HBsAg declines observed with VRON-0200 alone are rapidly enhanced with the addition of combination antiviral therapies: results from a Phase 1b study for functional cure in chronically HBV-infected patients

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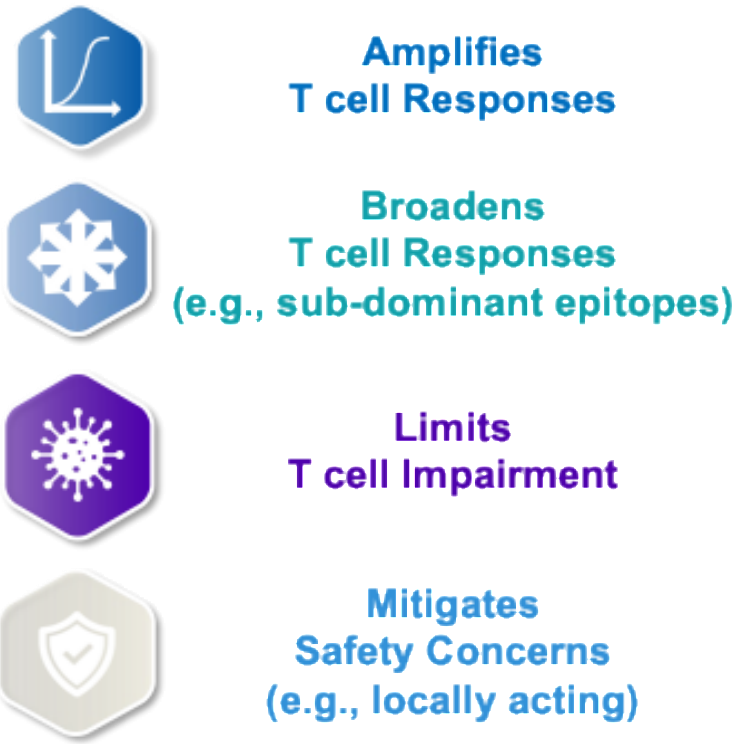
Disclosures of Conflict of Interest

- **Grace Wong** Grace Wong has served as an advisory committee member for AstraZeneca, Gilead Sciences, GlaxoSmithKline, Janssen, & Virion Therapeutics, and as a speaker for Abbott, Abbvie, Ascletis, Bristol-Myers Squibb, Echosens, Ferring, Gilead Sciences, GlaxoSmithKline, Janssen, and Roche. She has also received research grants from Gilead Sciences.
- **Ed Gane** has served as an advisor and/or speaker for AbbVie, Abbott Diagnostics, Aligos, Arbutus, Arrowhead, Assembly, Dicerna, Gilead Sciences, Glaxo Smith Kline, Intellia, Janssen, Merck, Novartis, Precision Biosciences, Genentech-Roche, Tune, Vaccitech, Vir Bio & Virion Therapeutics
- **Tien-Huey Lim** has nothing to disclose
- **Marie Bonhomme** is an employee of PPD®, part of Thermo Fisher Scientific, who is the laboratory contracted to perform work on the VRON-0200 study
- **Sue Currie** and **Andrew Luber** work at Virion Therapeutics, LLC and own shares in the company

VRON-0200: Background

- VRON-0200 is a therapeutic vaccine for HBV functional cure designed to enhance and broaden immune responses to HBV core & pol[1]
- VRON-0200 contains a novel checkpoint modifier which works by lowering the T cell activation threshold*
- In chronically HBV-infected patients, VRON-0200 has demonstrated[2]:
  - ✓ A favorable safety and tolerability profile
  - ✓ Immunogenicity
  - ✓ Anti-HBV activity (HBsAg declines)

Benefits of Checkpoint Modification



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*More information about MOA available at www.VirionTx.com;

