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Re: Appeal, Exclusive Licenses in Bicistronic Chimeric Antigen Receptor (CAR) Constructs Targeting CD19 and CD20 to Kite Pharma, Inc., a Wholly-Owned Subsidiary of Gilead Sciences, as Described in Federal Register Notices 84 FR 33270 and 84 FR 33272

Dear Director Collins and Dr. Lambertson:

Knowledge Ecology International (KEI), Union for Affordable Cancer Treatment (UACT), Universities Allied for Essential Medicines (UAEM), Social Security Works (SSW), and Clare Love (collectively, "Appellants"), write to appeal the decision of the National Institutes of Health (NIH) to grant exclusive licenses in "Bicistronic Chimeric Antigen Receptor (CAR) Constructs Targeting CD19 and CD20" to Kite Pharma, Inc. ("Kite"), a wholly-owned subsidiary of Gilead Sciences ("Gilead"), as described in 84 FR 33270 and 84 FR 33272.

This appeal addresses six important issues:

1. Did the NIH properly evaluate the necessity of granting an exclusive license, for example, by considering other incentives such as FDA regulatory protection of test data, and patent protection from non-NIH patent holders?

2. Assuming that the NIH can establish that an exclusive license was necessary in this case, did the NIH meet its statutory responsibility to limit the scope of rights to that which is "reasonably necessary" to induce the investment required to bring the invention to practical application, for example by analyzing the expected costs of investment and annual revenues to determine how many years of exclusivity are warranted?

3. Did the NIH request the antitrust advice of the Attorney General, pursuant to 40 U.S.C. § 559?

4. Will the licenses tend to substantially lessen competition by creating undue market concentration, in violation of 35 U.S.C. § 209(a)(4)?

5. Was the public's right to evaluate a proposed license under 35 U.S.C. § 209(e) undermined by the NIH's lack of transparency?

6. Has the NIH done anything to implement the objectives in the Public Health Service (PHS) Technology Transfer Policy Manual regarding promoting access in developing countries?

We request a hearing on this appeal.

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A. BACKGROUND AND PROCEDURAL HISTORY

The licenses at issue grant Gilead exclusive rights to manufacture and sell a chimeric antigen receptor (CAR or CAR T) therapy designed to treat B-cell lymphomas and leukemia.

Two CAR therapies have received FDA approval to treat hematological cancers: Kymriah® (tisagenlecleucel-T), sold by Novartis for $475,000 per treatment,[1] and Yescarta® (axicabtagene ciloleucel), sold by Gilead for $373,000 per treatment.[2] Hospital bills could bring total costs to receive the treatments as high as $1.5 million.[3]

CAR treatments have not been widely accessible to patients, in part due to questions about whether hospitals will be reimbursed for the costs of the treatment, which is exclusive of the hospital stays necessary to administer CAR therapies and care for their potential side effects.

The CAR inventions at issue here, as well as KEI's correspondence about the licenses with the NIH and the procedural history of this appeal, are discussed below.

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[1] Matthew Harper, *Patient Advocate Says Novartis' $475,000 Breakthrough Should Cost Just $160,000*, Forbes.com, February 8, 2018, available at https://www.forbes.com/sites/matthewherper/2018/02/08/patient-advocate-says-novartis-475000-breakthrough-should-cost-just-160000/#13e8be1b5152.

[2] Toni Clarke, Bill Berkrot, *FDA Approves Gilead cancer gene therapy; price set at $373,000*, Reuters, October 18, 2017, available at https://www.reuters.com/article/us-gilead-sciences-fda/fda-approves-gilead-cancer-gene-therapy-price-set-at-373000-idUSKBN1CN35H.

[3] Liz Szabo, *Cascade of Costs Could Push New Gene Therapy Above $1 Million Per Patient, Kaiser Health News*, Kaiser Health News, October 17, 2017, available at https://khn.org/news/cascade-of-costs-could-push-new-gene-therapy-above-1-million-per-patient/.

