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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of an NCI Exclusive Patent License: Use of Anti-Mesothelin Immunotoxins for the Treatment of Mesothelin-Expressing Cancers

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 NCI Exclusive Patent License to practice the inventions embodied in the patents listed in the Supplementary Information section of this notice to Lysin Therapeutics, Inc. (Lysin), a company located in Silver Spring, 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 FROM DATE OF PUBLICATION OF NOTICE IN THE FEDERAL REGISTER] will be considered.

ADDRESSES: All patents included in the Intellectual Property below have issued and are publicly available. Inquiries and comments relating to the contemplated NCI Exclusive Patent License should be directed to: Laurie Whitney, Ph.D., Supervisory Technology Transfer Manager, NCI Technology Transfer Center, Telephone: (240)-276-5505; E-mail: *WhitneyL@mail.nih.gov*.

SUPPLEMENTARY INFORMATION:

Intellectual Property

(1) E-269-2009-0 Technology entitled "Improved Pseudomonas Exotoxin A With Reduced Immunogenicity"

- U.S. Provisional Patent Application 61/241,620 (HHS Reference E-269-2009-0-US-01),

filed 9/11/2009;

- PCT Application PCT/US2010/048504 (HHS Reference E-269-2009-0-PCT-02), filed 9/10/2010;
- Australian Patent 2010292069 (HHS Reference E-269-2009-0-AU-03), issued 11/26/2015;
- Canadian Patent 2773665 (HHS Reference E-269-2009-0-CA-04), issued 2/20/2018;
- European Patent 2544805 (HHS Reference E-269-2009-0-EP-06), issued 5/20/2015 and validated in the following jurisdictions:
    - Germany (HHS Reference E-269-2009-0-DE-11);
    - Spain (HHS Reference E-269-2009-0-ES-12);
    - France (HHS Reference E-269-2009-0-FR-13);
    - The United Kingdom (HHS Reference E-269-2009-0-GB-14); and
    - Italy (HHS Reference E-269-2009-0-IT-15)
- Japanese Patent 5795765 (HHS Reference E-269-2009-0-JP-08), issued 8/21/2015; and
- United States Patent 8,936,792 (HHS Reference E-269-2009-0-US-10), issued 1/20/2015;

(2) E-263-2011-0 Technology entitled "Pseudomonas Exotoxin A With Less Immunogenic B Cell Epitopes"

- U.S. Provisional Patent Application 61/535,668 (HHS Reference E-263-2011-0-US-01), filed 9/16/2011;
- PCT Application PCT/US2012/055034 (HHS Reference E-263-2011-0-PCT-02), filed 9/13/2012;
- Australian Patent 2012308591 (HHS Reference E-263-2011-0-AU-03), issued 6/8/2017;
- Canadian Patent 2846608 (HHS Reference E-263-2011-0-CA-04), filed 4/25/2023;
- European Patent 2755993 (HHS Reference E-263-2011-0-EP-05), issued 11/8/2017 and validated in the following jurisdictions:

    - Germany (HHS Reference E-263-2011-0-DE-11);
    - Spain (HHS Reference E-263-2011-0-ES-12);
    - France (HHS Reference E-263-2011-0-FR-13);
    - The United Kingdom (HHS Reference E-263-2011-0-GB-14); and
    - Italy (HHS Reference E-263-2011-0-IT-15)
    - Netherlands (HHS Reference E-263-2011-0-NL-16)
    - Poland (HHS Reference E-263-2011-0-PL-17);
- United States Patent 9,206,240 (HHS Reference E-263-2011-0-US-6), issued 12/8/2015;
- United States Patent 9,657,066 (HHS Reference E-263-2011-0-US-8), issued 5/23/2017; and
- United States Patent 10,111,927 (HHS Reference E-263-2011-0-US-9), issued 10/30/2018;

(3) E-174-2011-0 Technology entitled " Pseudomonas Exotoxin A With Less Immunogenic T Cell And/Or B Cell Epitopes"

