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Re: Prospective Grant of an Exclusive Patent License: High ASS1 Expressing Tumors Embody a Purine Rich Genomic Signature and Sensitivity to Purine Depletion (86 FR 36567)

Dear Dr. Chang:

Knowledge Ecology International (KEI) would like to offer the following comments regarding the "Prospective Grant of an Exclusive Patent License: High ASS1 Expressing Tumors Embody a Purine Rich Genomic Signature and Sensitivity to Purine Depletion" (86 FR 36567). The technology is to be licensed to Yeda Research & Development Co, Ltd (YEDA). YEDA is identified in the Federal Register notice as "the technology transfer company of the Weizmann Institute of Science, a non-profit research institution located in Rehovot, Israel."

The technology to be licensed concerns "treating a high argininosuccinate synthase (ASS1) expressing solid tumor with a combination of a purine synthase inhibitor or an agent that increases the pyrimidine to purine ratio in a cell, and an immune-modulating drug, such as a checkpoint inhibitor." The rights to the inventions to be licensed are jointly owned by the US government and YEDA, and the license is intended to consolidate the rights to expedite development and commercialization.

As the license is to be sublicensable, and tumors expressing ASS1 are seen in a variety of cancer types, the NIH must ensure that any license or sublicense of the inventions include terms that protect patient access to any resultant treatment.

Further, as noted above, YEDA is based in Israel, and intends to sublicense the technology. Per the Bayh-Dole Act, one of the requirements of granting an exclusive license is that licensees "substantially" manufacture the invention in the United States. The NIH should include license terms that protect US patients from paying higher prices than other high income countries.

KEI suggest a provision in the license (to be included in any sublicense) that requires that any medical technology using the patented invention be available in the United States at a price that does not exceed the median price in the seven largest economies by GDP that have at least 50 percent of the GNI per capita as the United States, using the World Bank Atlas method.

The above is a modest safeguard. The US government has recently incorporated similar terms in agreements related to COVID-19 vaccines and other technology contracts. For example, in the contract with Sanofi Pasteur (Sanofi) for a COVID-19 vaccine, the federal government included a term that stated that Sanofi will not sell the vaccine to any member of the G7 or Switzerland at a price lower than what the U.S. government paid. The NIH should apply this standard to its exclusive licensing practices, and prevent licensees from charging U.S. residents a higher price for products embodying the licensed invention than they charge residents of these high-income countries.

KEI also urges the NIH to include the following provisions in the terms of any license, as well as any sublicense entered into by YEDA.

Transparency

Transparency of R&D outlays. The licensees should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product or service that uses the inventions, including reporting separately and individually the outlays on each clinical trial. We note that this is not a request to see a company business plan or license application. We are asking that going forward YEDA or any sublicensees be required to report on actual R&D outlays to develop the subject inventions. Reporting on actual R&D outlays is important for determining if the NIH is meeting the requirements of 35 U.S.C. § 209, that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application[.]" Specifically, having data on actual R&D outlays on each clinical trial used to obtain FDA approval provides evidence that is highly relevant to estimating the risk adjusted costs of bringing NIH licensed inventions to practical application.

Acknowledgement of federal funding - publication and publicity. The licensee should be required to include, when issuing statements, press releases, and other documents describing the development of any product that includes the licensed inventions, a statement that describes the role of the licensed inventions and the total and proportionate contribution of federal funding to the research and development performed to bring the inventions to market.

Additional transparency issues. The license should have provisions that give effect to the transparency norms set out in WHA72.8 "Improving the transparency of markets for medicines, vaccines, and other health products", a resolution enthusiastically supported by HHS in 2019.

Additional Provisions to Protect the Public Interest

Global registration and affordability. The licenses should require the licensee to disclose the steps that each will take to enable the timely registration and availability of the medical technology at an affordable price in the United States and in every country with a demonstrated need, according to the Centers for Disease Control and Prevention (CDC) and/or the World Health Organization (WHO), either by supplying a country directly at an affordable, publicly disclosed price and with sufficient quantities, or by providing technology transfer and rights to all intellectual property necessary for third parties to do so.

Low- and middle-income countries. The NIH should ensure that the exclusive license does not extend to countries with a per capita income less than 30 percent of the United States, in order to ensure that the patents do not lead to restricted and unequal access in developing countries. If the NIH rejects this suggestion, it needs to provide something that will give effect to the policy objective in the "United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy," which states the following: "PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries."

Medicines Patent Pool. The NIH should retain a right to grant the WHO, the Medicines Patent Pool or other governments the rights to use the patent rights to procure the medical technology from competitive suppliers, including technology transfer, in LMICs, upon a finding by HHS or the WHO that people in these markets do not have sufficient access to the medical technology.

Conclusion

It is critical that the NIH ensure that the terms of this license promote the public interest in the invention and protect patients' equitable access to the technology, should it come to market. In the event that the NIH grants the license, KEI asks that it incorporates the provisions listed above in order to achieve those goals.

Please notify us if and when a license is granted, so we can request a copy under the Freedom of Information Act.

Sincerely,

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Knowledge Ecology International