The Inventions

On July 12, 2019, the NIH published two notices of proposed exclusive licenses in the Federal Register: (1) Prospective Grant of an Exclusive Patent License: Allogeneic Therapy Using Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20 (84 FR 33270);[4] and (2) Prospective Grant of an Exclusive Patent License: Autologus Therapy Using Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20 (84 FR 33272).[5]

The licenses involve the same intellectual property (Bicistronic Chimeric Antigen Receptor (CAR) Constructs Targeting CD19 and CD20, U.S. Provisional Patent Application No. 62/732,263), the same prospective licensee (Kite Pharma), and the same terms (exclusive, worldwide rights). They differ in their application. The first license would pertain to an *allogeneic* use of CAR targeting CD19 and CD20, while the second license pertains to *autologic* use.

The potential indications of the subject technology are "B cell malignancies expressing CD19, CD20, or both."[6] According to the Federal Register notices, "CD19 and CD20 are expressed on the cell surface of several hematological malignancies, including Non-Hodgkins Lymphoma (NHL), acute lymphoblastic leukemia (ALL) and chronic lymphocytic leukemia (CLL)."[7]

Correspondence about the Licenses between KEI and the NIH

On July 12, 2019, Claire Cassedy, Research Associate and Assistant for Development with KEI, emailed Dr. David Lambertson, Senior Technology Transfer Officer with the National Cancer Institute (NCI), a list of ten questions designed to elicit information about whether the prospective licenses satisfy federal law and regulations governing the licensing of federally-owned technology.[8]

Dr. Lambertson responded on July 16, 2019. Of the 10 questions submitted by Ms. Cassedy, he answered only Questions 6, 8, and 9, erroneously stating that "[t]he other questions either ha[d] been answered previously or [were] not related to the criteria set forth in federal regulations."[9]

KEI Director James Love responded to Dr. Lambertson by email dated July 16, 2019, explaining the relevance of Ms. Cassedy's questions to the criteria governing exclusive licenses.[10] Dr. Lambertson did not respond to that email.

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[4] 84 Fed. Reg. 33270 (July 12, 2019).
[5] 84 Fed. Reg. 33272 (July 12, 2019).
[6] https://www.ott.nih.gov/technology/e-205-2018.
[7] 84 FR 33270; 84 FR 33272.
[8] *See* Attachment A.
[9] See *id.*
[10] *See* Attachment B.

Later that day, Mr. Love sent Dr. Lambertson an email asking why he refused to state whether the subject inventions were developed pursuant to a Cooperative Research and Development Agreement (CRADA) between the NIH and Kite. Dr. Lambertson did not respond to that email.[11]

Also on July 16, 2019, Mr. Love emailed Dr. Lambertson asking about the cost of manufacturing CAR T cells.[12] Dr. Lambertson responded, by email dated July 17, 2019, that he did not have access to such information.[13] Mr. Love replied by email that same day, asking who, within the NIH, does have access to such information.[14] Dr. Lambertson did not respond.

July 29, 2019 Comments

KEI timely submitted comments on the prospective licenses to the NIH on July 29, 2019, joined by UACT, SSW, UAEM, and Clare Love, a cancer patient who has suffered from lymphoma, one of the potential indications of the licensed invention.[15]

Final Determination Letters

On August 14, 2019, Dr. Lambertson emailed KEI two PDF documents which represented the final determinations of the National Cancer Institute regarding the licenses and which articulated the NCI's rationale for proceeding with the licenses over KEI's objections. The two documents, which are identical except that each pertains to a separate license, state that the comments did not persuade the NCI that the licenses were inconsistent with federal law.

The final determination letters are attached herein.[16]

B. STANDING

A right to appeal an exclusive license is afforded to: (1) A person whose 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 . . . and who can demonstrate . . . that such person may be damaged by the agency action. 37 C.F.R § 404.11(a).

Appellants satisfy the third basis for an appeal. We timely submitted our comments to the NIH, and appellant Clare Love is a lymphoma patient who could be damaged by the licenses.

[11] *See* Attachment C.
[12] *See* Attachment D.
[13] *See id.*
[14] *See* Attachment E.
[15] *See* Attachment F.
[16] *See* Attachments G, H.

