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February 26, 2018

Dear Director Collins and Dr. Lambertson:

Knowledge Ecology International ("KEI") writes to appeal the decision of the National Institutes of Health ("NIH") and National Cancer Institute ("NCI") to proceed with the exclusive license of a portfolio of patents to Kite Pharma, a wholly-owned subsidiary of Gilead, for chimeric antigen receptors ("CAR") that recognize the CD30 protein, as posted in the Federal Register notice 82 FR 60406.

Pursuant to 37 C.F.R. § 404.11, KEI requests a hearing as part of the appeal.

Procedural Background

On December 20, 2017, the NIH posted a notice of intent in the Federal Register (the "Notice") regarding the proposed grant of a worldwide exclusive license to Kite of patents for CAR technology for the treatment of human cancer.[1] The Notice specifically referred to "United States Provisional Patent Application No. 62/241,896, filed 15 October 2015 and entitled ''Anti-CD30 Chimeric Antigen Receptors'' [HHS Reference No. E–016–2018/0–US–01]; PCT Patent Application PCT/US2016/ 056262, filed 10 October 2016 and entitled ''Anti-CD30 Chimeric Antigen Receptors'' [HHS Reference No. E–016– 2018/0–PCT–02]; and U.S. and foreign patent applications claiming priority to the aforementioned applications" (collectively, the "CD30 CAR technology").

[1] 82 Fed. Reg. 60406-7 (Dec. 20, 2017).

The Notice additionally specified that this CD30 CAR technology would provide treatment for rare cancers, "including Hodgkin lymphoma (HL), Non-Hodgkin's Lymphoma (NHL), diffuse large B cell lymphoma (DLBCL), peripheral T cell lymphoma not otherwise specified (PTCL–NOS), anaplastic large cell lymphoma (ALCL), and angioimmunoblastic T cell lymphoma (AITL)."

The Notice provided a window for public comment on the proposed exclusive license that spanned two national holidays, closing on January 4, 2018.

On January 4, 2018, KEI timely submitted written comments ("Comments" or "KEI's Comments") to the NIH in response to the Notice, objecting to the exclusivity of the license and requesting the inclusion of public interest safeguards in any license to be executed.[2] KEI's comments are attached and incorporated by reference.

On January 25, 2018, Dr. David Lambertson, Senior Technology Transfer Manager at NCI, sent an email (attached) to KEI acknowledging receipt of KEI's comments, rejecting all of KEI's substantive suggestions and objections, providing a list of reasons for the "determination," and stating that ". . . NCI intends to proceed with the negotiation of the proposed exclusive license. . . ."

On February 13, 2018, KEI sent an email to Dr. Lambertson and Karen Rogers, Acting Director of NIH Office of Technology Transfer, asking whether NIH requests and obtains advice of the Attorney General with respect to antitrust laws prior to transferring patents and related rights from the NIH to private interests, as required by 40 U.S.C. § 559 of the Federal Property and Administrative Services Act ("FPASA").

On February 14, 2018, KEI sent an email to Dr. Lambertson and Dr. Francis Collins, Director of NIH, signaling an intent to appeal the decision to proceed with the exclusive license of the CD30 CAR technology to Kite.

On February 15, 2018, Ms. Rogers replied via email (attached) to KEI's February 13th inquiry to say that the NIH does not follow the requirements of 40 U.S.C. § 559 in its patent licensing activities.

KEI Has a Legal Basis for Appeal Under 37 C.F.R. § 404.11 as a Public Interest Organization Representing Individuals Who Will be Damaged By the Decision to Proceed with the Exclusive License[3]

37 C.F.R. § 404.11 governs appeals concerning, "any decision or determination concerning the grant, denial, modification, or termination of a license." Dr. Lambertson's email rejecting KEI's

[2] https://www.keionline.org/wp-content/uploads/2018/01/KEI-KITE-CAR-T-NIH-4Jan2018.pdf

[3] KEI sent an email to Dr. Lambertson and Dr. Collins on February 14, 2018 (attached) stating the desire to appeal the decision to proceed, and requesting information regarding any formal procedures that the NIH requires for such an appeal as no such procedures are specified in regulations or available on the NIH website. To date, we have not received any reply. If there are formal requirements and this document does not conform to those requirements, KEI would ask for the opportunity to make any necessary corrections.

comments is self-evidently a determination/decision to proceed with the negotiation of the exclusive license subject to appeal.

