PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
01134-0060-00PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2019/040820	8 July 2019 (08-07-2019)	9 July 2018 (09-07-2018)
Applicant		
FIVE PRIME THERAPEUTICS, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 11 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out 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 (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [X] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [X] **Certain claims were found unsearchable** (See Box No. II)

3. [X] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. 37C
      [X] as suggested by the applicant
      [ ] as selected by this Authority, because the applicant failed to suggest a figure
      [ ] as selected by this Authority, because this figure better characterizes the invention
   b. [ ] none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/040820

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:

      [ ] 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 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

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

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

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

2. [ ] 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.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/040820

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.: 1, 61-63(all partially)
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:

see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
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 additional sheet

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 an 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.:

32-37(completely); 1-31, 38-63(partially)

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.:

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.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/040820

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28 A61K39/395
ADD.

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)
C07K A61K

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2016/144728 A2 (UNIV TEXAS [US]) 15 September 2016 (2016-09-15) figures 6,19 -----	1-63
X	WO 2016/111947 A2 (JOUNCE THERAPEUTICS INC [US]) 14 July 2016 (2016-07-14) claims page 106; example 8 -----	1-63
X	WO 2015/179633 A1 (HUTCHINSON FRED CANCER RES [US]; UNIV TEXAS [US]) 26 November 2015 (2015-11-26) page 53, paragraph 144 -----	1-63
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[X] Further documents are listed in the continuation of Box C.

[X] 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

"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
13 January 2020	23/01/2020

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Covone-van Hees, M

3

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ANONYMOUS: "Invitrogen Data sheet: CD85d (ILT4) Monoclonal Antibody (42D1),Functional Grade, eBioscience Catalog Number 16-5149-85", INTERNET CITATION, 1 January 2015 (2015-01-01), XP002788854, Retrieved from the Internet: URL:https://www.thermofisher.com/order/genome-database/generatePdf?productName=CD85d%20(ILT4)&assayType=PRANT&detailed=true&productId=16-5149-85 [retrieved on 1077] the whole document	1-49, 60-63
X	M. DENG ET AL: "A motif in LILRB2 critical for Angptl2 binding and activation", BLOOD, vol. 124, no. 6, 7 August 2014 (2014-08-07), pages 924-935, XP055204710, ISSN: 0006-4971, DOI: 10.1182/blood-2014-01-549162 page 925, column 1, paragraph 3	1,15,16, 20,60-63
A	XIAOYE LIU ET AL: "ANGPTL2/LILRB2 signaling promotes the propagation of lung cancer cells", ONCOTARGET, vol. 6, no. 25, 28 August 2015 (2015-08-28), XP055471907, DOI: 10.18632/oncotarget.4217 the whole document	1-63
X,P	WO 2019/126514 A2 (JOUNCE THERAPEUTICS INC [US]) 27 June 2019 (2019-06-27) the whole document	1-63
X,P	WO 2018/187518 A1 (MERCK SHARP & DOHME [US]; AGENUS INC [US] ET AL.) 11 October 2018 (2018-10-11) the whole document	1-63
X,P	HUI-MING CHEN ET AL: "Blocking immunoinhibitory receptor LILRB2 reprograms tumor-associated myeloid cells and promotes antitumor immunity", JOURNAL OF CLINICAL INVESTIGATION, vol. 128, no. 12, 22 October 2018 (2018-10-22), pages 5647-5662, XP055554809, GB ISSN: 0021-9738, DOI: 10.1172/JCI97570 the whole document	1-63

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3

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2018/013818 A2 (BRISTOL-MYERS SQUIBB COMPANY [US]) 18 January 2018 (2018-01-18) 100% identity with seq.11; sequence 30 -----	1,3,7,9, 11,20, 27-29
X	WO 2008/079246 A2 (MEDAREX INC [US]; PFIZER [US] ET AL.) 3 July 2008 (2008-07-03) 100% identity with seq.11; sequence 85 -----	1,3,7,9, 11,20, 27-29
X	WO 2015/189638 A2 (UNIV LONDON QUEEN MARY [GB]) 17 December 2015 (2015-12-17) 100% identity with seq.155-157 (3 LCDRs); sequence 1008 -----	1,3,7,9, 11,20, 27-29

