July 27, 2021

Hiba Alsaffar, Ph.D.
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National Institutes of Health
Via Email: hiba.alsaffar@nih.gov

Re: Prospective Grant of an Exclusive Patent License: RP2 AAV-Based Gene Human Therapy for Ocular Diseases and Disorders Including XLRP (86 FR 36565)

Dear Dr. Alsaffar:

Knowledge Ecology International (KEI) offers the following comments regarding the "Prospective Grant of an Exclusive Patent License: RP2 AAV-Based Gene Human Therapy for Ocular Diseases and Disorders Including XLRP" (86 FR 36565) to PTC Therapeutics GT, Inc.

The license would convey exclusive rights in AAV8/9 vectors encoding *RP2* or *RPGR* for the treatment of "any ocular disease, disorder or condition," which is a seemingly unlimited field of use. Because the *RP2* and *RPGR* genes are involved in vision function and disorders, there is no other conceivable use for the technology. The National Institutes of Health (NIH) erroneously takes the position that the only aspect of the scope of a license it must limit is the field of use. It thus appears the NIH has made no effort to limit the scope of the license.

All aspects of the scope of the license must not be broader than necessary to incentivize a company to invest in the licensed technology. 35 U.S.C. § 209(a)(2). In negotiating the terms of this license, the NIH must consider the commercial potential of the invention, as it relates to the necessary incentive and permissible scope of the license. Mutations to the *RP2* and *RPGR* genes can cause Retinitis Pigmentosa, a group of rare, inherited genetic disorders that cause vision loss starting at a young age. As such, any product arising from the licensed technology will likely qualify for the regulatory incentives associated with orphan drugs and rare pediatric diseases. These incentives include marketing exclusivity, rare pediatric disease priority review vouchers, and accelerated approval, which can hasten the clinical development timeline by half.

KEI reached out to you to ask questions about the development stage of the technology, including whether it has been investigated in any clinical trials. By the time of this submission, we had not received a response. At the very least, it appears this technology had strong preclinical results and is ready to enter clinical trials. The terms of the license must be narrow, to reflect the invention's many commercially valuable features.

The NIH must also consider the impact of the license on patients. FDA approved gene therapies for inherited genetic disorders command the highest prices in medicine, such as the $2.1 million price of Zolgensma, a one time treatment for spinal muscular atrophy, and the $850,000 price of Luxturna, a gene therapy for an inherited form of blindness. These prices restrict access and

harm health outcomes, particularly in low-income countries. Narrowing the term of exclusivity and field of use, as the NIH is required to do, would ensure that the licensee receives adequate remuneration for its investment in the technology, while balancing that interest against the requirement that the license serve the public interest. Patients do not benefit from gene therapies that they cannot afford, and it is a policy of the NIH to promote broad access to NIH-owned inventions in developing countries.

We ask the NIH to consider several measures in an exclusive license to protect the public interest.

Ensuring global access

Given the vast global inequality in access to gene therapies, 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."

Prohibition against prices that discriminate against US residents

Any license should ensure that U.S. residents are not asked to pay prices that exceed the median price from the seven economies of the largest GDP and at least 50 percent of U.S. per capita income. The per capita income can be based upon the World Bank's Atlas method.

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 PTC Therapeutics 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 licensees 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

In the event that the NIH grants an exclusive license, it must comply with the restrictions and safeguards in 35 U.S.C. § 209. We are concerned that the NIH is not imposing any meaningful limits on the scope of exclusivity, in violation of the Bayh-Dole Act. The license must include measures to ensure access and avoid unnecessary fiscal toxicity. An overbroad monopoly in a gene therapy to treat a rare disorder can be expected to result in excessive prices.

Please notify us if and when a license is granted, so we can request a copy under the Freedom of Information Act. The grant of a license is not confidential business information.

Sincerely,

Knowledge Ecology International