KEI is granted the right of appeal under subsection (a)(3) as a public interest organization that timely filed a written objection to the NIH's notice. Furthermore, KEI represents taxpayers and patients, including cancer patients, who are stakeholders in the outcome of the NIH decision as persons who need new treatments but who also need these treatments to be affordable.

Kite was purchased by Gilead Sciences in October 2017 for $11.9 billion, and is now a wholly-owned subsidiary. Gilead already has one CAR T treatment, axicabtagene ciloleucel (marketed as Yescarta), priced at $373,000 per treatment. A second CAR T therapy, tisagenlecleucel (marketed by Novartis as Kymriah), is priced at $475,000 per treatment. Prices for costs of care related to the treatment have been estimated to be as high as $1.5 million, creating severe hardship for patients, payers, and health budgets.[4]

KEI represents persons who will be damaged by the decision to proceed with an exclusive license on CAR T technology without safeguards against excessive pricing or access barriers.

§ 404.11 Appeals.
(a) In accordance with procedures prescribed by the Federal agency, the following parties may appeal to the agency head or designee any decision or determination concerning the grant, denial, modification, or termination of a license:
(1) A person whose application for a license has been denied;
(2) A licensee whose license has been modified or terminated, in whole or in part; or
(3) A person who timely filed a written objection in response to the notice required by § 404.7(a)(1)(i) or § 404.7(b)(1)(i) and who can demonstrate to the satisfaction of the Federal agency that such person may be damaged by the agency action.
(b) An appeal by a licensee under paragraph (a)(2) of this section may include a hearing, upon the request of the licensee, to address a dispute over any relevant fact. The parties may agree to Alternate Dispute Resolution in lieu of an appeal.

Argument

It is Premature to Grant an Exclusive License Prior to the Completion of Phase 1 Clinical Trials.

In KEI's submitted comments, we objected to the proposed exclusive license as being premature, given that Phase 1 clinical trials are underway and are not scheduled to be completed until 2021. KEI recommended waiting until the NIH could do an analysis of the costs

[4] Kaiser Health News, "Cascade of costs could push CAR-T therapy to $1.5M per patient," Oct. 17, 2017. https://endpts.com/cascade-of-costs-could-push-new-gene-therapy-above-1-million-per-patient/

that the NIH would incur were the agency to fund the clinical trials completely, versus the costs imposed on patients, employers, and taxpayers via the grant of the patents to Gilead:

> In an environment where there is widespread alarm over the escalating costs of treatments for cancer and Congressional concerns over the pricing of NIH-funded biomedical inventions, it is unwise for the NIH to create a monopoly on this NIH-funded invention, before the NIH can evaluate both the evidence from the ongoing Phase 1 trial and the costs of moving the technology forward to FDA approval, if the Phase 1 results are encouraging.[5]

The KEI comment went to the issue of whether or not the NIH decision to license was premature, both in determining if an exclusive license was necessary at all, and if, pursuant to 35 U.S.C. § 209, "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application."

In response to this point, Dr. Lambertson replied that (1) because the field of use in the proposed license is limited, "only to specific anti-CD30 CARs using a specific antibody targeting component," there will be no monopoly; and that (2) the NIH does not have the appropriate funding to conduct Phase 2 or Phase 3 trials, and that therefore the time to license is "immediate."[6]

With regard to Dr. Lambertson's first point, the grant of an exclusive license is designed to create a twenty-year right to exclude competitors from the marketplace via the patents (plus time added for patent extensions). The suggestion that the license field of use restriction creates a situation where there is "no monopoly" is patronizing and incorrect. The NIH could offer a non-exclusive license, and avoid a monopoly, but instead it has proposed an exclusive license that would grant a monopoly on "specific anti-CD30 CARs using a specific antibody targeting component." Considering the extremely high prices associated with the earlier Kite/Gilead CAR T treatment (more than the median sales price for new houses sold in the United States) also licensed from the NIH, it is hard to see how the NIH can claim no monopoly is involved.