An overly broad exclusive license that is inconsistent with 35 U.S.C. § 209 not only violates federal law but could harm patients, such as Mr. Love, who may need to access the licensed technology but could face unnecessary barriers to accessing the treatments, due to cost.

Also, KEI has had to divert resources in order to counteract the NIH's unlawful lack of transparency, which has frustrated KEI's mission.

C. ARGUMENT

Appellants appeal the NIH's decision to proceed with the licenses for the following six reasons:

1. The NIH did not properly evaluate the necessity of granting an exclusive license, for example, by considering other incentives such as FDA regulatory protection of test data, and patent protection from non-NIH patent holders;
2. Assuming that the NIH could establish that an exclusive license was necessary in this case, the NIH did not meet its statutory responsibility to limit the scope of rights to that which is "reasonably necessary" to induce the investment required to bring the invention to practical application, for example by analyzing the expected costs of investment and annual revenues to determine how many years of exclusivity are warranted;
3. The NIH did not request the advice of the Attorney General regarding whether the licenses would create or maintain a violation of federal antitrust laws;
4. The licenses violate 35 U.S.C. § 209(a)(4) because they will tend to substantially lessen competition by creating undue market concentration;
5. The public's right to evaluate a proposed license under 35 U.S.C. § 209(e) was undermined by the NIH's lack of transparency; and
6. The NIH has not done anything to implement to objectives in the PHS Technology Transfer Policy Manual regarding promoting access in developing countries.

This appeal addresses each issue in turn.

1. The licenses violate 35 U.S.C. § 209(a)(1) because the NIH did not properly evaluate the necessity of granting an exclusive license, for example, by considering other incentives such as FDA regulatory protection of test data, and patent protection from non-NIH patent holders.

Section 209 of the Bayh-Dole Act allows a federal agency to grant an exclusive license only if "granting the license is a reasonable and necessary incentive to . . . (A) call forth the investment capital and expenditures needed to bring the invention to practical application; or (B) otherwise promote the invention's utilization by the public[.]" 35 U.S.C. § 209(a)(1).

It is our understanding that the NIH has not undertaken a serious evaluation of the adequacy of existing incentives and subsidies, relating to practical application of the inventions, in order to evaluate whether or not granting an exclusive license was a "reasonable and necessary incentive."

Our comments note that in the United States, Gilead/Kite and Novartis have both received seven years of Orphan Drug exclusivity for Yescarta and Kymriah, as well as 12 year of test data protection.[17] In the European Union, those protections are 10 and 11 years, respectively. Similar protections exist in Japan, Canada, and in many other countries.

Table 1: Three U.S. Orphan Designations and Approvals for Yescarta and Two Orphan Designations and Approvals for Kymriah

Product	Basis of Designation	Date of Designation
axicabtagene ciloleucel	Treatment of follicular lymphoma	04/25/201
axicabtagene ciloleucel	Treatment of primary mediastinal B-cell lymphoma	04/20/2016
axicabtagene ciloleucel	Treatment of diffuse large B-cell lymphoma	03/27/2014
tisagenlecleucel	For the treatment of acute lymphoblastic leukemia	01/31/2014
tisagenlecleucel	Treatment of diffuse large B-cell lymphoma	02/03/2015

We also note that the FDA granted Novartis a priority review voucher for Kymriah,[18] an incentive that we estimate to be worth at least $80 million in the current market.

The NIH must take into consideration the likelihood that the new technologies will receive Orphan Drug market exclusivities and/or priority review vouchers, and evaluate the incentive that the 12 years of test data provides, even in the absence of an exclusive patent license.

The NIH/NCI's final determination letters do not address our argument about the necessity of granting additional exclusivities to Gilead as an incentive to market the technology. Rather, after briefly addressing competition-related issues, the letters conclusorily state: "Your other questions and statements either have been addressed in many previous responses to you or are not relevant to the statutory criteria for licensing."[19]

[17] https://www.accessdata.fda.gov/scripts/opdlisting/oopd/detailedIndex.cfm?cfgridkey=463114; https://www.accessdata.fda.gov/scripts/opdlisting/oopd/detailedIndex.cfm?cfgridkey=423914.
[18] 82 Fed. Reg. 42686 (Sept. 11, 2017).
[19] *See* Attachments G & H.