1. Ertl H, et al. EASL 2023: TOP107; 2. Gane E, et al. EASL 2025: Abstract #1404.

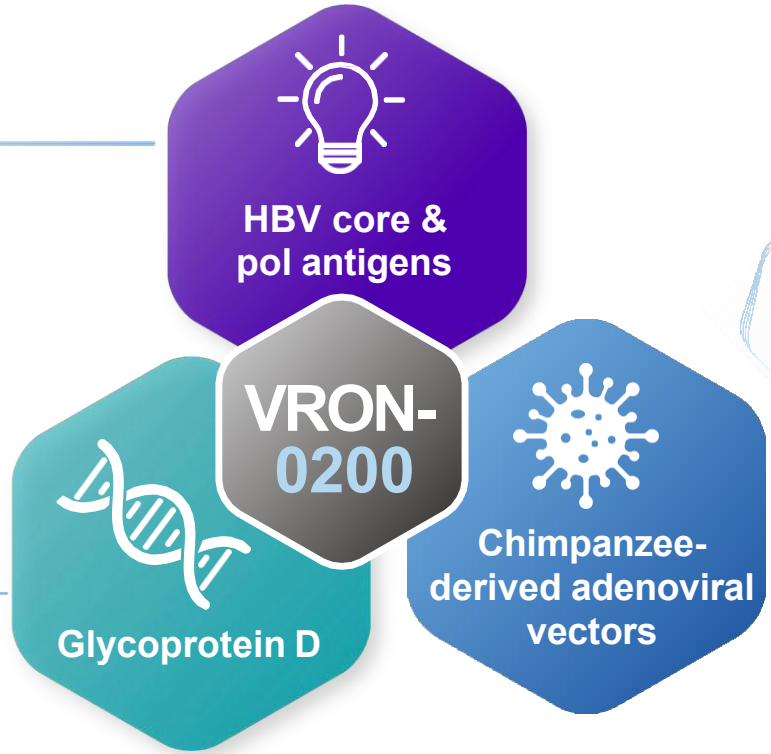
VRON-0200: A Potential First-in-Class Immunotherapy for HBV Functional Cure

HBV antigens

- Optimized **HBV core & pol antigens**
- Pan genotypic (A, B, C, D)
- **S antigen not included**

Checkpoint modifier*

- **Amplifies** and **broadens** immune responses



Viral vector platform

- Limited pre-existing vector immunity

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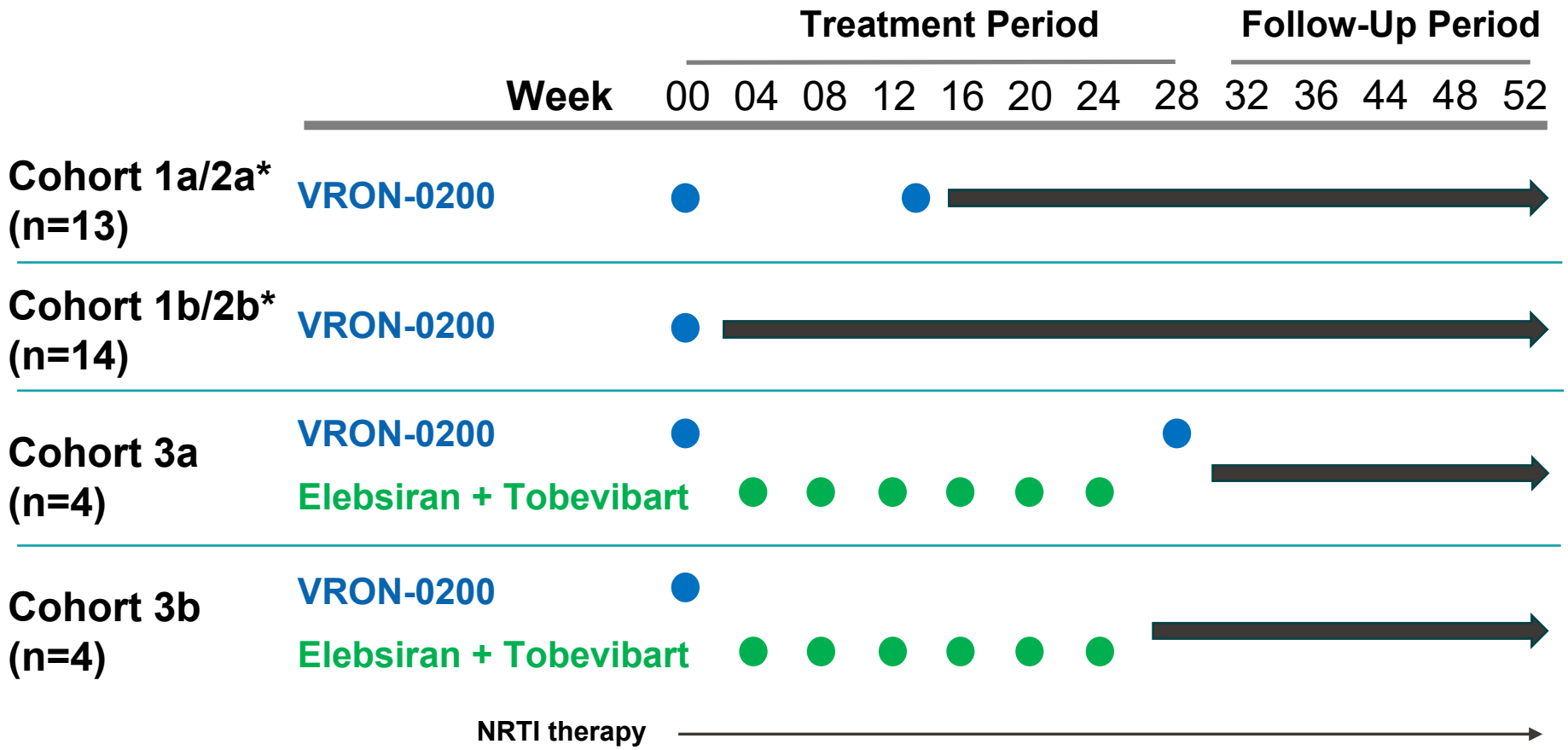
*More information about MOA available at www.VirionTx.com

