

Vir Biotechnology, Inc. EASL ILC 2021 Hepatitis B Data Call June 25, 2021

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Vir C	Clinica	al Dev	elopm	ent P	ipelin	e Antib	ody siRNA	T cell	
Disease Area	Product Candidate	Treatment/ Prophylaxis	Pre-clinical	Phase 1	Phase 2	Phase 3	Authorized	Collabo	orator
	Sotrovimab*	Treatment					U.S., EU <sup>†</sup>	gsk GlaxoSmithKline	
	Sotrovimab + bamlanivimab	Treatment	N.					gsk GlaxoSmithKline	Lilly
00110-13	Sotrovimab*	Prophylaxis						gsk GlaxoSmithKline	
	VIR-7832	Treatment						gsk GlaxoSmithKline	
	VIR-2218	Treatment	É						
	VIR-2218 + PEG-IFN-α	Treatment	É						
	VIR-3434	Treatment							
HBV	VIR-2218 + VIR-3434	Treatment	\$	Planned 2H:202	1 start				
	VIR-2218 + TLR8 <sup>1</sup> + PD-1 <sup>2</sup>	Treatment	¥	Planned 2H:202	1 start				🚺 GILEAD
	VIR-2218 + BRII-179	Treatment	€ ₹						<b>Brii</b> Biosciences
Influenza A	VIR-2482	Prophylaxis							
HIV	VIR-1111**	Prophylaxis	<b></b>					BILL& MELINDA GATES founda	tion

\*Sotrovimab (VIR-7831) IV formulation used in Phase 3 COMET-ICE trial; IM formulation currently in Phase 2 COMET-PEAK and COMET-TAIL trials, and pending in prophylaxis trial \*\*Vaccine designed to establish proof of concept in Phase (Ph) 1 clinical trial to determine whether unique immune response observed in non-human primates can be replicated in humans; ultimately, any candidates we advance as a potential HIV vaccine will require modifications to VIR-1111 before further clinical development. 1: GS-9688 2: nivolumab <sup>1</sup>In the U.S., EUA received on 5/26/2021. In the EU, EMA

positive opinion under Article 5(3) received on 5/21/2021.

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# Chronic HBV: Our Approach to Functional Cure

- We believe that chronic HBV (CHB) is a viral disease resulting in immune dysfunction
- We believe that chronic HBV infection results in immune dysfunction via the expression of a large amount of HBV antigens, which act to suppress the immune system
- We believe a functional cure for CHB results from regaining immunologic control

We hypothesize that knocking down HBV antigens will remove the block on the immune system, and in the setting of an immune modulator, result in immune control

# Chronic HBV: HBV T cells become dysfunctional in infected mice



### **Chronic HBV: Reversal of Functional Cure Via Immunosuppression**





# Vir's Broad HBV Functional Cure Portfolio

VIR-2218 Phase 2 Data Potential Best-In-Class siRNA as "backbone" of therapy



#### Substantial, Durable, and Dose Dependent Reduction of HBsAg through 48 weeks<sup>1</sup>

#### **Ongoing / Planned Combination Trials Currently in** IR **PEG-IFN-**α Phase 2 **VIR-3434** Start Phase 2 trial in 2H:2021 mAb **GS-9688** TLR-8 agonist Start Phase 2 GILEAD trial in 2H:2021 nivolumab PD-1 antagonist **BRII-179 Currently in Brii** Biosciences T cell vaccine Phase 2

Note: current and planned trials are/will be conducted in patients with chronic HBV on nucleotide/nucleoside reverse transcriptase inhibitors (NRTIs), which are standard of care treatment



# Higher VIR-2218 Dose Levels Associated With a More Sustained Response through Week 48



- With only 2 doses, at Week
  0 and Week 4, four subjects
  achieved a sustained
  response through Week 48
- In combination studies, VIR is exploring 3-6 doses of VIR-2218
- Diversity of response being explored through immune biomarkers and biopsy/FNA study

All participants on nucleos(t)ide reverse transcriptase inhibitors (NRTI) therapy

# **ESC+ Decreases Off-target Activity**



Enhanced stabilization chemistry plus (ESC+)\* decreases off-target seed-mediated binding while maintaining on-target activity and is hypothesized to improve the hepatic safety profile.