- U.S. Provisional Patent Application 61/495,085 (HHS Reference E-174-2011-0-US-01), filed 6/9/2011;
- PCT Application PCT/US2012/041234 (HHS Reference E-174-2011-0-PCT-02), filed 6/7/2012;
- Australian Patent 2012268013 (HHS Reference E-174-2011-0-AU-03), issued 3/2/2017;
- Canadian Patent 2838013 (HHS Reference E-174-2011-0-CA-05), issued 3/7/2023;
- Chinese Patent 201280039071.1 (HHS Reference E-174-2011-0-CN-06), issued 6/2/2020;
- European Patent 2718308 (HHS Reference E-174-2011-0-EP-07), issued 5/17/2017 and validated in the following jurisdictions:
    - Germany (HHS Reference E-174-2011-0-DE-19 and E-174-2011-0-DE-25);

- Spain (HHS Reference E-174-2011-0-ES-20);
- France (HHS Reference E-174-2011-0-FR-21 and E-174-2011-0-FR-26);
- The United Kingdom (HHS Reference E-174-2011-0-GB-22 and HHS Reference E-174-2011-0-GB-27); and
- Italy (HHS Reference E-174-2011-0-IT-23);

- Japanese Patent 6100764 (HHS Reference E-174-2011-0-JP-09), issued 3/22/2017;
- Russian Patent 2627216 (HHS Reference E-174-2011-0-RU-12), issued 8/3/2017;
- United States Patent 9,346,859 (HHS Reference E-174-2011-0-US-13), issued 5/24/2016;
- United States Patent 9,765,123 (HHS Reference E-174-2011-0-US-15), issued 3/25/2020;
- Australian Patent 2017200541 (HHS Reference E-174-2011-0-AU-16), issued 2/21/2019;
- European Patent 3231812 (HHS Reference E-174-2011-0-EP-017), issued 3/25/2020;
- Japanese Patent 6449359 (HHS Reference E-174-2011-0-JP-18), issued 1/9/2019; and
- United States Patent 10,428,119 (HHS Reference E-174-2011-0-US-24), issued 10/1/2019;

4) E-117-2011-0 Technology entitled ” Recombinant Immunotoxin Targeting Mesothelin”

- U.S. Provisional Patent Application 61/483,531 (HHS Reference E-117-2011-0-US-01), filed 5/6/2011;
- PCT Application PCT/US2012/036456 (HHS Reference E-117-2011-0-PCT-02), filed 5/4/2012;
- Australian Patent 2012253896 (HHS Reference E-117-2011-0-AU-03), issued 1/5/2017;
- Canadian Patent 2835070 (HHS Reference E-117-2011-0-CA-05), issued 7/6/2021;
- European Patent 2704739 (HHS Reference E-117-2011-0-EP-09), issued 7/12/2017 and validated in the following jurisdictions:
  - Germany (HHS Reference E-117-2011-0-DE-35);
  - Spain (HHS Reference E-117-2011-0-ES-36);

- France (HHS Reference E-117-2011-0-FR-37);
- The United Kingdom (HHS Reference E-117-2011-0-GB-38);
- Italy (HHS Reference E-117-2011-0-IT-39); and

- Russian Patent 2600067 (HHS Reference E-117-2011-0-RU-16), issued 9/22/2016;
- United States Patent 10,683,362 (HHS Reference E-117-2011-0-US-22), issued 6/16/2020;
- Japanese Patent 6169561 (HHS Reference E-117-2011-0-JP-23), issued 7/7/2017;
- Chinese Patent ZL201280033583.7 (HHS Reference E-117-2011-0-CN-24), issued 8/24/2016;

(5) E-292-2007-0 Technology entitled "Deletions in Domain II of Pseudomonas Exotoxin A that Reduce Non-Specific Toxicity"

