First-in-Human, First-in-Class, Phase 1B Preliminary Safety Data of VRON-0200, a Novel Checkpoint Modifier Containing Immunotherapy, for HBV Functional Cure

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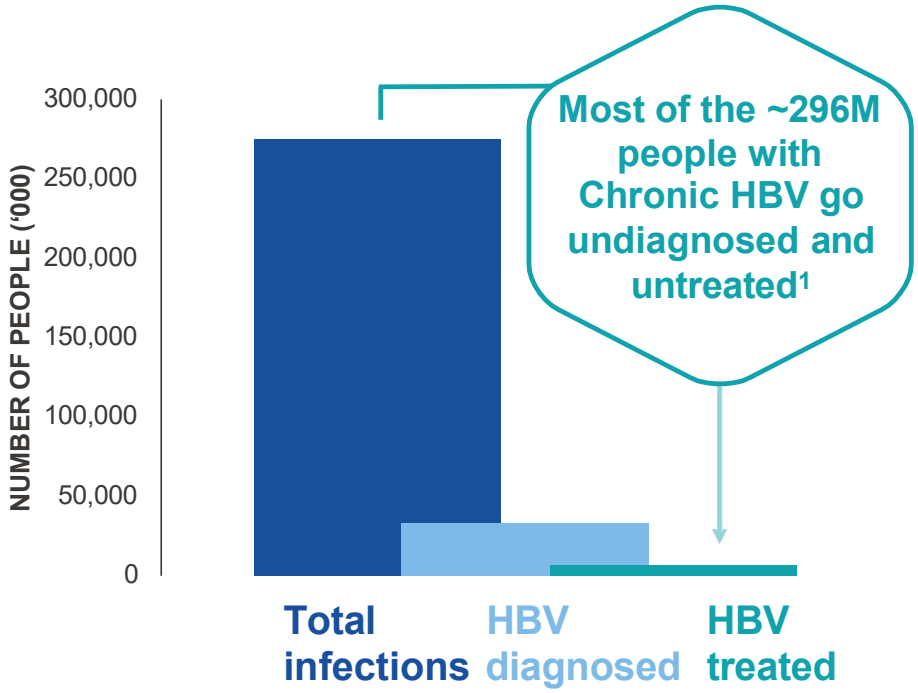
Disclosure of Conflict of Interest

- **Grace Wong** has served as an advisory committee member for AstraZeneca, Gilead Sciences, GlaxoSmithKline and Janssen, 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
- **Hildegund Ertl** is a Scientific Founder of Virion Therapeutics, LLC and owns shares in the company
- **Sue Currie** and **Andrew Luber** work at Virion Therapeutics, LLC and own shares in the company

Chronic HBV Infection is a High Unmet Need



- Chronic HBV remains a **global public health problem** despite vaccination[2]
- Antivirals **rarely achieve functional cure** and **require lifelong drug therapy**[3]
- Addition of **immune-based treatments now considered necessary** for HBV Functional Cure[4]

HBV, hepatitis B virus

1. WHO Hepatitis B Report; June 24, 2022; 2. Bertoletti A, et al. J Hepatol 2016; 64(1 Suppl):S71–S83; 3. Tsounis EP, et al. World J Gastroenterol 2021;27:2727–57.; 4. Wong, GL, et al. JHEP. 2022; 76: 1249-62.

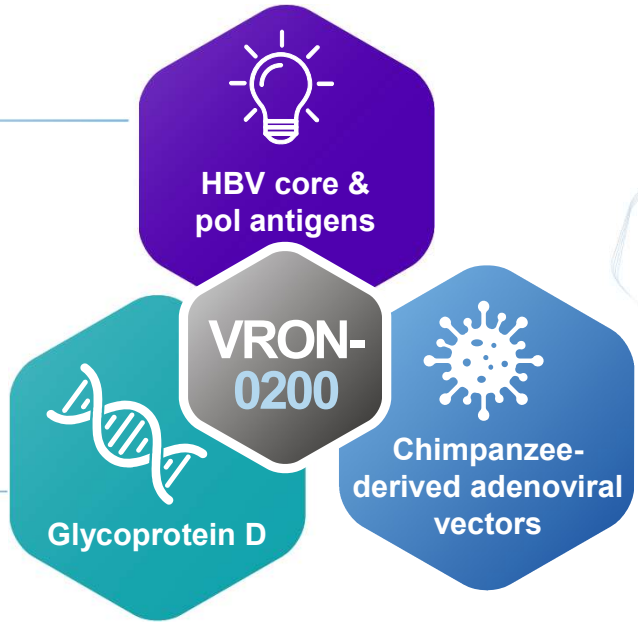
VRON-0200: A First-in-Class Immunotherapy for Chronic HBV

HBV antigens

- Optimized **HBV core & pol antigens**
- Pan genotypic (A, B, C, D)