Dr. Lambertson provides no evidence to support his second point regarding NIH funding. In considering this point, it would be helpful to know what the NIH is actually spending on the current Phase 1 trial. On February 14, 2018, KEI called Brenna Hansen, who is listed as the NIH contact for the clinical trials for the CD30 CAR technology at issue, to ask what the budget was for the current CAR T trial being funded by the NIH.[7] She declined to provide any information. The NIH/NCI can and should divulge this information, as well as estimates of what it believes a necessary budget would be for Phase 2 and/or Phase 3 trials.

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[5] KEI Objection, at p. 3.
[6] Email of Dr. Lambertson to James Love, Jan. 25, 2018.
[7] https://www.keionline.org/25808

We do know that for the first two CAR T treatments approved by the FDA, the number of patients in the trials were very small. According to the FDA press release for the initial approval of Kymriah (updated August 30, 2017), "the safety and efficacy of Kymriah were demonstrated in one multicenter clinical trial of 63 pediatric and young adult patients with relapsed or refractory B-cell precursor ALL."[8] The FDA press release for Gilead's Yescarta cited evidence from "over 100" patients. As of January 27, 2017, 111 patients were enrolled in the ZUMA-1 Phase 1/2 trials.[9]

The NIH is currently funding the Phase 1 trial NCT03049449, titled "T Cells Expressing a Fully-Human Anti-CD30 Chimeric Antigen Receptor for Treating CD30-Expressing Lymphomas," which has an expected enrollment of 76 patients, more than were enrolled in the trial cited by the FDA for the approval of Kymriah and nearly as many as in the Zuma-1 trial used to approve Yescarta.

If the NIH invented the technology and is funding the development through a 76-patient trial, it is reasonable to ask why the NIH believes an exclusive license is needed to fund the remaining trials, and how extensive the scope of rights should be to meet the 35 USC § 209 obligations to restrict such rights to those that are "reasonably necessary to provide the incentive for bringing the invention to practical application." The NIH needs to offer more information about the projected costs of the trials to justify the term of the monopoly the NIH proposes to give Gilead.

Any License Should Include Safeguards Against Excessive Pricing and Barriers to Access for U.S. Residents, and Should Limit the Exclusive Rights in Poorer Countries.

In KEI's Comments, in addition to objecting to the proposed exclusive license, we also made a number of suggestions regarding the need to include safeguards in any license that may be executed, including safeguards against excessive pricing and barriers to access, both for U.S. residents and for poorer countries. These recommendations included:

> (1) a clause to protect against excessive prices in the U.S. relative to a set of reference countries;
> (2) provisions to terminate monopoly rights if the price creates access barriers in the U.S.;
> (3) provisions preventing the price from exceeding that of CAR-T treatments of similar efficacy (*e.g.* Yescarta);
> (4) provisions to terminate monopoly rights upon achieving certain global revenue benchmarks; and
> (5) provisions to either limit exclusive rights or otherwise require that the treatment be made affordable in countries with less than one-third the per capita income of the U.S.

[8] https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm574058.htm
[9] http://cancerres.aacrjournals.org/content/77/13_Supplement/CT019

In reply, Dr. Lambertson simply points to the fact that the NIH has not included pricing provisions for years, a fact we do not dispute. However, the failure of the NIH in the past to limit the scope of rights to that which is reasonably necessary to induce investments in the development of a product is not an argument as to why it should never enforce this requirement to protect the public from unreasonable use of inventions.

