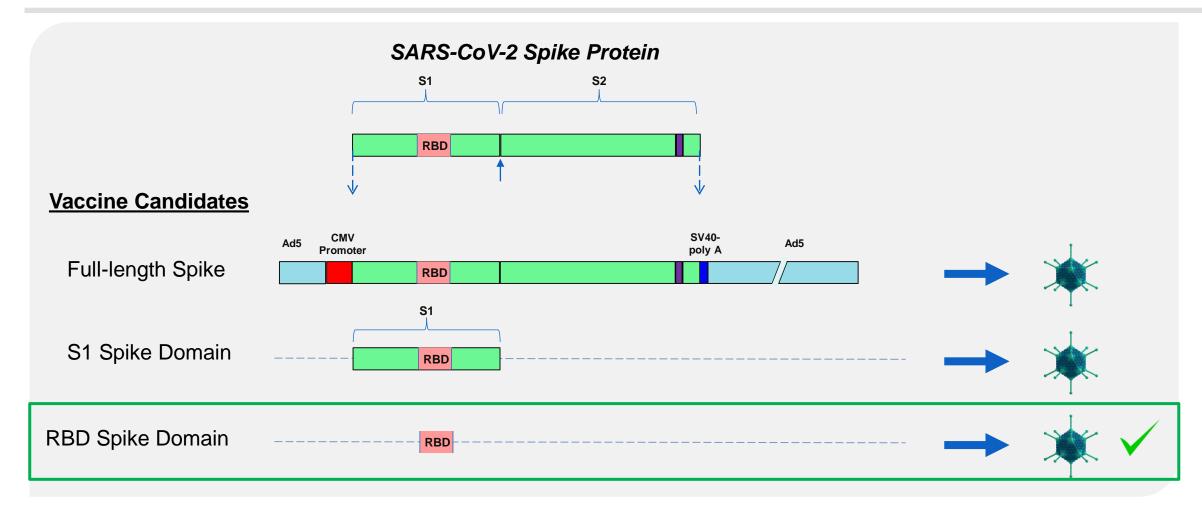
## AdCOVID: COMPELLING PRECLINICAL DATA

- Potent induction of multiple arms of the immune system
  - Systemic neutralizing antibody
  - Mucosal IgA response
  - Mucosal and systemic T cell responses
- Longevity of serum antibody responses
- Rapid recruitment of innate and adaptive immune cells into respiratory tract and draining lymph nodes consistent with induction of mucosal and systemic immunity
- Potent CD8+ T cell response in lung with resident memory phenotype



# AdCOVID: SINGLE-DOSE INTRANASAL VACCINE FOR COVID-19

VACCINE CANDIDATES BASED ON REPLICATION-DEFICIENT Ad5 PLATFORM





# AdCOVID: IMPROVING UPON CURRENTLY AUTHORIZED VACCINES

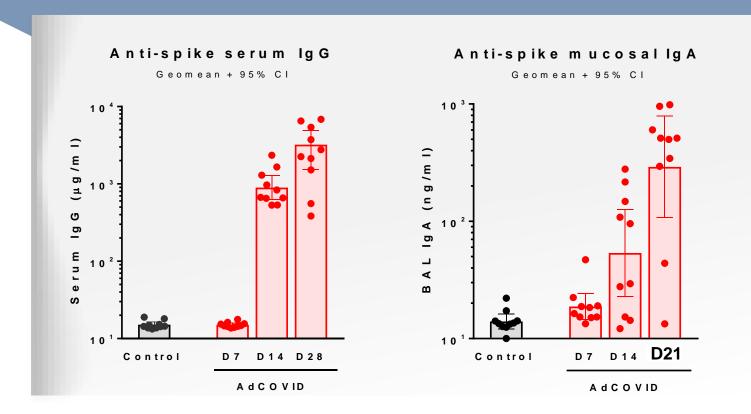
#### Greater ease and comfort of administration

- Single dose, simple nasal spray, <u>not</u> an intramuscular injection
- Broader immunity
  - Induces neutralizing antibody, T cells and <u>nasal mucosal immunity</u>
- Potential to block infection AND transmission
  - Stimulates mucosal immunity at the site of viral entry—the <u>nasal</u> cavity
- Room temperature stable for several months
  - Allows for distribution and deployment <u>without</u> refrigeration or ultra low-temp freezers
- Improved safety profile
  - <u>Indistinguishable</u> from placebo in Altimmune's clinically tested vaccine platform
- Durable antibody response
  - <u>13+ months of protective response</u> demonstrated by Altimmune's clinically tested vaccine platform



# AdCOVID: STIMULATION OF BOTH SERUM AND MUCOSAL ANTIBODIES

#### **Potent Antibody Responses in Serum and Respiratory Tract**



Single intranasal dose of AdCOVID

Anti-Spike IgG over 800 μg/mL IgG in serum by Day 14

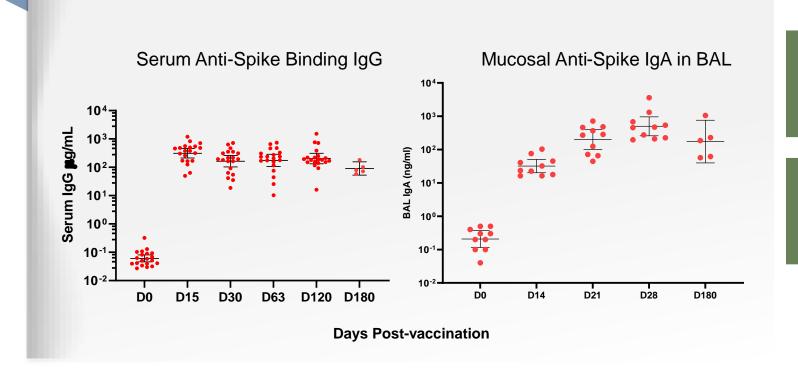
29-fold induction of mucosal IgA in the respiratory tract by Day 21



