

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference ABH-00725	<b>FOR FURTHER ACTION</b>	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US2020/030435	International filing date ( <i>day/month/year</i> ) 29 Apr 2020	(Earliest) Priority Date ( <i>day/month/year</i> ) 30 Apr 2019
Applicant ATARA BIOTHERAPEUTICS, 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 7 sheets.

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:

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 43.6bis(a)).

c.  With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2.  **Certain claims were found unsearchable** (see Box No. II).

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

4. With regard to the **title**,

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**,

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. \_\_\_\_\_

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.

**Box No. 1** 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 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).
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/US2020/030435

<p><b>A. CLASSIFICATION OF SUBJECT MATTER</b>                  IPC (20200101) C07K 16/28, C07K 16/46, C12N 5/0783, A61K 35/28, A61K 39/395, A61P 35/02                  CPC (20130101) C07K 16/28, C07K 16/2896, C07K 16/46, C12N 5/0636, A61K 35/28, A61K 39/39558, A61P 35/02                  According to International Patent Classification (IPC) or to both national classification and IPC</p>														
<p><b>B. FIELDS SEARCHED</b></p> <p>Minimum documentation searched (classification system followed by classification symbols)                  IPC (20200101) C07K 16/28, C12N 5/00, A61K 39/395, A61P 35/02                  CPC (20130101) C07K 16/28, C12N 5/00, A61K 39/395, A61P 35/02</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)                  Databases consulted: Esp@cenet, Google Patents, CAPLUS, BIOSIS, EMBASE, MEDLINE, Google Scholar, Derwent Innovation                  Search terms used: car t cell, cd19, GPC3, MAGE-A1, MAGE-A2, MAGE-C2, SSX-2, Ny-ESO-1, hTERT, "bi specific", "chimeric antigen receptor", "co-stimulatory signaling domain", ymmn, prp, pyap, ITAM mutant, EBV-sensitized.</p>														
<p><b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b></p> <table border="1"> <thead> <tr> <th>Category*</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>                     Kochenderfer, James N., et al. "B-cell depletion and remissions of malignancy along with cytokine-associated toxicity in a clinical trial of anti-CD19 chimeric-antigen-receptor-transduced T cells." Blood, The Journal of the American Society of Hematology 119.12 (2012): 2709-2720.  <a href="https://ashpublications.org/blood/article/119/12/2709/29857/B-cell-depletion-and-remissions-of-malignancy">https://ashpublications.org/blood/article/119/12/2709/29857/B-cell-depletion-and-remissions-of-malignancy</a>                       22 Mar 2012 (2012/03/22)                      The whole document                 </td> <td>1-4,6-12,16,17,24, 25,28-37,66,67,69-74</td> </tr> <tr> <td>Y</td> <td>The whole document</td> <td>5,13-15,18-27,38-65, 68,73-82</td> </tr> <tr> <td>X</td> <td>                     Kochenderfer, James N., et al. "Construction and pre-clinical evaluation of an anti-CD19 chimeric antigen receptor." Journal of immunotherapy (Hagerstown, Md.: 1997) 32.7 (2009): 689.  <a href="https://journals.lww.com/immunotherapy-journal/Abstract/2009/09000/Construction_and_Preclinical_Evaluation_of_an.2.aspx">https://journals.lww.com/immunotherapy-journal/Abstract/2009/09000/Construction_and_Preclinical_Evaluation_of_an.2.aspx</a>                       30 Sep 2009 (2009/09/30)                      The whole document                 </td> <td>1-4,6-12,16,17,24, 25,28-37,66,67,69-74</td> </tr> </tbody> </table>			Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	Kochenderfer, James N., et al. "B-cell depletion and remissions of malignancy along with cytokine-associated toxicity in a clinical trial of anti-CD19 chimeric-antigen-receptor-transduced T cells." Blood, The Journal of the American Society of Hematology 119.12 (2012): 2709-2720. <a href="https://ashpublications.org/blood/article/119/12/2709/29857/B-cell-depletion-and-remissions-of-malignancy">https://ashpublications.org/blood/article/119/12/2709/29857/B-cell-depletion-and-remissions-of-malignancy</a>  22 Mar 2012 (2012/03/22) The whole document	1-4,6-12,16,17,24, 25,28-37,66,67,69-74	Y	The whole document	5,13-15,18-27,38-65, 68,73-82	X	Kochenderfer, James N., et al. "Construction and pre-clinical evaluation of an anti-CD19 chimeric antigen receptor." Journal of immunotherapy (Hagerstown, Md.: 1997) 32.7 (2009): 689. <a href="https://journals.lww.com/immunotherapy-journal/Abstract/2009/09000/Construction_and_Preclinical_Evaluation_of_an.2.aspx">https://journals.lww.com/immunotherapy-journal/Abstract/2009/09000/Construction_and_Preclinical_Evaluation_of_an.2.aspx</a>  30 Sep 2009 (2009/09/30) The whole document	1-4,6-12,16,17,24, 25,28-37,66,67,69-74
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<p><input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.      <input checked="" type="checkbox"/> See patent family annex.</p>														
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"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</td> </tr> <tr> <td>"D" document cited by the applicant in the international application</td> <td>"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</td> </tr> <tr> <td>"E" earlier application or patent but published on or after the international filing date</td> <td>"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</td> </tr> <tr> <td>"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)</td> <td>"&amp;" document member of the same patent family</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td></td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"D" document cited by the applicant in the international application	"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	"E" earlier application or patent but published on or after the international filing date	"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	"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)	"&" document member of the same patent family	"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	
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"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														
Date of the actual completion of the international search 23 Jul 2020		Date of mailing of the international search report 27 Jul 2020												
Name and mailing address of the ISA: Israel Patent Office Technology Park, Bldg.5, Malcha, Jerusalem, 9695101, Israel Email address: pctoffice@justice.gov.il		Authorized officer PACE Umberto  Telephone No. 972-73-3927148												