To meet the requirements of 35 USC § 209, the NIH could choose to include safeguards on pricing, a concession that would limit the scope of rights associated with a monopoly. Alternatively, the NIH could limit the number of years of exclusivity, which was the approach taken for the NIH/ddI license to BMS.[10] According to an NIH report on the negotiation:[11]

> "The technology transfer challenge was to negotiate a license that would provide a strong incentive for a drug company to make the significant investment necessary for the rapid development of a new drug while ensuring the long-term public health benefits. This balance was struck by offering a license that was initially exclusive, but which could became non-exclusive early, prior to the expiration of the NIH patents. Several companies competed for the license. Criteria for selecting the licensee included the company's technical ability to develop this compound into a drug and manufacture it in large quantities, its willingness to work cooperatively with the NIH, and its willingness to make development of this compound a priority. The Bristol-Myers Squibb plan was judged superior by the selection panel, and the license was signed in January 1988. NIH exercised its prerogative to have the license become nonexclusive in October 2001."

Instead the NIH seems to be offering to do neither measure to limit the scope of rights, and proposes to just give Gilead the maximum term of years and the maximum flexibility on pricing. This appears contrary to the statutory requirements of § 209.

KEI also notes that the Bayh-Dole Act does not begin and end with a mandate to bring products to market, but rather includes the need to, "protect the public against nonuse or unreasonable use of inventions"[12]

The inclusion of protections against "unreasonable use" is not inconsequential, and the Bayh-Dole Act contains related provisions in numerous places demonstrating that it is not

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[10] See *Exclusive Agreements Between Federal Agencies and Bristol-Myers Squibb Co. For Drug Development: Is the Public Interest Protected?: Hearing Before the Subcomm. On Regulation, Business Opportunities, and Energy of the H. Comm. on Small Business*, 102nd Congress 350-377 at 362 (NCI's Response to Questions Raised in Rep. Ron Wyden Letter dated Aug. 1, 1991) ("...NCI negotiated this term with Bristol, which originally requested an exclusive license for the duration of the life of the patent. ...At the time that this license was granted by the National Technical Information Service (NTIS) as the licensing agent for DHHS, NTIS frequently limited the exclusive period in license agreements to ten years.").

[11] Videx® Expanding Possibilities: A Case Study, National Institutes of Health Office of Technology Transfer, September 2003. https://www.ott.nih.gov/sites/default/files/documents/pdfs/VidexCS.pdf

[12] 35 U.S.C. § 200.

merely “nonuse” that is of concern. 35 U.S.C. § 209, governing the license of federally-owned inventions, includes a requirement of “practical application” — a defined term under 35 U.S.C. § 201(f) that requires the invention be made “available to the public in reasonable terms.”

“Reasonable terms” itself is understood both in the United States and abroad, in jurisprudence as well as official statutory/regulatory interpretative documents, to include reasonable pricing. *See* KEI 10 March 2017 Comments on Army Exclusive License on Zika Virus Vaccine Patents to Sanofi, attached and incorporated by reference.[13]

The inclusion of safeguards and conditions on access and affordability are consistent with the obligations in the Bayh-Dole Act to make the benefits of the inventions “available to the public on reasonable terms”, and are the right policy for protecting the public interest.

The NIH Should Require Transparency of R&D Outlays for the Public to Better Understand the Relationship of R&D to High Prices.

KEI’s Comments additionally suggested that the NIH should require transparency with regard to research and development (R&D) costs, along with public sector subsidies such as the Orphan Drug Tax Credit. This information would better allow the public to understand what relationship there is, if any, between the R&D expenditures and high prices.

Dr. Lambertson stated in his reply that NIH/NCI does not have authority to require such disclosures, and points to 37 CFR § 404.14 requiring that any plan submitted under 37 CFR § 404.8(h) and § 404.5(b)(6) be treated as confidential and not subject to disclosure under FOIA.