VRON-0200 Phase 1b Study Schema
Open Label, Randomized, Multi-Center Study

Key Inclusion Criteria (N=35)

- **Adults ≥ 18 to ≤ 55 years**
- BMI ≥ 18 to ≤ 32 kg/m^2
- Documented chronic HBV
- **HBsAg:**
  - **Cohorts 1/2 - ≤ 500 IU/mL**
  - **Cohort 3 - ≤ 1000 IU/mL**
- On stable NUC therapy > 12 mos
- HBV DNA < 40 IU/mL for > 12 mos
- ALT < 2x ULN
- AST < 2x ULN
- No clinical diagnosis of advance liver fibrosis and/or cirrhosis



*Cohort 1 – VRON-0200 i.m. 1x10^{10} vp; Cohort 2 – VRON-0200 i.m. 5x10^{10} vp; Boost at Day 91 (Week 13)
Both elebsiran (siRNA) and tobevibart (S-antigen targeted mAb) are part of Vir Biotechnology, Inc.'s, clinical-stage portfolio for Hepatitis

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Purpose

To report safety, immunogenicity, and HBsAg changes in chronically HBV-infected patients, up to 360 days, post VRON-0200 dosing

Methods: Clinical Assessments

Patients were evaluated for safety, immunologic, and virologic measures at multiple time points, and blood samples were collected at every visit:

Safety (data cutoff October 1, 2025)

- Adverse events(AEs) and SAEs (CTCAE) monitored and labs, including LFTs, vital signs, and PEs

Immunologic Assessments: IFNγ ELISpot (data cutoff July 7, 2025)

- IFNγ ELISpot to core and pol peptide pools

Virologic Assessments: HBsAg (data cutoff August 20, 2025)

- ELISA HBsAg II Quant; LLOD 0.05 IU/mL
- Absolute values (IU/mL), and absolute changes ($\log_{10}$ IU/mL)

Patient Demographics & Baseline Characteristics (N=35)

	Cohort 1 (n=13)	Cohort 2 (n=14)	Cohort 3# (n=8)
Median age, yrs (range)	45 (37-54)	46 (41-55)	51 (41-55)
Sex, n (%)			
Male	12 (92%)	10 (71%)	6 (75%)
Race, n (%)			
Asian	11 (85%)	13 (93%)	6 (75%)
Other	2 (15%)	1 (7%)	2 (25%)
BMI (kg/m^2), median (range)	26.3 (20.2-32)	25.9 (19.7-31.6)	21.7 (18.6-32)
Baseline HBsAg Levels (IU/mL), median (range)*	179 (16-623)	149 (10-563)	469 (12-1169)
Baseline HBsAg Levels, n (%)			
≥500 IU/mL	1 (8%)	1 (7%)	4 (50%)
200 to <500 IU/mL	6 (46%)	4 (29%)	1 (13%)
100 to <200 IU/mL	2 (15%)	6 (43%)	0 (0%)
<100 IU/mL	4 (31%)	3 (21%)	3 (38%)
Baseline ALT (x ULN), n (%)			
1.5 to ≤2x ULN	1 (8%)	0 (0%)	0 (0%)
1 to <1.5x ULN	0 (0%)	1 (7%)	0 (0%)
<1 x ULN	12 (92%)	13 (93%)	8 (100%)
HBeAg Status at Baseline, n (%)			
Negative	12 (92%)	14 (100%)	8 (100%)