- U.S. Provisional Patent Application 60/969,929 (HHS Reference E-292-2007-0-US-01), filed 9/4/2007;
- PCT Application PCT/US2008/075296 (HHS Reference E-292-2007-0-PCT-02), filed 9/4/2008;
- Australian Patent 2008296194 (HHS Reference E-292-2007-0-AU-03), issued 6/25/2013;
- Canadian Patent 2698357 (HHS Reference E E-292-2007-0-CA-04), issued 6/6/2017;
- European Patent 2197903 (HHS Reference E-292-2007-0-EP-05), issued 11/12/2014 and validated in the following jurisdictions:
  - Switzerland (HHS Reference E-292-2007-0-CH-12);
  - Germany (HHS Reference E-292-2007-0-DE-14 and E-292-2007-0-DE-40);
  - Spain (HHS Reference E-292-2007-0-ES-17 and E-292-2007-0-ES-43);
  - France (HHS Reference E-292-2007-0-FR-19 and E-292-2007-0-FR-39);
  - The United Kingdom (HHS Reference E-292-2007-0-GB-20 and E-292-2007-0-GB-41); and

- Italy (HHS Reference E-292-2007-0-IT-25 and E-292-2007-0-IT-42);

- United States Patent 8,871,906 (HHS Reference E-292-2007-0-US-06), issued 10/28/2014; and
- European Patent 2570425 (HHS Reference E-292-2007-0-EP-07), issued 8/23/2017

(6) E-262-2005-0 Technology entitled "Mutated Pseudomonas Exotoxins with Reduced Antigenicity"

- U.S. Provisional Patent Application 60/703,798 (HHS Reference E-262-2005-0-US-01), filed 7/29/2005;
- PCT Application PCT/US2006/028986 (HHS Reference E-262-2005-0-PCT-02), filed 7/25/2006;
- Australian Patent 2006275865 (HHS Reference E-262-2005-0-AU-03), issued 10/11/2012;
- Canadian Patent 2616987 (HHS Reference E-262-2005-0-CA-04), issued 10/11/2016;
- European Patent 1910407 (HHS Reference E-262-2005-0-EP-05), issued 9/14/2011 and validated in the following jurisdictions:
    - Switzerland (HHS Reference E-262-2005-0-CH-09 and E-262-2005-0-CH-16 and E-262-2005-0-CH-53);
    - Germany (HHS Reference E-262-2005-0-DE-10 and E-174-2011-0-DE-17 and E-262-2005-0-DE-23 E-262-2005-0-DE-35 and E-262-2005-0-DE-45 and E-262-2005-0-DE-54);
    - Spain (HHS Reference E-262-2005-0-ES-11 and E-262-2005-0-ES-18 and E-262-2005-0-ES-24 and E-262-2005-0-ES-36 and E-262-2005-0-ES-46 and E-262-2005-0-ES-55);
    - France (HHS Reference E-262-2005-0-FR-12 and E-262-2005-0-FR-19 and E-262-2005-0-FR-25 and E-262-2005-0-FR-37 and E-262-2005-0-FR-47 and E-262-2005-0-FR-56);

- The United Kingdom (HHS Reference E-262-2005-0-GB-13 and HHS Reference E-262-2005-0-GB-20 and E-262-2005-0-GB-26 and E-262-2005-0-GB-38 and E-262-2005-0-GB-48 and E-262-2005-0-GB-57); and
- Italy (HHS Reference E-262-2005-0-IT-14 and E-262-2005-0-IT-21 and E-262-2005-0-IT-27 and E-262-2005-0-IT-40 and E-262-2005-0-IT-50 and E-262-2005-0-IT-59);
- Austria (HHS Reference E-262-2005-0-AT-33 and E-262-2005-0-AT-43);
- Belgium (HHS Reference E-262-2005-0-BE-34 and E-262-2005-0-BE-44);
- Ireland (HHS Reference E-262-2005-0-IE-39 and E-262-2005-0-IE-49 and E-262-2005-0-IE-58);
- Netherlands (HHS Reference E-262-2005-0-NL-41 and E-262-2005-0-NL-51); and
- Poland (HHS Reference E-262-2005-0-PL-42 and E-262-2005-0-PL-52 and E-262-2005-0-PL-60);