Neither of the specified regulatory requirements referred to within § 404.14 are a flat bar to transparency obligations regarding the development of product, and the requests KEI made were not inconsistent with licensing regulations. § 404.8(h) is relevant to the plan itself submitted as part of an application for a license, but is silent as to the actual expenditures and subsidies themselves. § 404.5(b)(6) requires periodic reporting by the licensee, “on the utilization or efforts at obtaining utilization that are being made by the licensee, with particular reference to the plan submitted but only to the extent necessary to enable the agency to determine compliance with the terms of the license.” But this requirement does not explicitly refer to the costs of R&D or the extent of federal subsidy.

During an earlier dispute regarding the failure to adequately supply the market with Fabrazyme, Genzyme, Inc. and later Sanofi were required to provide the NIH with detailed monthly reports on patent litigation in Europe and on measures taken to address access to the drug in the United States. These documents were subsequently made public by the NIH and are on the KEI web page.[14]

[13] Also available at https://www.keionline.org/23296.
[14] https://keionline.org/sites/default/files/Fabrazyme-NIH-Sinai_2011u.pdf

The Decision to Proceed with the Exclusive License Should Be Stopped Until NIH Receives Antitrust Advice from the Attorney General Pursuant to 40 U.S.C. § 559.

By admission of Ms. Rogers, the NIH has not followed the law of 40 U.S.C. § 559, because it does not believe the law pertains to the licensing of patents. This interpretation is not supported by the law.

The Federal Property and Administrative Services Act (40 U.S.C. §§ 101 *et seq.*) was enacted to govern the procurement, utilization and disposal of property.[15]

Under 40 U.S.C. § 559(b), the NIH as a federal executive agency is required to seek and obtain the antitrust advice of the Attorney General prior to disposing of property to a private interest.

"Property" is defined at 40 U.S.C. § 102 to mean "any interest in property", with certain exceptions that do not include patents. Similarly, § 559 includes certain exceptions for where the requirement does not apply, but these exceptions do not include patents.

40 U.S. Code § 559 - Advice of Attorney General with respect to antitrust law

(a)Definition.—In this section, the term "antitrust law" includes—

(1) the Sherman Act (15 U.S.C. 1 et seq.);
(2) the Clayton Act (15 U.S.C. 12 et seq., 29 U.S.C. 52, 53);
(3) the Federal Trade Commission Act (15 U.S.C. 41 et seq.); and
(4) sections 73 and 74 of the Wilson Tariff Act (15 U.S.C. 8, 9).

(b)Advice Required.—

(1)In general.—
An executive agency shall not dispose of property to a private interest until the agency has received the advice of the Attorney General on whether the disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law.
(2)Exception.—This section does not apply to disposal of—
(A)real property, if the estimated fair market value is less than $3,000,000; or
(B)personal property (other than a patent, process, technique, or invention), if the estimated fair market value is less than $3,000,000.

(c)Notice to Attorney General.—

(1)In general.—
An executive agency that contemplates disposing of property to a private interest shall promptly transmit notice of the proposed disposal, including probable terms and conditions, to the Attorney General.
(2)Copy.—

[15] 40 U.S.C. § 101.

Except for the General Services Administration, an executive agency that transmits notice under paragraph (1) shall simultaneously transmit a copy of the notice to the Administrator of General Services.

(d)Advice From Attorney General.—
Within a reasonable time, not later than 60 days, after receipt of notice under subsection (c), the Attorney General shall advise the Administrator and any interested executive agency whether, so far as the Attorney General can determine, the proposed disposition would tend to create or maintain a situation inconsistent with antitrust law.

(e)Request for Information.—On request from the Attorney General, the head of an executive agency shall furnish information the agency possesses that the Attorney General determines is appropriate or necessary to—

(1) give advice required by this section; or
(2)determine whether any other disposition or proposed disposition of surplus property violates antitrust law.

(f)No Effect on Antitrust Law.—
This subtitle does not impair, amend, or modify antitrust law or limit or prevent application of antitrust law to a person acquiring property under this subtitle.