1 pt withdrew consent at D28 (Group 3), and is included in demographics and baseline characteristics, and safety, but excluded from Clinical Data (not evaluable)
*As per protocol, participants had prior HBsAg at screening ≤500 IU/mL in Groups 1 and 2, and ≤1000 IU/mL in Group 3.

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Safety and Tolerability (N=35)
11,629 Patient Safety Days

	Cohort 1 (n=13)	Cohort 2 (n=14)	Cohort 3 (n=8)
Any AE, n	**16**	**29**	**40**
Grade 1	**13**	**19**	**35**
Grade 2	**3**	**10**	**5**
Grade 3 or 4	**0**	**0**	**1**
SAE, n	**0**	**0**	**1***
TRAEs, n	**5**	**16**	**16**
AEs leading to Study Drug Discontinuation, n	**0**	**0**	**0**
Study Discontinuations, n	**0**	**0**	**1****
ALT elevations, n	**0**	**0**	**1**
Grade 1	**0**	**0**	**0**
Grade 2	**0**	**0**	**1**

No serious TRAEs, treatment-related discontinuations or clinical laboratory abnormalities

86 AEs in 24 patients; 37 TRAEs included 4 - Grade 2: eczema, myalgia, headache, injection site reaction, all others Grade 1; All TRAE symptoms have resolved

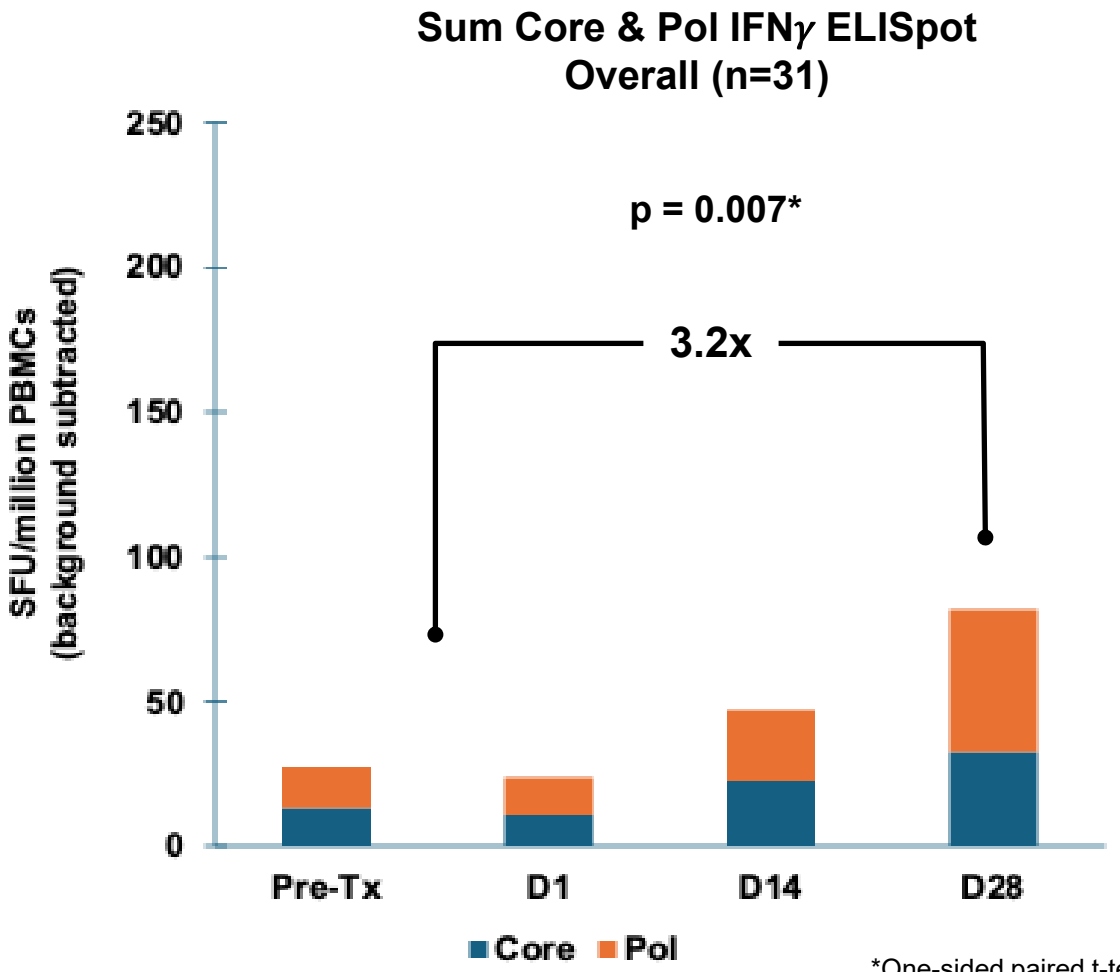
Safety data as of October 1, 2025.