- United States Patent 8,907,060 (HHS Reference E-262-2005-0-US-06), issued 12/9/2014;
- European Patent 2311854 (HHS Reference E-262-2005-0-EP-07), issued 4/17/2013;
- European Patent 2332970 (HHS Reference E-262-2005-0-EP-08), issued 12/23/2015;
- Australian Patent 2012216642 (HHS Reference E-262-2005-0-AU-15), issued 9/25/2014;
- Australian Patent 2014208269 (HHS Reference E-262-2005-0-AU-22), issued 6/16/2016;
- European Patent 3006456 (HHS Reference E-262-2005-0-EP-28), issued 9/19/2018;
- European Patent 3006457 (HHS Reference E-262-2005-0-EP-29), issued 11/22/2017;
- European Patent 3006458 (HHS Reference E-262-2005-0-EP-30), issued 11/22/2017;
- Australian Patent 2016202754 (HHS Reference E-262-2005-0-AU-31), issued 10/5/2017; and
- Canadian Patent 2,941,466 (HHS Reference E-262-2005-0-CA-32), issued 12/3/2019;

(7) E-231-2017-0 Technology entitled "Immunotoxins with Albumin Binding Domain"

- U.S. Provisional Patent Application 62/559,926 (HHS Reference E-231-2017-0-US-01), filed 9/18/2017;
- PCT Application PCT/US2018/051418 (HHS Reference E-231-2017-0-PCT-02), filed 9/18/2018;
- United States Patent 18/471,137 (HHS Reference E-269-2009-0-US-02), issued 2/4/2025; and
- United States Patent 16/648,369 (HHS Reference E-269-2009-0-US-03), issued 10/24/2023;

The patent rights in these inventions have been assigned to the Government of the United States of America.

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

"Use of the anti-mesothelin immunotoxins LMB-100 or SS1P for the treatment of mesothelin-expressing cancers."

Recent efforts have been directed to developing more specific cancer treatments in order to more effectively treat cancer with fewer side effects. These efforts include the development of antibody-based therapeutics such as unconjugated antibodies, antibody drug conjugates (ADCs), bispecific antibodies, chimeric antigen receptors (CARs), and recombinant immunotoxins (RITs). This technology concerns the development of RITs, specifically the SS1P or LMB-100 immunotoxins. These immunotoxins comprise a targeting domain and a toxin domain, where the targeting domain comprises the CDR sequences of the anti-mesothelin antibody known as SS1 (this antibody is not patented), and the toxin domain comprises a *Pseudomonas* exotoxin A (PE) variant that contains deletions and mutations to the native PE sequence which reduces its immunogenicity when administered to patients. The targeting domain serves the purpose of directing the immunotoxins to only those cells which express a protein known as mesothelin,

which is expressed on the surface of certain types of cancer cells (e.g., mesothelioma, ovarian cancer, pancreatic cancer, etc.), allowing healthy, essential cells to remain unaffected while tumor cells are killed.

All the Intellectual Property listed above is directed to the toxin domain of SS1P and LMB-100 (i.e. PE variants that contain deletions and mutations to the native PE sequence which reduces its immunogenicity when administered to patients). The scope of exclusivity for this license will be limited to the specific use of the LMB-100 or SS1P anti-mesothelin immunotoxins for the treatment of mesothelin-expressing cancers. Other fields of use will still be available if this license is granted, including use of other mesothelin-targeted immunotoxins using other anti-mesothelin antibodies in conjunction with the Intellectual Property, as well as the use of the antibodies directed to other targets in conjunction with the Intellectual Property.

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.

Complete applications for a license that are timely filed in response to this notice will be treated as objections to the grant of the contemplated exclusive patent license. 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 in these license applications will be made only as required and upon a request under the Freedom of Information Act, 5 USC 552.

Dated: September 8, 2025

Richard U. Rodriguez

Associate Director,

Technology Transfer Center,

National Cancer Institute.

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