DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of Exclusive License: The Use of Geldanamycin and Its Derivatives for the Treatment of Cancer

AGENCY: National Institutes of Health, Public Health Service, DHHS.

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:

1. PCT Patent Application No. PCT/US03/31962 filed October 8, 2003 [DHHS Ref. E–256–2002/0–PCT–02], entitled ''17–AAG Treatment of Diseases Sensitive to c-Kit Down Regulation:'',
2. U.S. Provisional Patent Application No. 60/598,752 filed October 3, 2003 [DHHS Ref. E–169–2003/0–US–01], entitled ''Geldanamycin Derivatives With Methyl Substituted Hydrogen Atom At N22 Position As Anticancer Agents'',
3. U.S. Provisional Patent Application No. 60/508,795 filed October 3, 2003 [DHHS Ref. E–064–2003/0–US–01], entitled ''Degradation And Transcriptional Inhibition Of HIF–2 Alpha Protein By 17–AAG''

and all related foreign patents/patent applications, to Kosan Biosciences, Inc., which is located in Hayward, CA. The patent rights in these inventions have been assigned to the United States of America.

The prospective exclusive license territory will be worldwide and the field of use may be limited to pharmaceutical use as anti-cancer agents, and as agents to prevent undesired cell growth or the deleterious effects thereof such as the prevention of re-stenosis and neurodegenerative diseases in humans and animals. This notice should be considered a modification of an earlier **Federal Register** notice (67 FR 9763, March 4, 2002).

DATES: Only written comments and/or applications for a license which are received by the NIH Office of Technology Transfer on or before April 13, 2004 will be considered.

ADDRESSES: Requests for copies of the patent application, inquiries, comments, and other materials relating to the contemplated exclusive license should be directed to: George G. Pipia, Ph.D., Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852–3804; Telephone: (301) 435–5560; Facsimile: (301) 402–0220; E-mail: *pipiag@mail.nih.gov*.

SUPPLEMENTARY INFORMATION: 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 404.7. The prospective exclusive license may be granted unless within sixty (60) days from the date of this published notice, the NIH receives written evidence and argument that establish that the grant of the license would not be consistent with the requirements of 35 U.S.C. 209 and 37 CFR 404.7.

Description of the Technologies

(1) *E–256–2003/0.* This invention directed to the use of 17-allylamino-17-demethoxygeldanamycin (17-AAG), a derivative of geldanamycin, in decreasing levels of a mutated protein called KIT (the product of proto-oncogene c-KIT), which has been identified as the protein responsible for transformation of certain human cell types into pathologic cells. By way of background, this invention is predicated on the discovery of a new method of inhibiting the activity of a mutated, constitutively active form of the tyrosine kinase, KIT. The method involves the administration of 17-AAG to a cell comprising the mutant KIT protein, whereby the activity level of KIT in the cell is reduced. The invention may prove to be useful for treating diseases such as mastocytosis, gastrointestinal stromal tumors (GIST), mast cell leukemia, myelogenenous leukemia, and testicular cancer, all of which are associated with mutations in the c-KIT proto-oncogene.

(2) *E–169–2003/0.* This invention is directed to an N22-methyl substituted analogue of geldanamycin. Preliminary studies have shown that providing a methyl substituent in the N22 position of geldanamycin derivatives stabilizes the cis-conformation of the compounds. Such compounds are expected to have an increased binding to and inhibition of heat shock protein 90 (Hsp9O). Inhibition of Hsp9O is considered useful in the treatment of many cancers.

(3) *E–064–2003/0.* The invention is directed to the use of 17-allylaminogeldanamycin (17–AAG) and, by analogy, other geldanamycin derivatives to inhibit the activity of hypoxia inducible factor-2α (HIF–2α). HIF–2α is thought to play an important role in tumor growth in the lung and endothelium, and is overexpressed in a majority of renal carcinomas. Accordingly, the technology suggests the use of 17–AAG and other geldanamycin derivatives to reduce levels of HIF–2α in cells that overexpress the protein, for example to treat cancer. According to the lead inventor, HIF–2α plays a central role behind the mechanism of action of geldanamycin in renal cancer. The inventors also predict that certain geldanamycin analogs will have therapeutic benefit in tumors overexpressing HIF–2α, and that those analogs could also find therapeutic utility in clinical conditions involving hypervascularization.

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.

Dated: February 5, 2004.

Steven M. Ferguson,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. 04–3167 Filed 2–12–04; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

List of Drugs for Which Pediatric Studies Are Needed

ACTION: Notice.

SUMMARY: The National Institutes of Health (NIH) is providing notice of a ''List of Drugs for Which Pediatric Studies Are Needed.'' The NIH developed the list in consultation with the Food and Drug Administration (FDA) and pediatric experts, as mandated by the Best Pharmaceuticals for Children Act (BPCA). This list prioritizes certain drugs most in need of study for use by children to ensure their safety and efficacy. The NIH will update the list at least annually until the Act expires on October 1, 2007.

DATES: The list is effective upon publication.

FOR FURTHER INFORMATION CONTACT: Dr. Anne Zajicek, National Institute of Child Health and Human Development, 6100 Executive Boulevard, Suite 4B–11, Bethesda, MD 20892–7510, e-mail *BestPharmaceuticals@mail.nih.gov,*