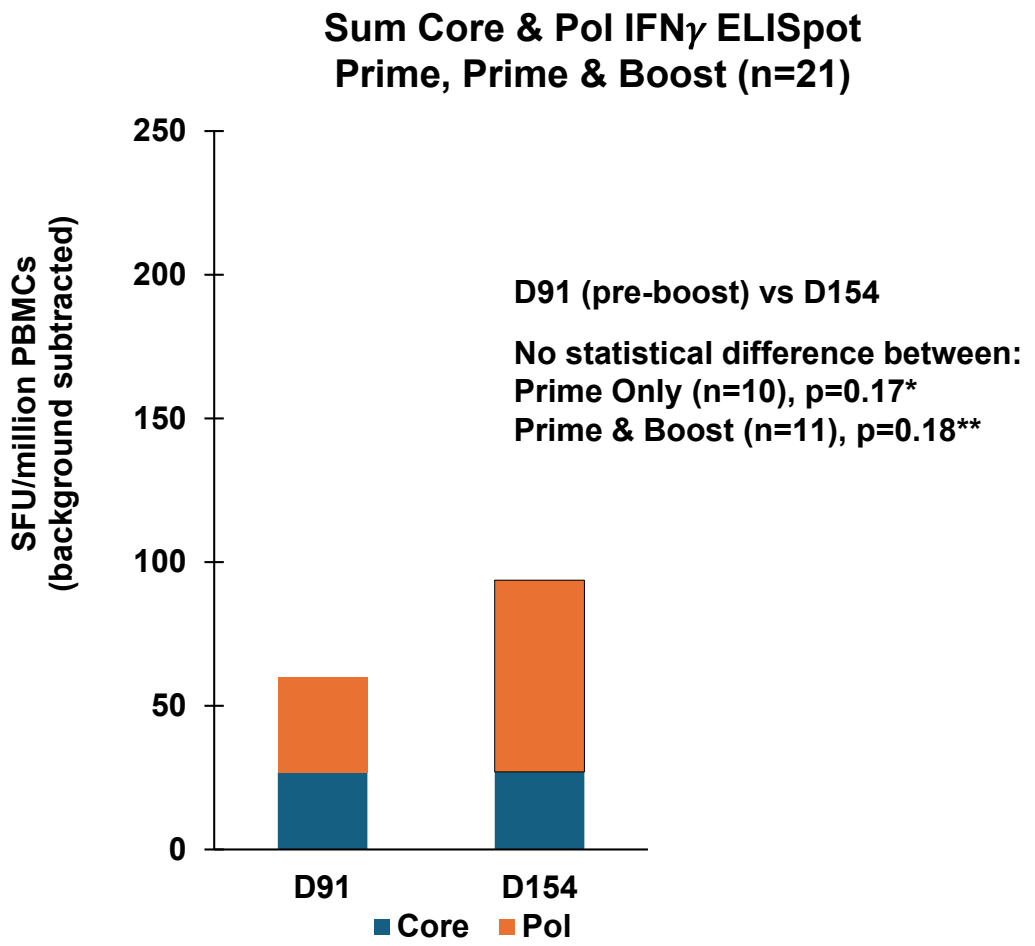
* 1 pt in Cohort 3 had a non-treatment-related significant adverse event that resulted in a 2-dose elebsiran+tobevibart treatment interruption.