## AdCOVID: DURABLE SYSTEMIC AND MUCOSAL ANTIBODY RESPONSES

SERUM IgG AND MUCOSAL IgA TITERS MAINTAINED FOR AT LEAST 6 MONTHS

## Spike-specific serum IgG and respiratory IgA titers over time



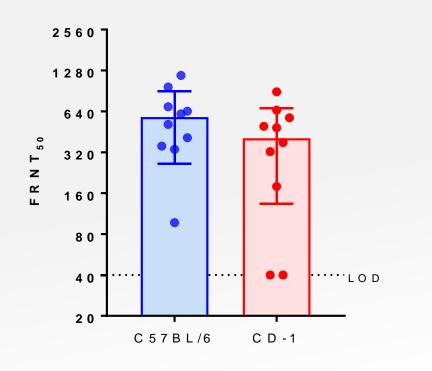
Single intranasal dose of AdCOVID

IgG measured in serum, IgA in bronchoalveolar lavages (BAL)



# AdCOVID: POTENT INDUCTION OF SERUM NEUTRALIZATION TITERS

#### **Mean Neutralizing Antibodies Against Wild-type SARS-CoV-2**



Single intranasal dose of AdCOVID

Consistent results in two strains of mice

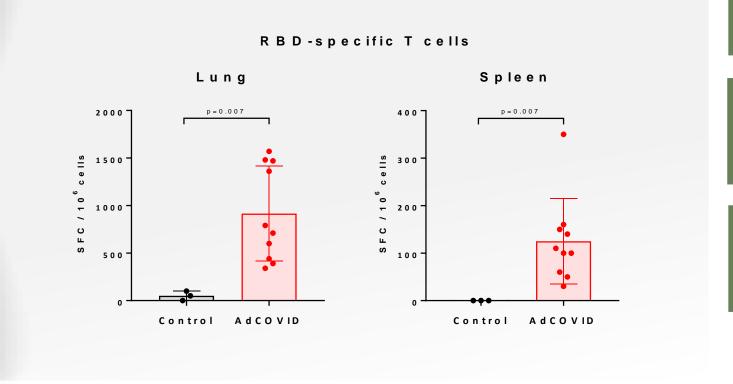
Responses are several fold higher than reported for most convalescent sera



# AdCOVID: STIMULATION OF MUCOSAL & SYSTEMIC T CELL IMMUNITY

#### RBD-SPECIFIC T CELLS IN THE LUNG AND SPLEEN

## **RBD-specific T Cell Responses**



Single intranasal dose of AdCOVID

Mucosal (lung) and systemic (spleen) T cell responses

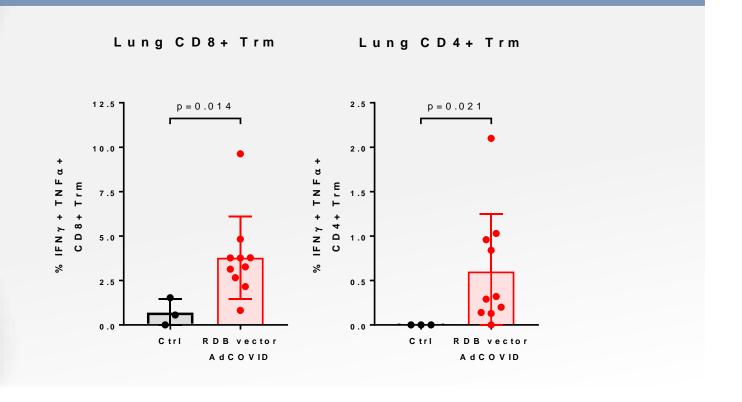
T cell response especially strong in lung



## AdCOVID: CELL IMMUNITY INCLUDED RESIDENT MEMORY T CELLS

#### TISSUE-LOCALIZED T CELLS POISED TO FIGHT LUNG INFECTION

## **RBD-specific Resident Memory T Cell Responses**



Single intranasal dose of AdCOVID

T cells with a resident memory phenotype stay in lung poised for protection

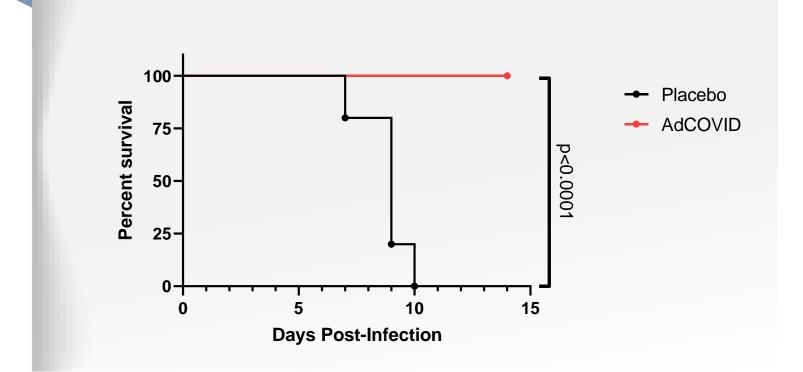
Strong CD8+ killer T cell response to clear infected lung cells



# AdCOVID: SINGLE DOSE EFFICACY

#### COMPLETE PROTECTION AGAINST DISEASE FOLLOWING LETHAL CHALLENGE

## **K18-hACE2 Transgenic Mouse Model**



Single intranasal dose of AdCOVID 1 month prior to challenge

Challenged with 1 x 10<sup>4</sup> FFU of SARS-CoV-2 (AZ1 isolate)