Genetically encoded checkpoint modifier

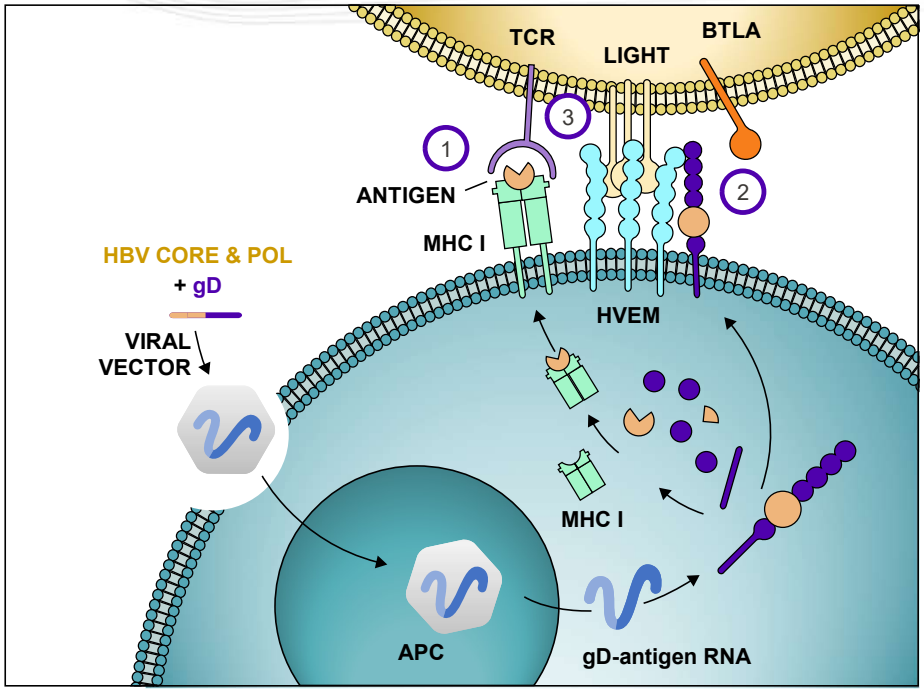
- Checkpoint modification amplifies and broadens $CD8^+$ T cell response to the target antigen(s)



Viral vector platform

- Limited pre-existing vector immunity
- Heterologous vectors (AdC6 & AdC7) allows for prime & boost administration

Checkpoint Modification of T cell Activation Enhances & Broadens T cell Responses*



1. Antigen(s) Presented to CD8⁺ T cell for Activation
2. Checkpoint Modifier Blocks Key Inhibitory Signaling
3. Increased T cell Receptor Signaling & Co-Stimulation

gD – HSV-1 glycoprotein D acts as a genetically encoded checkpoint modifier

Benefits of Checkpoint Modification

Amplifies
T cell Responses

Broadens
T cell Responses
(e.g., sub-dominant epitopes)

Limits
T cell Impairment

Mitigates
Safety Concerns
(e.g., locally acting)

*More information about preclinical data and MOA are available at www.VirionTx.com

