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HBsAg Declines and Immune Responses Following a Single Dose of VRON-0200: Interim Results from a Phase1B Study for HBV Functional Cure in Chronic HBV-Infected Patients

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Disclosure of Conflict of Interest

- **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, Gilead Sciences, Janssen, and Roche. She has also received a research grant 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

Background

- Despite preventative vaccines, chronic HBV infection remains a high unmet medical need [1]
- Immune-based treatments are now considered necessary for HBV Functional Cure [2]
- VRON-0200 is a therapeutic vaccine for functional cure of HBV infection designed to enhance and broaden $CD8^+$ T cells to HBV core & pol [3-6]
- In chronically HBV-infected patients, VRON-0200 has demonstrated [7]:
  - A favorable safety and tolerability profile
  - Immunogenicity
  - Anti-HBV activity (HBsAg declines)

1. Bertoletti A, et al. J Hepatol 2016; 64 (1 Suppl):S71-S83. 2. Wong GL, et al. JHEP. 2022; 76: 1249-62. 3. Luber A, et al. ESMO TAT 2021: Abstract 143. 4. Xiang ZQ, et al. ASCO-SITC Clinical Immuno-Oncology Symposium 2020: Abstract 71. 5. Stiles KM, et al. J Virol. 2010; 84: 11640-60. 6. Virion Therapeutics, LLC. Data on File; 2024. 7. Wong GL, et al. AASLD 2024: Abstract #LBA-5029.

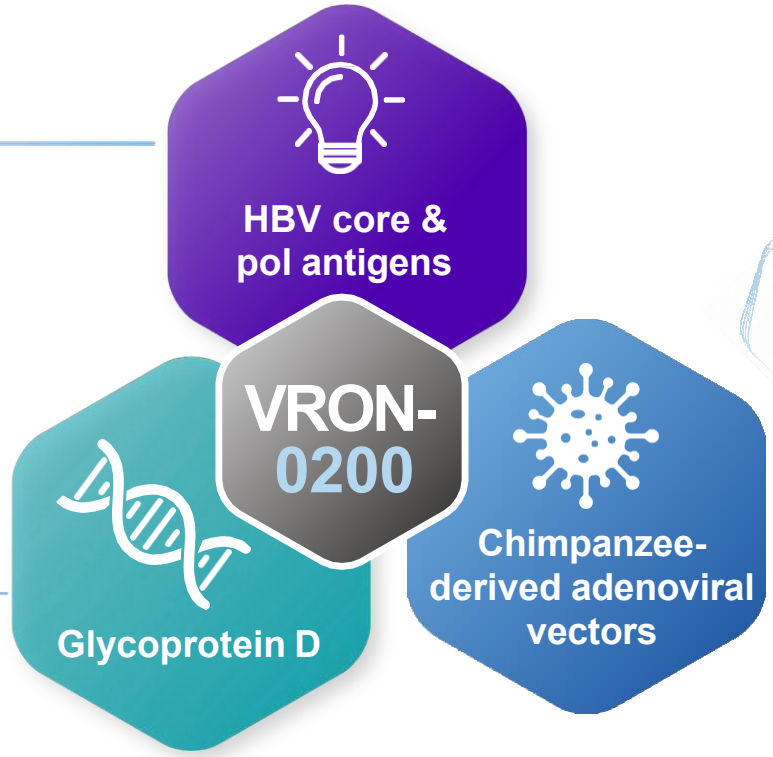
VRON-0200: A Potential First-in-Class, Best-In-Class Immunotherapy for HBV Functional Cure

HBV antigens

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

Genetically encoded checkpoint modifier*

- Checkpoint modification **amplifies** and **broadens** CD8⁺ T cell response to the target antigen(s)



Viral vector platform

- Limited pre-existing vector immunity
- Allows for optimized CD8⁺ T cell responses

HBV, hepatitis B virus.