NIH has never addressed our arguments regarding the necessity of granting these specific exclusive licenses. As such, the NIH apparently takes the view that it is not required to consider that issue, in direct contradiction with 35 U.S.C. § 209(a)(1).

2. Assuming that the NIH could establish that an exclusive license was necessary in this case, the licenses violate 35 U.S.C. § 209(a)(2) because the NIH did not meet its statutory responsibility to limit the scope of rights to that which is "reasonably necessary" to induce the investment required to bring the invention to practical application, including in particular the number of years of exclusivity.

When proposing to license government-owned technology on an exclusive basis, a federal agency must not only determine whether exclusivity is a reasonable and necessary incentive to encourage a licensee to commercialize the licensed invention. Rather, before granting the license, the agency must also determine "that the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application[.]" 35 U.S.C. § 209(a)(2).

The scope of a license in federally-sponsored technology may vary along the following (non-exhaustive) parameters:

- The period of exclusivity - how long the licensee may claim a monopoly on the right to market and sell the invention (*i.e.*, five years, ten years, life of patent, etc.);
- Territorial reach (worldwide or limited to the U.S. or a particular geographic region); and
- Field of use (*i.e.*, targeted diseases).

The scope of the license must not exceed the incentive needed to induce a company to bring a government-owned invention to market. Factors that pertain to the necessary incentive include:

- The expected profitability of the invention;
- The costs of financing research and development and bringing the invention to market, including obtaining FDA approval;
- The government's investment in R&D and the development stage of the technology; and
- The cost to manufacture the invention.

a. It appears that the NIH has not performed the necessary analysis to determine the appropriate scope of the licenses.

For several reasons, it appears that the NIH has not performed the necessary analysis to determine the appropriate scope of the licenses.

First, as indicated by its response to KEI's questions regarding the licenses, the NIH appears to hold the erroneous view that information such as the government's contribution to the licensed technology and the stage of research and development of the invention is irrelevant to Section

209. That view is confirmed by the brief analysis in NIH's final determinations about the licenses. After giving a perfunctory nod to our objections about the anticompetitive effects of the licenses, the NIH states that our "other questions and statements have either been addressed in many previous responses to you or are not relevant to the statutory criteria for licensing."[20]

One of the questions posed by KEI, that the NIH refused to answer in advance of the comment deadline and did not address in its final determination letters, was as follows:

> "[H]as/will the NIH seek license terms that will ensure the resultant therapy is available to patients on reasonable terms?"[21]

It goes without saying that if the NIH views the issues presented by KEI as irrelevant, it does not consider them when executing licenses, in violation of the Bayh-Dole Act. But those issues relate directly to the criteria the NIH must consider under 35 U.S.C. § 209 and 37 C.F.R. § 404.7, since the incentive that is reasonably necessary is related to the prices that will be charged.

Rather than answering several of KEI's questions about the licenses, the NIH referred KEI to the NIH's past answers to questions about separate, unrelated licensing decisions. This strongly implies that the NIH assumes across-the-board positions about the appropriate scope of licenses without engaging in the individualized assessments mandated by Section 209.

One area in which the NIH fails to determine the appropriate scope of a license on a case-by-case basis is the duration of exclusivity.

The NIH's continued refusal to answer KEI's question about the duration of proposed licenses indicates that the NIH routinely grants licenses for the life of a patent, even though the number of years of exclusivity is directly and unambiguously related to the incentive to invest.