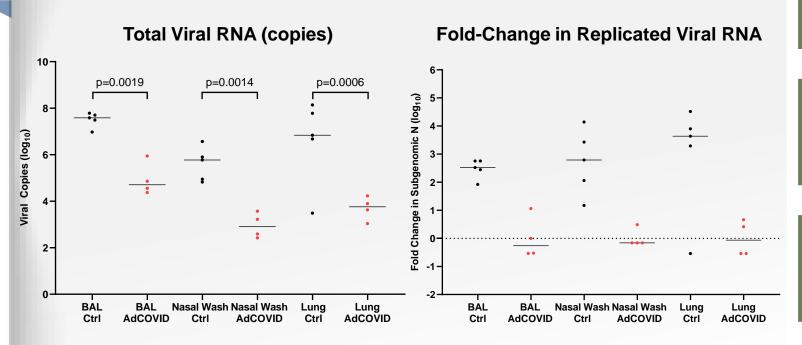
No weight loss in the AdCOVID vaccinated group



# AdCOVID: REPRESSION OF VIRAL REPLICATION

#### 1000-FOLD REDUCTION IN TOTAL AND REPLICATING VIRUS

## **K18-hACE2 Transgenic Mouse Model**



Single intranasal dose of AdCOVID 1 month prior to challenge

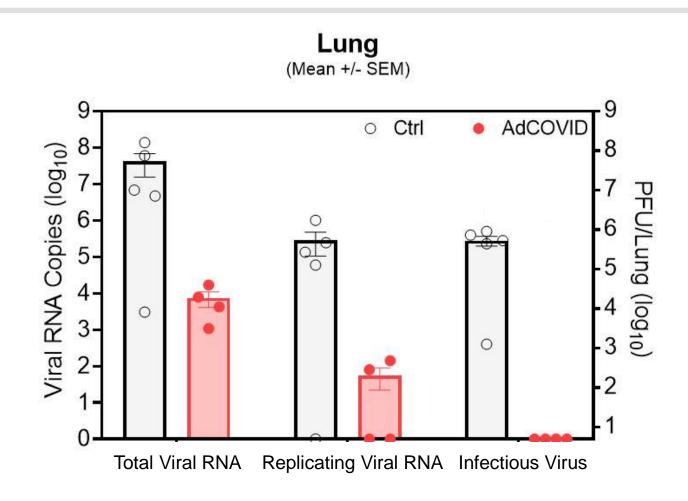
Challenged with 5 x 10<sup>3</sup> pfu SARS-CoV-2 (WA1 isolate)

Viral titers determined Day 3 post-challenge



# AdCOVID PROVIDES STERILIZING IMMUNITY IN MICE

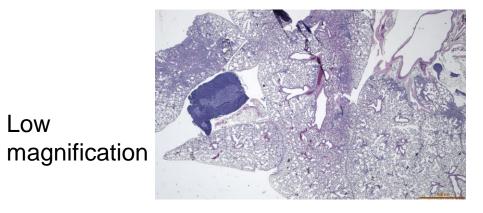
- Single intranasal dose of AdCOVID administered 28 days prior to SARS-CoV-2 challenge
- Heavy viral RNA burden reduced ~1000-fold over nonvaccinated controls
- Infectious virus undetectable in lungs of AdCOVID vaccinated mice (≥50,000-fold reduction in PFU over nonvaccinated controls)





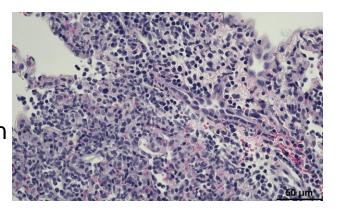
# SINGLE DOSE AdCOVID PROTECTS AGAINST LUNG DISEASE IN MICE

#### **Control**

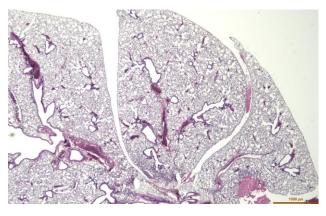


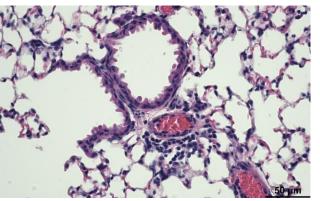
High magnification

Low



**AdCOVID** 







## AMENDED ADCOVID PHASE 1 STUDY DESIGN

- Approximately 80 subjects randomized 5:1 to receive one or two doses of AdCOVID or placebo
- Three dose groups
  - Low dose—1 x 10<sup>10</sup> vp
  - Medium dose—3 x 10<sup>10</sup> vp
  - High dose—1 x 10<sup>11</sup> vp
- Immunogenicity readouts will include neutralizing Ab, anti-spike IgG, and anti-spike IgA (mucosal immunogenicity) measured 28 days after the first and second doses
- Enrollment target met, and topline results expected June 2021
- T cell readouts expected to follow in 4-6 weeks



# KEY STUDIES TO SUPPORT AdCOVID TARGET PRODUCT PROFILE

Target Product Profile	Key Anticipated Phase 2 Trials		
Boosts natural immune response to wild-type and variant viruses in previously infected but unvaccinated individuals	Naïve and previously-infected populations in Low-Access Countries		
Boosts immune response to wild-type and variant viruses in vaccinated individuals	<ul> <li>Revaccination with parental and variant vaccines in previously vaccinated individuals</li> </ul>		
<ul> <li>Safe and well-tolerated in children down to 2 years of age</li> </ul>	<ul> <li>Age-based de-escalation study in young children and adolescents</li> </ul>		
<ul> <li>Safe for use in pregnant and breast-feeding women</li> </ul>	Maternal immunization study		





# NasoShield: FUNDED THROUGH A DEVELOPMENT CONTRACT WITH BARDA

## Phase 1b clinical trial completed



Received \$3.7M BARDA funding to conduct Phase 1b clinical trial

\$133.7M total contract value through Phase 2

Stockpiling of vaccine may occur prior to licensure<sup>1</sup>

 Nuthrax<sup>®</sup> initial stockpiling valued at \$261M with a \$1.6 billion total potential contract value



### **DIFFERENTIATED**

## **COMPETITION**

Only single-dose vaccine currently in development

**Intranasal spray** 

**Faster** protection

Superior logisticsNo cold chain distributionPotentially self-administered/ no injection required NasoShield
Differentiated
Anthrax Vaccine