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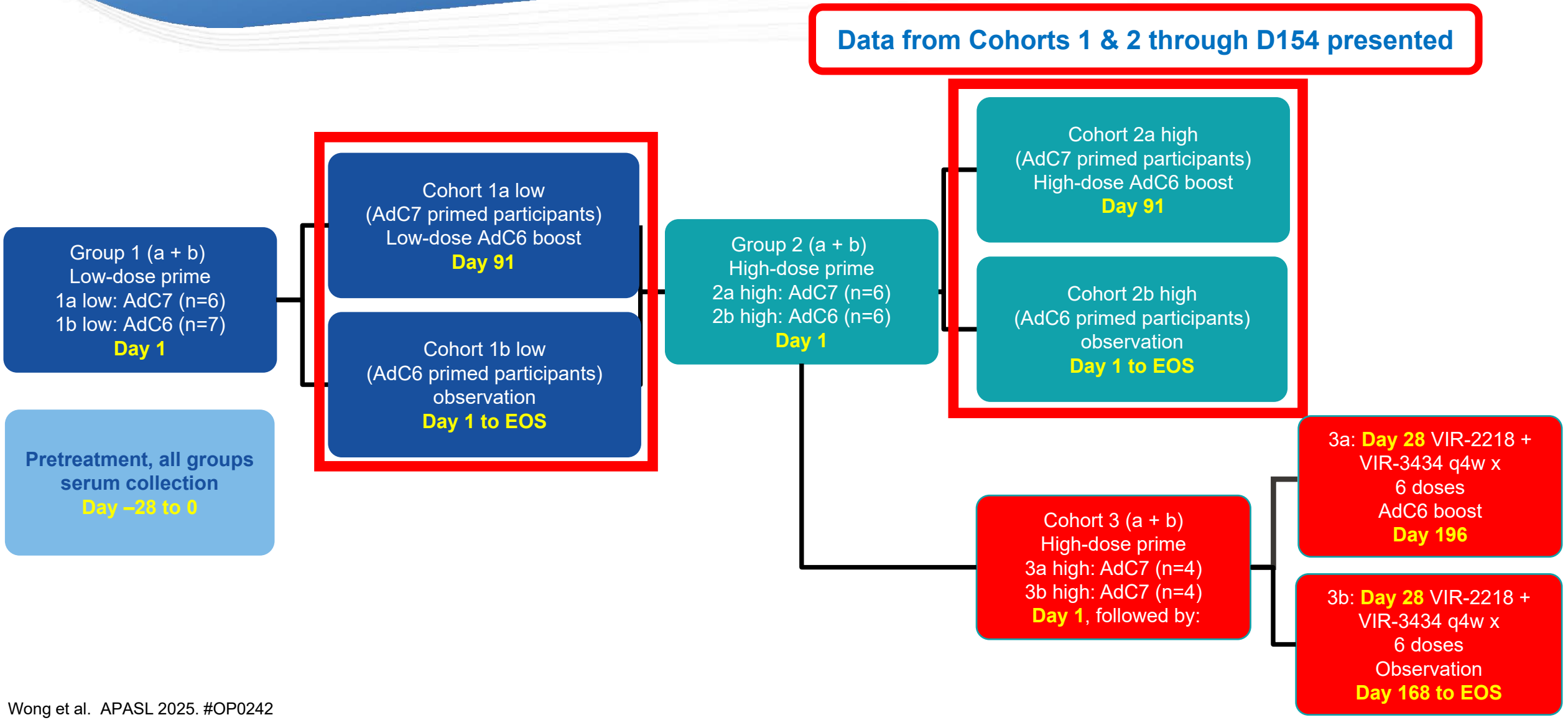
*More information about MOA available at www.VirionTx.com

Purpose

To report ongoing safety, immunogenicity data, and HBsAg changes in chronically HBV-infected patients vaccinated with VRON-0200

Study Schema

Data from Cohorts 1 & 2 through D154 presented



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Key Inclusion Criteria

1. **Adults ≥ 18 to ≤ 55 years**
2. BMI ≥ 18 to ≤ 32 kg/m^2
3. Documented chronic HBV infection
4. **HBsAg ≤ 500 IU/mL (Cohort 3 ≤ 1,000 IU/mL)**
5. On entecavir or tenofovir > 12 months and expected to stay on therapy
6. HBV DNA < 40 IU/mL > 12 months
7. ALT < 2x ULN
8. AST levels < 2x ULN
9. No clinical diagnosis of advanced liver fibrosis and/or cirrhosis

