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OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Published:

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23 July 2020 (23.07.2020)

(54) Title: METHODS OF TREATING DISEASES USING KINASE MODULATORS

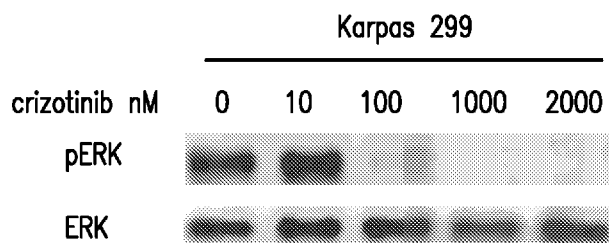


FIG. 1A

(57) Abstract: Provided herein are methods of modulating immune response, including methods of treating a cancer or an infection using a combination of kinase modulators and immunotherapy that promotes immune response. Also provided herein are methods of treating an autoimmune disease or graft-versus-host disease, and methods of reducing the risk of solid organ transplant rejection using a combination of kinase modulators and immunosuppressive therapy.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2019/059125

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. ☐ 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 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/US2019/059125

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.:
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.:
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, 2, 5-9, 37, 38, 60(all partially)

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/US2019/059125

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/506 A61K39/00 A61P35/00 C07K16/00 A61K31/517
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 A61P

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, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2017/160717 A2 (MEMORIAL SLOAN KETTERING CANCER CENTER [US]) 21 September 2017 (2017-09-21) the whole document	1,2,5-9, 37,38,60
A	WO 2017/058780 A1 (MERCK PATENT GMBH [DE]; PFIZER [US] ET AL.) 6 April 2017 (2017-04-06) claims 1-57; examples 2-6 ----- -/-	1,2,5-9, 37,38,60



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

"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

12 February 2020

Date of mailing of the international search report

24/06/2020

Name and mailing address of the ISA/

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Authorized officer

Noë, Veerle

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/059125

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	C. VOENA ET AL: "Efficacy of a Cancer Vaccine against ALK-Rearranged Lung Tumors", CANCER IMMUNOLOGY RESEARCH, vol. 3, no. 12, 1 December 2015 (2015-12-01), pages 1333-1343, XP055609811, US ISSN: 2326-6066, DOI: 10.1158/2326-6066.CIR-15-0089	1,2,5,9, 37,38,60
Y	the whole document	1,2,5-9, 37,38,60
X	----- VOENA C ET AL: "ALK Inhibitors and Vaccination Against Anaplastic Lymphoma Kinase (ALK) Induce Potent Anti-tumor Activity Improving Overall Survival in Non Small Cell Lung Carcinoma (NSCLC)", EUROPEAN JOURNAL OF CANCER, vol. 48, no. Suppl. 5, July 2012 (2012-07), page S211, XP002797564, & 22ND BIENNIAL CONGRESS OF THE EUROPEAN-ASSOCIATION-FOR-CANCER-RESEARCH; BARCELONA, SPAIN; JULY 07 -10, 2012	1,5,9, 37,38,60
Y	the whole document	1,2,5,9, 37,38,60
X	----- WO 2016/040880 A1 (NOVARTIS AG [CH]; LEBWOHL DAVID [US] ET AL.) 17 March 2016 (2016-03-17) abstract page 3, paragraph 3 - page 4, paragraph 1 page 8, last paragraph page 9, paragraph 2 page 13, paragraph 4-1 page 17, last paragraph page 27, paragraph 3 page 49, paragraph 2 page 53, paragraph 2 page 61, paragraph 3 - page 62, paragraph 4 page 73, paragraph 3-4	1,2,5,9, 37,38,60
A	----- WO 2016/044774 A1 (PHARMACYCLICS LLC [US]) 24 March 2016 (2016-03-24) paragraphs [0052] - [0054], [0198]; claim 47 ----- -/--	1,2,5-9, 37,38,60

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2019/059125

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	CARPENTER E L ET AL: "Antibody targeting of anaplastic lymphoma kinase induces cytotoxicity of human neuroblastoma.", ONCOGENE 15 NOV 2012, vol. 31, no. 46, 15 November 2012 (2012-11-15), pages 4859-4867, XP002797565, ISSN: 1476-5594 the whole document -----	6,7