** Pt withdrew consent at D28 - included in demographics, baseline characteristics, and safety, but excluded from Clinical Data (not evaluable).

AE – adverse event; SAE – serious adverse event; TRAE – treatment-related adverse event

VRON-0200 Prime Significantly Improved IFNγ ELISpot Responses, but was NOT enhanced with a Boost





*One-sided paired t-test; **Two-tailed paired t-test

VRON-0200 Added to SOC Produces Sustained and/or Continued HBsAg Declines

VRON-0200 Does NOT Target HBsAg

Log Change from BL
≤ –0.06
–0.07 to –0.49
–0.50 to –0.99
≥ –1.00

Boost D91

Pt #	D1
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	

N/A – not available

EOT - Day 1 for Prime Only: 6 mos post-tx (D180)
EOT - Day 91 for Prime and Boost: 6 mos post-tx (D271)

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VRON-0200 Added to SOC Produces Sustained and/or Continued HBsAg Declines

VRON-0200 Does NOT Target HBsAg

Log Change from BL
≤ –0.06
–0.07 to –0.49
–0.50 to –0.99
≥ –1.00

Boost D91

Pt #	D1	D14	D28
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			
14			
15			
16			
17			
18			
19			
20			
21			
22			
23			

- **Declines begin around Day 28**

EOT - Day 1 for Prime Only: 6 mos post-tx (D180)
EOT - Day 91 for Prime and Boost: 6 mos post-tx (D271)

N/A – not available

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VRON-0200 Added to SOC Produces Sustained and/or Continued HBsAg Declines

VRON-0200 Does NOT Target HBsAg

Log Change from BL
≤ –0.06
–0.07 to –0.49
–0.50 to –0.99
≥ –1.00

Boost D91

Pt #	D1	D14	D28	D60	D91
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					
16					
17					
18					
19					
20					
21					
22					N/A
23					

- **Declines begin around Day 28**

EOT - Day 1 for Prime Only: 6 mos post-tx (D180)
EOT - Day 91 for Prime and Boost: 6 mos post-tx (D271)

N/A – not available

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VRON-0200 Added to SOC Produces Sustained and/or Continued HBsAg Declines

VRON-0200 Does NOT Target HBsAg

Log Change from BL
≤ –0.06
–0.07 to –0.49
–0.50 to –0.99
≥ –1.00

Boost D91

Pt #	D1	D14	D28	D60	D91	D104	D118	D154	D360
1						N/A			
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									
13									
14									
15									
16									
17									
18									
19									
20									
21									#
22					N/A				
23									

- **Declines begin around Day 28**
- **Day 91 boost does not appear to improve HBsAg declines**
- **At Day 360**:
  - **19/23 (83%)** pts with sustained control and/or continued declines
  - **4 pts** with **≥ 1 $\log_{10}$ IU/mL** decline#

EOT - Day 1 for Prime Only: 6 mos post-tx (D180)
EOT - Day 91 for Prime and Boost: 6 mos post-tx (D271)

N/A – not available

#-0.97 $\log_{10}$ IU/mL decline

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VRON-0200 Added to SOC Produces Sustained and/or Continued HBsAg Declines

VRON-0200 Does NOT Target HBsAg

Log Change from BL
≤ –0.06
–0.07 to –0.49
–0.50 to –0.99
≥ –1.00

Boost D91

Pt #	D1	D14	D28	D60	D91	D104	D118	D154	D360
1	622.9					N/A			**406.9**
2	562.6								**39.8**
3	441.9								**297.7**
4	322.2								**184.8**
5	319.2								323.7
6	273.4								**195.5**
7	271.0								**127.9**
8	265.4								271.2
9	226.0								**101.1**
10	225.3								**187.4**
11	221.8								197.9
12	178.9								**141.2**
13	177.1								155.3
14	150.2								**67.0**
15	112.8								**81.9**
16	101.3								**77.5**
17	94.2								**56.3**
18	43.2								**20.1**
19	28.6								**22.9**
20	25.4								**0.7**
21	17.1								**1.8#**
22	15.5				N/A				**0.1**
23	9.7								**3.8**

- **Declines begin around Day 28**
- **Day 91 boost does not appear to improve HBsAg declines**
- **At Day 360**:
  - **19/23 (83%)** pts with sustained control and/or continued declines
  - **4 pts** with **≥ 1 $\log_{10}$ IU/mL** decline#
  - HBsAg declines **independent of BL levels**
  - 9/19 **(47%)** had **> 50% declines**

