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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
02 October 2025 (02.10.2025)

WIPO | PCT

(10) International Publication Number
WO 2025/207946 A1

(51) International Patent Classification:
C07K 16/28 (2006.01) *A61K 51/10* (2006.01)
A61K 47/68 (2017.01) *A61P 25/00* (2006.01)

(21) International Application Number:
PCT/US2025/021853

(22) International Filing Date:
27 March 2025 (27.03.2025)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/571,018 28 March 2024 (28.03.2024) US
24175277.3 10 May 2024 (10.05.2024) EP

(71) Applicant: **GENZYME CORPORATION** [US/US]; 450 Water Street, Cambridge, MA 02141 (US).

(72) Inventors: **CORNELIS, Sigrid**; c/o Ablynx N.V., Patent Department, Technologiepark 21, 9052 Ghent-Zwijnaarde (BE). **LEKSA-GORDON, Nina**; c/o Sanofi, Patent Department, 450 Water Street, Cambridge, MA 02141 (US). **LESUISSE, Dominique**; c/o Sanofi, Patent Department, 46 avenue de la Grande Armée, 75017 Paris (FR). **MOONENS, Kristof**; c/o Ablynx N.V., Patent Department, Technologiepark 21, 9052 Ghent-Zwijnaarde (BE). **NONNE, Christelle**; c/o Ablynx N.V., Patent Department, Technologiepark 21, 9052 Ghent-Zwijnaarde (BE). **RAPISARDA, Chiara**; c/o Sanofi, Patent Department, 46 avenue de la Grande Armée, 75017 Paris (FR). **T'SYEN, Joeri**; c/o Ablynx N.V., Patent Department, Technologiepark 21, 9052 Ghent-Zwijnaarde (BE).

(74) Agent: **VELEMA, James, H.** et al.; Lathrop GPM LLP, 28 State Street, Boston, MA 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, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, 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, UY, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, 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, ME, 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:
— *of inventorship (Rule 4.17(iv))*

Published:
— *with international search report (Art. 21(3))*
— *with sequence listing part of description (Rule 5.2(a))*

WO 2025/207946 A1

(54) Title: POLYPEPTIDES BINDING TO A SPECIFIC EPITOPE OF THE TRANSFERRIN RECEPTOR 1

(57) Abstract: The present invention relates to polypeptides that are capable of binding to a specific pH-dependent epitope on the (human) transferrin receptor 1 (TfR1). In particular, the present invention relates to novel and improved immunoglobulin single variable domains (ISVDs), such as heavy-chain single variable domains, which are capable of binding to a specific epitope on TfR1. The invention further relates to polypeptides, nucleic acids, vectors, host cells, conjugates, or pharmaceutical compositions that comprise at least one of these ISVDs binding to a specific epitope on TfR1. The present invention further relates to methods for producing such ISVDs as well as to uses of such polypeptides for diverse therapeutic, diagnostic and/or medical imaging applications, including but not limited to the delivery of therapeutic, diagnostic and/or medical imaging agents across the blood-brain barrier (BBB), and/or into a cell of a subject.