



(51) International Patent Classification:

A61K 47/68 (2017.01) *C07K 16/00* (2006.01)
A61K 47/60 (2017.01)

(21) International Application Number:

PCT/US2021/019958

(22) International Filing Date:

26 February 2021 (26.02.2021)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/982,943 28 February 2020 (28.02.2020) US

(71) Applicant: **GENZYME CORPORATION** [US/US]; 50
Binney Street, Cambridge, Massachusetts 02142 (US).

(72) Inventors: **BRUN, Marie-Priscille**; c/o Sanofi, 54 rue
La Boétie, 75008 Paris (FR). **DUFFIEUX, Francis**; c/o

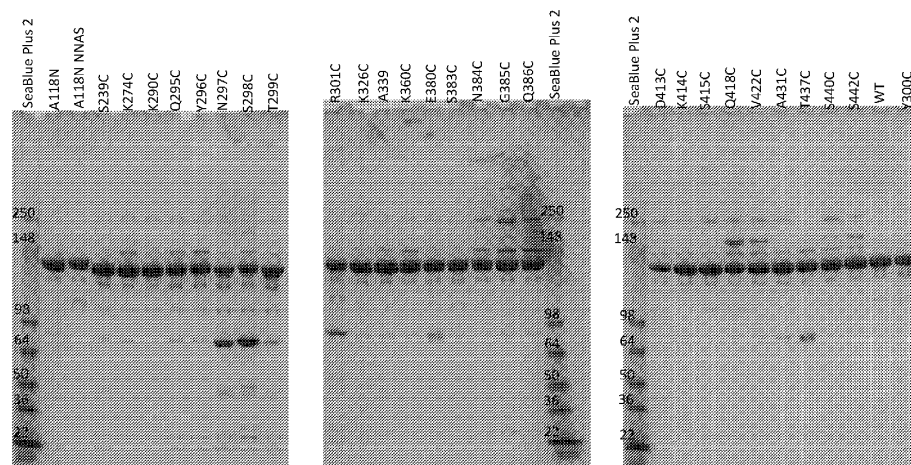
Sanofi, 54 rue La Boétie, 75008 Paris (FR). **PARK, Sung-hae**; c/o Sanofi, 55 Corporate Drive, Mail Code 55A-525, Bridgewater, New Jersey 08807 (US). **QIU, Huawei**; c/o Sanofi, 55 Corporate Drive, Mail Code 55A-525, Bridgewater, New Jersey 08807 (US). **ZHOU, Qun**; c/o Sanofi, 55 Corporate Drive, Mail Code 55A-525, Bridgewater, New Jersey 08807 (US).

(74) Agent: **VELEMA, James H.**; LATHROP GPM LLP, 28 State Street, Boston, Massachusetts 02109 (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, 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,

(54) Title: MODIFIED BINDING POLYPEPTIDES FOR OPTIMIZED DRUG CONJUGATION

Fig. 1



(57) Abstract: Engineered antibodies that are stable and can be conjugated to a ligand or drug at a ligand/drug to antibody ratio of above 3, making these conjugates suitable for treatment of a variety of indications, are provided. Methods of producing these engineered antibodies are also provided. In a first embodiment, the antibody comprises a first engineered reactive amino acid residue at position 274 according to the numbering of the EU index of Kabat and a second engineered reactive amino acid residue at position 339, 360, 384, 385, 422 and/or 440. In a second embodiment, the antibody comprises a first engineered reactive amino acid residue at position 339 according to the numbering of the EU index of Kabat and a second engineered reactive amino acid residue at position 290, 360, 384, 385, 422 and/or 440. In a third embodiment, the antibody comprises a first engineered reactive amino acid residue at position 118 according to the numbering of the EU index of Kabat and a second engineered reactive amino acid residue at position 274, 339, 384, 385, 422 and/or 440. In a fourth embodiment, the antibody comprises a first engineered reactive amino acid residue at position 384

[Continued on next page]

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).

Published:

— with international search report (Art. 21(3))

according to the numbering of the EU index of Kabat and a second engineered reactive amino acid residue at position 118, 274, 290 and/or 339. In a preferred embodiment, the engineered reactive amino acid residue is cysteine.