Biothrax® - Only approved vaccine

- 3 dose regimen
- Requires an adjuvant
- Subcutaneous injections

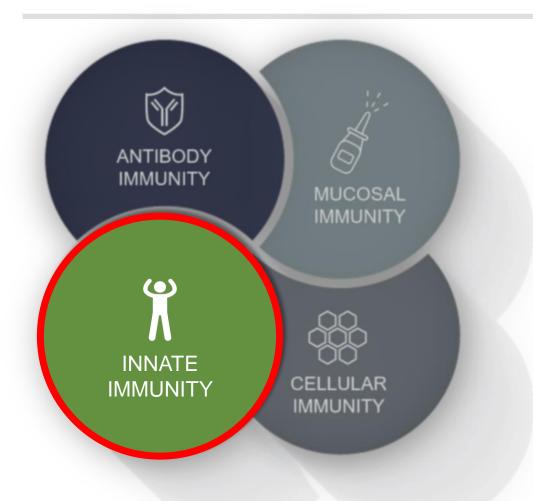
NuThrax® (AV7909) – Phase 3

- 2 dose regimen
- Requires 2 adjuvants
- Intramuscular injections



# T-COVID: BASED ON RD-Ad5 VECTOR VACCINE PLATFORM

SINGLE DOSE INTRANASAL THERAPEUTIC FOR THE TREATMENT OF EARLY COVID-19



## Single dose intranasal therapeutic

Potentially self-administered

### Modulates the innate immune response

 Reduced lung inflammation and inflammatory cytokine response in preclinical models

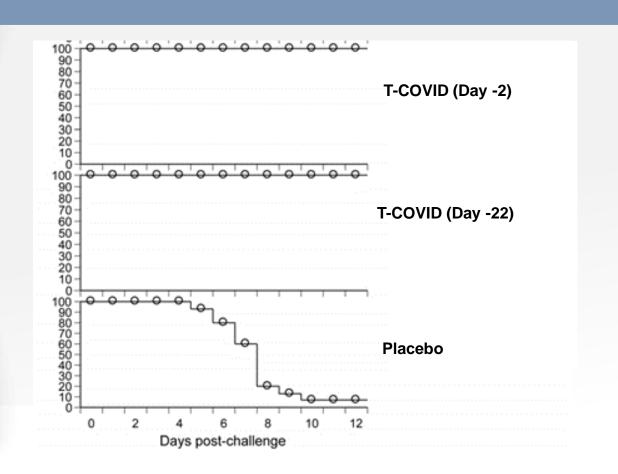
## **Acts rapidly**

 Provided protection within days of administration in preclinical models



# T-COVID: RAPID PROTECTION FROM RESPIRATORY PATHOGENS

#### Survival curves following lethal influenza challenge



Near immediate protection from challenge with influenza virus

Mechanism based on reduction of exaggerated lung inflammatory cytokine response

Pathogen-independent mechanism suggests efficacy against broad panel of respiratory pathogens



# T-COVID PHASE 1/2 CLINICAL TRIAL ONGOING

- 96 community-based patients with fever, cough, or shortness of breath, with onset of symptoms and confirmed diagnosis of COVID-19 within 72 hours
- Randomized 1:1 to T-COVID or placebo administered as a single 0.5 mL nasal spray on the day of diagnosis
- 3 cohorts of increasing age and risk for complications of COVID-19
- Primary efficacy endpoint:
  - Proportion of patients with clinical worsening, defined as a 4% decrease in pulse oxygen saturation (SpO<sub>2</sub>), or hospitalization
- Secondary endpoints:
  - Average decrease in resting SpO<sub>2</sub>
  - Average increase in resting pulse rate
  - Proportion of patients requiring oxygen supplementation and mechanical ventilation





## NASH AND NAFLD

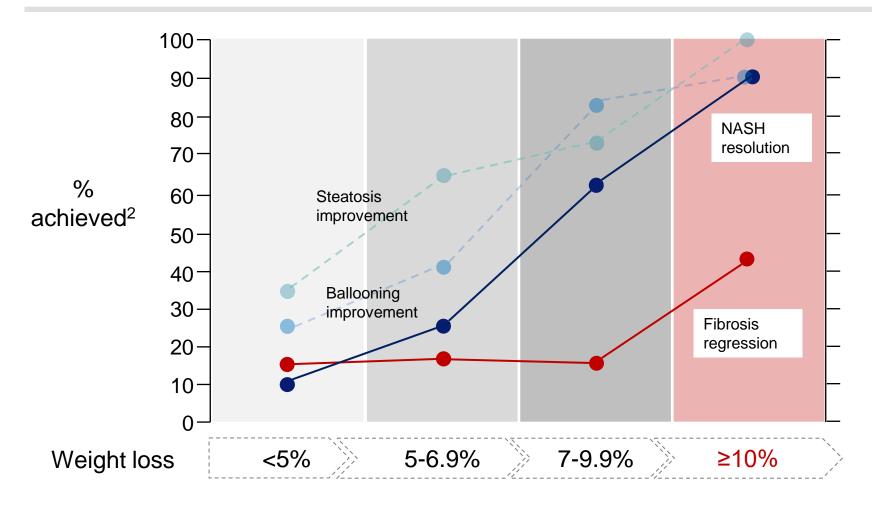
#### HEPATIC MANIFESTATIONS OF OBESITY AND METABOLIC SYNDROME

- NAFLD is present in up to 90% of obese patients, and ~20% of NAFLD patients progress to NASH<sup>1</sup>
- Up to 40% of NASH patients develop NAFLD recurrence one year after liver transplant—we believe the underlying metabolic disease is still present<sup>2</sup>
- The treatment of obesity is the cornerstone of treating NASH and the principal morbidities of NASH<sup>1,3</sup>
- Drugs in development should target the weight loss range achieved by bariatric surgery<sup>4</sup>