#### and potential hepatotoxicity

#### Minimal off-target effects and improved hepatic safety

### No Dose-Dependent Changes in Post-Treatment ALT Levels through Week 48





- No grade >1 ALT elevations\*; no bilirubin >ULN
- No clinically relevant changes or trends in other lab parameters, vital signs, or ECGs

All participants on nucleos(t)ide reverse transcriptase inhibitors (NRTI) therapy

ALT, alanine transaminase; CTCAE, common terminology criteria for adverse events; ECG, electrocardiogram;

ULN, upper limit of normal \*Grade based on CTCAE v5.0

## VIR-2218 With and Without PEG-IFNα



- Open-label study to evaluate the safety and antiviral activity of VIR-2218 alone or in combination with PEG-IFNα in noncirrhotic, HBeAg-negative and positive adults with chronic HBV infection on NRTI therapy
- Participants will be followed for safety and antiviral endpoints for a minimum of 24 to 48 weeks after treatment; NRTI therapy may be discontinued if the pre-specified criteria are met to assess if functional cure is achieved
- The study is ongoing; preliminary safety and HBsAg through Week 12 are presented

### VIR-2218 with Pegylated Interferon Alfa-2a Mediated HBsAg Decreases from Baseline



#### PO-824

#### Preliminary On-Treatment Data From a Phase 2 Study Evaluating VIR-2218 in Combination With Pegylated Interferon <u>Alfa-2a in Patients With Chronic Hepatitis B Infection</u>



Man-Fung Yuen<sup>1</sup>, Young-Suk Lim<sup>2</sup>, Daniel Cloutier<sup>3</sup>, Ling Shen<sup>3</sup>, Andre Arizpe<sup>3</sup>, Phillip S. Pang<sup>3</sup>, Chin Tay<sup>3</sup>, Vaidehi Thanawala<sup>3</sup>, Sneha V. Gupta<sup>3</sup>, Andrea L. Cathcart<sup>3</sup>, and Edward Gane<sup>4</sup> <sup>1</sup>Queen Mary Hospital, University of Hong Kong, Hong Kong, China; <sup>2</sup>Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; <sup>3</sup>Vir Biotechnology, Inc., San Francisco, California, United States; <sup>4</sup>University of Auckland, Auckland, New Zealand



- Co-administration of VIR-2218 with PEG-IFNα (Cohort 3) resulted in a more rapid and substantial HBsAg decline compared to VIR-2218 alone
  - The mean HBsAg reduction in Cohort 3 was 0.6 log<sub>10</sub> IU/mL greater than in Cohorts 1 and 2 at Week 12
  - In published studies, PEG-IFN $\alpha$  alone in virally suppressed patients was associated with  $\leq 0.25 \log_{10}$  IU/mL HBsAg decline, on average, over the first 12 weeks <sup>1,2,3,4</sup>
- Additional follow-up in Cohort 2 will provide insight into the antiviral effects of the combination when PEG-IFNα is administered following a 12-week lead-in period of VIR-2218

All participants on nucleos(t)ide reverse transcriptase inhibitors (NRTI) therapy. Study is ongoing, N values at each timepoint per cohort are indicated below the graph HBsAg, hepatitis B surface antigen; PEG-IFNG, pegylated interferon alfa

1. Marcellin P, et al. Gastroenterology. 2016;150(1):134-144; 2. Bourlière M, et al. Lancet Gastroenterol Hepatol.

2017;2(3):177-188; 3. Chi H, et al. J Infect Dis. 2017;215(7):1085-1093; 4. Farag MS, et al. Oral presentation at: The Liver Meeting of The American Association for the Study of Liver Diseases; November 11, 2019; Boston, MA, USA.



