

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
30 December 2021 (30.12.2021)



(10) International Publication Number
WO 2021/262840 A1

- (51) **International Patent Classification:**
A61P 31/20 (2006.01) *C07K 16/08* (2006.01)
- (21) **International Application Number:**
PCT/US2021/038667
- (22) **International Filing Date:**
23 June 2021 (23.06.2021)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
63/043,692 24 June 2020 (24.06.2020) US
- (71) **Applicants:** **VIR BIOTECHNOLOGY, INC.** [US/US]; 499 Illinois Street, Suite 500, San Francisco, California 94158 (US). **HUMABS BIOMED SA** [CH/CH]; Via dei Gaggini 3, 6500 Bellinzona (CH).
- (72) **Inventors:** **ROSEN, Laura**; 499 Illinois Street, Suite 500, San Francisco, California 94158 (US). **CZUDNO-CHOWSKI, Nadine**; 499 Illinois Street, Suite 500, San Francisco, California 94158 (US). **LEMPP, Florian**; 499 Illinois Street, Suite 500, San Francisco, California 94158 (US). **SNELL, Gyorgy**; 499 Illinois Street, Suite 500, San Francisco, California 94158 (US). **CORTI, Davide**; Via dei Gaggini 3, 6500 Bellinzona (CH). **CAMERONI, Elisabetta**; Via dei Gaggini 3, 6500 Bellinzona (CH).
- (74) **Agent:** **MORGAN, John, A.** et al.; SEED INTELLECTUAL PROPERTY LAW GROUP LLP, Suite 5400, 701 Fifth Avenue, Seattle, Washington 98104-7064 (US).
- (81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,

(54) **Title:** ENGINEERED HEPATITIS B VIRUS NEUTRALIZING ANTIBODIES AND USES THEREOF

mAb name	titer 5 ml transfection (mg/L)	titer 100ml transfections (mg/L)	average titer in 100 ml scale (mg/L)
HBC34-v35-rlgG1 (G1m17,1)	89.4	149.0, 172.3, 212.0 (N=3)	177.8
HBC34-v40-rlgG1 (G1m17,1)	237.261	535.5, 583.0, 669.4 (N=3)	596.0
HBC34-v44-rlgG1 (G1m17,1)	157.8	588.2, 563.0 (N=2)	575.6
HBC34-v45-rlgG1 (G1m17,1)	140.9	269.2, 256.0 (N=2)	262.6
HBC34-v50rlgG1 (G1m17,1)	163.7	363.8, 371.0 (N=2)	367.4

FIG. 19

(57) **Abstract:** The present disclosure relates, in part, to antibodies, and antigen-binding fragments thereof, that can bind to the antigenic loop region of hepatitis B surface antigen (HBsAg) and, optionally, can neutralize infection hepatitis B virus (HBV), and further optionally, of hepatitis delta virus (HDV). Presently disclosed antibodies and antigen-binding fragments have advantageous production characteristics, such as reduced formation of aggregates and/or improved production titer in transformed host cells, as compared to a reference antibody or antigen-binding fragment. The present disclosure also relates to fusion proteins that comprise an antigen-binding fragment, and to nucleic acids that encode and cells that produce such antibodies, antigen-binding fragments, and fusion proteins. In addition, the present disclosure relates to the use of the antibodies, antigen-binding fragments, fusion proteins, and related polynucleotides, vectors, host cells, and compositions of the present disclosure in the diagnosis, prophylaxis and treatment of hepatitis B and hepatitis D. Also provided are combination therapies comprising (i) an antibody or antigen-binding fragment and (ii) an agent that is an inhibitor of HBV gene expression and/or that reduces HBV antigenic load.

[Continued on next page]

HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

- (84) Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

- *with international search report (Art. 21(3))*
 - *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*
 - *with sequence listing part of description (Rule 5.2(a))*
-