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Re: Prospective Grant of an Exclusive Patent License: The Development of Natural Killer (NK) Cell Kita-Kyushu Lung Cancer Antigen 1 (KK-LC-1) T Cell Receptor (TCR) Therapy for the Treatment of KK-LC-1 Expressing Human Cancers (86 FR 16603)

Dear Dr. Dhal:

Knowledge Ecology International (KEI) would like to offer the following comments regarding the "Prospective Grant of an Exclusive Patent License: The Development of Natural Killer (NK) Cell Kita-Kyushu Lung Cancer Antigen 1 (KK-LC-1) T Cell Receptor (TCR) Therapy for the Treatment of KK-LC-1 Expressing Human Cancers," to Zelluna Immunotherapy (Zelluna) in Oslo, Norway.

The geographic scope of the license is worldwide, and the field of use conveys the rights to the Kita-Kyushu Lung Cancer Antigen 1 (KK-LC-1) expressing cancers.

As noted in the the *Federal Register* (*FR*) announcement:

> *"Currently, there for [sic] no effective immunotherapies for patients with these various solid tumors. The NK-TCRs can potentially be used for the treatment of triple negative breast cancer, gastric cancer, and lung cancer."*

Considering that the inventions to be licensed could potentially lead to treatments for breast cancer, stomach cancer, and lung cancer patients for whom there are currently no effective immunotherapies, it is important that the NIH ensures that the terms of this license protect equitable and affordable access to any resultant treatments. The terms included in these exclusive licenses must ensure that desperate patients without alternative treatment options are not held hostage to high prices.

We also note that the firm to receive the exclusive license is based in Norway. One of the requirements of granting an exclusive license per the Bayh-Dole Act is that licensees "substantially" manufacture the invention in the United States. The NIH should factor this in

while negotiating terms of any exclusive license to a foreign firm and should only grant a waiver if a compelling reason is shown.

Among several questions that KEI asked regarding the details of this invention and license, was whether the NIH was in any concurrent negotiations to waive the domestic manufacturing requirement (35 USC 204) for this license, i.e. whether the proposed licensee was seeking such a waiver. The NIH did not provide a response to this question.

In fact, KEI asked nine basic questions regarding the inventions to be licensed and the terms of the proposed license, including:

1. *At what development stage are the inventions listed?*
2. *Are there any clinical trials of the licensed technology planned or already conducted?*
3. *Has the government funded any clinical trials relevant to these technologies? Can you provide NCT numbers?*
4. *If the government has provided funding, how much has been spent by the government on these trials? Can you please provide relevant grant and/or contract numbers?*
5. *Is the term in the proposed licenses to be life of patent or less than life of patent?*
6. *Is there a Cooperative Research and Development Agreement associated with this technology?*
7. *What analysis did the NIH undertake, if any, in order to conclude that exclusivity is a reasonable and necessary incentive?*
8. *How will the NIH ensure that the scope of exclusivity is not broader than reasonably necessary?*
9. *Is the NIH in any concurrent negotiations to waive the domestic manufacturing requirement (35 USC 204) for this license?*

In response, the NIH did inform us that the inventions were in preclinical stage, with a clinical trial planned for the future, but declined to answer any of the rest of the questions, instead stating,

> *"NIH has determined that the proposed exclusive license satisfies the criteria required for an exclusive license under 37 CFR Part 404. The other questions you have asked have been answered by NIH previously in explanations that the license application is proprietary to the applicant and the terms of the license have not yet been negotiated."*

The NIH is required to consider the incentive necessary to induce development of technologies on a case-by-case basis, and each license is to be given individual consideration. Therefore, effectively saying "see previous response" is not an acceptable response to the questions asked.

Since Zelluna is not based in the US, it is important that the NIH ensures license terms that will protect US patients from paying higher prices than other high income countries, for any resultant treatment. Any medical technology using the patented invention should 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.

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 Zelluna 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.

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