Methods: Clinical assessments (Data Cutoff: Feb. 20, 2025)

Safety

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

HBsAg

- ELISA for absolute changes (log_{10} IU/mL; LLOD 0.05 IU/mL)
- Day 91 – all prime patients
- Day 154 – included prime, and prime and boost, patients

HBsAb (Qualitative)

- anti-HBs concentration detected at ≥ 10 mIU/mL is considered positive

Immunologic Assessments

- IFNγ ELISpot to core, pol, and surface peptide pools
- Immunologic "**responder**" – 2 consecutive core + pol ELISpot measurements at Day 28 > average of the 2 pre-treatment timepoints, and above the LLOD
- One-side paired t-test – assess sum of core + pol ELISpot measurements from average of the pre-treatment values compared to Day 28, and Day 91, respectively, for each patient

Demographics and Baseline Characteristics

	Cohort 1a (n=6)	Cohort 1b (n=7)	Cohort 2a (n=7)	Cohort 2b (n=7)	Overall (N=27)
Median age, yrs (range)	43 (37-52)	49 (41-54)	47(45-54)	46(41-55)	46 (37-55)
Sex, n (%)					
Male	6 (100%)	6 (86%)	4 (57%)	6 (86%)	22 (81%)
Female	0 (0%)	1 (14%)	3 (43%)	1 (14%)	5 (19%)
Race, n (%)					
Asian	5 (83%)	6 (86%)	6 (86%)	7 (100%)	24 (89%)
Native Hawaiian or Other Pacific Islander	0 (0%)	0 (0%)	1 (14%)	0 (0%)	1 (4%)
White	0 (0%)	1 (14%)	0 (0%)	0 (0%)	1 (4%)
Other	1 (17%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
BMI (kg/m^2), median (range)	29.3 (27.3 – 31.7)	24.6 (20.2 – 32)	27.4 (22.9 – 31.6)	23 (19.7-27.7)	26.7 (19.7 – 32)
Baseline HBsAg Levels (IU/mL), median (range)	222 (29-319)	273 (16-623)	124.8(17.1-322.2)	226 (9.66-562.6)	177.1 (9.66 - 623*)
Baseline HBsAg Levels, n (%)					
>500 IU/mL	0 (0%)	1 (14%*)	0 (0%)	1 (14%)*	2 (7%*)
200 - ≤ 500 IU/mL	4 (67%)	2 (29%)	1 (14%)	3 (43%)	10 (37%)
100 - 199 IU/mL	0 (0%)	2 (29%)	4 (57%)	1 (14%)	7(26%)
< 100 IU/mL	2 (33%)	2 (29%)	2 (29%)	2 (29%)	8 (30%)
Baseline ALT (x ULN), n (%)					
< 1 x ULN	5 (83%)	7 (100%)	6 (86%)	6 (86%)	24 (89%)
1 to 1.5 x ULN	0 (00%)	0 (0%)	1 (14%)	1 (14%)	2 (7%)
1.6 x ≤ 2 x ULN	1 (17%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
HBeAg Status at Baseline, n (%)					
Negative	6 (100%)	6 (80%)	7 (100%)	7 (100%)	26 (96%)
Positive	0 (0%)	1 (20%)	0 (0%)	0 (0%)	1 (4%)

* As per protocol, participant had prior HBsAg ≤500 IU/mL at screening

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Safety and Tolerability

	Cohort 1a (n=6)	Cohort 1b (n=7)	Cohort 2a (n=7)	Cohort 2b (n=7)	Overall (N=27)
Any AE, n	6	9	13	10	38
Grade 1	5	7	9	6	27
Grade 2	1	2	4	4	12
Grade 3 or 4	0	0	0	0	0
SAE, n	0	0	0	0	0
TEAEs, n	2	3	10	5	20
AE Leading to Study Drug Discontinuation, n	0	0	0	0	0
Study Discontinuations, n	0	0	0	0	0
ALT elevations, n					
Grade 1	0	0	0	0	0
Grade 2	0	0	0	0	0

Of 7,680 Patient Safety Days: 38 AEs were reported in 17 patients; 20 TEAEs included 3 – Grade 2: eczema, myalgia, and runny nose, and 17 – Grade 1 events. All TEAE symptoms have resolved.

