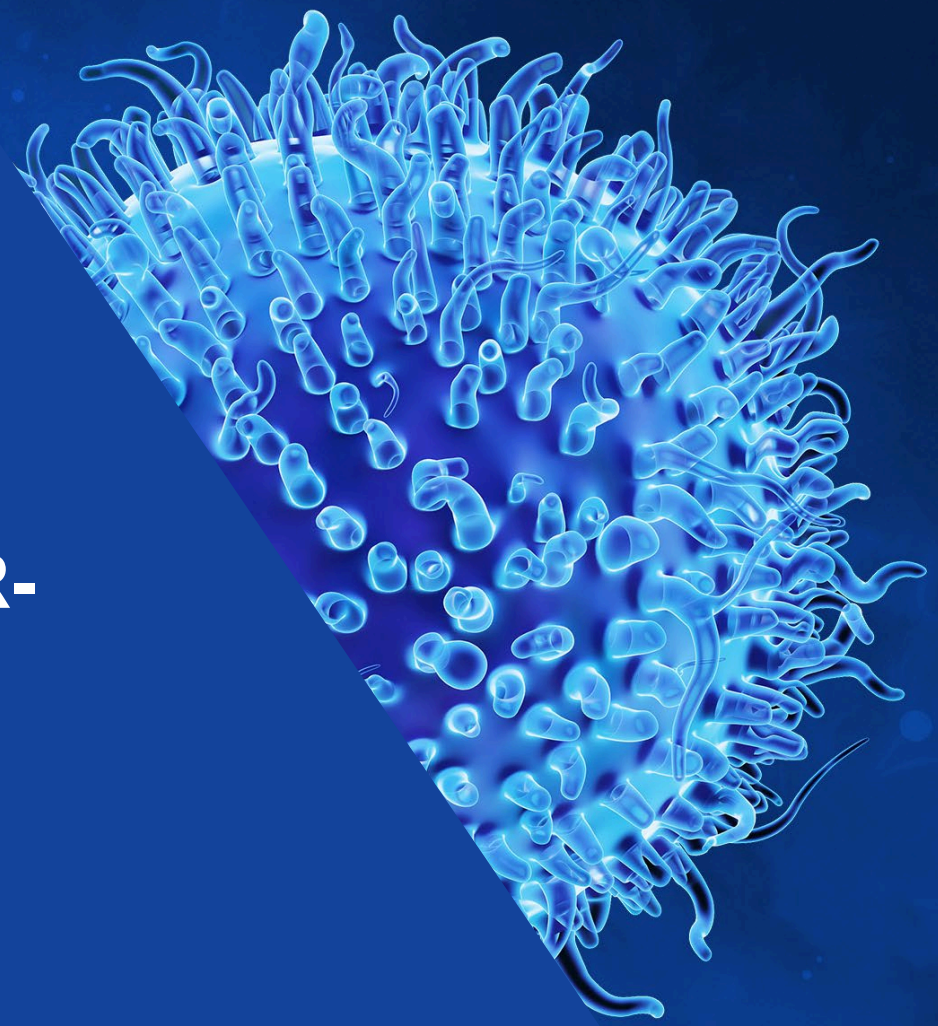
VIR-3434, an investigational monoclonal antibody neutralizing Hepatitis B virus and facilitating FcγR-mediated elimination of HBsAg

– *Preclinical Studies*



Michael A. Schmid, PhD, Vir Biotechnology

The HBV Forum – Webinar on January 18th 2022

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Statements in this presentation that are not statements of historical fact are forward-looking statements. Such forward-looking statements include, without limitation, statements regarding the near-term financial performance of Vir Biotechnology, Inc. (the "Company"), the timing and expected number of therapeutic doses that the Company will be able to supply to patients, the expected success, cost, and timing of the Company's research and clinical development plans and clinical trials, the Company's goals with respect to the prophylaxis or treatment of COVID-19, HBV, influenza A and HIV, the Company's objectives, strategy, technology platform and clinical trial designs, the potential benefits of the Company's collaborations, and the Company's ability to complete certain milestones. Words such as "believe," "anticipate," "plan," "expect," "intend," "will," "may," "goal," "potential" and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain these identifying words. These forward-looking statements are based on the beliefs of the management of the Company as well as assumptions made by and information currently available to the Company. Such statements reflect the current views of the Company with respect to future events and are subject to known and unknown risks, including business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company, including, without limitation, risks inherent in developing the Company's products and technologies, future results from the Company's ongoing and planned clinical trials such as unexpected data or clinical site activation rates or clinical trial enrollment rates that are lower than expected, difficulties arising from the Company's collaborations, challenges in accessing adequate manufacturing capacity, the Company's ability to obtain adequate financing to fund its planned clinical trials and other expenses, statements related to regulatory authorizations and approvals, trends in the industry, changes in the competitive landscape, delays or disruptions due to the COVID-19 pandemic, including supply chain disruptions, the legal and regulatory framework for the industry, unexpected litigation or disputes and future expenditures. In light of these risks and uncertainties, the events or circumstances referred to in the forward-looking statements may not occur. The actual results may vary from the anticipated results and the variations may be material. Other factors that may cause the Company's actual results to differ from current expectations are discussed in the Company's filings with the U.S. Securities and Exchange Commission, including the section titled "Risk Factors" contained therein. These forward-looking statements should not be taken as forecasts or promises nor should they be taken as implying any indication, assurance or guarantee that the assumptions on which such forward-looking statements have been made are correct or exhaustive or, in the case of the assumptions, fully stated in this presentation. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this presentation is given. Except as required by law, the Company undertakes no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise. The Company claims the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995 for all forward-looking statements.