Purpose and Methods

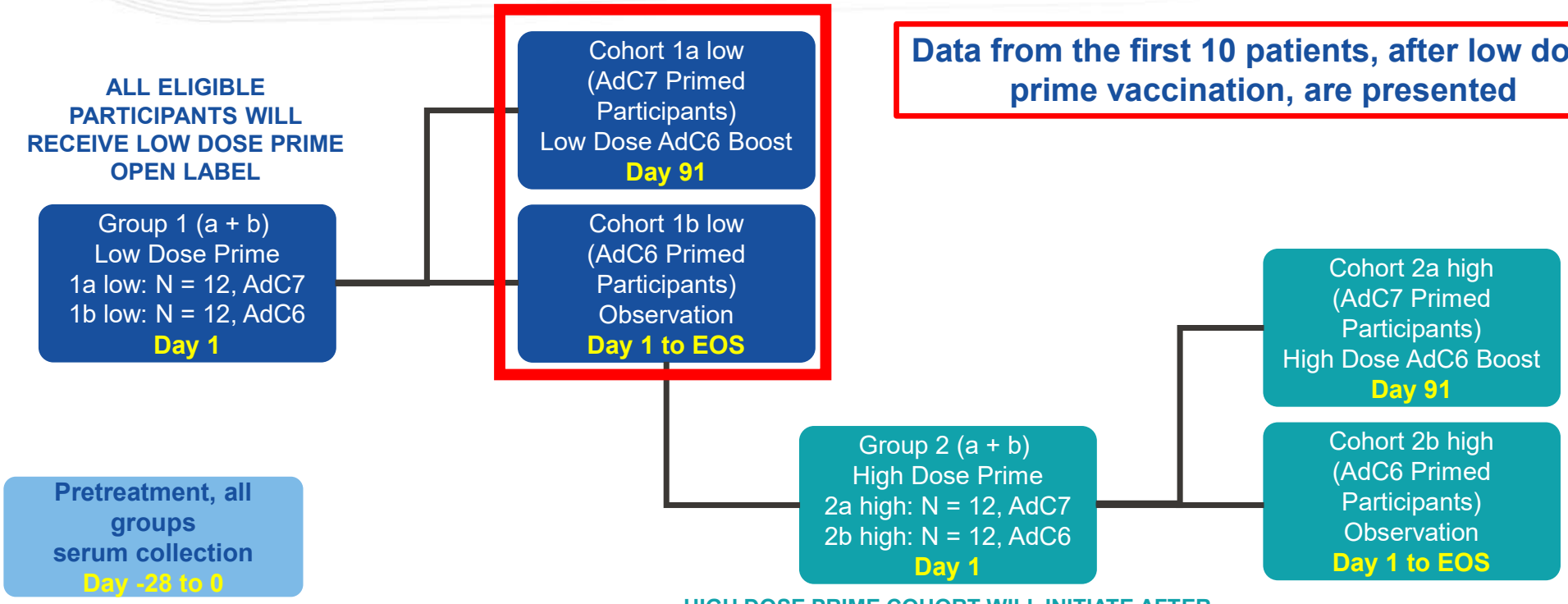
- **Methods:**
  - Patients randomized to receive either AdC7 or AdC6
  - Patients who received a prime vaccination included in this analysis (data cutoff as of March 15, 2024)
- **Study Objectives:**
  - Primary objectives – safety and tolerability
  - Secondary objectives – $CD8^+$ T cell frequencies
  - Exploratory objectives – antiviral, immunologic, and anti-vector antibody assessments

Purpose: To evaluate the safety and tolerability of VRON-0200 in chronically HBV-infected patients who received a low dose, prime vaccination

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**
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

VRON-0200 P1B Study Design



- 1a – low dose Prime vaccination (1×10^{10} vp) of AdC7
- 1b – low dose Prime vaccination (1×10^{10} vp) of AdC6
- 2a – high dose Prime vaccination (5×10^{10} vp) of AdC7
- 2b – high dose Prime vaccination (5×10^{10} vp) of AdC6
- Randomized in a 1:1 Ratio

EOS – End of Study

Demographics and Baseline Characteristics

	Cohort 1a (n=5)	Cohort 1b (n=5)	Overall (n=10)
Median age, yrs (range)	43 (42-52)	49 (41-54)	44.5 (41-54)
Sex, n (%)			
Male	5 (100%)	5 (100%)	10 (100%)
Female	0 (0%)	0 (0%)	0 (0%)
Race, n (%)			
Asian	4 (80%)	4 (80%)	8 (80%)
Native Hawaiian or Other Pacific Islander	0 (0%)	0 (0%)	0 (0%)
White	0 (0%)	1 (20%)	1 (10%)
Other	1 (20%)	0 (0%)	1 (10%)
BMI (kg/m^2), median (range)	29.4 (27.3 – 31.7)	25 (23.2 – 32)	28.2 (23.2 – 32)
Baseline HBsAg Levels (IU/mL), median (range)	222 (29-319)	273 (16-623)	244 (16-623*)
Baseline HBsAg Levels, n (%)			
>500 IU/mL	0 (0%)	1 (20%*)	1 (10%*)
200 - ≤ 500 IU/mL	3 (60%)	2 (40%)	5 (50%)
100 - 199 IU/mL	0 (0%)	0 (0%)	0 (0%)
< 100 IU/mL	2 (40%)	2 (40%)	4 (40%)
Baseline ALT (x ULN), n (%)			
< 1 x ULN	4 (80%)	5 (100%)	9 (90%)
1 to 1.5 x ULN	0 (00%)	0 (0%)	0 (0%)
1.6 x ≤ 2 x ULN	1 (20%)	0 (0%)	1 (10%)
HBeAg Status at Baseline, n (%)			
Negative	5 (100%)	4 (80%)	9 (90%)
Positive	0 (0%)	1 (20%)	1 (10%)

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

Data cutoff as of March 15, 2024

Study Subject Disposition

Number of Patients with Study Visit at Day of Follow Up

	Day 1	Day 7	Day 14	Day 28	Day 60	Day 91*
Cohort 1a (n=5)	5	5	5	4	3	3
Cohort 1b (n=5)	5	5	5	4	3	2
Overall (n=10)	10	10	10	8	6	5

*For those subjects randomized to receive a boost vaccination, this visit is prior to receipt of the boost vaccination

As of March 15, 2024, 641 total on-treatment prime (up to and including Day 91) patient safety days are included in this analysis