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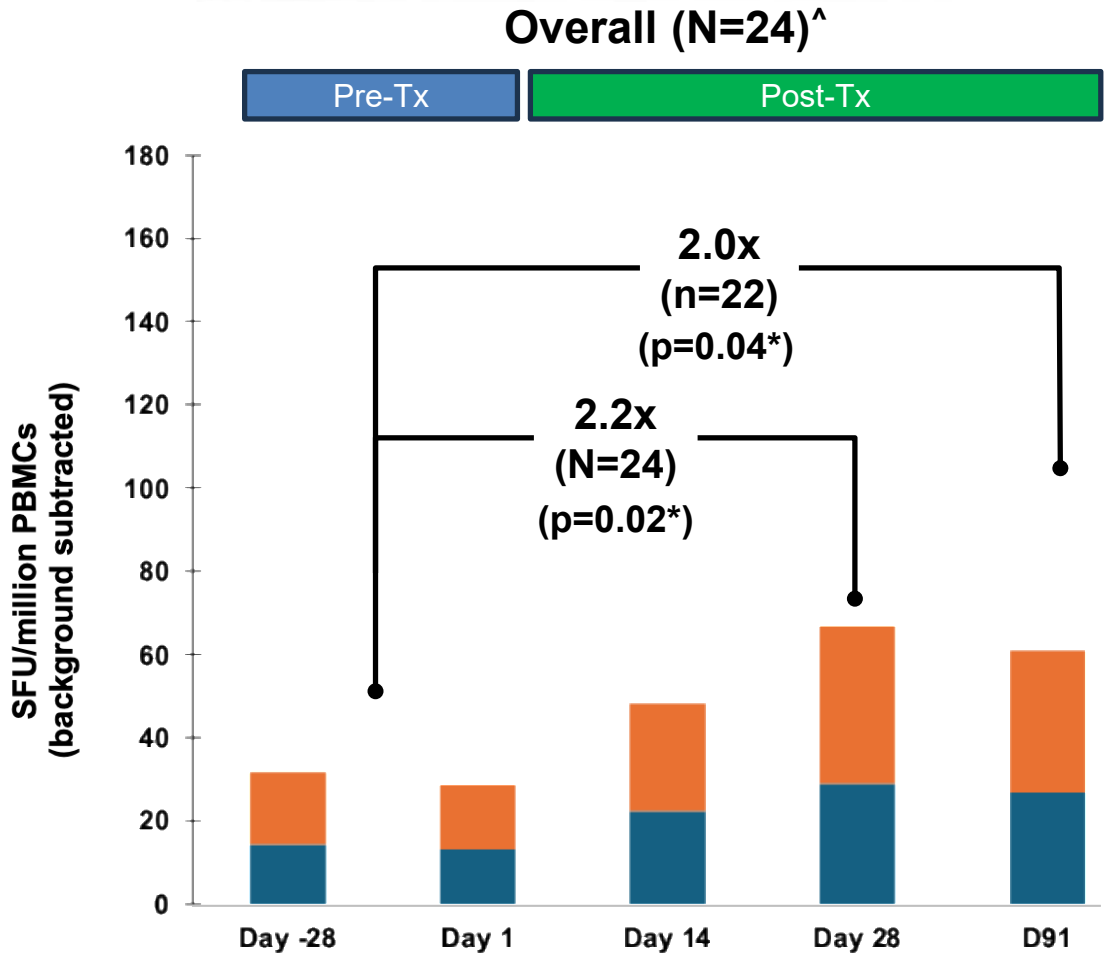