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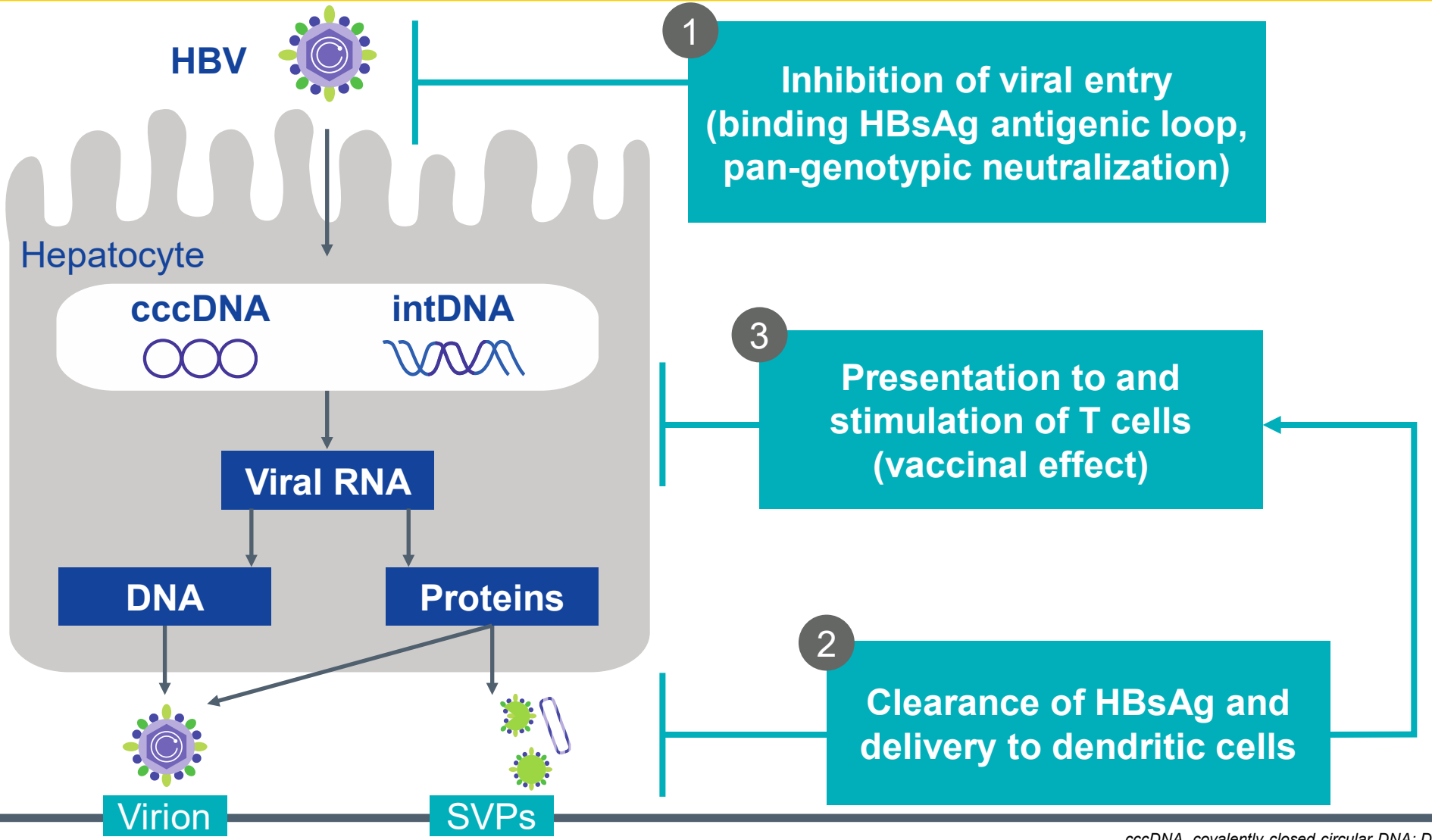
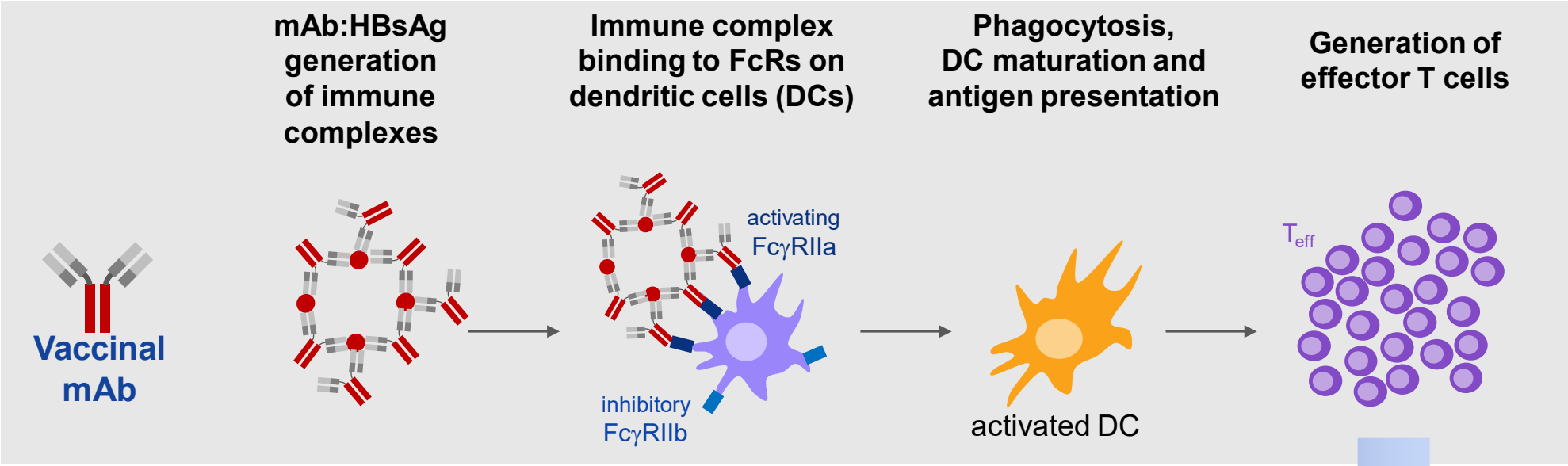
VIR-3434: an Fc-engineered human antibody against HBsAg with multiple potential mechanisms of action