# SUBSTANTIAL BODY WEIGHT LOSS IS NECESSARY TO BLUNT NASH PROGRESSION

10% OR MORE WEIGHT LOSS MUST BE ACHIEVED1



The treatment of obesity remains the cornerstone of NASH and NAFLD therapy

Meaningful weight loss is rarely achieved without medical intervention

Current drugs have failed to deliver the weight loss achieved by bariatric surgery

altimmune

<sup>&</sup>lt;sup>1</sup> Promrat et al Hepatology 2010; Glass et al Dig Dis Sci 2015; Vilar-Gomez et al Gastroenterology 2015; Marchesini et al Hepatology 2016; Koutowkidis et al JAMA Intern Med 2019

# SNAPSHOT OF COMPOUNDS IN ADVANCED NASH DEVELOPMENT

#### MOST AGENTS FAIL TO ACHIEVE MEANINGFUL LEVELS OF WEIGHT LOSS

Agent	Author (year)	Mechanism	Weight Loss (%)
Obeticholic acid	Younossi, ZM 2019 <sup>1</sup>	FXR agonist	~2%
Resmetirom	Harrison, SA 2018 <sup>2</sup>	THRβ agonist	no change
Aldafermin (3mg)†	Harrison, SA 2019 <sup>3</sup>	FGF19 agonist	1.3%
Pegbelfermin (10 mg) <sup>††</sup>	Sanyal, A 2018 <sup>4</sup>	FGF21 agonist	2.2%
AKR-001 (70 mg)	Ritchie, M 2020 <sup>5</sup>	FGF21 agonist	no change
Firsocostat	Lawitz, EJ 2018 <sup>6</sup>	ACC inhibitor	no change
Elafibranor	Ratziu, V 2016 <sup>7</sup>	PPARα/δ agonist	no change

<sup>†</sup> No information has been made public on 1mg dose



<sup>††</sup> Gain of 0.6% on 20mg dose

<sup>&</sup>lt;sup>1</sup>Younossi, YM, et al. (2019) Lancet 394: 2184-96; <sup>2</sup>Harrison, SA, et al. Lancet 394: 2012-24; <sup>3</sup> Harrison, SA, et al. (2019) Lancet 391:1174-85; <sup>4</sup>Sanyal, A, et al. (2018) Lancet 392:2705-17; <sup>5</sup>Ritchie, M, et al. (2020) Exp Opin Invest Drugs, 29:2, 197-204; <sup>6</sup> Lawitz, EJ, et al. (2018) Clin Gastroenterol Hepatol 16:1983-91; <sup>7</sup>Ratziu, V, et al. (2016) Gastroenterol 150: 1147-59

# ALT-801: GLP-1/GLUCAGON RECEPTOR DUAL AGONIST

OPTIMIZED FOR NASH AND WEIGHT LOSS

#### **GLP-1**

blood glucose

appetite

inflammation

Indirect effects on liver

#### **GLUCAGON**

energy expenditure

adipose browning

lipolysis/ gluconeogenesis

mobilization of liver fat

Direct effects on liver

# DESIGNED FOR SIGNIFICANT REDUCTIONS IN

body weight

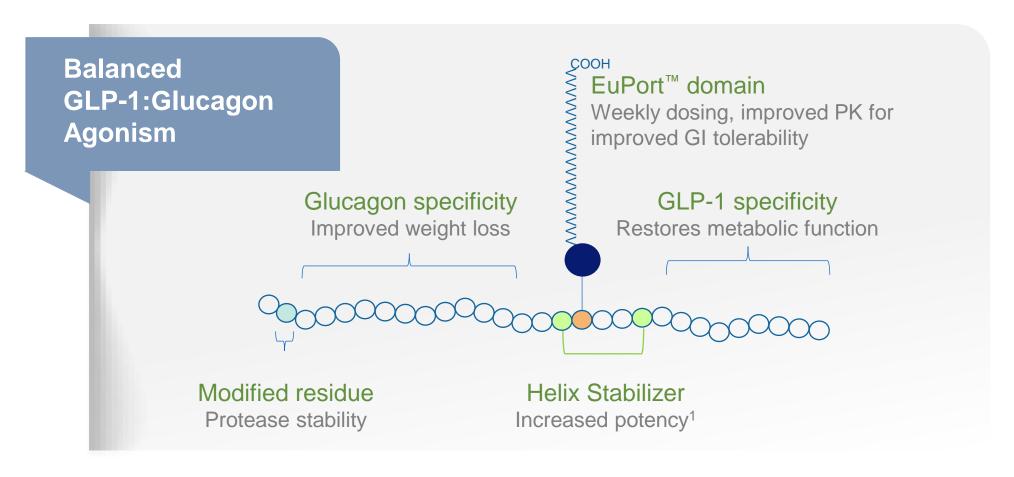
liver fat, inflammation and resulting fibrosis

blood glucose



# ALT-801: RATIONALLY DESIGNED AND HIGHLY DIFFERENTIATED

PROPRIETARY EuPort™ DOMAIN PROVIDES PROLONGED SERUM HALF-LIFE AND REDUCED PEAK CONCENTRATION





## ALT-801 SUMMARY OF PRECLINICAL STUDIES

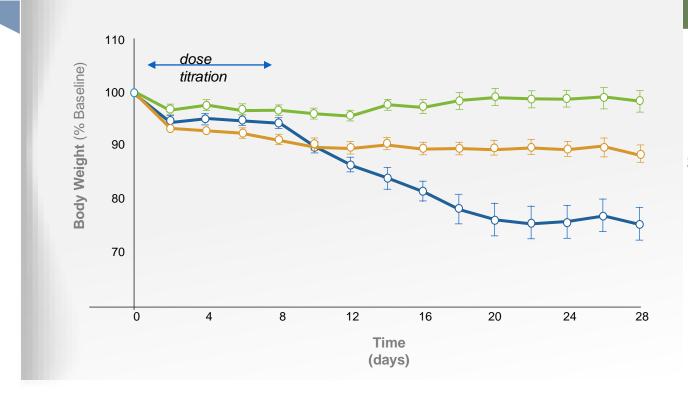
- ALT-801 preclinical results in diet induced obesity models showed superior reductions in nearly all measured NASH parameters compared to semaglutide or elafibranor, returning many parameters to lean normal range:
  - Body and liver weight
  - NAS and ALT
  - Collagen (COL1A1 and galectin-3) content
  - Liver fat, cholesterol and triglycerides
- ALT-801 improved metabolic function and exhibited pleiotropic effects in preclinical testing across multiple pathways involved in NASH
- ALT-801 resulted in more profound suppression of genes associated with steatosis, inflammation and stellate cell fibrosis by RNA sequencing compared to elafibranor