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2019/040820

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2016144728 A2	15-09-2016	AU 2016229201 A1	14-09-2017
		CA 2977544 A1	15-09-2016
		CN 107530402 A	02-01-2018
		EP 3265113 A2	10-01-2018
		JP 2018510340 A	12-04-2018
		KR 20170123323 A	07-11-2017
		US 2018086829 A1	29-03-2018
		WO 2016144728 A2	15-09-2016
WO 2016111947 A2	14-07-2016	US 2016200815 A1	14-07-2016
		WO 2016111947 A2	14-07-2016
WO 2015179633 A1	26-11-2015	AU 2015264120 A1	24-11-2016
		CA 2948871 A1	26-11-2015
		EP 3146041 A1	29-03-2017
		JP 6533912 B2	26-06-2019
		JP 2017517259 A	29-06-2017
		KR 20170007449 A	18-01-2017
		US 2017260508 A1	14-09-2017
		US 2019330593 A1	31-10-2019
		WO 2015179633 A1	26-11-2015
WO 2019126514 A2	27-06-2019	TW 201930357 A	01-08-2019
		US 2019194327 A1	27-06-2019
		WO 2019126514 A2	27-06-2019
WO 2018187518 A1	11-10-2018	AR 111362 A1	03-07-2019
		AU 2018248294 A1	10-10-2019
		CA 3057378 A1	11-10-2018
		CO 2019011155 A2	21-10-2019
		KR 20190136064 A	09-12-2019
		SG 11201909081Y A	30-10-2019
		TW 201839014 A	01-11-2018
		US 2018298096 A1	18-10-2018
		WO 2018187518 A1	11-10-2018
WO 2018013818 A2	18-01-2018	AU 2017297506 A1	21-02-2019
		BR 112019000431 A2	09-07-2019
		CA 3030765 A1	18-01-2018
		CL 2019000100 A1	10-05-2019
		CN 109757103 A	14-05-2019
		CO 2019000372 A2	18-01-2019
		EP 3484920 A2	22-05-2019
		JP 2019533981 A	28-11-2019
		KR 20190027384 A	14-03-2019
		PE 20190418 A1	19-03-2019
		SG 11201900026T A	30-01-2019
		TW 201811829 A	01-04-2018
		US 2018016336 A1	18-01-2018
		US 2018298097 A1	18-10-2018
		US 2019248893 A1	15-08-2019
		UY 37325 A	31-01-2018
		WO 2018013818 A2	18-01-2018
WO 2008079246 A2	03-07-2008	AR 064456 A1	01-04-2009
		AU 2007338844 A1	03-07-2008
		BR PI0720477 A2	14-01-2014
		CA 2672916 A1	03-07-2008

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2019/040820

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		CL 2007003807 A1	09-05-2008
		CN 101605812 A	16-12-2009
		EP 2102238 A2	23-09-2009
		JP 2010512790 A	30-04-2010
		KR 20090094848 A	08-09-2009
		PE 20081478 A1	07-12-2008
		RU 2009128064 A	27-01-2011
		TW 200846365 A	01-12-2008
		US 2010092484 A1	15-04-2010
		UY 30776 A1	03-07-2008
		WO 2008079246 A2	03-07-2008
WO 2015189638 A2	17-12-2015	EP 3155012 A2	19-04-2017
		US 2017129948 A1	11-05-2017
		WO 2015189638 A2	17-12-2015

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-31, 38-63(all partially)

   Antibody binding to ILT4 designated 9G4, isolated nucleic acid and set of nucleic acid encoding the antibody, composition and cell comprising said nucleic acid, method to prepare the antibody by culturing the said cell, combination with pharmaceutically acceptable carrier, cancer and infectious disease treatment with the said antibody, use of the said antibody of detection

