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(71) Applicant: **CSPC DOPHEN CORPORATION** [US/US]; 302 Carnegie Center Blvd., Suite 100, Princeton, NJ 08540 (US).

(72) Inventors: **ZHANG, Wen**; 302 Carnegie Center Blvd., Suite 100, Princeton, NJ 08540 (US). **SUN, Zhaopeng**; 302 Carnegie Center Blvd., Suite 100, Princeton, NJ 08540 (US). **HU, Xixin**; 302 Carnegie Center Blvd., Suite 100, Princeton, NJ 08540 (US). **HUI, Xiwu**; 302 Carnegie Center Blvd., Suite 100, Princeton, NJ 08540 (US). **DAN, Mo**; 302 Carnegie Center Blvd., Suite 100, Princeton, NJ 08540 (US). **YUAN, Can**; 302 Carnegie Center Blvd., Suite 100, Princeton, NJ 08540 (US). **LV, Lu**; 302 Carnegie Center Blvd., Suite 100, Princeton, NJ 08540 (US).

(74) Agent: **ZHONG, Ling**; RatnerPrestia, 2200 Renaissance Boulevard, Suite 350, King of Prussia, PA 19406 (US).

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(54) Title: ANTIBODY IMMUNE-STIMULANT CONJUGATES AND USE THEREOF

Fig. 1: Schematic structure of DP001

DP001 Hc

1 EVQLVESGGG LVQPGGSLRL SCAASGFNIK DTYIHWVRQA PGKGLEWVAR IYPTNGYTRY

61 ADSVKGRFTI SADTSKNTAY LQMNSLRAED TAVYYCSRWG GDGFYAMDYW GQGTLVTVSS

121 ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS

181 GLYSLSSVVT VPSSSLGTQT YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG

241 PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN

301 STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ VYTLPPSREE

361 MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY SKLTVDKSRW

421 QQGNVFSCSV MHEALHNHYT QKSLSLSPGK

LC

1 DIQMTQSPSS LSASVGDRVT ITCRASQDVN TAVAWYQQKP GKAPKLLIYS ASFLYSGVPS

61 RFSGSRSGTD FTLTISSLQP EDFATYYCQQ HYTTPPTFGQ GTKVEIKRTV AAPSVFIFPP

121 SDEQLKSGTA SVVCLLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSTLT

181 LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEC

(57) Abstract: The present disclosure provides, in some embodiments, antibody-immune stimulant conjugates for cancer immunotherapy. Methods for making and using the antibody-immune stimulant conjugates are also provided herein.

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[Continued on next page]

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))*
— *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:
20 April 2023 (20.04.2023)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2022/043820

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - INV. - C07D 487/04 (2023.01)
ADD. - A61K 31/437; A61P 35/00 (2023.01)

CPC - INV. - C07D 487/04 (2023.01)

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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 2021/0017238 A1 (SANOFI) 21 January 2021 (21.01.2021) entire document	1, 6, 7
A	US 2012/0294885 A1 (DAVID et al) 22 November 2012 (22.11.2012) entire document	1, 6, 7
A	US 2021/0154316 A1 (BOLT BIOTHERAPEUTICS INC. et al) 27 May 2021 (27.05.2021) entire document	1, 6, 7
A	WO 2021/086981 A1 (CSPC DOPHEN CORPORATION) 06 May 2021 (06.05.2021) entire document	1, 6, 7

☐ 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
27 January 2023	FEB 28 2023
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/US2022/043820

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:

   ISA/225 was mailed on 18 October 2022. No approved electronic sequence listing was submitted in response to the ISA/225. The sequence listing filed on 21 October 2022 contained errors which resulted in the listing not being entered into ISA/US's search system.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2022/043820

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.: 19
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:

Claim 19 is held unsearchable as a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit, furnish a sequence listing in the form of an Annex C/ST.26 XML file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

3. ☒ Claims Nos.: 8-18, 20-24
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, 6, 7

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 1-7 are drawn to compounds having Formula A3 or Formula A4, or a pharmaceutically acceptable salt or an isotopic derivative thereof, and antibody conjugates thereof.

The first invention of Group I+ is restricted to a compound having Formula A3, or a pharmaceutically acceptable salt or an isotopic derivative thereof, wherein X is shown succinimide ring moiety; Y is the upper-left shown moiety, m is 1; and n is 1. It is believed that claims 1, 6, and 7 read on this first named invention and thus these claims will be searched without fee to the extent that they read on the above embodiment.

Applicant is invited to elect additional formula(e) for each additional compound to be searched in a specific combination by paying an additional fee for each set of election. Each additional elected formula(e) requires the selection of a single definition for each compound variable. An exemplary election would be a compound having Formula A3, or a pharmaceutically acceptable salt or an isotopic derivative thereof, wherein X is NH2; Y is the upper-right shown moiety, m is 2; and n is 2. Additional formula(e) 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+ formulae do not share a significant structural element requiring the selection of alternatives for the compound variables X, Y, m, n, and accordingly these groups lack unity a priori.

Additionally, even if Groups I+ were considered to share the technical features of a compound having the core structure of Formula A3 or Formula A4, or a pharmaceutically acceptable salt or an isotopic derivative thereof; and an antibody conjugate comprising a compound conjugated to an antibody or an antigen-binding fragment thereof, these shared technical features do not represent a contribution over the prior art as disclosed by US 2012/0294885 A1 to David et al. (hereinafter, "David") and US 2021/0154316 A1 to Bolt Biotherapeutics, Inc. et al. (hereinafter, "Bolt").

David teaches a compound having the core structure of Formula A3 or Formula A4 (Para. [0006], imidazoquinoline derived compounds of Formula I, as well as derivatives and analogues, and pharmaceutically acceptable salts of the compounds).

Bolt teaches an antibody conjugate comprising a compound conjugated to an antibody or an antigen-binding fragment thereof (Para. [0004], the invention provides an immunoconjugate comprising (a) an antibody construct comprising (i) an antigen binding domain and (ii) an Fc domain and (b) 1-8 adjuvant cores, wherein each adjuvant core is covalently bonded to the antibody construct via a linker, wherein each adjuvant core comprises a 2-amino nitrogen moiety with a pendant nitrogen atom and a point of attachment of the linker to the adjuvant core).

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