### **ALT-801**

#### 25% REDUCTION IN BODY WEIGHT TO CHOW-FED LEAN NORMAL RANGE

#### **Mouse DIO Model After 4 Weeks of Treatment**



More than **2x** the weight loss of **semaglutide** 

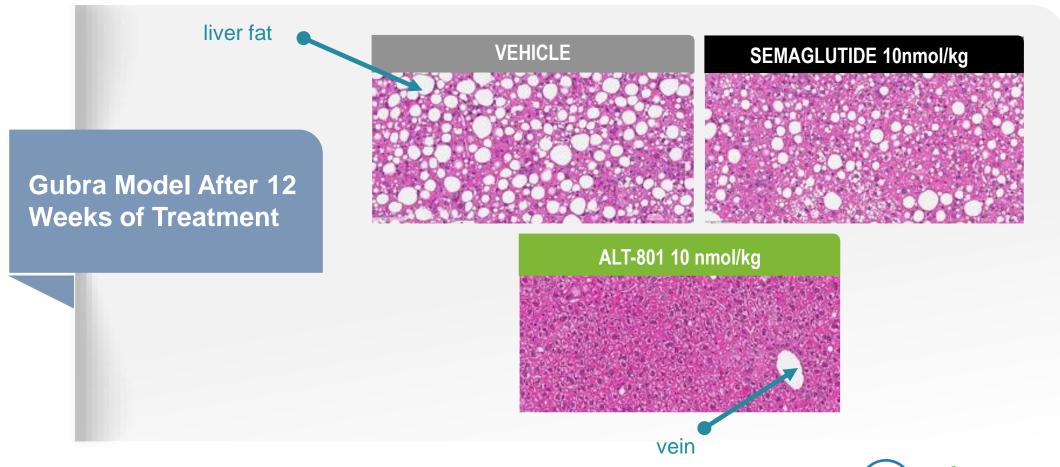
**Vehicle** 

Semaglutide (12nmol/kg)

**ALT-801 (12nmol/kg)** 

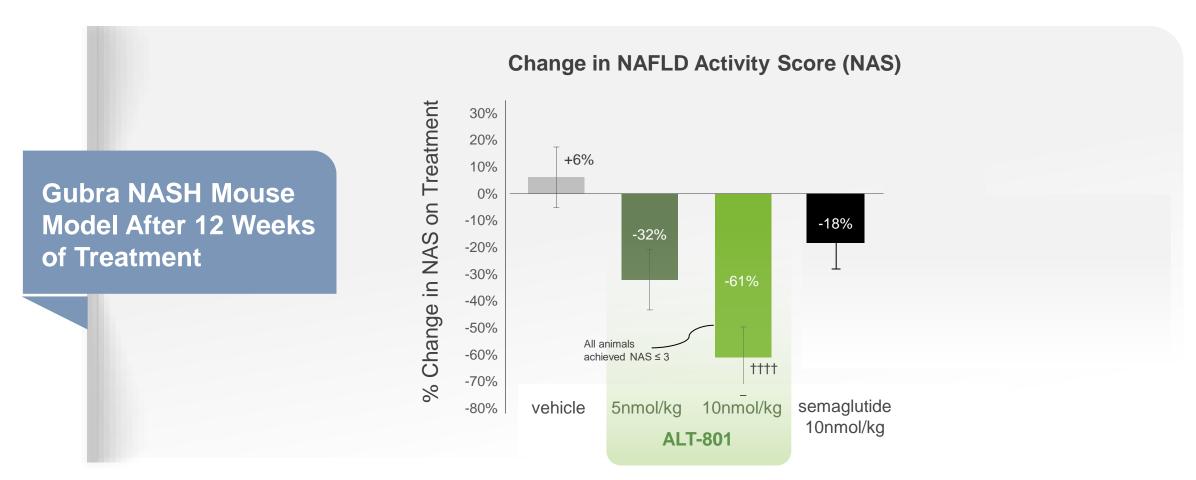


# ALT-801 REDUCTION IN LIVER FAT AND LIVER WEIGHT TO LEAN NORMAL RANGE



### **ALT-801**

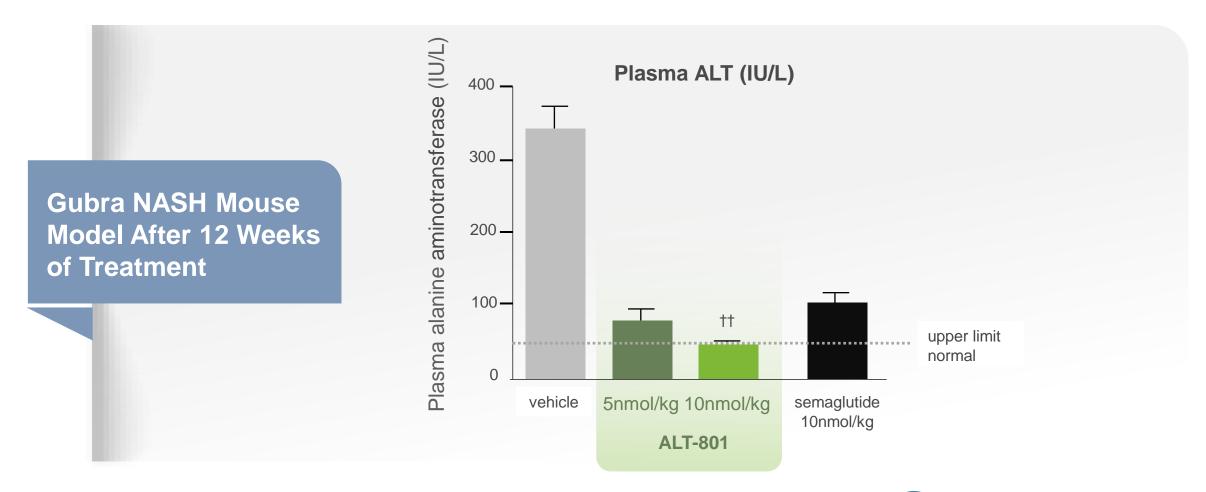
### IMPROVEMENT IN NAFLD ACTIVITY SCORE (NAS)

