

Knowledge Ecology International
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Rose M. Freel, Ph.D.
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NCI Technology Transfer Center
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October 12, 2021

Re: Prospective Grant of an Exclusive Patent License: Development of a Bispecific T Cell Engager for the Treatment and Cure of HIV-1 ([86 FR 53334](#))

Dear Dr. Freel:

Knowledge Ecology International (KEI) would like to offer the following comments regarding the “Prospective Grant of an Exclusive Patent License: Development of a Bispecific T Cell Engager for the Treatment and Cure of HIV-1” (86 FR 53334) to Gilead Sciences, based in Foster City, CA.

The field of use of this exclusive, worldwide license is “For use in an HIV Bispecific T cell engager construct comprising the CD4 mD1 which will be utilized in therapeutic regimens to treat and cure people living with HIV.” If the development of the invention advances and comes to market, it would be the first cure for people living with HIV.

KEI asked the NIH nine questions regarding the license (attached), and while they answered very promptly, for the five questions regarding various terms of the license, the NIH declined to provide information, stating that “the license has yet to be negotiated” and “The specific terms of the license will be considered business confidential.” How are the public supposed to be able to provide detailed, informed comments on a license about which the only term published is the field of use? And what dictates that the term concerning field of use is not business confidential, while every other term is?

KEI also asked the NIH whether, in working towards executing this license, the NIH has sought advice from the Attorney General (as is required under 40 USC § 559) to determine if the “disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law”. The NIH’s response was that “This question has been previously addressed by the NIH.”

The NIH has previously made clear that it does not seek the advice of the Attorney General regarding antitrust concerns in the execution of exclusive licenses. 40 USC § 559, however, is not preempted by the Bayh-Dole Act. The Bayh-Dole Act provides that “[n]othing in this chapter shall be deemed to convey to any person immunity from civil or criminal liability, or to create any defenses to actions, under any antitrust law[.]” 35 U.S.C. § 211. The Bayh-Dole Act sets out the areas where the statute “shall take precedence over any other Act which would require a disposition of rights in subject inventions[.]” 35 U.S.C. § 210, and mentions 21 separate statutes, but does not include 40 U.S.C. § 559.

Of the information gleaned from our questions to the NIH, KEI ascertained that the family of inventions has been available for licensing since May 2010, and there is no Cooperative Research and Development Agreement (CRADA) associated with this technology. When asked about the stage of development of the inventions to be licensed, the NIH stated, “For the field of use and products contemplated in this license, it is in preclinical stage.” From looking at the descriptions of the inventions, it would seem that the technology to be licensed is related to Gilead’s Vesatolimod TLR-7 agonist (GS-9620), although Gilead’s website states that technology is in Phase 2 of trials.

As the NIH considers licensing this potentially very significant technology to Gilead, KEI urges the NIH to include terms in the license that protect affordable, equitable access to patients in the US and around the world. Gilead’s U.S. pricing of its HIV products have been aggressive, and in the past, the high prices have been a barrier to the deployment of PrEP to prevent HIV infections. The company has been the subject of a Congressional inquiry into its high pricing of its hepatitis C virus treatment, Sovaldi. Gilead’s CD19-targeting therapy, Yescarta (axicabtagene ciloleucel), which was also developed using technology invented by and licensed from the NIH and was the subject of a separate NIH Cooperative Research and Development Agreement (CRADA), was also aggressively priced.

Given Gilead’s track record of aggressively pricing its treatments, including other HIV-related technologies, the NIH must negotiate and include terms in this license that protect and safeguard affordable patient access to any resultant treatment. KEI strongly urges the NIH to include the following considerations and provisions in the terms of these licenses.

Price Discrimination

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. This is a modest safeguard.

KEI notes that 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.

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 Kyverna 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

We further request that the NIH includes the following additional provisions to protect the public’s interest in this NIH-funded technology:

Years of exclusivity. We propose the license include terms that reduce the years of exclusivity when revenues are large. The NIH has many options, including by providing an option for non-exclusive licensing, such as was done in the ddi case. We propose that the terms stipulate that in any sublicense that the exclusivity of the license be reduced when the global cumulative sales from products or services using the inventions exceed certain benchmarks. For example, the period of exclusivity in the sublicense could be reduced by one year for every \$500 million in

global cumulative revenue after the first one billion in global sales. This request is consistent with the statutory requirements of 35 U.S.C. § 209, which requires that “the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application.”

Low and middle income countries. The exclusive license should 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 countries with significantly lower incomes. 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.”