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2020/030435

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	The whole document	5,13-15,18-27,38-65, 68,73-82
Y	US 2016362472 A1 BITTER HANS [US] et al. 15 Dec 2016 (2016/12/15) Sequence 111	5,26
Y	Boucher, Justin C., et al. "Mutation of the CD28 costimulatory domain confers decreased CAR T cell exhaustion." Blood 132.Supplement 1 (2018): 966-966. <a href="https://ashpublications.org/blood/article/132/Supplement%201/966/266122/Mutation-of-the-CD28-Costimulatory-Domain-Confers">https://ashpublications.org/blood/article/132/Supplement%201/966/266122/Mutation-of-the-CD28-Costimulatory-Domain-Confers</a> This document teaches that incorporating null mutations of the CD28 subdomains (YMNM, PRRP, or PYAP) optimizes CAR T cell signaling and reduces exhaustion (see the whole document).  29 Nov 2018 (2018/11/29) The whole document	13-15,56-58
Y	D5: Boucher, Justin C., et al. "Mutation of the CD28 costimulatory domain confers increased CAR T cell persistence and decreased exhaustion." (2018): 57-28. <a href="https://www.jimmunol.org/content/200/1_Supplement/57.28.abstract">https://www.jimmunol.org/content/200/1_Supplement/57.28.abstract</a>  01 May 2018 (2018/05/01) The whole document	13-15,56-58
Y	Love, Paul E., and Sandra M. Hayes. "ITAM-mediated signaling by the T-cell antigen receptor." Cold Spring Harbor perspectives in biology 2.6 (2010): a002485. <a href="https://cshperspectives.cshlp.org/content/2/6/a002485.short">https://cshperspectives.cshlp.org/content/2/6/a002485.short</a> 28 Apr 2010 (2010/04/28) Table 2	18-21
Y	Qin, Le, et al. "Incorporation of a hinge domain improves the expansion of chimeric antigen receptor T cells." Journal of hematology & oncology 10.1 (2017): 1-11. <a href="https://jhoonline.biomedcentral.com/articles/10.1186/s13045-017-0437-8">https://jhoonline.biomedcentral.com/articles/10.1186/s13045-017-0437-8</a>  13 Mar 2013 (2013/03/13) The whole document, especially page 2, second paragraph of the right column, Fig. 1 and the "Results" section	22,23,59
Y	FMC63-28Z receptor protein [synthetic construct] GenBank: ADM64594.1 <a href="https://www.ncbi.nlm.nih.gov/protein/ADM64594.1?report=genbank&amp;log\$=protalign&amp;blast_rank=1&amp;RID=HAN7S91A014">https://www.ncbi.nlm.nih.gov/protein/ADM64594.1?report=genbank&amp;log\$=protalign&amp;blast_rank=1&amp;RID=HAN7S91A014</a>  11 Jun 2012 (2012/06/11) The whole document	27
Y	Pule, M. A., Savoldo, B., Myers, G. D., Rossig, C., Russell, H. V., Dotti, G., ... & Yvon, E. (2008). Virus-specific T cells engineered to coexpress tumor-specific receptors: persistence and antitumor activity in individuals with neuroblastoma. Nature medicine, 14(11), 1264. <a href="https://www.nature.com/articles/nm.1882">https://www.nature.com/articles/nm.1882</a>  02 Nov 2008 (2008/11/02) The whole document	38-41,68

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International application No.

PCT/US2020/030435

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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Y	WO 2017027291 A1 SEATTLE CHILDREN'S HOSPITAL (SEATTLE CHILDREN'S RESEARCH INSTITUTE) 16 Feb 2017 (2017/02/16) Paragraphs 32-33 and figures 3 and 4, paragraph 39, figure 9, paragraph 46 and figure 11, (paragraph 11	42-55
Y	Rafiq, Sarwish, et al. "Targeted delivery of a PD-1-blocking scFv by CAR-T cells enhances anti-tumor efficacy in vivo." Nature biotechnology 36.9 (2018): 847-856. <a href="https://www.nature.com/articles/nbt.4195">https://www.nature.com/articles/nbt.4195</a>  01 Oct 2018 (2018/10/01) The whole document	63-65
Y	Zhang, Yongping, et al. "CRISPR-Cas9 mediated LAG-3 disruption in CAR-T cells." Frontiers of medicine 11.4 (2017): 554-562. <a href="https://link.springer.com/article/10.1007/s11684-017-0543-6">https://link.springer.com/article/10.1007/s11684-017-0543-6</a>  17 Jun 2017 (2017/06/17) The whole document	60,61,78,81,82
Y	Yoon, Dok Hyun, et al. "Incorporation of immune checkpoint blockade into chimeric antigen receptor T cells (CAR-Ts): combination or built-in CAR-T." International journal of molecular sciences 19.2 (2018): 340. <a href="https://www.mdpi.com/1422-0067/19/2/340">https://www.mdpi.com/1422-0067/19/2/340</a>  24 Jan 2018 (2018/01/24) The whole document	60-65,75-82

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International application No.  
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		US 10253086 B2	09 Apr 2019
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		EP 3331920 A1	13 Jun 2018

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

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Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		EP 3331920 A4	03 Apr 2019
		JP 2018522567 A	16 Aug 2018
		MX 2018001568 A	25 Apr 2019
		US 2020215108 A1	09 Jul 2020