Agarwal, et al. Rapid HBsAg Reduction in Chronic Hepatitis B Virus Infection: Preliminary Results From a Phase 1 Study Evaluating a Single Dose of VIR-3434, a Novel Neutralizing, Vaccinal Monoclonal Antibody. Poster presented at AASLD 2021. Nov 12-15, 2021. Virtual; Lempp, et al. Preclinical Characterization of VIR-3434, a Monoclonal Antibody Neutralizing Hepatitis B Virus That Facilitates FcγR-Mediated Elimination of HBsAg. Poster presented at AASLD 2021. Nov 12-15, 2021. Virtual.

cccDNA, covalently closed circular DNA; DNA, deoxyribonucleic acid; HBsAg, hepatitis B s antigen; HBV, hepatitis B virus; intDNA, integrated DNA; RNA, ribonucleic acid; SVPs, subviral particles

Vaccinal Effect: VIR-3434, an Fc-engineered antibody as a potential therapeutic vaccine against HBV



Fc engineered (GAALIE)
to increase binding to FcgRs IIA & IIIA (activating) and to decrease binding to FcgRIIB (inhibitory)

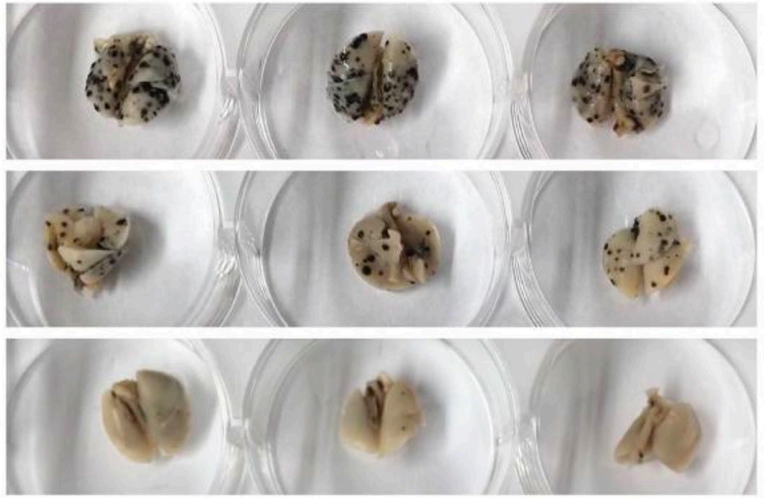
Durable HBV-specific immunity, potential functional cure

Agarwal, et al. A Phase 1 Study Evaluating the Neutralizing, Vaccinal Monoclonal Antibody VIR-3434 in Participants With Chronic Hepatitis B Virus Infection: Preliminary Results. Oral presentation at EASL 2021. 23–26 June 2021. Virtual.