Recent correspondence between KEI and the NIH appears to confirm this. On August 20, 2019, KEI asked NIH Technology Transfer Officer Michael Shmilovich whether he was aware of any NIH exclusive licenses for which the term of the license is shorter than the term of the patent. Mr. Shmilovich responded that he did not "personally have any licenses on my docket granted for a term shorter than the full patent term" and that he was "unaware of any that may have been granted by my colleagues at other Institutes."[22]

This also seems to be confirmed by the NIH's model license agreements, which it publishes on its website,[23] and which serve as the basis of license negotiations.[24] The NIH's model Exclusive

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[20] *See* Attachments G & H.
[21] *See* Attachment A.
[22] *See* Attachment I.
[23] https://www.ott.nih.gov/resources#MLA.
[24] https://www.ott.nih.gov/licensing.

Patent License Agreement contains the following duration-of-exclusivity term: “This Agreement . . . shall extend to the expiration of the last to expire of the Licensed Patent Rights[.]”[25]

Finally, all of the NIH exclusive licenses granted by the NIH to Kite that were disclosed in Kite’s annual and quarterly SEC reports extend until the expiration of the last-filed patent.[26] KEI has no objections to the NIH collecting royalties for the life of patents, and indeed, often this is precisely what the government should do. But the term of exclusive rights should be limited in years to be shorter than the term of the patents, as it has in the past for several NIH licenses.

The idea that the NIH may default to negotiating license agreements that last the entire life of a patent is concerning for several reasons. As a legal matter, if the term of exclusivity is life of patent, no matter what the facts are, then the NIH is no longer meeting the requirements of 35 U.S.C. § 209 to ensure that the “scope of exclusivity is not greater than reasonably necessary.”

Factually, past experience refutes the notion that, in all cases, exclusivity extending for the life of a patent is necessary to incentivize a company to market the licensed technology. The NIH has granted licenses that were shorter than the life of a patent, and those collaborations succeeded.

In earlier years, the Department of Health and Human Services (HHS) regulated the term of exclusivity even for extramural funded inventions. For example, the cancer drug cisplatin (cisplatinum) was licensed to Bristol-Myers Squibb (BMS) by Research Corporation for a term of three years from the date of the first commercial sale in the United States, or eight years from the date of the exclusive license, whichever occurred first.[27] BMS petitioned HHS for and was granted an extension of the original exclusivity period to five years from the first commercial sale.[28] Before that exclusivity period expired, BMS requested a seven-year extension.[29] Several other companies competed for the license.[30] The NIH negotiated a five-year extension of the term with BMS, in order to incentivize additional research related to cisplatin, but in return BMS was required to lower the price of cisplatin by 30 percent[31] and contribute $35 million to cancer

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[25] https://www.ott.nih.gov/sites/default/files/documents/pdfs/NIH-Patent-License-Exclusive-model-102015.pdf. The Exclusive Patent Agreement provides grounds for earlier termination, such as if the licensee commits a material breach of the agreement or fails to commercialize the technology, but what KEI here seeks to emphasize is the fact that the default license term is the life of the latest-filed patent.

[26] *See* Table B, *supra*.

[27] 48 Fed. Reg. 53177 (Nov. 25, 1983).

[28] *Id.*

[29] *Id.*

[30] *Exclusive agreements between Federal agencies and Bristol-Myers Squibb Co. for drug development is the public interest protected?* Hearing before the H. Subcommittee on Regulation, Business Opportunities, and Energy of the Committee on Small Business, 102nd Cong. (1991), 350-377 at 354.

[31] 48 FR 53177.

research directed by the NIH staff.[32] HHS explained its rationale for granting a five-year extension, rather than the seven years requested by BMS, as follows:

> [G]iven the fact that Bristol has already had almost five years of an exclusive market for cisplatinum, and that the market for cisplatinum is expected to expand dramatically in the next few years, we believe that five years of additional exclusivity is a sufficient incentive to induce Bristol to undertake the commitments which it has offered and is the best decision in the public interest.[33]

In another example involving a National Cancer Institute invention, the NIH licensed the HIV drug ddI (didanosine) to BMS. The license term was initially exclusive, but gave the NIH the option of making the license nonexclusive before the expiration of the NIH patents,[34] which the NIH exercised in 2001.[35] A term of exclusivity less than the life of patent did not chill investment - several companies competed for the license.[36] Around the time of the ddI license, the NIH frequently granted 10 year periods of exclusivity.[37]

Whatever exclusivity period the NIH ultimately negotiates, it must do so on a case-by-case basis, in order to fulfill Section 209's mandate that before granting an exclusive license, a federal agency determines that "the proposed scope of exclusivity is no greater than reasonably necessary to provide the incentive for bringing the invention to practical application." The apparent failure to do so here violates the Bayh-Dole Act.

b. If the NIH had performed the analysis required by law, it would have concluded that even if an exclusive license was warranted, it would not need to be for the life of the patent.

