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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
01 February 2024 (01.02.2024)

WIPO | PCT

(10) International Publication Number
WO 2024/026199 A3

(51) International Patent Classification:
C07K 14/705 (2006.01) *C12N 15/62* (2006.01)
A61K 35/12 (2015.01) *C12N 15/85* (2006.01)
A61P 35/00 (2006.01) *C07K 16/28* (2006.01)
C07K 19/00 (2006.01) *C12N 5/10* (2006.01)

(21) International Application Number:
PCT/US2023/069829

(22) International Filing Date:
07 July 2023 (07.07.2023)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/369,480 26 July 2022 (26.07.2022) US

(71) Applicant: **SENTI BIOSCIENCES, INC.** [US/US]; 2 Corporate Drive, First Floor, South San Francisco, California 94080 (US).

(72) Inventors: **FRANKEL, Nicholas**; c/o SENTI BIOSCIENCES, INC., 2 Corporate Drive, First Floor, South San Francisco, California 94080 (US). **GORDLEY, Russell Morrison**; c/o SENTI BIOSCIENCES, INC., 2 Corporate Drive, First Floor, South San Francisco, California 94080 (US). **HUA, Jun Jie**; c/o SENTI BIOSCIENCES, INC., 2 Corporate Drive, First Floor, South San Francisco, California 94080 (US).

(74) Agent: **LANGE, Kevin** et al.; Goodwin Procter LLP, 100 Northern Avenue, IP DOCKETING DEPT./7TH FL, Boston, Massachusetts 02210 (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, 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,

(54) Title: INHIBITORY CHIMERIC RECEPTOR ARCHITECTURES

(57) Abstract: Provided herein are inhibitory chimeric antigen receptor compositions and cells comprising such compositions. Also provided are methods of using inhibitory chimeric antigen receptors and cells.

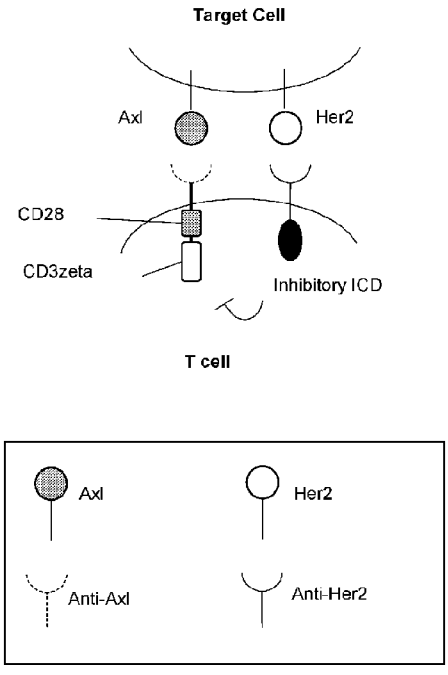

FIG. 1

WO 2024/026199 A3

[Continued on next page]

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))*
— *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))*

(88) Date of publication of the international search report:
11 April 2024 (11.04.2024)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2023/069829

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - INV. - C07K 14/705; A61K 35/12; A61P 35/00; C07K 19/00; C12N 15/62, 15/85 (2023.01)
ADD. - C07K 16/28; C12N 5/10 (2023.01)

CPC - INV. - A61K 39/4621; A61P 35/00; C07K 14/4703, 14/705; C12N 15/85 (2023.08)

ADD. - A61K 2039/5156; C07K 16/28, 2319/02; C12N 5/10 (2023.08)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History document

Electronic database consulted during the international search (name of database and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2007/0083334 A1 (MINTZ et al.) 12 April 2007 (12.04.2007) entire document	1-3
A	US 2022/0089750 A1 (NOVARTIS AG et al.) 24 March 2022 (24.03.2022) entire document	1-3
A	WO 2021/168298 A1 (SENTI BIOSCIENCES INC.) 26 August 2021 (26.08.2021) entire document	1-3
A	WO 2021/168317 A1 (SENTI BIOSCIENCES INC. et al.) 26 August 2021 (26.08.2021) entire document	1-3

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
08 December 2023	JAN 31 2024
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Taina Matos Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2023/069829

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed.

   b. ☒ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)),

      ☒ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2023/069829

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 7-21
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See extra sheet(s).

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-3

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

Continued from Box No. III Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees need to be paid.

Group I+: claims 1-6 are drawn to chimeric inhibitory receptors.