GAALIE mutation: Bournazos *et al.* 2020; *CD, cluster of differentiation; DC, dendritic cell; FcR, fragment crystallizable receptor; T_{eff}, effector T cell; WT, wild-type*

Fc engineering & the vaccinal effect protect during cancer cell & influenza virus infection studies

7E3-GAALIE (anti-sLeA carbohydrate) reduced lung metastatic foci of B16 tumor cells compared to 7E3-WT

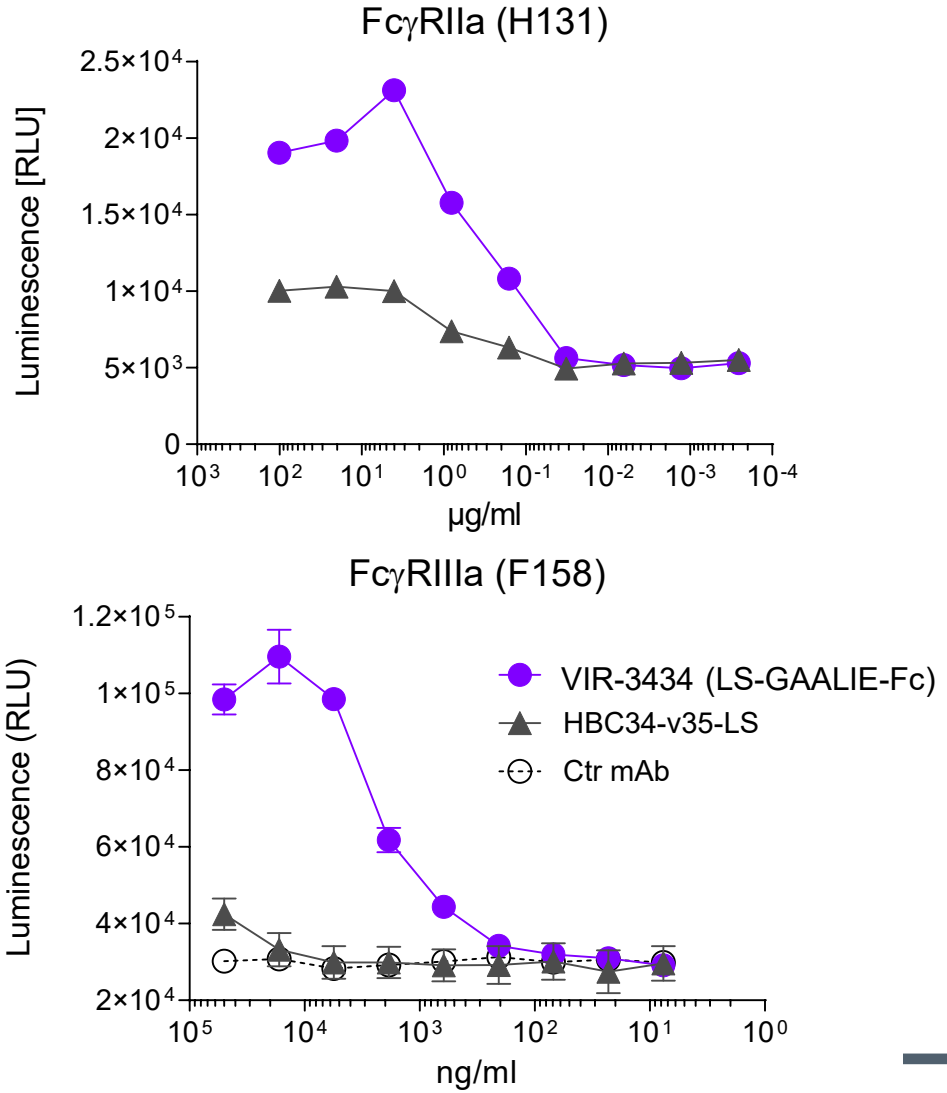


FY1-GAALIE (anti-HA stem mAb) induced a CD8+ T cell -mediated vaccinal effect and better protected huFcgR mice from infection with influenza virus

