

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
26 January 2023 (26.01.2023)



(10) International Publication Number
WO 2023/002952 A1

(51) International Patent Classification:

C07K 19/00 (2006.01) *C40B 40/10* (2006.01)
C07K 14/54 (2006.01) *C12N 15/13* (2006.01)
C07K 16/24 (2006.01) *C12N 15/62* (2006.01)
C12P 21/02 (2006.01)

(21) International Application Number:

PCT/JP2022/027893

(22) International Filing Date:

15 July 2022 (15.07.2022)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

2021-119178 19 July 2021 (19.07.2021) JP

(71) Applicant: **CHUGAI SEIYAKU KABUSHIKI KAISHA**
[JP/JP]; 5-1, Ukima 5-chome, Kita-ku, Tokyo, 1158543
(JP).

(72) Inventors: **CHICHILI, Vishnu Priyanka Reddy**; c/o
Chugai Pharmabody Research Pte. Ltd., 3, Biopolis Drive,
#07-11 to 16 Synapse, 138623 (SG). **NAMBU, Takeru**; c/o
Chugai Pharmabody Research Pte. Ltd., 3, Biopolis Drive,
#07-11 to 16 Synapse, 138623 (SG). **IGAWA, Tomoyuki**;
c/o CHUGAI SEIYAKU KABUSHIKI KAISHA, 1-1, Ni-
honbashi-Muromachi 2-chome, Chuo-ku, Tokyo, 1038324

(JP). **YAMAMOTO, Yohei**; c/o CHUGAI SEIYAKU
KABUSHIKI KAISHA, 135, Komakado 1-chome, Gotem-
ba-shi, Shizuoka, 4128513 (JP). **SATO, Motohiko**; c/o
CHUGAI SEIYAKU KABUSHIKI KAISHA, 135, Ko-
makado 1-chome, Gotemba-shi, Shizuoka, 4128513 (JP).
HIRONIWA, NAOKA; c/o Chugai Pharmabody Research
Pte. Ltd., 3, Biopolis Drive, #07-11 to 16 Synapse, 138623
(SG).

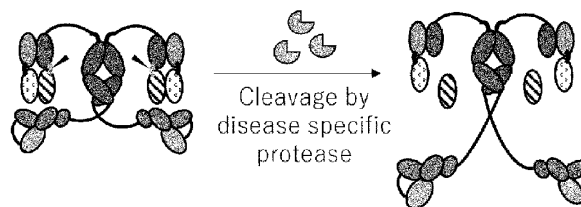
(74) Agent: **HARUNA, Masao** et al.; Kantetsu Tsukuba Bldg.
6F, 1-1-1, Oroshi-machi, Tsuchiura-shi, Ibaraki, 3000847
(JP).

(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, 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,

(54) Title: PROTEASE-MEDIATED TARGET SPECIFIC CYTOKINE DELIVERY USING FUSION POLYPEPTIDE

[Fig. 1]



- Inactive IL12
- Long systemic half life
- Active IL12
- Retention in disease site
- Short systemic half life

(57) Abstract: The present invention relates to fusion proteins comprising a ligand binding domain, a protease cleavage site, and a ligand moiety. The fusion proteins of the invention comprise a ligand binding domain, a ligand moiety, and a protease cleavage site that, when activated by cleavage by a protease, restores biological activity of the ligand. The invention also relates to methods of producing the fusion proteins, their uses and pharmaceutical compositions comprising said fusion proteins. The present invention also relates to a method of reducing the association between heavy chain variable domain (VH) and light chain variable domain (VL) within the ligand binding domain that promotes dissociation of one from the other. The present disclosure provides fusion proteins in which the ligand is fused to the C-terminus of the constant region, or the N-terminus of the ligand binding domain.

[Continued on next page]

WO 2023/002952 A1

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 applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

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