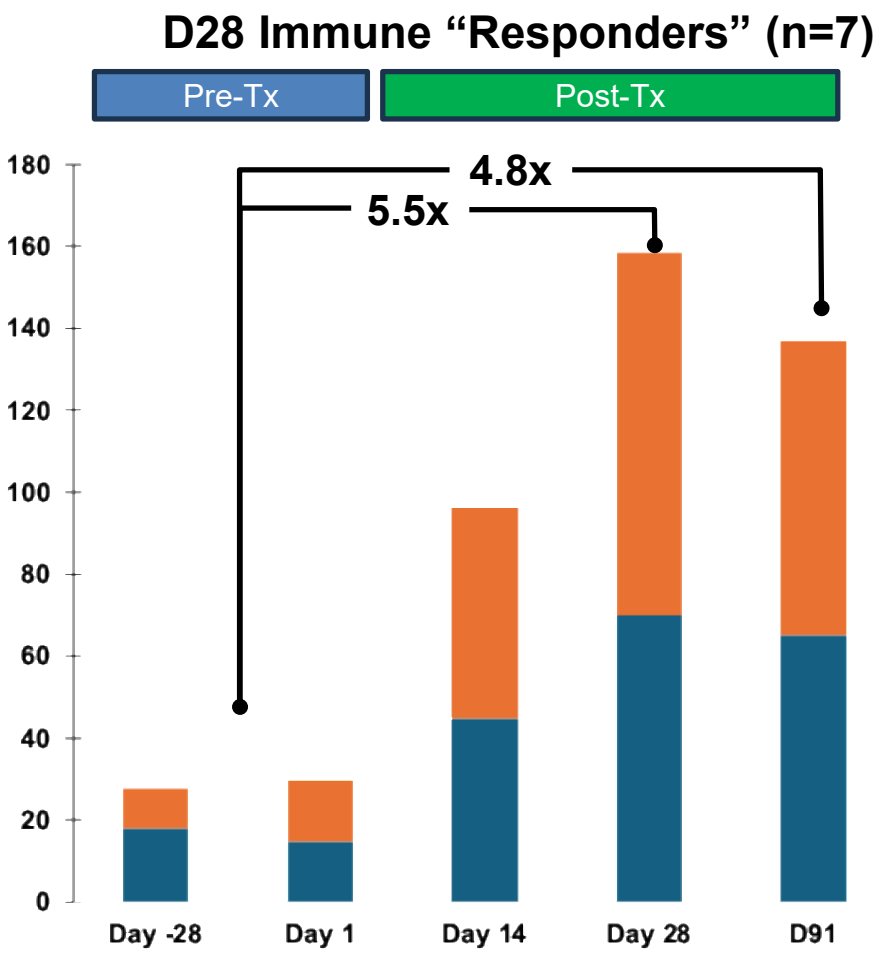
VRON-0200 Significantly Improved HBV IFNγ ELISpot Responses Post Prime Vaccination