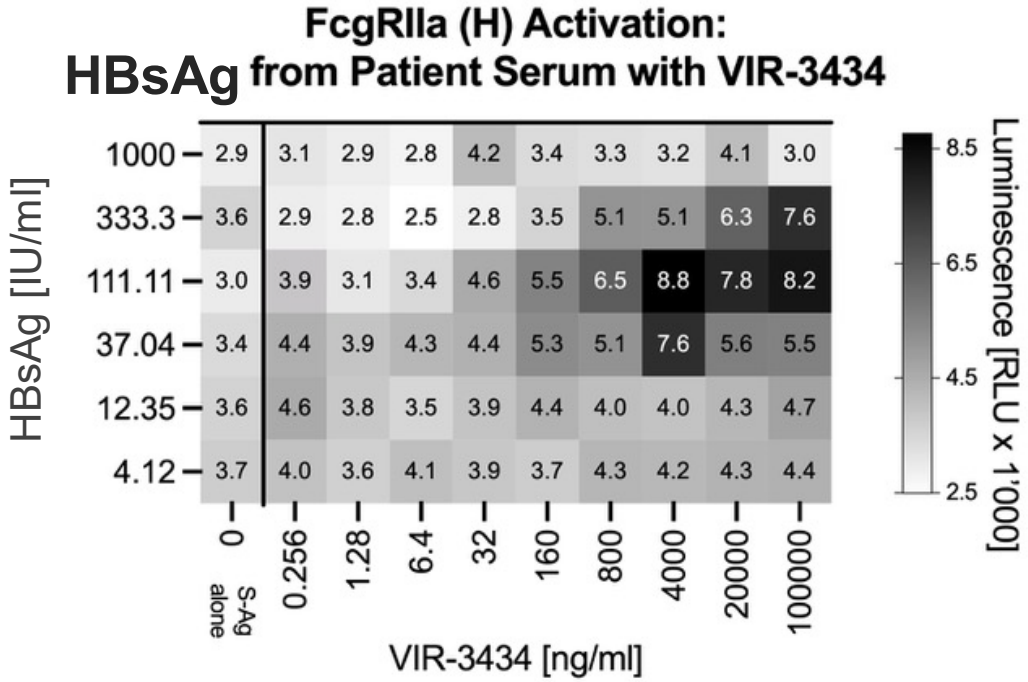
Weizenfeld, P, et al. JClinInvest. 2019; 129(9):3952–3962.

Bournazos, S, et al. Nature. 2020; 588,485–490.

FcγR signaling inducing effector functions that could mediate HBsAg elimination and potentially lead to functional cure



GAALIE-Fc mutation & mAb:HBsAg ratios are crucial



HBsAg source: Serum from HBV+ patients
Readout: FcgR reporter cell assay (Promega)

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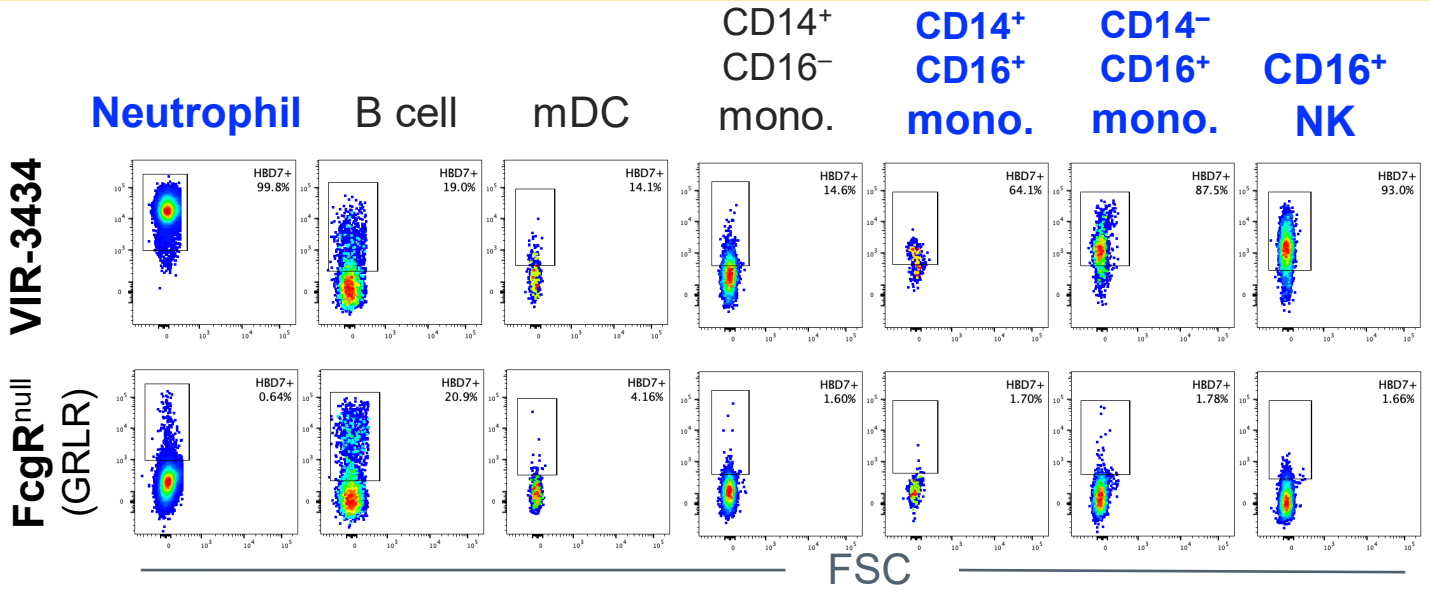
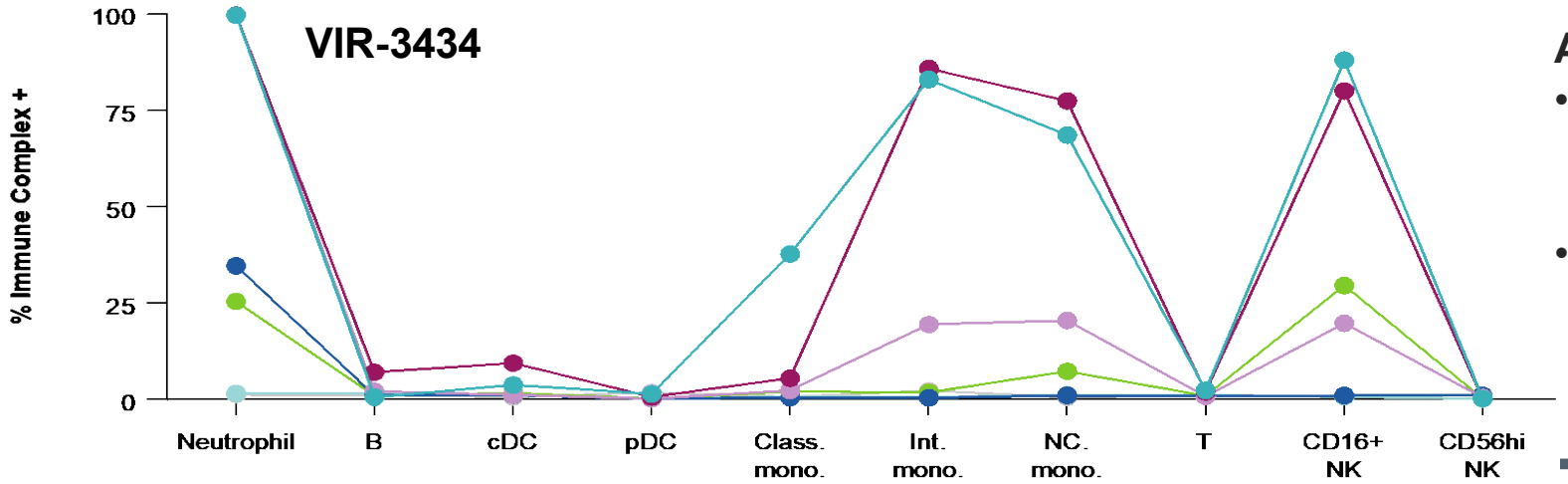
VIR-3434 promotes FcγR-mediated association of HBsAg to immune cells in whole blood from HBV+ donors





