

Knowledge Ecology International  
1621 Connecticut Ave NW  
Washington, DC 20009  
[www.keionline.org](http://www.keionline.org)

David A Lambertson, Ph.D.  
Senior Technology Transfer Manager  
NCI Technology Transfer Center  
National Institutes of Health  
Email: [david.lambertson@nih.gov](mailto:david.lambertson@nih.gov)

March 5, 2021

**Re: Prospective Grant of an Exclusive Patent License: Allogeneic Therapy for the Treatment of Autoimmune Disease Using Chimeric Antigen Receptors Targeting CD19 (86 FR 10092); and Prospective Grant of an Exclusive Patent License: Autologous Therapy for the Treatment of Autoimmune Disease Using Chimeric Antigen Receptors Targeting CD19 (86 FR 10081)**

Dear Dr. Lambertson:

Knowledge Ecology International (KEI) would like to offer the following comments regarding the prospective grant of exclusive patent licenses concerning allogeneic and autologous therapies using anti-CD19 targeting chimeric antigen receptor (CAR)-based immunotherapy to Kyverna Therapeutics (Kyverna) located in Berkeley, CA.

The National Cancer Institute (NCI) of the National Institutes of Health (NIH) is separately seeking to enter into the “Prospective Grant of an Exclusive Patent License: Allogeneic Therapy for the Treatment of Autoimmune Disease Using Chimeric Antigen Receptors Targeting CD19” (86 FR 10092) and the “Prospective Grant of an Exclusive Patent License: Autologous Therapy for the Treatment of Autoimmune Disease Using Chimeric Antigen Receptors Targeting CD19 (86 FR 10081). The following comments are offered jointly to the respective licenses.

The fields of use for the licenses of both therapies state that they are for “the treatment of autoimmune diseases.”

There are over 80 types of autoimmune diseases, affecting 3-5% of the global population ([ref](#)). Incidence of autoimmune diseases is growing at a rate of 19.1% per year worldwide, with high DALY-burden ([ref](#)).

As the Federal Register notices state, the CD19 cell surface protein is expressed on the cell surface of several autoimmune disease cells, and “For many autoimmune diseases there are no FDA-approved therapies, underscoring that there is an unmet need. The development of an autoimmune disease therapeutic targeting CD19 will benefit public health by providing a treatment for patients who may not have any options.”

Considering that, as the NIH says, these patients “may not have any options”, it is imperative that the NIH ensures that these licenses contain terms that ensure equitable and affordable access to any resultant treatment. The terms included in these exclusive licenses ensure that desperate patients without alternative treatment options are not held hostage to high prices.

As the NIH considers this exclusive license to Kyverna, KEI would also like to highlight the potential anticompetitive practices and market consolidation of this technology. Although this license is to Kyverna, KEI notes that in this treatment area, Kyverna has entered into a close partnership with Gilead Sciences (Gilead):

“Kyverna also announced that it has entered into a strategic collaboration and license agreement with Gilead to develop engineered T cell therapies for the treatment of autoimmune disease based on Kyverna's synthetic Treg platform and synNotch™ technology from Kite, a Gilead Company. Kyverna will be responsible for conducting research activities and initial clinical studies through proof-of-concept and Gilead will be granted an option, upon the exercise of which Gilead will be solely responsible for further clinical development and commercialization efforts for these programs.”<sup>1</sup>

Gilead also has a seat on the Board of Directors of Kyverna. Through this partnership, and Gilead’s acquisition of Kite Pharma (now a wholly-owned subsidiary of Gilead), the company has existing CAR T treatments, including therapies targeting the CD19 cell surface proteins.

The NIH has previously announced exclusive licenses involving CAR technologies and CD19 to Kite/Gilead, and the partnership between Kyverna-Gilead in this area expands upon that. This consolidation may have consequences for access and affordability to any resultant therapy.

The first Gilead 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 aggressively priced. Gilead has received repeated scrutiny and criticism for the aggressive pricing of its products, including having been the subject of a Congressional inquiry into its high pricing of its hepatitis C virus treatment, Sovaldi. 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.

---

1

<https://www.prnewswire.com/news-releases/kyverna-therapeutics-secures-25-million-series-a-funding-from-key-investors-and-enters-into-strategic-collaboration-with-gilead-sciences-300985379.html>

Did the NIH seek the antitrust advice of the U.S. Attorney General with respect to the license, as required by 40 U.S.C. § 559? Considering Gilead's partnership with Kyverna in the very area of these technologies, these licenses should be carefully scrutinized for their potential for anticompetitive impact and subsequent pricing abuses resulting from that impact.

Considering the breadth of the treatment area of the proposed fields of use for these licenses, the prevalence of autoimmune diseases, the dearth of current treatment options for these patients, and the close relationship of Kyverna and Gilead, the NIH must ensure that these licenses include protections and safeguards to ensure 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 ddl 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.

**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](mailto:claire.cassedy@keionline.org)