Data cutoff as of March 15, 2024

Safety and Tolerability

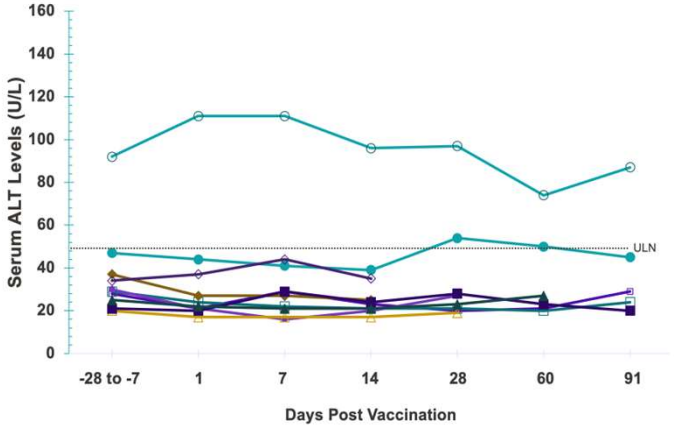
	Cohort 1a (n=5)	Cohort 1b (n=5)	Overall (n=10)
Any AE, n	0	2	2
Grade 1	0	2	2
Grade 2	0	0	0
Grade 3 or 4	0	0	0
SAE, n	0	0	0
TEAEs, n	0	1	1
AE Leading to Study Drug Discontinuation, n	0	0	0
Study Discontinuations, n	0	0	0
ALT elevations, n			
Grade 1	0	0	0
Grade 2	0	0	0

The two Grade 1 AEs in Cohort 1b were discrete events in a single patient and consisted of a leg cramp (not considered treatment related) and flu like symptoms (considered treatment related) – all symptoms resolved without treatment

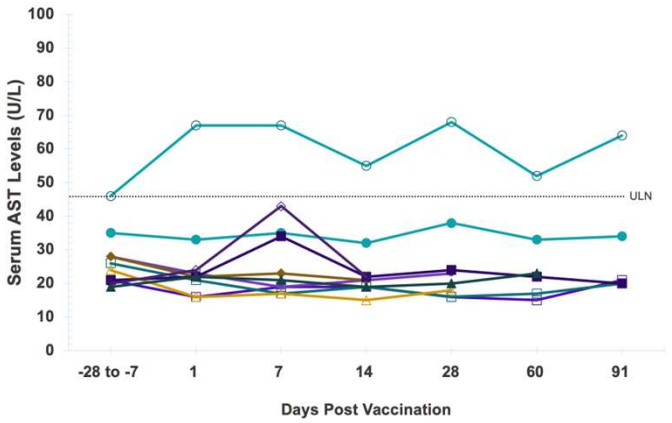
Data cutoff as of March 15, 2024

Select Liver Function Tests

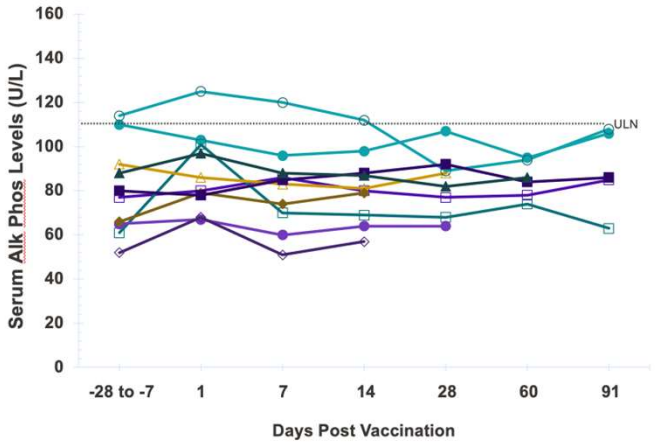
ALT



AST



ALP



No alterations observed in any other liver function tests, post vaccination

Data cutoff as of March 15, 2024;
ALT: alanine transaminase; AST: aspartate aminotransferase; ALP: Alkaline Phosphatase

Day 1 samples taken prior to vaccination

Open symbols – Cohort 1a; Solid symbols – Cohort 1b

Conclusions

- **These are the first ever clinical safety data from a checkpoint modifier containing immunotherapy**
- **To date, VRON-0200 Cohort 1 (low dose prime vaccinated patients):**
  - Has been well tolerated with no SAEs
  - No safety concerns
  - No unexpected laboratory abnormalities, including liver function tests

These data demonstrate that VRON-0200 is safe, well tolerated, and easy to administer, and support its continued evaluation as a potential interferon-sparing option for HBV Functional Cure

- **Study is progressing with Cohort 1 nearing completion, boost vaccinations underway, and immunologic assessments ongoing**

- **The first-ever immunologic (i.e. interferon-gamma), as well other serologic data, are planned for presentation later this year**

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