Methods

- Whole blood from HBV+ donor (9,400 IU/mL HBsAg) with 50 µg/mL VIR-3434 for 2 hours at 37°C
- Flow cytometry: HBsAg stained with anti-HBs mAb that is not competing with VIR-3434

Additional Data & Conclusions

- GAALIE-Fc is essential to mediate HBsAg binding to immune cells
- HBsAg binding is in line with FcgRIIIa (CD16) expression

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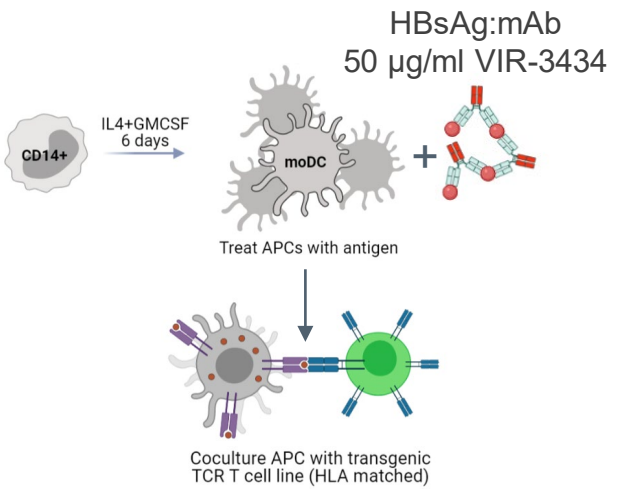
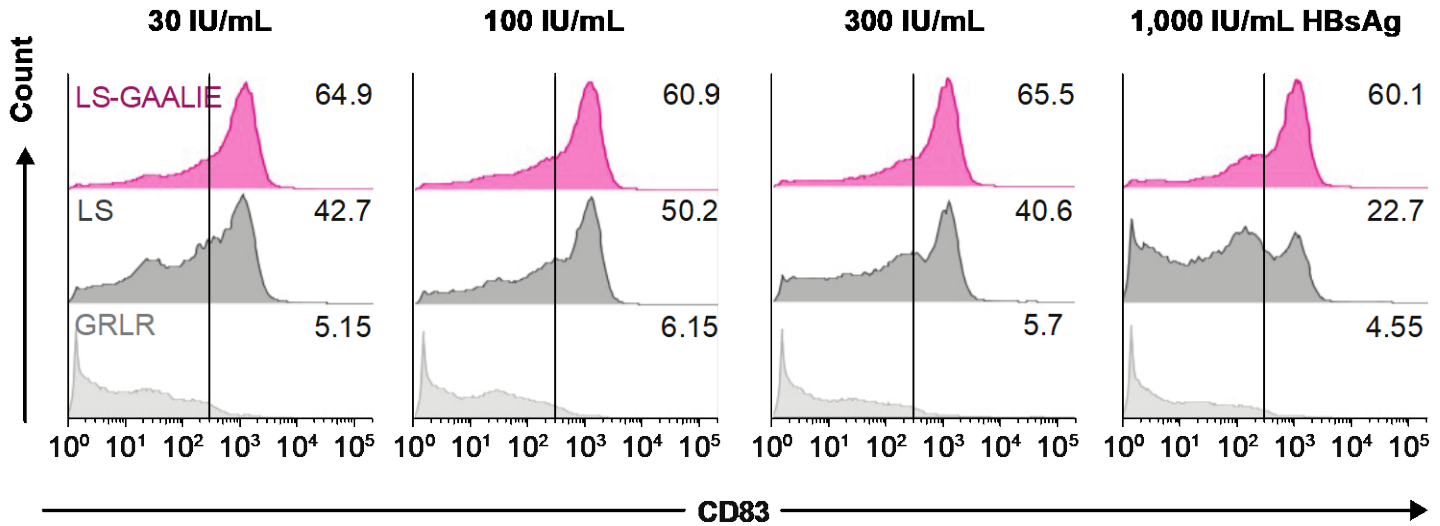
Vaccinal effect: VIR-3434 in complex with HBsAg activates moDCs and stimulates antigen-specific reporter CD4+ T cells