The factors bearing on the appropriate term of a license necessarily involve making estimates of such items as:

1. The government's investment in R&D and the development stage of the technology;
2. The costs of financing the additional trials and other research and development costs necessary to obtain FDA approval;
3. The cost to manufacturing the product; and

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[32] *Exclusive agreements between Federal agencies and Bristol-Myers Squibb Co. for drug development is the public interest protected?* Hearing before the H. Subcommittee on Regulation, Business Opportunities, and Energy of the Committee on Small Business, 102nd Cong. (1991), 350-377 at 355.
[33] 48 FR 53177.
[34] *Id*.
[35] *See* National Institutes of Health Office of Technology Transfer, *Videx® Expanding Possibilities: A Case Study* (hereinafter, "Videx"), September 2003, available at https://www.ott.nih.gov/sites/default/files/documents/pdfs/VidexCS.pdf.
[36] *Id.*
[37] *Exclusive agreements between Federal agencies and Bristol-Myers Squibb Co. for drug development is the public interest protected?* Hearing before the H. Subcommittee on Regulation, Business Opportunities, and Energy of the Committee on Small Business, 102nd Cong. (1991), 350-377 at 362.

4. The expected profitability of the invention, over time.

If such analysis exists, it should have been provided to the public, in order to evaluate the proposed license terms. If such analysis does not exist, the NIH is not doing its job.

Profitability/Revenues

Yescarta, one of the two CAR therapies approved by the FDA, has been highly profitable for Gilead. As noted previously, Yescarta's list price is $373,000 per patient. In the first six quarters since its initial approval, Yescarta has netted $366 million, and its quarterly revenues from sales of Yescarta have increased significantly every quarter since its launch.[38] Kymriah's revenues have been doubling every six months, with $58 million in revenue in the 2nd quarter of 2019.[39]

As government and private sector third party payers sort out reimbursement issues, company revenues are expected to increase.

R&D Costs

The estimated costs to develop CAR therapies are low relative to their profit yields. The FDA reported that the approval of Kymriah and Yescarta were based upon evidence from clinical trials consisting of 63[40] and 108[41] patients, respectively. Carl June, M.D., the lead investigator for Kymriah's clinical trials, has estimated the per-patient costs of CAR T clinical trials at roughly $150,000 per patient,[42] making the total trial costs ($10 to $16 million before tax-credits and subsidies) trivial when compared to the profitability of such treatments.

Appellants noted in their comments that Yescarta and Kymriah were granted Orphan Drug status under the Orphan Drug Act of 1983, 21 U.S.C. §§ 360aa–360ee. Because the subject invention's field of use applies to similar rare disease indications, it is likely that it, too, will qualify for such status. The subsidies associated with Orphan Drug designation, including a 25% tax credit on clinical trials, must be taken into account when analyzing whether the scope of exclusivity is not greater than reasonably necessary to incentivize Kite/Gilead or some other company to commercialize the technology.

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[38] *See* Table 3, Appendix.
[39] *See id*.
[40] https://www.fda.gov/news-events/press-announcements/fda-approval-brings-first-gene-therapy-united-states
[41] https://www.fda.gov/downloads/BiologicsBloodVaccines/CellularGeneTherapyProducts/ApprovedProducts/UCM585388.pdf.
[42] https://www.keionline.org/30869.