#### "We hypothesize that knocking down HBV antigens will remove the block on the immune system, and in the setting of an immune modulator, result in immune control"

We believe that this VIR-2218+ PEG-IFNα data suggests that treatment with an siRNA could help unlock the potential of immunomodulators

# VIR-3434: An Engineered Human Antibody Against HBsAg WR with Multiple Potential Mechanisms of Action



**cccDNA**, covalently closed circular DNA; **intDNA**, integrated DNA; **SVPs**, subviral particles; **HBsAg**, hepatitis B surface antigen; **PEG-IFNα**, pegylated interferon alfa VIR-3434 incorporates Xencor's Xtend<sup>TM</sup> and other Fc technologies

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## VIR-3434-1002 Phase 1 Design





- In Part B, 8 participants per cohort were randomized 6:2 to receive a single dose of VIR-3434 or placebo by SC injection
- Blinded preliminary safety, tolerability, and HBsAg data up to 4 weeks post-dose are presented for Part B cohorts evaluating low doses of 6 mg and 18 mg

### Preliminary PK of VIR-3434 After Single SC or IV Dose in Healthy Volunteers



P

#### Preliminary Pharmacokinetics and Safety in Healthy Volunteers of VIR-3434, a Monoclonal Antibody for the Treatment of Chronic Hepatitis B Infection





Preliminary VIR-3434 Serum Concentration Profiles

PO-43

Subjects with 5 1 AE	VIR-3434 or Placebo							
n (%)	90mg SC n=9*	300 mg SC n=8	900 mg SC n=8	900 mg IV n=8	3000 mg IV n=8			
Grade 1	5 (55.6)	5 (62.5)	7 (87.5)	5 (62.5)	3 (37.5)			
Grade 2	0	1 (12.5)	0	0	1 (12.5)			
Grade <u>&gt;</u> 3	0	0	0	0	0			
Serious AE	0	0	0	0	0			
AE leading to study discontinuation	0	0	0	0	0			

- The most common reported AE across all groups was headache, which was observed in 10/41 (24.4%) participants
- Injection site reactions were reported in 6/41 (14.6%) participants, and all were grade 1 in severity except for a grade 2 AE of injection site erythema which resolved without intervention
- No grade 3/4 AEs, SAEs, or AEs leading to study discontinuation were observed
- No clinically significant laboratory abnormalities were observed
- VIR-3434 was generally well tolerated in healthy volunteers following single doses of up to 3000 mg; AEs were generally mild, and no AEs led to study discontinuation
- The bioavailability and half-life following SC administration of VIR-3434 is estimated to be 76% and 25 days respectively
- Favorable PK properties of SC VIR-3434 and safety profile are supportive of continued development for the treatment of chronic HBV infection

### VIR-3434 Mediated HBsAg Decreases from Baseline

VIR-3434 6 mg or Placebo
 VIR-3434 18 mg or Placebo

- Most participants rapidly achieved ≥ 1 log10 IU/mL decline in HBsAg
- The largest reductions in HBsAg were in the 18 mg cohort, who also had higher baseline HBsAg levels
- Full analysis of VIR-3434 PK and HBsAg:VIR-3434 complex disposition is ongoing



<sup>2</sup> Free VIR-3434 concentrations were lower than anticipated in all available samples

## **VIR-3434 Next Steps**



- Higher single doses of VIR-3434 are being evaluated
- Patients with higher baseline HbsAg are being evaluated
- NRTI-naïve patients will be evaluated
- Multiple and higher doses of VIR-3434 will be evaluated in combination with VIR-2218 in the MARCH trial

## **2H:2021 Anticipated Catalysts**



HBV



	<b>Sotrovimab (mAb)</b> BLA (Early Treatment, COMET-ICE, IV)	File
	Sotrovimab (mAb) EMA rolling review (Early Treatment, COMET-ICE, IV)	Complete
	Sotrovimab (mAb) Phase 2 (Early Treatment, COMET-PEAK, IM)	Data
	VIR-7832 (mAb) Phase 1b (Early Treatment, AGILE, IV)	Data
	VIR-2218 (siRNA) + VIR-3434 (mAb) Phase 2	Start
	VIR-2218 (siRNA) + GS-9688 + nivolumab Phase 2	Start
	VIR-3434 (mAb) Phase 1 additional clinical data	Data
	VIR-2218 (siRNA) + PEG-IFN-α Phase 2 additional clinical data	Data
	VIR-1111 (T cell) Phase 1	Data