The first invention of Group I+ is restricted to a chimeric inhibitory receptor comprising: an extracellular protein binding domain; a transmembrane domain, wherein the transmembrane domain is operably linked to the extracellular protein binding domain; and an intracellular signaling domain, wherein the intracellular signaling domain is operably linked to the transmembrane domain, and where the intracellular signaling domain is selected to be SEQ ID NO: 100 (MPZL1). The first named invention has been selected based on the guidance set forth in section 10.54 of the PCT International Search and Preliminary Examination Guidelines. Specifically, the first named invention was selected based on the intracellular signaling domains listed in instant claim 1, and intracellular signaling domain sequences listed in instant claim 3. It is believed that claims 1-3 read on this first named invention and thus these claims will be searched without fee to the extent that they read on SEQ ID NO: 100.

Applicant is invited to elect additional intracellular signaling domains, and their respective, corresponding, SEQ ID NOs to be searched in a specific combination by paying additional fee for each set of election. An exemplary election would be a chimeric inhibitory receptor comprising: an extracellular protein binding domain; a transmembrane domain, wherein the transmembrane domain is operably linked to the extracellular protein binding domain; and an intracellular signaling domain, wherein the intracellular signaling domain is operably linked to the transmembrane domain, and where the intracellular signaling domain is selected to be SEQ ID NO: 108 (IRTA1). Additional intracellular signaling domains, and their respective, corresponding, SEQ ID NOs will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined.

The inventions listed in Groups I+ do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The Groups I+ formulas do not share a significant structural element responsible for inhibiting or reducing immunomodulatory cell activity, requiring the selection of alternative intracellular signaling domains where "A chimeric inhibitory receptor comprising: - an extracellular protein binding domain; - a transmembrane domain, wherein the transmembrane domain is operably linked to the extracellular protein binding domain; and - one or more intracellular signaling domains, wherein the one or more intracellular signaling domains are operably linked to the transmembrane domain, wherein the one or more intracellular signaling domains are each derived from a protein selected from the group consisting of: MPZL1, IRTA1, LIR8, PECAM-1, CD72, IRTA2, IRTA4, NKIR, ILIRAP, PTPRO, PTPRZ1, TLT1, SLAMIF1, SLAMF5, PCDHGC3, LIFR, ERMAP, IL1RAPL2, CDH5, MPZ, FCGR2B, SIGLEC-6, MPIG6B, VSIG4, SIGLEC-12, KIR2DL4, KIR2DL5, SIGLEC-7, FCRH3, PCDHGC5, CDH11, IMPG2, and DSCAM, and wherein at least one of the one or more intracellular signaling domains is capable of preventing, attenuating, or inhibiting activation of a tumor-targeting chimeric receptor expressed on an immunomodulatory cell."

Additionally, even if Groups I+ were considered to share the technical features of a chimeric inhibitory receptor comprising: an extracellular protein binding domain; a transmembrane domain, wherein the transmembrane domain is operably linked to the extracellular protein binding domain; and one or more intracellular signaling domains, wherein the one or more intracellular signaling domains are operably linked to the transmembrane domain, wherein at least one of the one or more intracellular signaling domains is capable of preventing, attenuating, or inhibiting activation of a tumor-targeting chimeric receptor expressed on an immunomodulatory cell. However, these shared technical features do not represent a contribution over the prior art.

Specifically, US 2022/0089750 to Novartis Ag et al. discloses a chimeric inhibitory receptor (a Chimeric Antigen Receptor ... inhibit one or more checkpoint inhibitors of the immune response, Abstract) comprising: an extracellular protein binding domain (an extracellular antigen binding domain, Para. [0129]); a transmembrane domain (a transmembrane domain, Para. [0129]), wherein the transmembrane domain is operably linked to the extracellular protein binding domain (construct comprising at least an extracellular antigen binding domain, a transmembrane domain, Para. [0129]); and one or more intracellular signaling domains, wherein the one or more intracellular signaling domains are operably linked to the transmembrane domain (and a cytoplasmic signaling domain (also referred to herein as "an intracellular signaling domain") comprising a functional signaling domain, Para. [0129]), wherein at least one of the one or more intracellular signaling domains is capable of preventing, attenuating, or inhibiting activation of a tumor-targeting chimeric receptor expressed on an immunomodulatory cell (conditional CAR as described herein, an agent that inhibits a checkpoint inhibitor, or a cytokine, Para. [0062]).

The inventions listed in Groups I+ therefore lack unity under Rule 13 because they do not share a same or corresponding special technical features.