Government Investment in the Technology

Gilead has benefitted from the government's investment in CAR T. Through its ownership of Kite, Gilead has assumed the benefit of at least three CRADAs between Kite and the NCI and seven exclusive license agreements, including the CRADA that led to the development of Yescarta. Many of those partnerships involve cell or gene therapies to treat cancer. Kite has acknowledged the role that public funding has played in developing its CAR therapies. Kite's 2015 SEC 10-k disclosure states: "A substantial portion of our research and development has been conducted by the NCI under the 2012 CRADA."[43]

Kite's relationship with the NCI is discussed in greater detail in Section C(4), *supra*.

Cost of Manufacturing CAR Therapies

Dr. Walid Gellad, co-director of the Center for Pharmaceutical Policy and Prescribing at the University of Pittsburgh, called Kymriah's $475,000 list price "outrageous" given the cost to manufacture it.[44]

Because the NIH declined to answer KEI's questions about the cost of manufacturing CAR T-cells, KEI must rely on the best available data. Dr. June once estimated that it costs about $15,000 to manufacture Kymriah,[45] a CAR therapy that is similar to the licensed inventions. Our discussions with European manufacturers of CAR T cells suggest that even with current bottlenecks in markets for reagents and other inputs, cells can be manufactured for between €25,000 to €50,000 per treatment, with costs expected to fall dramatically. Since the NIH is conducting and funding CAR T trials, it clearly has relevant information it is declining to make available.

The disparity between the cost of manufacturing CAR therapies and the prices that Gilead and Novartis charge for them weigh against granting additional, broad exclusive rights in the technology to Gilead, since it is predictable that patients and employers, governments and insurance companies that pay for the treatments will be gouged by Gilead.

3. As far as KEI can determine, the NIH did not request the advice of the DOJ regarding whether the licenses would create or maintain a violation of federal antitrust laws.

Under the Federal Property and Administrative Services Act, 40 U.S.C. §§ 101 *et seq.*, "[a]n 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." 40 U.S.C. § 559(b)(1).

[43] https://www.sec.gov/Archives/edgar/data/1510580/000156459016013699/kite-10k_20151231.htm.
[44] https://khn.org/news/cascade-of-costs-could-push-new-gene-therapy-above-1-million-per-patient/.
[45] https://khn.org/news/cascade-of-costs-could-push-new-gene-therapy-above-1-million-per-patient/.

This includes when the NIH proposes to grant an exclusive license in federally-owned technology. “Property” is defined at 40 U.S.C. § 102 to mean “any interest in property,” with certain exceptions that do not include patents. Similarly, Section 559 creates certain exceptions that do not include patents.

41 C.F.R. § 102-75.270 supports the notion that the term “property” in Section 559 includes intellectual property rights such as patents.

41 C.F.R. § 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.

KEI asked the NIH whether it requested the advice of the U.S. Attorney General concerning the licenses. The NIH declined to answer, instead referring KEI to its past answers to the question.

On February 13, 2018, KEI emailed Dr. Lambertson and Karen Rogers, Acting Director of the 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 Section 559.

Ms. Rogers responded as follows:

> “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 government by the Bayh-Dole Act and its regulations.”[46]

The NIH’s statement about the applicability of 40 U.S.C. § 559 is incorrect.

The Bayh-Dole Act expressly incorporates federal antitrust laws. 35 U.S.C. § 209(a)(4) allows a federal agency to grant an exclusive license only if the license “will not tend to substantially lessen competition or create or maintain a violation of the Federal antitrust laws.” 35 U.S.C. § 211 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[.]” The Bayh-Dole Act sets out the areas in which the statute “shall take precedence over any other Act

[46] *See* Attachment J.

which would require a disposition of rights in subject inventions[,]" 35 U.S.C. § 210, and mentions 21 separate statutes, but not the FPASA.

Second, 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.

Finally, by granting a fully-exclusive license in a federally-owned invention for life of patent, and allowing termination of the license only in narrow, vaguely-defined circumstances, the NIH is effectively disposing of a government property interest so as to trigger 40 U.S.C. § 559.

4. The licenses are unauthorized under 35 U.S.C. § 209(a)(4) because they "tend to substantially lessen competition or create or maintain a violation of Federal antitrust laws."