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 developing countries, 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. KEI therefore requests that the license 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,

Claire Cassedy
Knowledge Ecology International

claire.cassedy@keionline.org

ATTACHMENT

From: **Freel, Rose (NIH/NCI) [E]** <rose.freel@nih.gov>

Date: Mon, Sep 27, 2021 at 11:29 AM

Subject: RE: Questions Regarding Prospective Exclusive License to Gilead Science

To: Claire Cassedy <claire.cassedy@keionline.org>

Cc: James Love <james.love@keionline.org>

Dear Ms. Cassedy,

Below please find my responses to your questions in red text:

1. At what stage of development are the inventions listed? **For the field of use and products contemplated in this license, it is in preclinical stage.**
2. Are there any clinical trials of the licensed technology planned or already conducted? **None that I'm aware of that relate to the subject matter of the license.** If so:
 - a. Can you provide NCT numbers?
 - b. Has the government funded or planned to spend any clinical trials relevant to these technologies?
 - i. If so, how much has been spent or planned to be spent by the government on these trials? Can you please provide relevant grant and/or contract numbers?
1. Is the term in the proposed licenses to be life of patent or less than life of patent? **The license has yet to be negotiated.**
2. For how long have the instant patents and applications been available for licensing? **This family has been available for licensing since May 2010.**
3. In working towards executing this license, has the NIH sought advice from the Attorney General (as is required under 40 USC § 559) to determine if the "disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law"? **This question has been previously addressed by the NIH.**
4. Is there a Cooperative Research and Development Agreement associated with this technology? **No**
5. What analysis did the NIH undertake, if any, in order to conclude that exclusivity is a reasonable and necessary incentive? **NIH has reviewed the proposed license and determined that the proposed exclusive license satisfies the criteria required for an exclusive license under 37 CFR Part 404.**

6. Considering Gilead has a history of pricing medical technologies aggressively (as investigated by Congress), including those involving NIH-licenses and CRADAs, how will the NIH ensure that any resultant technology is available to the public on reasonable terms? **The license has yet to be negotiated. The specific terms of the license will be considered business confidential.**
7. What provisions will be made in the license to address the unequal access to treatments in developing countries, in order to give effect to PHS policy? **As above in question 8, the license has yet to be negotiated however, the specific terms of the license will be considered business confidential.**
8. Has the NIH considered limiting the geographic scope of the exclusive rights to exclude countries with lower incomes? **Same as above in question 8.**
9. Has the NIH considered a system of non-exclusive rights for the US, and exclusive rights in other high income countries? **Same as above in question 8.**

Best Regards,
Rose

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Rose Santangelo Freel, Ph.D.
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From: Claire Cassedy <claire.cassedy@keionline.org>
Sent: Friday, September 24, 2021 3:55 PM
To: Freel, Rose (NIH/NCI) [E] <rose.freel@nih.gov>
Cc: James Love <james.love@keionline.org>
Subject: Questions Regarding Prospective Exclusive License to Gilead Science

Dear Dr. Freel,

I am writing in reference to the Federal Register notice, "Prospective Grant of an Exclusive Patent License: Development of a Bispecific T Cell Engager for the Treatment and Cure of HIV-1" (FR Doc. 2021-20908). You were listed as the contact for all inquiries regarding the prospective license.

1. At what stage of development are the inventions listed?
2. Are there any clinical trials of the licensed technology planned or already conducted? If so:
 1. Can you provide NCT numbers?
 2. Has the government funded or planned to spend any clinical trials relevant to these technologies?

1. If so, how much has been spent or planned to be spent by the government on these trials? Can you please provide relevant grant and/or contract numbers?
3. Is the term in the proposed licenses to be life of patent or less than life of patent?
4. For how long have the instant patents and applications been available for licensing?
5. In working towards executing this license, has the NIH sought advice from the Attorney General (as is required under 40 USC § 559) to determine if the “disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law”?
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. Considering Gilead has a history of pricing medical technologies aggressively (as investigated by Congress), including those involving NIH-licenses and CRADAs, how will the NIH ensure that any resultant technology is available to the public on reasonable terms?
9. What provisions will be made in the license to address the unequal access to treatments in developing countries, in order to give effect to PHS policy?
10. Has the NIH considered limiting the geographic scope of the exclusive rights to exclude countries with lower incomes?
11. Has the NIH considered a system of non-exclusive rights for the US, and exclusive rights in other high income countries?

Thank you in advance for the information.

Best Regards,
Claire Cassedy

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