PATENT COOPERATION TREATY

From the:
INTERNATIONAL SEARCHING AUTHORITY

To:

FB RICE PTY LTD
Level 14, 90 Collins Street
Melbourne, Victoria 3000
Australia

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*
30 January 2020

Applicant's or agent's file reference	**FOR FURTHER ACTION**
524787PCT	See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/AU2019/051325	04 December 2019	04 December 2018

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

C07K 16/28 (2006.01) A61K 39/395 (2006.01) A61P 17/06 (2006.01) A61P 17/10 (2006.01) A61P 37/06 (2006.01)

Applicant

CSL INNOVATION PTY LTD

1. This opinion contains indications relating to the following items:

- [X] Box No. I — Basis of the opinion
- [X] Box No. II — Priority
- [ ] Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV — Lack of unity of invention
- [X] Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- [X] Box No. VI — Certain documents cited
- [ ] Box No. VII — Certain defects in the international application
- [ ] Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA	Date of completion of this opinion	**Authorised Officer**
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA Email address: pct@ipaustralia.gov.au	30 January 2020	Lauren Howitt AUSTRALIAN PATENT OFFICE (ISO 9001 Quality Certified Service) Telephone No. +61262256130

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/AU2019/051325

Box No. I Basis of this opinion

1. With regard to the **language,** this opinion has been established on the basis of:

   [X] The international application in the language in which it was filed

   [ ] A translation of the international application into, , which is the language of a translation furnished for the purposes of international search (under Rules 12.3(a) and 23.1(b)).

2. [ ] This opinion has been established taking into account **the rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(b))

3. [X] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   a. [X] forming part of the international application as filed:

      [X] in the form of an Annex C/ST.25 text file.

      [ ] on paper or in the form of an image file.

   b. [ ] furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. [ ] furnished subsequent to the international filing date for the purposes of international search only:

      [ ] in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).

      [ ] on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).

4. [ ] In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

   SEQ ID NO: 4-11 searched.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/AU2019/051325

Box No. II Priority

1. [X] The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. [ ] This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY	International Application No. PCT/AU2019/051325

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims **1-2, 11-12 and 18-23**	**YES**
	Claims **3-10 and 13-17**	**NO**
Inventive step (IS)	Claims **NONE**	**YES**
	Claims **1-23**	**NO**
Industrial applicability (IA)	Claims **1-23**	**YES**
	Claims **NONE**	**NO**

2. CITATIONS AND EXPLANATIONS:

CITATIONS

D1: SCALZO-INGUANTI, K. et al., 'A neutralizing anti-G-CSFR antibody blocks G-CSF-induced neutrophilia without inducing neutropenia in nonhuman primates', JOURNAL OF LEUKOCYTE BIOLOGY. 2017, Vol. 102, No. 2, pages 537-549
D2: WO 2012/171057 A1 (CSL LIMITED) 20 December 2012
D3: Document cited in International Search Report only
D4: Document cited in International Search Report only
D5: Document cited in International Search Report only
D6: Document cited in International Search Report only

NOVELTY (N)

D1 discloses administration of humanized mAb CSL324 (C1.2G) to cynomolgus monkeys at doses ranging from 0.1 to 10mg/kg reduced G-CSF–induced neutrophilia without inducing neutropenia (Abstract, Materials and Methods, Results, Figure 3). Hence claims 3-10 and 13-16 are not novel in light of D1.

D2 discloses administration of between 0.1 to 10mg/kg G-CSFR antibody C1.2G to cynomolgus monkeys reduced the level of neutrophils compared to control animals without inducing neutropenia (Example 6, Figure 3, SEQ ID NO: 2-5, 64-65 and 68). Hence claims 3-10 and 13-17 are not novel in light of D2.

Claims 3-10 and 13-17 are not novel and therefore do not meet the requirements of Article 33(2) of the PCT.

With regard to claims 1-2, 11-12 and 18-23, none of the cited documents explicitly disclose treatment of a human subject, administration of the antibody once every 14-28 days or the treatment of the neutrophil-mediated conditions, as claimed and hence meet the requirements of Article 33(2) of the PCT.