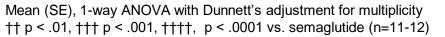


Mean (SE), 1-way ANOVA with Dunnett's adjustment for multiplicity  $\uparrow \uparrow p < .01, \uparrow \uparrow \uparrow p < .001, \uparrow \uparrow \uparrow \uparrow \uparrow$ , p < .0001 vs. semaglutide (n=11-12)



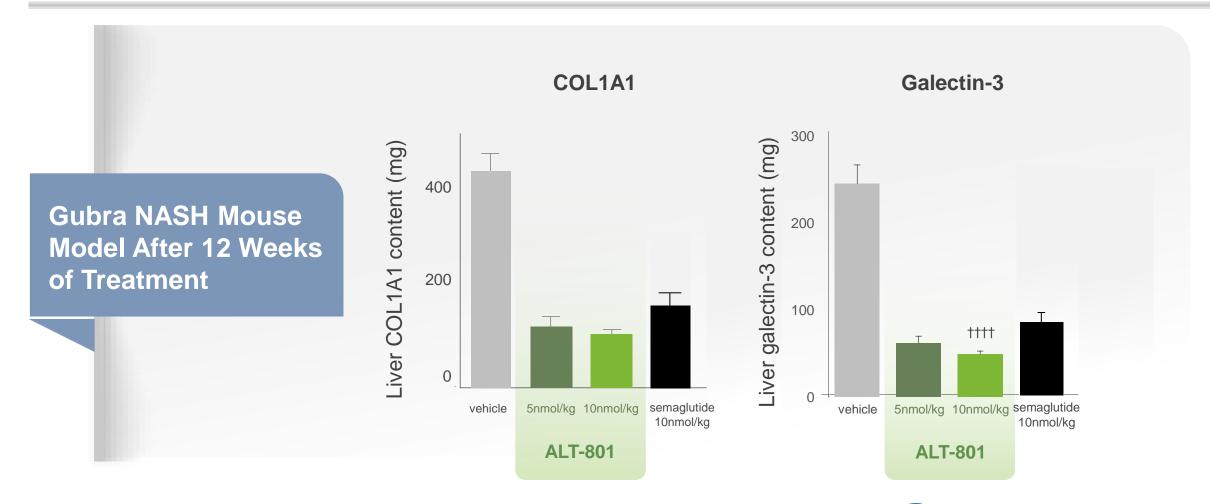
# ALT-801 NORMALIZATION OF PLASMA ALT







# ALT-801 GREATER EFFECTS ON FIBROSIS



Mean (SE), 1-way ANOVA with Dunnett's adjustment for multiplicity  $\uparrow \uparrow p < .01, \uparrow \uparrow \uparrow p < .001, \uparrow \uparrow \uparrow \uparrow \uparrow$ , p < .0001 vs. semaglutide (n=11-12)



#### ALT-801 PHASE 1 TRIAL UPDATE

- Phase 1 study is advancing to data readout
  - Enrollment completed in the single ascending dose (SAD) phase and the 3 planned cohorts
    of multiple ascending dose (MAD) phase of the trial
  - 6-week data anticipated in June 2021; 12-week data anticipated in Q3 2021
- Anticipate mid-year IND filing to initiate NASH studies in the US
- A 52-week, Phase 2, biopsy-trial based on NASH endpoints is expected to commence in early 2022



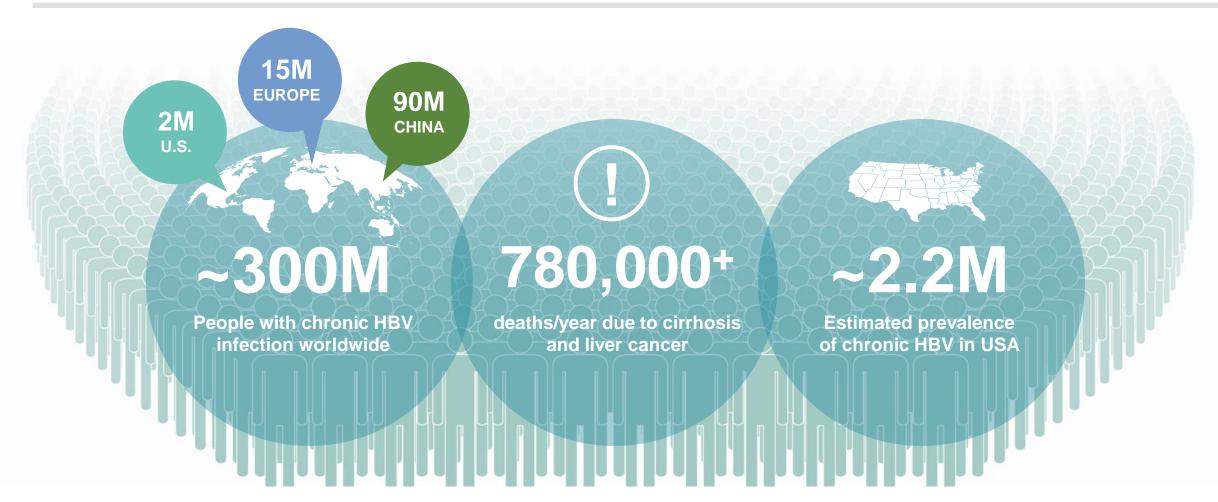
### ALT-801 – POTENTIAL IND FILING FOR OBESITY IN 2H 2021