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2019/059125

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2017160717 A2	21-09-2017	US 2019077856 A1 WO 2017160717 A2	14-03-2019 21-09-2017
WO 2017058780 A1	06-04-2017	CA 3000386 A1 EP 3355902 A1 JP 2018529719 A US 2018282415 A1 WO 2017058780 A1	06-04-2017 08-08-2018 11-10-2018 04-10-2018 06-04-2017
WO 2016040880 A1	17-03-2016	AU 2015314756 A1 AU 2018250507 A1 BR 112017004826 A2 CA 2960824 A1 CN 107206071 A EP 3191097 A1 EP 3191126 A1 EP 3191127 A1 EP 3659621 A1 JP 6681905 B2 JP 2017532372 A KR 20170060042 A RU 2017112379 A US 2017281624 A1 US 2017296659 A1 US 2017304443 A1 WO 2016040880 A1 WO 2016040882 A1 WO 2016040892 A1	16-03-2017 15-11-2018 12-12-2017 17-03-2016 26-09-2017 19-07-2017 19-07-2017 19-07-2017 03-06-2020 15-04-2020 02-11-2017 31-05-2017 15-10-2018 05-10-2017 19-10-2017 26-10-2017 17-03-2016 17-03-2016 17-03-2016
WO 2016044774 A1	24-03-2016	NONE	

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, 2, 5-9, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ALK inhibitor and a vaccine.

2. claims: 1, 2, 5-8, 10-13, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ALK inhibitor and an immune checkpoint blockade immunotherapy

3. claims: 1, 2, 5-8, 14-17, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ALK inhibitor and adoptive cell therapy.

4. claims: 1, 2, 5-8, 18, 19, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ALK inhibitor and a TCR mimic antibody or a TCR based construct

5. claims: 1, 2, 5-8, 20, 23, 24, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ALK inhibitor and a cytokine.

6. claims: 1, 2, 5-8, 20, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ALK inhibitor and a CD47 antibody.

7. claims: 1, 2, 5-8, 20, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ALK inhibitor and a SIRP alpha antagonist.

8. claims: 1, 2, 5-8, 20, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ALK inhibitor and a HDAC inhibitor.

9. claims: 1, 2, 5-8, 20, 25-27, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ALK inhibitor and a TLR agonist.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

10. claims: 1, 2, 5-8, 20-22, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ALK inhibitor and an epigenetic modulator that upregulates the expression of one or more MHCs or upregulates antigen presentation.

11. claims: 3-9, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ERBB2 inhibitor and a vaccine.

12. claims: 3-8, 10-13, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ERBB2 inhibitor and an immune checkpoint blockade immunotherapy.

13. claims: 3-8, 14-17, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ERBB2 inhibitor and adoptive T-cell therapy.

14. claims: 3-8, 18, 19, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ERBB2 inhibitor and a TCR mimic antibody or a TCR based construct.

15. claims: 3-8, 20, 23, 24, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ERBB2 inhibitor and a cytokine.

16. claims: 3-8, 20, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ERBB2 inhibitor and a CD47 antibody.

17. claims: 3-8, 20, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ERBB2 inhibitor and a SIRP alpha antagonist.

18. claims: 3-8, 20, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ERBB2

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

inhibitor and a HDAC inhibitor.

19. claims: 3-8, 20, 25-27, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ERBB2 inhibitor and a TLR agonist.

20. claims: 3-8, 20-22, 37, 38, 60(all partially)

Method of treating cancer comprising administering an ERBB2 inhibitor and an epigenetic modulator that upregulates the expression of one or more MHCs or upregulates antigen presentation.

21. claims: 28-30(completely); 34-38, 60(partially)

Method for generating a population of antigen-presenting cells for therapeutic administration to a cancer patient comprising culturing antigen-presenting cells with an ALK inhibitor.

22. claims: 31-33(completely); 34-38, 60(partially)

Method for generating a population of antigen-presenting cells for therapeutic administration to a cancer patient comprising culturing antigen-presenting cells with an ERBB2 inhibitor.

23. claims: 39(completely); 41, 48-60(partially)

Method of treating an autoimmune disease comprising administering an ALK activator and an immunosuppressive therapy.

24. claims: 40(completely); 41, 48-60(partially)

Method of treating an autoimmune disease comprising administering an ERBB2 activator and an immunosuppressive therapy.

25. claims: 42(completely); 44, 45, 48-60(partially)

Method of treating graft-versus-host disease comprising administering an ALK activator and an immunosuppressive therapy.

26. claims: 43(completely); 44, 45, 48-60(partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Method of treating graft-versus-host disease comprising administering an ERBB2 activator and an immunosuppressive therapy.

27. claims: 46(completely); 48-60(partially)

Method of reducing the risk of solid organ transplant rejection comprising administering an ALK activator.

28. claims: 47(completely); 48-60(partially)

Method of reducing the risk of solid organ transplant rejection comprising administering an ERBB2 activator.