INVENTIVE STEP (IS)

Given the above novelty objection, claims 3-10 and 13-17 do not involve an inventive step and do not meet the requirements of Article 33(3) of the PCT.

Claims 1-2, 11-12 and 17-23 lack an inventive step in light of D1.

The relevant disclosures of D1 are described above.

The claimed invention differs from D1 in that it does not explicitly disclose treatment of a human subject, administration of the antibody once every 14-28 days, an antibody comprising SEQ ID NO: 14-16 or the treatment of the neutrophil-mediated conditions claimed.

D1 further discloses that neutrophils contribute to the pathogenesis of a number of human diseases, including chronic obstructive pulmonary disease, rheumatoid arthritis and Behcet's disease. The data provided further supports anti–G-CSFR therapy for the treatment of various neutrophil-driven inflammatory conditions (Introduction, Discussion).

In light of the disclosures of D1 it would be obvious to use G-CSFR antibodies to reduce circulating neutrophils in humans and for the treatment or prevention of the neutrophil-mediated conditions claimed with a reasonable expectation of success.

Furthermore it is considered that there are no difficulties for a person skilled in the art to overcome in administering the antibody once every 14-28 days or optimizing antibody CSL324. These differences merely represent features achieved by routine optimization when compared to the citation. Therefore the person skilled in the art would directly and without difficulty, by routine steps, arrive at a solution which is the same as the claimed solution and therefore the claimed invention lacks an inventive step.

For similar reasons stated above claims 1-2, 11-12 and 18-23 lack an inventive step in light of D2. D2 further discloses that the G-CSFR antibodies are suitable for treating or preventing GCSF-mediated conditions including autoimmune disease, inflammatory disease or cancer (page 18, lines 21-29, page 53, line 14 – page 54, line 3, page 57, lines 31-35). In light of the disclosures of D2 it would be obvious to use G-CSFR antibodies to reduce circulating neutrophils in humans and for the treatment or prevention of the neutrophil-mediated conditions claimed with a reasonable expectation of success.

Claims 1-23 are obvious and do not meet the requirements of Article 33(3) of the PCT.

INDUSTRIAL APPLICABILITY (IA)

The invention defined in the claims is considered to meet the requirements of Industrial Applicability under Article 33(4) of the PCT because it can be made by, or used in, industry.

P Category Document/s listed in Box VI:

There is a document(s) listed as a P category document in Box VI because it:

- discloses subject matter that is of particular relevance to this application and
- is published before the international filing date but after the priority date of this application.

Under the PCT, only documents published before the priority date of the instant application can deprive the claims of that application of novelty or inventive step.

However, the relevance of a document published after the priority date of the application under consideration is dependent on national law in individual countries.

P category document/s may become significant in the National Phase.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International Application No.

PCT/AU2019/051325

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
P,X : WO 2019/178645 A1	26 September 2019	22 March 2019	23 March 2018
P,X : WO 2019/104385 A1	06 June 2019	29 November 2018	29 November 2017

See Supplemental Box for Details

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

Continuation of: **Box VI**

WO 2019/178645 A1 discloses methods of treating asthma, such as neutrophilic asthma comprising administration of an antibody that inhibits G-CSF signaling. WO 2019/178645 A1 further discloses that the dose is administered at an initial dose of between about 0.1mg/kg to about 30mg/kg, such as from about 1mg/kg to about 10mg/kg. The antibody may be administered every 21 days. The compound that inhibits G-CSF signaling reduces the number of neutrophils without inducing neutropenia (Abstract, page 45, lines 9-10, page 50, lines 34-36, page 51, lines 19-23, Example 3, Claims 1-20, SEQ ID NO: 2-5, 14-15 and 18). WO 2019/178645 A1 is relevant to claims 3-19.

WO 2019/104385 A1 discloses a method for preventing or treating ischemia-reperfusion injury in a subject comprising administering an antibody that inhibits G-CSF signaling. The dose may be administered at about 0.1mg/kg to about 1mg/kg. The maintenance doses may be administered every 10-15 days (Abstract, page 8, lines 8-14, page 58, lines 8-9, Examples 3, 6 and 9, Claims 1-26, SEQ ID NO: 2-5, 14-15 and 18). WO 2019/104385 A1 is relevant to claims 3, 9-11 and 13-18.