[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of Exclusive Patent License: MicroRNA Therapeutics for Treating Squamous Cell Carcinomas

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The National Heart, Lung and Blood Institute (NHLBI), National Institutes of Health, Department of Health and Human Services, is contemplating the grant of an Exclusive Patent License to MiRecule, Inc., located in Rockville, Maryland, to practice the inventions embodied in the patent applications listed in the Supplementary Information section of this notice.

DATES: Only written comments and/or applications for a license which are received by the NHLBI Office of Technology Transfer and Development [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: Michael Shmilovich, Esq., Senior Licensing and Patent Manager, 31 Center Drive Room 4A29, MSC2479, Bethesda, MD 20892-2479, phone number 301-435-5019, or shmilovm@mail.nih.gov.

SUPPLEMENTARY INFORMATION:

The following represents the intellectual property to be licensed under the prospective agreement:
HHS Ref. No. E-043-2016/0, including provisional patent application 62/304,844 filed March 7, 2016 and International Patent Application PCT/US2017/021178 filed March 7, 2017 both entitled "MicroRNAs And Methods Of Their Use," and all continuing U.S. and foreign patents/patent applications for the technology family, to MiRecule. The patent rights in these inventions have been assigned to and/or exclusively licensed to the Government of the United States of America.

With respect to persons who have an obligation to assign their right, title and interest to the Government of the United States of America, the patent rights in these inventions have been assigned to the Government of the United States of America.

The prospective Exclusive Patent License territory may be worldwide for the following field of use: MicroRNA therapeutics for squamous cell carcinomas.

The invention relates to the use of microRNAs (miRs), miR mimics, miR mimetics, and a combination thereof as anti-proliferative cancer therapeutics. In this case, miRs will be administered in a form complexed with nanoparticles in the form of liposomes decorated with anti-transferrin receptor (TfR) scFv fragments. Generally, miRs are a highly conserved class of small RNA molecules (about 18-24bp) that primarily bind the 3'-UTR region of mRNA molecules and either block translation or promote nuclease mediated degradation. The inventors found that mimics or mimetics derived from several members of the miR-30-5p family; and miR-30a-5p and miR-30e-5p, have potential as anti-proliferative therapeutics in cancers including but not limited to squamous cell carcinomas and currently have a CRADA with NIDCD exploring their uses in treating head and neck squamous cell carcinoma (HNSSC). In an *in vivo* proof-of-concept using a murine xenograft tumor model for HNSSC, the inventors demonstrated that intraperitoneal administration of a nanoliposome formulated with an anti-transferrin receptor antibody fragment and a synthetic miR-30a-5p mimic strongly delayed tumor growth. Other anti-cancer miR therapeutic mimics can be combines with miR-30 including miR-145-5p, miR-26a-5p, miR-26b-5p, miR-375-5p, miR-30b-5p, miR-30d-5p, or miR-338-3p. Modes of administration can be by intravenous injection, intraperitoneal injection, subcutaneous injection, or intratumoral injection. Therapeutic design employing miR mimicry focuses on nucleic acid modifications that exhibit better cytotoxicity than unmodified miRs or commercially available mimics. For example, it is accepted that modification of the 2' position of individual nucleic acids in an oligonucleotide can improve affinity to complementary strands and confer resistance to nucleases and reduce adverse immunogenic reactions. By way of another example, bases 1, 6, and 20 of a passenger strand miR can be mutated to increase the stability of the resulting duplex; however, these mutation sites may differ from one therapeutic miR to another. Tumor suppressing miR mimics can be synergistically combined with standard chemo- and radiation therapies in an anti-cancer regimen.

This notice is made in accordance with 35 U.S.C. 209 and 37 CFR Part 404. The prospective Exclusive Patent License will be royalty bearing and may be granted unless within fifteen (15) days from the date of this published notice, the NHLBI 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 in the prospective field of use that are timely filed in response to this notice will be treated as objections to the grant of the contemplated Exclusive Patent 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.

Dated: July 25, 2017.

Michael Shmilovich,

Senior Licensing and Patenting Manager,

NHLBI Office of Technology Transfer and Development.

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