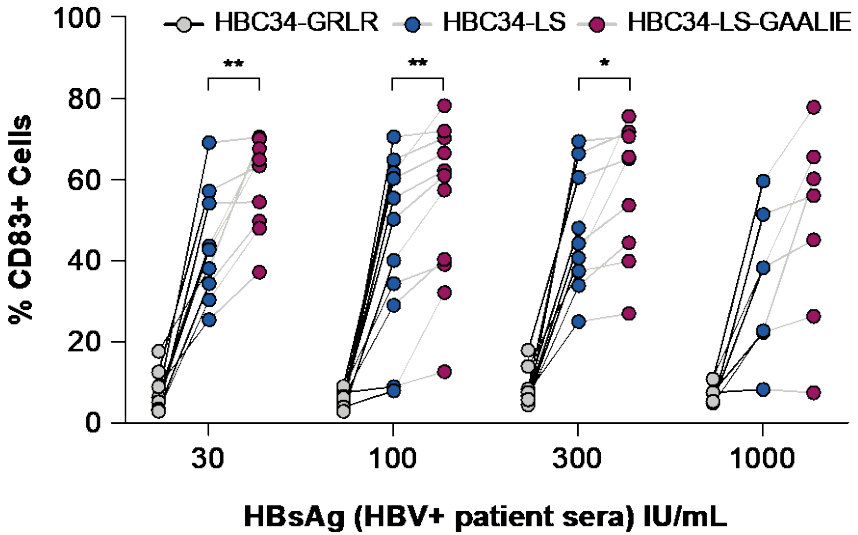


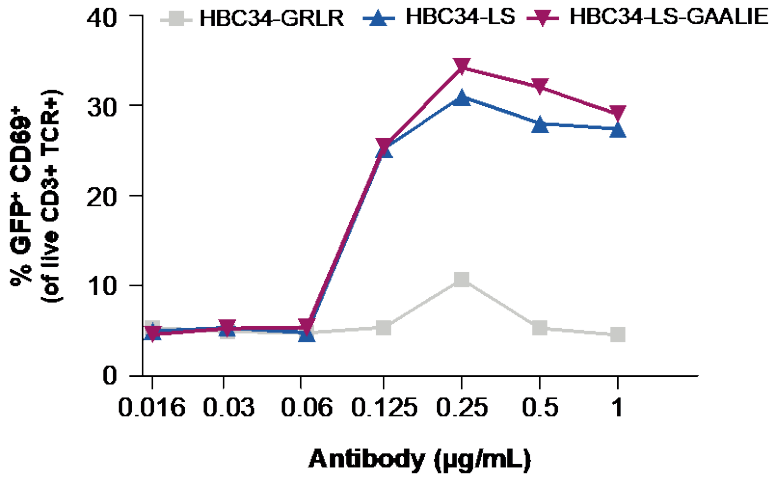


LS-GAALIE
FcγRIIA↑IIB↓IIIA↑

LS

GRLR
No FcγR binding





moDC activation marker CD83, similar for CD86 and cytokines in supernatant

TCR-transgenic Jurkat reporter cells as model for CD4+ **T cells**

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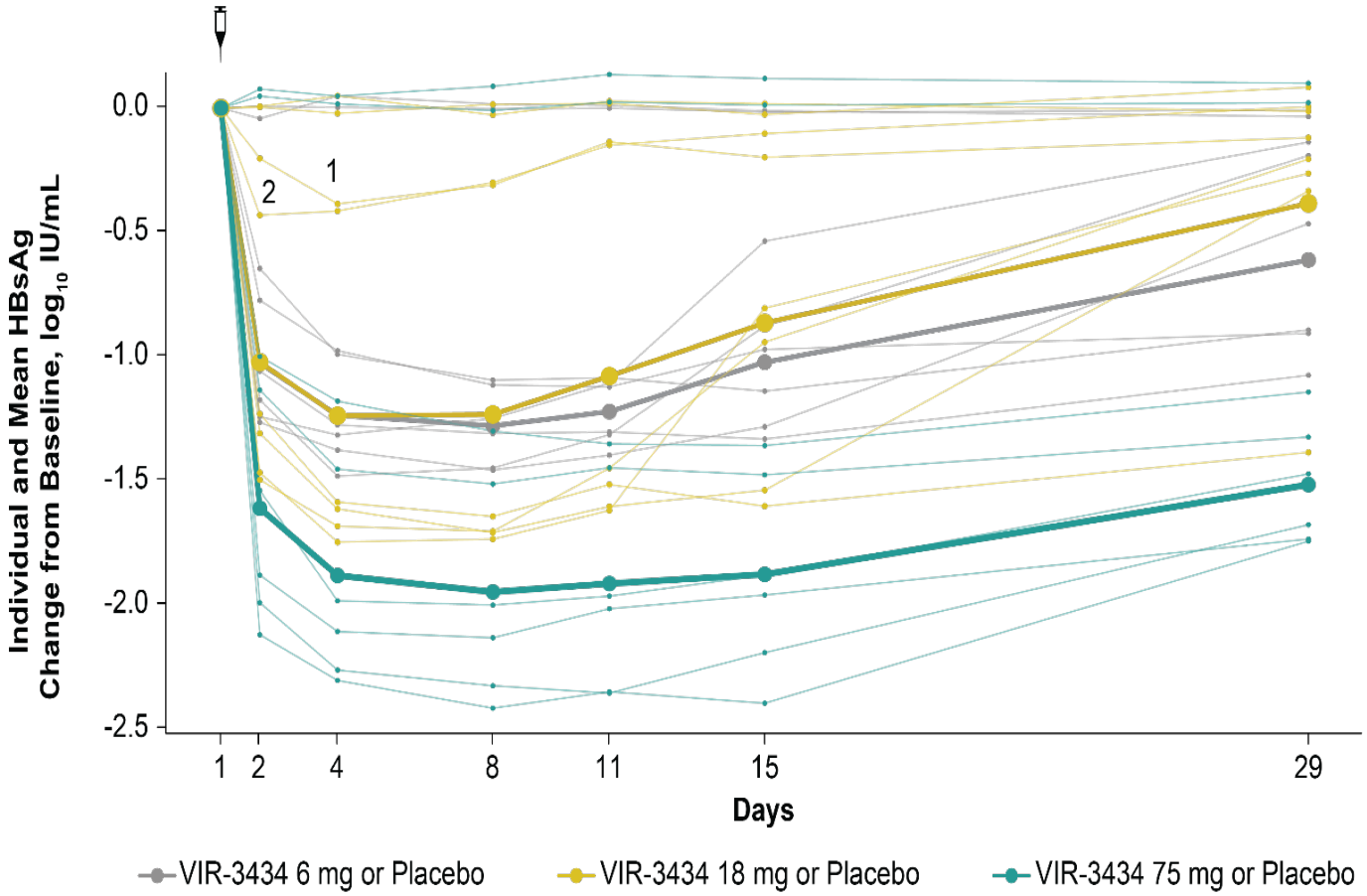
Clinical data, phase 1: single dose of VIR-3434: preliminary HBsAg change from baseline

- Virally suppressed participants with **chronic HBV infection** and HBsAg < 3,000 IU/mL
- **Single doses** of 6, 18, or 75 mg of VIR-3434 were generally well tolerated; all AEs were grade 1-2
- Rapid **decline in HBsAg** ≥ 1 log_{10} IU/mL **within 7 days**
- The largest (> 2 log_{10}) reductions in HBsAg were observed for 75 mg
- Full analysis of VIR-3434 PK and HBsAg:VIR-3434 complex disposition is ongoing



Note: HBsAg measured with Abbott ARCHITECT®. [1,2] Two participants in the 18 mg cohort had undetectable or lower-than-expected free PK and < 0.5 log_{10} IU/mL reductions in HBsAg

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Conclusions

- VIR-3434 targets the conserved antigenic loop within HBsAg and mediates pan-genotypic **neutralization** of HBV in vitro
- In vitro, Fc-engineered VIR-3434 bound and **activated FcγRIIa** and IIIa more efficiently compared to the mAb with wild-type Fc
- VIR-3434 mediated the **association** of HBsAg to immune cells (neutrophils, monocytes, and NK cells) in whole blood of patients with CHB
- VIR-3434 in complex with HBsAg **activated moDCs** more efficiently and induced CD4+ reporter **T cell responses**, in vitro. These results are a first step towards potential **long-term immunity** and functional cure via a vaccinal effect.
- **In patients** with CHB, a single low dose of 6, 18 or 75 mg of VIR-3434 resulted in rapid reductions in HBsAg within 1 week.

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