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2. claims: 1-31, 38-63(all partially)

   Antibody binding to ILT4 designated 9C8, isolated nucleic acid and set of nucleic acid encoding the antibody, composition and cell comprising said nucleic acid, method to prepare the antibody by culturing the said cell, combination with pharmaceutically acceptable carrier, cancer and infectious disease treatment with the said antibody, use of the said antibody of detection

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3. claims: 1-31, 38-63(all partially)

   Antibody binding to ILT4 designated 2H2, isolated nucleic acid and set of nucleic acid encoding the antibody, composition and cell comprising said nucleic acid, method to prepare the antibody by culturing the said cell, combination with pharmaceutically acceptable carrier, cancer and infectious disease treatment with the said antibody, use of the said antibody of detection

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4. claims: 1-31, 38-63(all partially)

   Antibody binding to ILT4 designated 2E5, isolated nucleic acid and set of nucleic acid encoding the antibody, composition and cell comprising said nucleic acid, method to prepare the antibody by culturing the said cell, combination with pharmaceutically acceptable carrier, cancer and infectious disease treatment with the said antibody, use of the said antibody of detection

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5. claims: 1-31, 38-63(all partially)

   Antibody binding to ILT4 designated 24E5, isolated nucleic acid and set of nucleic acid encoding the antibody, composition and cell comprising said nucleic acid, method to prepare the antibody by culturing the said cell, combination with pharmaceutically acceptable carrier, cancer and infectious disease treatment with the said antibody, use of

the said antibody of detection

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6. claims: 32-37(completely); 1-31, 38-63(partially)

Antibody binding to ILT4 designated 21D9 including the mutants in the framework mutations, isolated nucleic acid and set of nucleic acid encoding the antibody, composition and cell comprising said nucleic acid, method to prepare the antibody by culturing the said cell, combination with pharmaceutically acceptable carrier, cancer and infectious disease treatment with the said antibody, use of the said antibody of detection

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7. claims: 1-31, 38-63(all partially)

Antibody binding to ILT4 designated 21A5 including the mutants in the framework mutations, isolated nucleic acid and set of nucleic acid encoding the antibody, composition and cell comprising said nucleic acid, method to prepare the antibody by culturing the said cell, combination with pharmaceutically acceptable carrier, cancer and infectious disease treatment with the said antibody, use of the said antibody of detection

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8. claims: 1-31, 38-63(all partially)

Antibody binding to ILT4 designated 10F10 including the mutants in the framework mutations, isolated nucleic acid and set of nucleic acid encoding the antibody, composition and cell comprising said nucleic acid, method to prepare the antibody by culturing the said cell, combination with pharmaceutically acceptable carrier, cancer and infectious disease treatment with the said antibody, use of the said antibody of detection

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Continuation of Box II.2

Claims Nos.: 1, 61-63(all partially)

Present claims 1,61-63 relate to antibodies defined only by reference functional features, including unusual parameters e.g. competes for binding, interacts to one or more of a amino acid residues, has binding profile shown in figures etc.
This definition comprises an extremely large number of possible products. Support and disclosure in the sense of Article 6 and 5 PCT is to be found however for only a very small proportion of the products claimed, namely the specific human anti-ILT4 Ab produced in the application.
In addition, the use of functional features and unusual parameters in the present context is considered to lead to a lack of clarity because the claims do not clearly identify the products encompassed by them as not all the parameters can be clearly and reliably determined by indications in the description or by objective procedures which are usual in the art. This makes it impossible to compare the claims to the prior art. As a result, the application does not comply with the requirement of clarity under Article 6 PCT.
The lack of clarity, support and/or disclosure is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of the said claims.

The search of claims 1,61-63 was restricted to the specific exemplified antibodies (as defined in claims 2-14)

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.