Billing Code 4140-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of an Exclusive Patent License: Development and Commercialization of Cell Therapies for Cancer

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The National Cancer Institute, an institute of the National Institutes of Health, Department of Health and Human Services, is contemplating the grant of an Exclusive Patent License to practice the inventions embodied in the Patents and Patent Applications listed in the Supplementary Information section of this Notice to Tailored Therapeutics, LLC. ("Tailored"), located in Potomac, MD**.**

DATES: Only written comments and/or applications for a license which are received by the National Cancer Institute's Technology Transfer Center on or before **[INSERT DATE 15 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]** will be considered.

ADDRESSES: Requests for copies of the patent applications, inquiries, and comments relating to the contemplated Exclusive Patent License should be directed to: Andrew Burke, Senior Technology Transfer Manager, NCI Technology Transfer Center, 9609 Medical Center Drive, RM 1E530, MSC 9702, Bethesda, MD 20892-9702 (for business mail), Rockville, MD 20850-9702; Telephone: (240)-276-5484; Facsimile: (240)-276-5504; E-mail: andy.burke@nih.gov.

SUPPLEMENTARY INFORMATION:

Intellectual Property

GROUP A

E-028-2015: Anti-Mutated KRAS T Cell Receptors

1. US Provisional Patent Application 62/084,654, filed November 26, 2014 (E-028-2015-0-US-01);
2. International Patent Application PCT/US2015/062269, filed November 24, 2015 (E-028-2015-1-PCT-01);
3. Australian Patent Application 2015353720, filed May 18, 2017 (E-028-2015-1-AU-02);
4. Canadian Patent Application 2968399, filed May 18, 2017 (E-028-2015-1-CA-03);
5. Chinese Patent Application 201580070673.7, filed June 23, 2017 (E-028-2015-1-CN-04);
6. European Patent Application 15807756.0 filed June 23, 2017 (E-028-2015-1-EP-05);
7. Israeli Patent Application 252258, filed May 14, 2017 (E-028-2015-1-IL-06);
8. Japanese Patent Application 527874/2017, filed May 24, 2017 (E-028-2015-1-JP-07);
9. Korean Patent Application 2017-7017289, filed June 23, 2017 (E-028-2015-1-KR-08);
10. Mexican Patent Application MX/a/2017/006865, filed May 25, 2017 (E-028-2015-1-MX-09);

11. New Zealand Patent Application 732045, filed May 18, 2017 (E-028-2015-1-NZ-10);
12. Saudi Arabian Patent Application 517381608, filed May 25, 2017 (E-028-2015-1-SA-11);
13. Singapore Patent Application 11201704155U, filed May 23, 2017 (E-028-2015-1-SG-12);
14. United States Utility Patent Application 15/528,813, filed May 23, 2017 (E-028-2015-1-US-13); and
15. Hong Kong Patent Application 18103250.9, filed March 7, 2018 (E-028-2015-1-HK-14).

E-180-2015: Anti-Mutated KRAS T Cell Receptors

1. US Provisional Patent Application 62/171,321, filed June 5, 2015 (E-180-2015-0-US-01).

E-265-2015: T Cell Receptors Recognizing HLA-CW8 Restricted Mutated KRAS

1. US Provisional Patent Application 62/218,688, filed September 15, 2015 (E-265-2015-0-US-01);
2. International Patent Application PCT/US2016/050875, filed September 9, 2016 (E-265-2015-0-PCT-02);
3. Australian Patent Application 2016323017, filed March 6, 2018 (E-265-2015-0-AU-03);
4. Canadian Patent Application 2998869, filed March 15, 2018 (E-265-2015-0-CA-04);

5. Chinese Patent Application 201680058891.3, filed April 3, 2018 (E-265-2015-0-CN-05);
6. European Patent Application 16770408.9 filed March 7, 2018 (E-265-2015-0-EP-06);
7. Israeli Patent Application 257840, filed March 4, 2018 (E-265-2018-0-IL-07);
8. Japanese Patent Application 513423/2018, filed March 13, 2018 (E-265-2015-0-JP-08);
9. Korean Patent Application 2018-7010326, filed April 12, 2018 (E-265-2015-0-KR-09);
10. Mexican Patent Application MX/a/2018/003062, filed March 12, 2018 (E-265-2015-0-MX-10);
11. New Zealand Patent Application 740714, filed March 14, 2018 (E-265-2015-0-NZ-11);
12. Saudi Arabian Patent Application 518391109, filed March 13, 2018 (E-265-2015-0-SA-12);
13. Singapore Patent Application 11201802069U, filed March 13, 2018 (E-265-2015-0-SG-13); and
14. United States Utility Patent Application 15/758,954, filed March 9, 2018 (E-265-2015-0-US-14).