- Novo Nordisk (semaglutide) and Lilly (tirzepatide) have executed successful Phase 3 programs
- These programs have de-risked the obesity space previously occupied by unsafe and ineffective drugs
- GI intolerability has been problematic for GLP-1 based treatments, with side effects leading to treatment discontinuation
- If the impressive weight loss and tolerability of ALT-801 in preclinical studies translate to the clinical setting, ALT-801 could be ideally suited in this indication
- The filing of a 2nd IND in obesity in 2H 2021 is being evaluated, with the final decision based on the upcoming Phase 1 trial readout





# HepTcell: T CELL IMMUNOTHERAPEUTIC FOR CHRONIC HEPATITIS B SIGNIFICANT OPPORTUNITY TO IMPROVE CURRENT HBV CURE RATES





## CURRENTLY APPROVED HBV THERAPEUTICS DO NOT LEAD TO A CURE

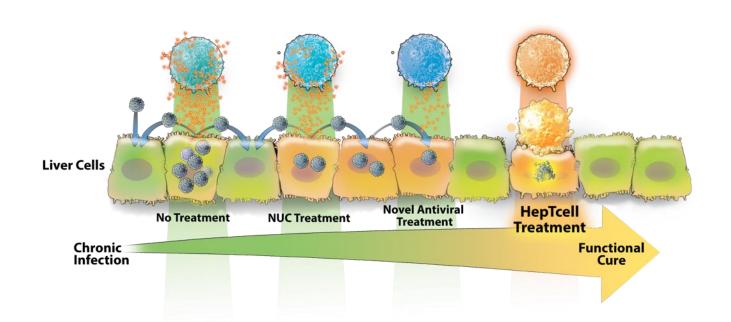
IMMUNE ACTIVATION WILL BE REQUIRED FOR SIGNIFICANT IMPACT

Current antivirals prevent disease progression but rarely clear chronic infection

Breaking T cell immune tolerance is key to functional cure

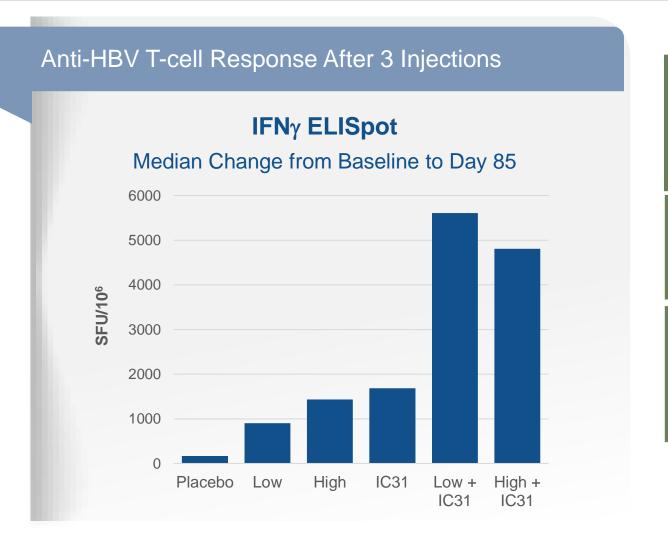
Newer direct-acting antivirals unlikely to result in immune reactivation alone

HepTcell is designed to "wake up" dormant T-cells to eliminate infection





## HepTcell: PHASE 1 SAFETY AND IMMUNOGENICITY STUDY



HepTcell is designed to break immune tolerance in chronic hepatitis B patients

T cell responses strongest when combined with IC31<sup>TM</sup> adjuvant

HepTcell dose and use of adjuvant confirmed for Phase 2 studies



## HepTcell: PHASE 2 CLINICAL TRIAL

#### MULTINATIONAL, MULTICENTER TRIAL OF HEPTCELL IN INACTIVE CHRONIC HEPATITIS B

- 80 patients with HBeAg negative inactive chronic hepatitis B and HBsAg ≤ 100 IU/mL randomized 1:1 to HepTcell or placebo administered every 4 weeks for 24 weeks
- Follow-up study phase of 48 weeks after the last dose will assess the safety and durability of response of treatment
- Study to be conducted at 20 sites in the US, Canada and Europe
- Efficacy endpoints
  - Primary endpoint: proportion of patients with 1.0-log reduction in HBsAg from baseline at Week 24
  - Secondary endpoints: HBsAg clearance, changes from baseline in HBsAg, HBV DNA, HBcrAg, pg-RNA at Week 24

### Phase 2 data readout expected H1 2022





## STRONG ANTICIPATED NEWS FLOW

Program	Event	Timing
AdCOVID	Phase 1 clinical trial readout	Q2 2021
	Phase 2 clinical trial initiation	Q2 2021
ALT-801	Phase 1 SAD/MAD clinical trial readout	Q2 2021
	Phase 1 (12-week dosing) readout	Q3 2021
T-COVID	Phase 1/2 clinical trial readout	Q2 2021
HepTcell	Phase 2 clinical trial readout	H1 2022



#### **ALTIMMUNE: INVESTMENT HIGHLIGHTS**

- Diversified portfolio with 2 proprietary technology platforms

  Intranasal vaccines & peptide therapeutics
- Highly-differentiated intranasal vaccine approach
  Offers advantages over other vaccine approaches
- Strong clinical focus and momentum 5 ongoing clinical programs in 2021
- Multiple valuation catalysts anticipated over the next 12 months

  Data read-outs from multiple clinical programs
- Solid cash position to reach value-generating milestones ~\$227 million as of March 31, 2021



