[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of Exclusive License: The Development of Anti-mesothelin Targeted Immunotoxins for the Treatment of Cancer

AGENCY: National Institutes of Health, Public Health Service, HHS

ACTION: Notice

SUMMARY: This is notice, in accordance with 35 U.S.C. 209(c)(1) and 37 CFR Part 404.7(a)(1)(i), that 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 US Patent application 61/535,668 entitled "Pseudomonas Exotoxin A with Less Immunogenic B Cell Epitopes" [HHS Ref. E-263-2011/0-US-01], US Patent application 61/495,085 entitled "Pseudomonas Exotoxin A with Less Immunogenic T Cell Epitopes" [HHS Ref. E-174-2011/0-US-01], US Patent application 61/483,531 entitled "Recombinant Immunotoxin Targeting Mesothelin" [HHS Ref. E-117-2011/0-US-01], U.S. Patent Application 61/241,620 entitled "Development of an Immunotoxin in Which All B-Cell Epitopes Have Been Removed and Which Has High Cytotoxic Activity" [HHS Ref. E-269-2009/0-US-01], U.S. Patent Application 60/969,929 entitled "Deletions in Domain II of Pseudomonas Exotoxin A That Reduce

Non-Specific Toxicity" [HHS Ref. E-292-2007/0-US-01], U.S. Patent Application 60/703,798 entitled "Mutated Pseudomonas Exotoxins with Reduced Antigenicity" [HHS Ref. E-262-2005/0-US-01], U.S. Patent Application 60/160,071 entitled "Immunoconjugates Having High Binding Affinity" [HHS Ref. E-139-1999/0-US-01], U.S. Patent Application 60/067,175 entitled "Antibodies, Including Fv Molecules, and Immunoconjugates Having High Binding Affinity for Mesothelin and Methods for Their Use" [HHS Ref. E-021-1998/0-US-01], U.S. Patent Application 60/010,166 entitled "Molecular Cloning of Mesothelin, a Differentiation Antigen Present on Mesothelium, Mesotheliomas and Ovarian Cancers" [HHS Ref. E-002-1996/0-US-01], PCT Application PCT/US97/00224 entitled "Mesothelin Antigen and Methods and Kits for Targeting It" [HHS Ref. E-002-1996/1-PCT-01], U.S. Patent 5,747,654 entitled "Recombinant Disulfide-Stabilized Polypeptide Fragments Having Binding Specificity" [HHS Ref. E-163-1993/0-US-01], PCT application PCT/US96/16327 entitled "Immunotoxin Containing A Disulfide-Stabilized Antibody Fragment" [HHS Ref. E-163-1993/2-PCT-01], and all continuing applications and foreign counterparts, to Hoffman-La Roche, Inc. The patent rights in these inventions have been assigned to and/or exclusively licensed 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 use of anti-mesothelin targeted immunotoxins for the treatment of mesothelin-expressing cancers, wherein the immunotoxins have: (1) a targeting domain containing the complementary determining regions (CDR) of the SS1 antibody and (2) a *Pseudomonas* exotoxin A ("PE") toxin domain that is (a) lysosomal protease resistant (PE-LR) and (b) lacks at least one major B-cell epitope due to the alteration of an amino acid. The immunotoxin may include additional alterations to B-cell and T-cell epitopes for reduction of immunogenicity, as well as a peptide linker sequence.

DATE: Only written comments and/or applications for a license which are received by the NIH Office of Technology Transfer on or before [Insert date 30 days from date of publication of notice in the FEDERAL REGISTER] will be considered.

ADDRESS: Requests for copies of the patent application, inquiries, comments, and other materials relating to the contemplated exclusive license should be directed to: David A. Lambertson, Ph.D., Senior Licensing and Patenting Manager, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852-3804; Telephone: (301) 435-4632; Facsimile: (301) 402-0220; E-mail: lambertsond@od.nih.gov.

SUPPLEMENTARY INFORMATION: These inventions concern immunotoxins which are targeted to mesothelin-expressing cancer cells, and methods of using the immunotoxins for the treatment of mesothelin-expressing cancers (such as mesothelioma, ovarian cancer and pancreatic cancer). The specific immunotoxin will have an antibody targeting domain that contains the CDRs of the antibody identified as SS1, which was invented at the NIH. The specific immunotoxin will also have a toxin domain derived from PE that is resistant to lysosomal proteases due to the deletion of a large portion of the exotoxin, and which lacks at least one major B-cell epitope due to the alteration an amino acid. Ultimately, the PE used in the immunotoxin may lack multiple B-cell epitopes, as well as multiple T-cell epitopes, in an effort to minimize immunogenicity.

Alterations to the toxin that reduce immunogenicity improve the therapeutic value of the immunotoxin while maintaining its ability to trigger cell death. Since mesothelin

is preferentially expressed on certain types of cancer cells, the immunotoxins selectively bind and kill only those cancer cells, allowing healthy, essential cells to remain unharmed. This results in an effective therapeutic strategy with fewer side effects.

The prospective exclusive license will be royalty bearing and will comply with the terms and conditions of 35 U.S.C. 209 and 37 CFR Part 404.7. The prospective exclusive license may be granted unless the NIH 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 404.7 within thirty (30) days from the date of this published notice.

Applications for a license in the field of use filed in response to this notice will be treated as objections to the grant of the contemplated exclusive license. Comments and objections submitted to this notice will not be made available for public inspection and, to the extent permitted by law, will not be released under the Freedom of Information Act, 5 U.S.C. 552.

February 8, 2012
Date

Richard U. Rodriguez,
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Division of Technology Development & Transfer
Office of Technology Transfer
National Institutes of Health

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