EOT - Day 1 for Prime Only: 6 mos post-tx (D180)
EOT - Day 91 for Prime and Boost: 6 mos post-tx (D271)

N/A – not available

#-0.97 $\log_{10}$ IU/mL decline

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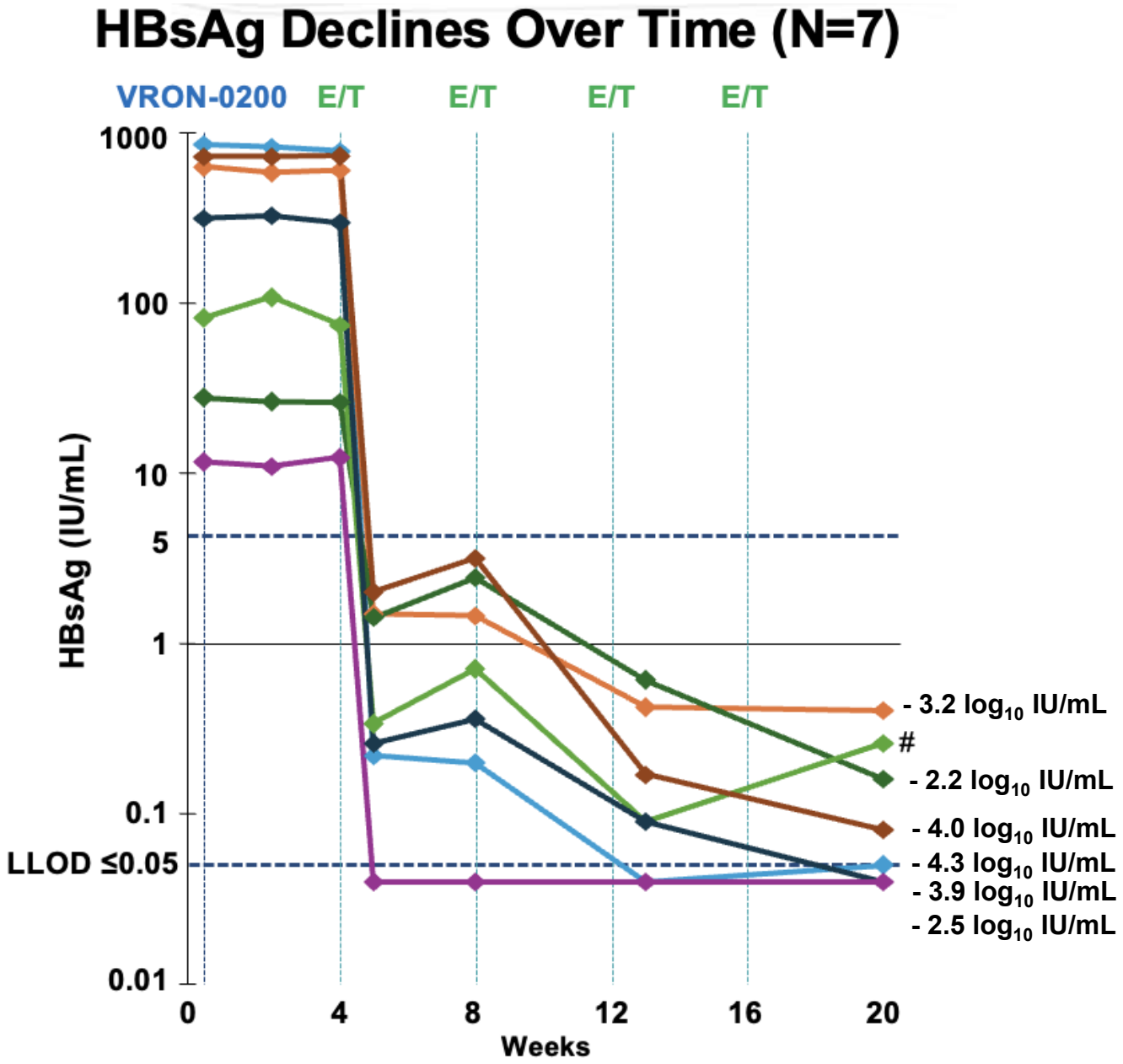
Cohort 3: VRON-0200 plus Antiviral Combination (N=7)
Rapid & Profound HBsAg Declines Observed in All Patients