Core Pol N & C

D28 Responders are defined as having ELISpot measurement above the LOD with 2 consecutive timepoint measurements greater than the average of the two pre-treatment timepoints

*One-sided paired t-test; ^D91 unavailable for 2 patients - replaced with D104

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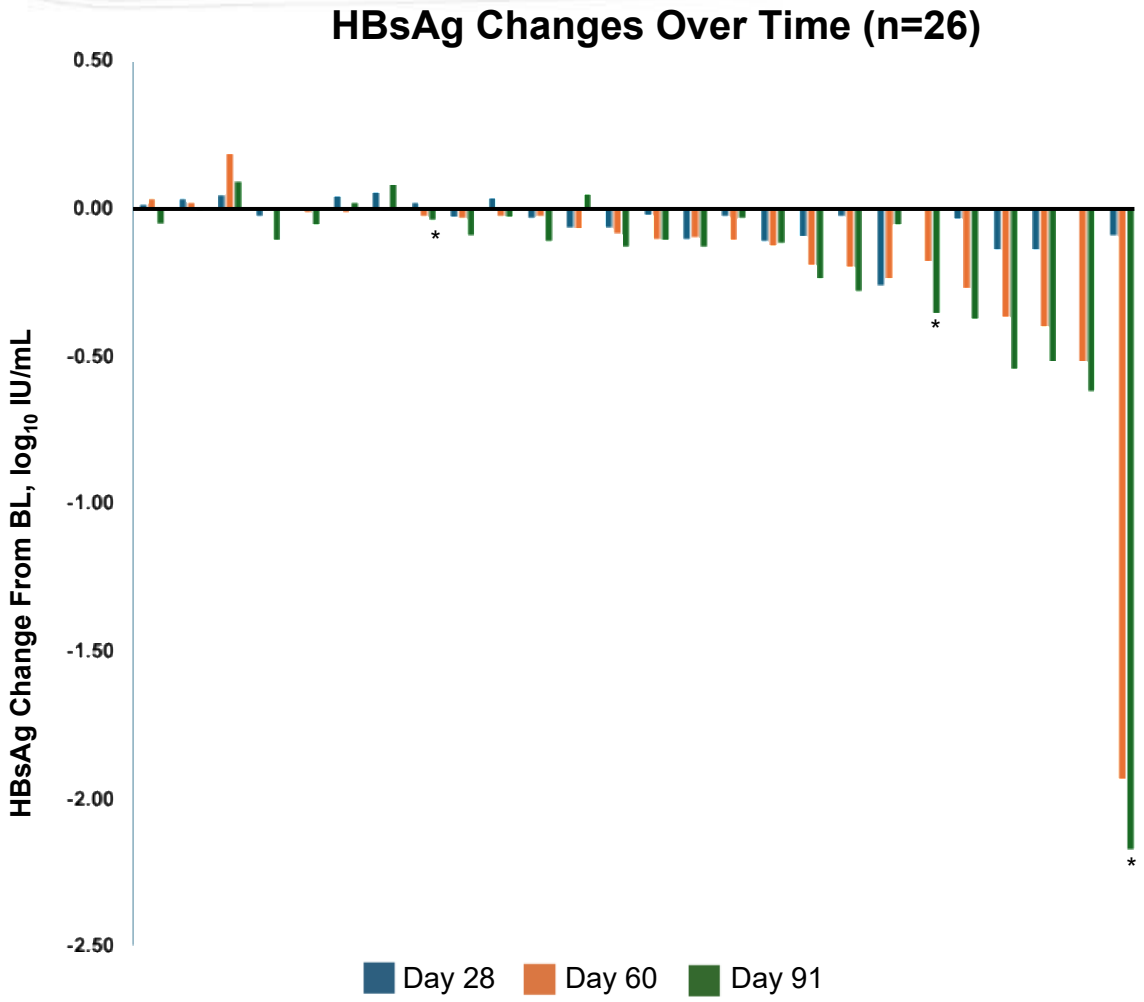
A Single VRON-0200 Prime Dose Lowers HBsAg Levels Despite NOT Targeting Surface Antigen



Cohorts 1 & 2
Single Prime Dose Day 1

6/26 (23%) had HBsAg ≥ 0.4 log_{10} IU/mL declines at Day 91

-2.2 log_{10} IU/mL
-0.6 log_{10} IU/mL
-0.5 log_{10} IU/mL
-0.5 log_{10} IU/mL
-0.4 log_{10} IU/mL
-0.4 log_{10} IU/mL