E-175-2016: Anti-KRAS G12D T Cell Receptors

1. US Provisional Patent Application 62/369,883, filed August 2, 2016 (E-175-2016-0-US-01); and

2. International Patent Application PCT/US2017/044615, filed July 31, 2017 (E-175-2016-0-PCT-02).

E-181-2017: HLA Class II-Restricted T Cell Receptors Against Mutated RAS

1. US Provisional Patent Application 62/560,930, filed September 20, 2017 (E-181-2017-0-US-01).

E-239-2017: HLA Class I-Restricted T Cell Receptors Against Mutated RAS

1. US Provisional Patent Application 62/594,244, filed December 4, 2017 (E-239-2017-0-US-01).

GROUP B

E-237-2017-0: T Cell Receptors Recognizing Mutated P53

1. US Provisional Patent Application 62/565,383, filed September 29, 2017 (E-237-2017-0-US-01).

GROUP C

E-237-2017-1: Methods of Isolating T Cells Having Antigenic Specificity for a P53 Cancer-Specific Mutation

1. US Provisional Patent Application 62/565,464, filed September 29, 2017 (E-237-2017-1-US-01).

The patent rights in these inventions have been assigned and/or exclusively licensed to the government of the United States of America.

The prospective exclusive license territory may be worldwide, and the fields of use may be limited to the following:

Fields of Use Applying to Intellectual Property Group A

"Development, manufacture and commercialization of autologous, peripheral blood T cell therapy products engineered by CRISPR to express T cell receptors reactive to mutated KRAS, as claimed in the Licensed Patent Rights, for the treatment of human cancers. Specifically excluded from this field of use are retrovirally-engineered peripheral blood T cell therapy products for the treatment of human cancers.

Development, manufacture and commercialization of companion diagnostics approved or cleared by the FDA or equivalent foreign regulatory agency for Licensee-proprietary T cell therapy products."

Fields of Use Applying to Intellectual Property Group B

"Development, manufacture and commercialization of autologous, peripheral blood T cell therapy products engineered by CRISPR to express T cell receptors reactive to mutated p53, as claimed in the Licensed Patent Rights, for the treatment of cancer in humans.

Development, manufacture and commercialization of companion diagnostics approved or cleared by the FDA or equivalent foreign regulatory agency for Licensee-proprietary T cell therapy products."

Fields of Use Applying to Intellectual Property Group C

"Development, manufacture and commercialization of autologous, tumor infiltrating lymphocyte-based adoptive T cell therapy products reactive to mutated p53, isolated as claimed in the Licensed Patent Rights, for the treatment of human cancers. Specifically excluded from this field of use are genetically engineered TIL cell therapy products for the treatment of human cancers.

Development, manufacture and commercialization of companion diagnostics approved or cleared by the FDA or equivalent foreign regulatory agency for Licensee-proprietary T cell therapy products."

Intellectual Property Group A is primarily directed to isolated T cell receptors (TCRs) reactive to mutated Kirsten rat sarcoma viral oncogene homolog (KRAS), within the context of several human leukocyte antigens (HLAs). Mutated KRAS, which plays a well-defined driver role in oncogenesis, is expressed by a variety of human cancers, including: pancreatic, lung, endometrial, ovarian and prostate. Due to its restricted expression in precancerous and cancerous cells, this antigen may be targeted on mutant KRAS-expressing tumors with minimal normal tissue toxicity.

Intellectual Property Group B is primarily directed to isolated TCRs reactive to mutated tumor protein 53 (TP53 or P53), within the context of several HLAs. *P53* is the archetypal tumor suppressor gene and the most frequently mutated gene in cancer. Contemporary estimates suggest that >50% of all tumors carry mutations in *P53*. Because of its prevalence in cancer and its restricted expression to precancerous and cancerous cells, this antigen may be targeted on mutant P53-expressing tumors with minimal normal tissue toxicity.

Intellectual Property Group C is primarily directed to methods of isolating T cells which are reactive to mutated P53 antigens. Briefly, pools of 25-mer peptides covering known P53 "hotspot" mutations have been generated. These peptides may be pulsed into autologous antigen presenting cells which are subsequently co-cultured with the patient's isolated T cells. Reactive T cells may be purified and expanded *in vitro* to generate an

autologous cell therapy product. The expanded cells may be administered to the patient and mediate tumor regression.

This Notice is made in accordance with 35 U.S.C. 209 and 37 CFR Part 404. The prospective exclusive license will be royalty bearing, and the prospective exclusive license may be granted unless within fifteen (15) days from the date of this published Notice, the National Cancer Institute receives written evidence and argument that establishes that the grant of the license would not be consistent with the requirements of 35 U.S.C. 209 and 37 CFR Part 404.

In response to this Notice, the public may file comments or objections. Comments and objections, other than those in the form of a license application, will not be treated confidentially, and may be made publicly available.

License applications submitted in response to this Notice will be presumed to contain business confidential information and any release of information from these license applications will be made only as required and upon a request under the Freedom of Information Act, 5 USC 552.

Dated: September 18, 2018.

Richard U. Rodriguez,

Associate Director,

Technology Transfer Center,

National Cancer Institute.

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