At Week 5 (7 days post 1st E/T Dose):

- Rapid and profound HBsAg declines in all patients
- 100% ≤ 2 IU/mL
- These types of responses have not been observed with any antiviral regimen, alone or in combination with PEG-IFN
- Responses independent of BL HBsAg

At Week 20 (4 of 6 E/T doses):

- 3 of 6 pts had HBsAg loss (LLOD)

Patient missed E/T Doses 2 & 3 for non-treatment related AE; Cohort ongoing – to receive a total of 6 E/T doses

E/T – elebsiran plus tobevibart

Both elebsiran (siRNA) and tobevibart (S-antigen targeted mAb) are part of Vir Biotechnology, Inc.'s, clinical-stage portfolio for Hepatitis

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Key Take Aways

VRON-0200, which does NOT target HBsAg:

- Was safe and well tolerated
- A single dose induced immune responses, starting around Day 28
- HBV-specific immune activation and restoration occurred in the majority of patients (e.g., HBsAg declines)
- HBsAg declines were sustained and/or deepened up to 360 days after end of treatment
  - A long-term study has been implemented to follow these patients
- VRON-0200 prime, followed by the addition of an antiviral combination, resulted in rapid and profound HBsAg declines in all patients
- A “Spark and Fan” model, using VRON-0200 first (“Spark”), followed by an antiviral agent(s) (“Fan”), could position VRON-0200 to be THE immune-modulator backbone for future functional cure regimens

A Phase 2b SPARK-B combination study is in development

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    - **Middlemore Hospital** – Tien huey Lim, Ethan Chiddicks, Emma Dorsey, Iram Khan, Mhairi McIntyre
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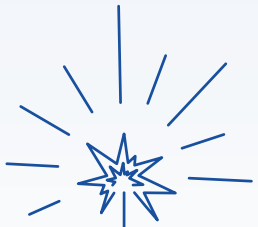
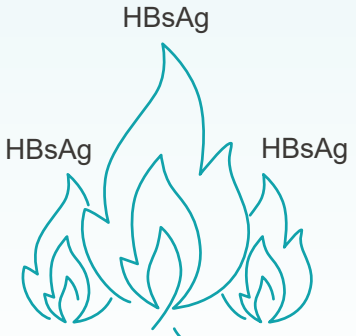
”Spark and Fan” Model for Chronic HBV: VRON-0200 as the “Spark”

VRON-0200 PRIME

VRON-0200 “Sparks” a new, and broadened, anti-HBV immune response



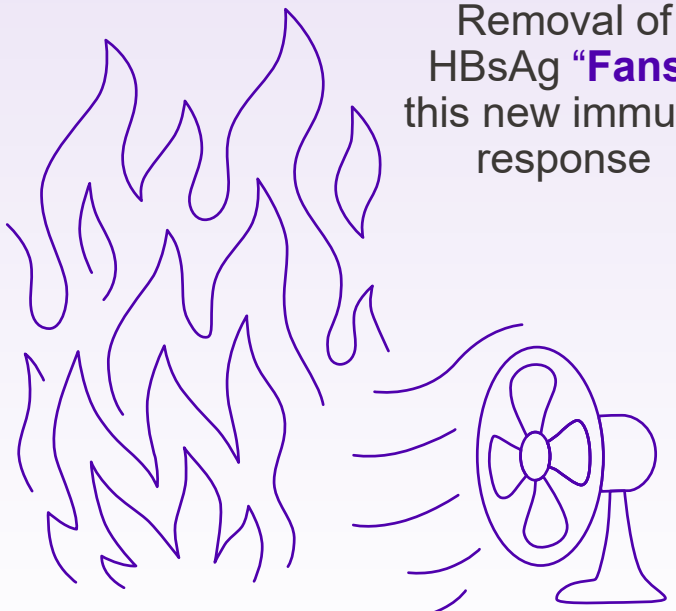
New immune response **reacts to antigen** (e.g. HBsAg)



Any antiviral or agent that can remove HBsAg can be a “Fan” for VRON-0200

BOOST

Removal of HBsAg **“Fans”** this new immune response



VRON-0200 could be **the immune-modulator backbone** for many different potential HBV Functional Cure regimens

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