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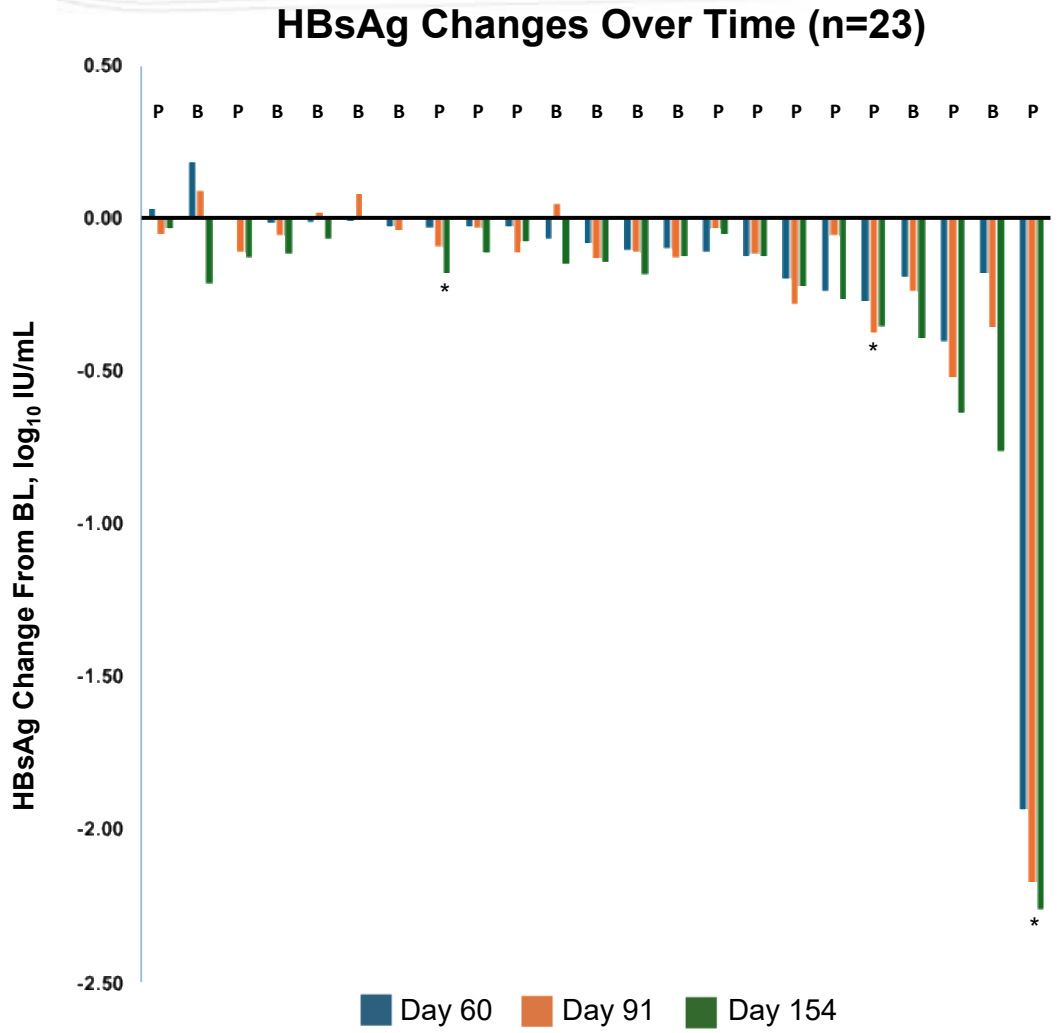
*D91 Sample missing; D104 sample used

VRON-0200 HBsAg Declines Deepen Over Time



Cohorts 1 & 2
Single Prime & Prime/Boost (D91)

6/24 (25%) had HBsAg ≥ 0.4 log_{10} IU/mL declines at Day 118 and beyond**

-2.3 log_{10} IU/mL
-0.8 log_{10} IU/mL
-0.6 log_{10} IU/mL
-0.5 log_{10} IU/mL**
-0.4 log_{10} IU/mL
-0.4 log_{10} IU/mL

VRON-0200 Does NOT Target Surface Antigen

*D91 Sample missing; D104 sample used; P – Prime Only, B – Prime & Boost (D91)
**3 patients at D91 have not reached D154; 2 have continued to trend downward at D118, with 1 patient -0.5 log_{10} IU/mL decline; 1 patient has not reached D118 but had -0.6 log_{10} IU/mL decline at D91

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Conclusions

This is the first clinical report of VRON-0200 monotherapy Prime, and Prime and Boost:

- With 7,680 patient safety days reported (N=27), VRON-0200 was safe and well-tolerated
  - No differences have been observed between low- and high-doses, and Prime, and Prime and Boost regimens
- S-antigen declines were observed in ~25% of patients despite the fact VRON-0200 does NOT target S
  - In patients with HBsAg declines, it continued over time, regardless of baseline S antigen levels or a boost dose at Day 91
- All Cohorts, including the combination Cohort, are now fully enrolled and ongoing
  - Factors associated with immunologic responses and HBsAg declines are being evaluated further
  - Future data to be presented in 2025