Federal regulations at 41 C.F.R. 102-75.270 clarify the point by explicitly including patents among the property that trigger the requirement of considering the antitrust ramifications in a contemplated disposal to a private interest:

41 CFR 102-75.270 - Must antitrust laws be considered when disposing of property?

Yes, antitrust laws must be considered in any case in which there is contemplated a disposal to any private interest of -

(a) Real and related personal property that has an estimated fair market value of $3 million or more; or

(b) Patents, processes, techniques, or inventions, irrespective of cost.

Furthermore, 40 U.S.C. § 113 provides for limitations on the reach of the FPASA by explicitly enumerating a list of departments, agencies, and heads of those departments and agencies that retain authority that cannot be impaired or affected by the FPASA. This list does not include the Department of Health and Human Services, the Secretary of Health and Human Services, the National Institutes of Health, or the Director of the National Institutes of Health. The omission of

these entities and offices evidences the fact that NIH licensing activities are not exempt from the requirements of the FPASA.

"Disposal" under the FPASA Includes Licensing, and the Bayh Dole Act does not Create an Exception to the FPASA Requirement Regarding Antitrust Advice..

Ms. Rogers's email errantly suggests that "disposal" under the FPASA does not touch licensing activities: "The statute you reference is directed to the disposal (assignment) of government property. It has little relevance to our patent licensing activities, which are principally governed by the Bayh-Dole Act and its regulations."

While the Bayh-Dole Act and its attendant regulations govern the licensing of federally-owned and federally-funded patents by NIH, there is no exception within the Bayh-Dole Act that would exempt the agency from having to abide by the requirements of the FPASA. 35 U.S.C. § 209(a)(4) in fact creates an obligation that the licensing federal agency may only grant a license on a federally-owned invention if it, "will not tend to substantially lessen competition or create or maintain a violation of the Federal antitrust laws." Logically, this suggests that the FPASA requirement applies; the NIH has abundant expertise in developing new medical technologies but does not have the antitrust expertise of the Attorney General.

Furthermore, the term "disposal" is not a defined term under 40 U.S.C. § 102 of the FPASA, and is not limited to "assignment" or "sale." In fact, there are many examples of regulations and laws that include licensing amongst dispositions, either explicitly or by implication.

For example, in the State Department's Foreign Affairs Manual, licenses are included as a method of disposal along with sale, assignment, and lease.[16] The manual distinguishes between "permanent" disposals (e.g. sale) and licenses, which are "preferable because a license generally creates no enforceable rights for the licensee and does not diminish the U.S. Government's title rights. . . [and] require prior review and approval by OBO/PRE/RPL and the Office of the Legal Adviser (L/BA) for properties controlled by Department of State, or USAID/W-M/MS/OMD for properties controlled by USAID."[17]

Likewise, General Services Administration regulations in many places include licenses among the possible methods of disposal. *See, e.g.*, FMR §102-75.296 ("A landholding agency may be the disposal agency for real and related personal property when— …(c) The agency is disposing of —(1)...licenses…").

The Uniform Commercial Code defines "account" to include a right to payment for "property that has been or is to be sold, leased, licensed, assigned, or otherwise disposed of." Unif.Commercial Code § 9-102.

[16] 15 FAM 521.1.
[17] 15 FAM 521.5.

Conclusion

For all of the reasons stated above, KEI requests that the NIH reverse its determination to proceed with this license (1) unless it includes the public interest safeguards referred to in our submitted comments, and (2) until the NIH seeks and obtains antitrust advice from the Attorney General.

We request a hearing for this appeal.

Sincerely,

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Attachments:

(1) Email from Dr. Lambertson to James Love, January 25, 2018.
(2) Objection of Knowledge Ecology International to Proposed Exclusive License to Gilead of Chimeric Antigen Receptors that Recognize the CLD30 Protein, Jan. 4, 2017.
(3) Email from Karen Rogers to Andrew Goldman and James Love, Feb. 15, 2018.
(4) Email from Andrew Goldman to Dr. Lambertson and Dr. Collins, Feb. 14, 2018.
(5) KEI Comments on Army Exclusive License on Zika Virus Vaccine Patents to Sanofi, March 10, 2017.