19 April 2016

Michael Shmilovich, Esq., CLP
Senior Licensing and Patent Manager
Office of Technology Transfer and Development
National Heart, Lung, and Blood Institute
31 Center Drive Room 4A29, MSC2479
Bethesda, MD 20892-2479
phone number 301-435-5019
Via E-Mail: shmilovm@mail.nih.gov.

These comments pertain to two Federal Register notices regarding proposed licenses of exclusive rights in NIH patents. Both notices involved the same patents on Boron Neutron technologies, licensed to Beijing Lanyears Communication Technology, Ltd., a company formed under the laws of the People's Republic of China and having its principle place of business in Beijing, China. Once notice would limit the field of technology to skin cancer. The other field of use involves brain tumors.

KEI opposes the grant of exclusive license in this case unless:

1. The NIH conducts sufficient analysis and limits the terms and scope of the license as required under 404.7(a)(1)(ii-iii),
2. The license contains sufficient safeguards regarding affordability and reasonable pricing of the products developed under the patent licenses,
3. The license places restrictions on charging US residents higher prices than the median prices charged in countries with the seven largest GDP and per capita incomes of 50 percent or more than the United States per capita income,
4. The license quires products are affordable in developing countries, and explicitly allows the NIH to grant licenses to the patents to the Medicines Patent Pool (MPP) for use in developing countries;
5. The license requires transparent reporting on drug development costs, royalties and revenues.

We also ask the NIH to create a requirement for annual reports on R&D outlays, including an obligation that the company reports the following for each clinical trial that tests products covered by the patents:

- ClinicalTrials.Gov identifier
- Phase
- Conditions:
- Interventions:
- Title Acronym/Titles:
- Outcome Measures:
- Sponsor/Collaborators:
- Other Study IDs:
- Expenditure: (for that year)

With regard to sales prices, we request an annual report that provide data on the following variables:

- Units of sales, by country
- Revenue for sales, by country

With regard to government subsidies for research, we request a report that provides data for the following, by year:

- Grants and research contracts from government agencies, with data on the funding agency, the identifier of the grant or contract, and the amount of the grant or contact.
- Tax credits associated with R&D for the product, including the U.S. orphan drug tax credit, broken out by the type of credit and the expenditure the credit was associated with (such as a specific trial).
- Other government R&D subsidies.

Since the statute governing the grant of exclusive licenses requires that the "scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application" we request a copy of any analysis, if any, that was done to consider how many years of exclusive rights were necessary to bring the invention to practical application. We also propose the following terms for the contract:

> The exclusive rights will extend to five years from the first sale of a product receiving approval by the U.S. FDA, or until the license holder recovers at least $1 billion in global sales from the product, whichever is shorter, and thereafter, the license will become non-exclusive. After the first five years of exclusivity, the NIH can extend the exclusivity by another 3 years, upon a showing that such extension is reasonable in

light on the risk adjusted R&D costs to bring the product market, and the net revenues from sales.

KEI notes that the 5 year period, with possible extensions, follows NIH practice, prior to 1984, and other NIH licenses have had terms shorter than the life of patent. For example, in October 2001, the NIH exercised an option to make the licenses for the AIDS drug DDI non-exclusive, ten years after the initial FDA registration (see: Videx® Expanding Possibilities: A Case Study, NIH, National Institutes of Health Office of Technology Transfer, September 2003) in order to expand access to the drug, and to obtain lower cost supplies for federal programs.

The NIH could consider different time periods for exclusivity, but if the answer is always life of patent, no matter what the facts are, and without an analysis to determine the the "scope of exclusivity is not greater than reasonably necessary," the NIH would have failed to meet the requirements of 35 U.S.C. 209.

Sincerely,

James Packard Love
Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009
http://keionline.org
Work: +1.202.332.2670; Mobile: +1.202.361.3040
james.love@keionline.org

Annex 1

Prospective Grant of an Exclusive Patent License for Commercialization: Boron Neutron Capture Therapy for Skin Cancer

Document Citation: 81 FR 19984; Page: 19984 -19985 (2 pages)
Document Number: 2016-07864
URL: https://federalregister.gov/a/2016-07864

The grant of a worldwide exclusive license to practice the inventions embodied in: HHS Ref. No. E-135-2015/0, U.S. Provisional Patent Application No. 62/155,085, filed April 30, 2015, entitled “Boron Mimics Of Amino Acids And Uses Thereof,” to Beijing Lanyears Communication Technology, Ltd., a company formed under the laws of the People's Republic of China and having its principle place of business in Beijing, China.

The contemplated exclusive license may be limited to boron neutron capture therapy for skin cancer.

Annex 2

Prospective Grant of an Exclusive Patent License for Commercialization: Boron Neutron Capture Therapy for Brain Tumors

Document Citation: 81 FR 19983; Page: 19983 -19984 (2 pages)
Document Number: 2016-07865
URL: https://federalregister.gov/a/2016-07865

The grant of a worldwide exclusive license to practice the inventions embodied in: HHS Ref. No. E-135-2015/0, U.S. Provisional Patent Application No. 62/155,085, filed April 30, 2015, entitled “Boron Mimics Of Amino Acids And Uses Thereof,” to Beijing Lanyears Communication Technology, Ltd., a company formed under the laws of the People's Republic of China and having its principle place of business in Beijing, China.

The contemplated exclusive license may be limited to boron neutron capture therapy for brain tumors.

Annex 3. Supplemental information from the FR notice.

The invention pertains to boramino acid compounds that can be used as imaging agents for positron emission tomography of cancer or for boron neutron capture therapy. Mimetics created by substituting the carboxylate group (-COO-) of an amino acid with trifluoroborate (-BF3-) are metabolically stable and allow for the use of fluorine-18 (18F) as the radiolabel (e.g., trifluoroborate phenylalanine (B-Phe)). Using boramino acid for 18F-labeling allows for integrating the 18F radiolabel into the core molecular backbone rather than the side-chains thus increasing the agent's target specificity. There is a direct relationship between amino acid uptake and cancer cell replication, where the uptake is extensively upregulated in most cancer cells. This uptake increases as cancer progresses, leading to greater uptake in high-grade tumors and metastases. Amino acids act as signaling molecules for proliferation and may also reprogram metabolic networks in the buildup of biomass. This invention provides for an unmet need for traceable amino acid mimics, including those based on naturally-occurring amino acids, which may be non-invasively detected by imaging technology, including for clinical diagnosis or BNCT. Boron neutron capture therapy (BNCT) is based on the nuclear capture and fission reactions that occur when non-radioactive boron-10 ([10] B, approximately 20% of natural elemental boron), is irradiated and thus activated with neutrons of the appropriate energy to yield excited boron-11 (11B*). This isotope turn decays into high energy alpha particles (“stripped” down 4He nuclei) and high energy lithium-7 (7Li) nuclei. Both the emitted alpha particles and the lithium ions are close proximity reactions, i.e., at a range of approximately 5-9 μm; the diameter of a target cell. The energies produced in this ionization and radio-decay is cytotoxic and thus exploited as the basis for cancer radiotherapy. The success of BNCT is dependent on the selective delivery of sufficient amounts of [10] B to the tumor site with only small amounts localized in the surrounding normal tissues thus sparing normal tissue from the nuclear capture and fission reactions.