These data support the continued study of VRON-0200 as a safe and well tolerated, easy-to-administer, potential IFN-sparing immunotherapy, alone or in combination, for HBV functional cure

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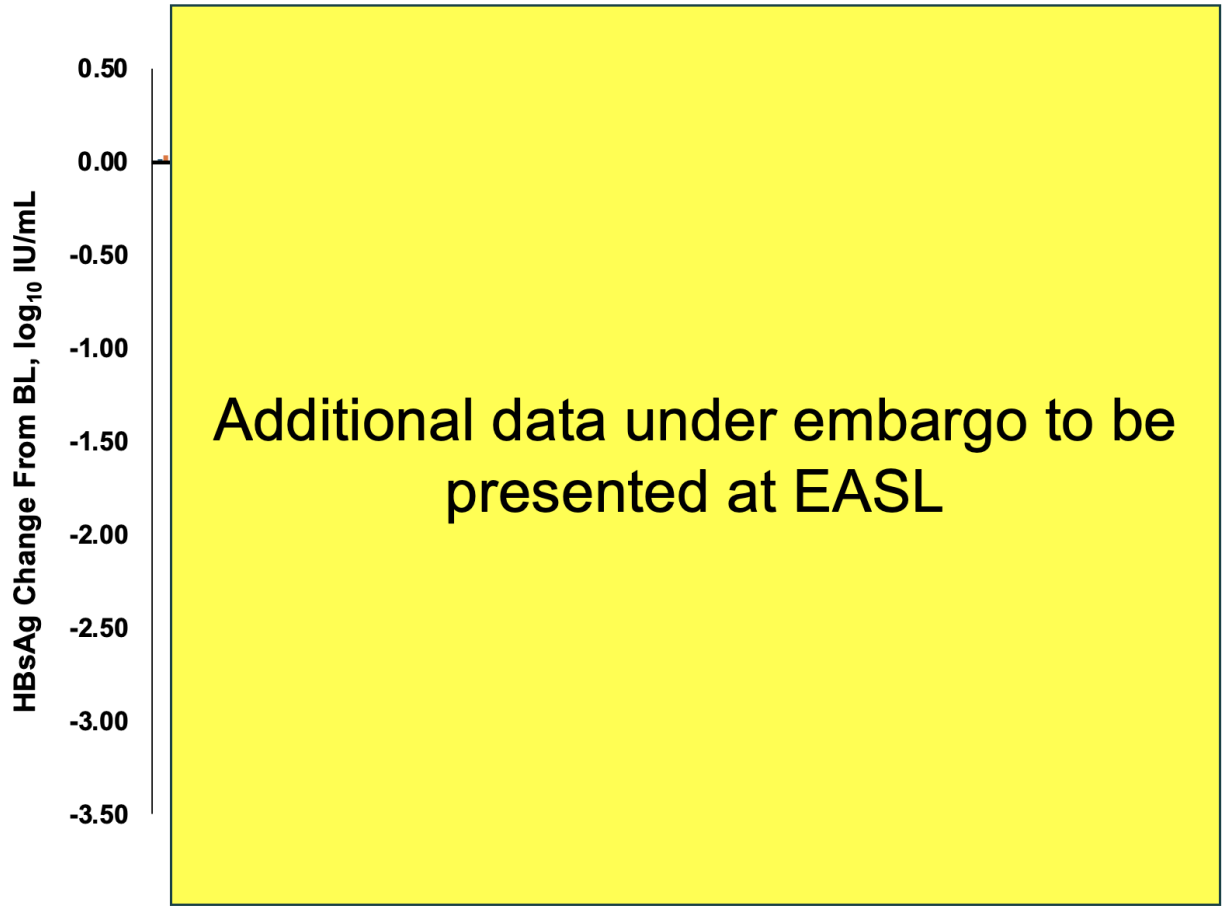
VRON-0200 Cohort 3: Embargoed Data To Be Presented at EASL

HBsAg Changes Over Time (N=30)



Cohort 3 – Combination Therapy with VRON-0200

Additional data under embargo to be presented at EASL

HBsAb

HBsAb	D1	D14	D28	D35	D56	D84
Additional data under embargo to be presented at EASL						

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