Under 35 U.S.C. § 209(a)(4), before granting an exclusive license, a federal agency must ensure that "granting the license will not tend to substantially competition or create or maintain a violation of the Federal antitrust laws."

The grant of two additional exclusive licenses in federally-sponsored CAR technologies to treat blood disorders to Gilead via Kite, which has already enjoyed an advantage over competitors through its relationship with the NCI, will tend to substantially lessen competition in the market of CAR T therapies to treat hematological disorders.

Since 2012, the NCI has entered into at least three CRADAs and seven exclusive licenses with Kite relating to CAR technologies and other cancer treatments. In its SEC filings, Kite touts its strong relationship with the NCI,[47] and the close relationship between Kite and the NIH/NCI was explored in a front page story in the New York Times titled "*Public Labs, Corporate Gains: Harnessing the U.S. Taxpayer to Fight Cancer and Make Profits*."[48]

NIH's partnerships with Kite are explained in greater detail below.

The 2012 NCI-Kite CRADA

Gilead acquired Kite in October 2017 for $11.2 billion. In so doing, Gilead acquired the rights to Yescarta,[49] a CAR therapy that benefited heavily from federal funding. The technology behind

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[47] *See, e.g.*, https://www.sec.gov/Archives/edgar/data/1510580/000151058017000003/kite20161231-10k.htm ("Our strong relationship with the NCI is bolstered by our President and Chief Executive Officer's relationship with Dr. Rosenberg of the NCI.").

[48] Matt Richtel and Andrew Pollack, *Public Labs, Corporate Gains: Harnessing the U.S. Taxpayer to Fight Cancer and Make Profits*, N.Y.Times, Dec. 19, 2019, available at https://www.nytimes.com/2016/12/19/health/harnessing-the-us-taxpayer-to-fight-cancer-and-make-profits.html.

[49] https://www.sec.gov/Archives/edgar/data/882095/000088209518000008/a2017form10-k.htm

Yescarta was developed in NCI labs pursuant to a CRADA executed in 2012 between NCI and Kite, with Dr. Steven A. Rosenberg as the Principal Investigator.[50]

The 2016 NCI-Kite CRADAs

Gilead likely will obtain even more rights in CAR therapies to treat B cell lymphomas through a second CRADA executed between Kite and the NIH in 2016. CRADAs typically grant the industry-collaborator the option of retaining exclusive rights in any intellectual property developed pursuant to the agreement. On January 4, 2016, Kite entered into a CRADA with NIH to develop anti-CD19 car therapies to treat B cell lymphomas and leukemias. The CRADA will expire January 4, 2021 and "will focus on the development of next-generation CAR programs directed against other novel antigens for the treatment of B cell lymphomas and leukemias."[51]

In June 2016, Kite entered into a CRADA with the NCI to pursue clinical development of "T-cell receptor (TCR) product candidates directed against human papillomavirus (HPV)-16 E6 and E7 oncoproteins for the treatment of HPV-associated cancers."[52]

Exclusive Licenses between Gilead (through Kite) and NCI

In 2017, NIH proposed a broad license to Kite in an autologus CAR immunotherapy targeting the CD30 antigen, for the treatment of diseases such as Hodgkin lymphoma, Non-Hodgkin lymphoma, and diffuse large B cell lymphoma, the same indications as the licensed invention.[53]

In addition, Gilead now owns exclusive licensing rights to a slew of government-financed cell or gene therapies, as the successor in interest to the following exclusive licenses with NIH.

Table 2: NIH Exclusive Licenses to Kite in Government-Owned Inventions

Date	Terms	Invention
April 11, 2013	Exclusive, worldwide, life of patent[54]	"a CAR-based product candidate that targets the EGFRvIII antigen for the treatment of brain cancer, head and neck cancer and melanoma, and a TCR-based product candidate that targets the SSX2 CTA for the treatment of head and neck cancer, hepatocellular carcinoma, melanoma, prostate cancer, and sarcoma"
May 29, 2014	Exclusive, worldwide,	"TCR-based product candidates that target the NY-ESO-1 antigen for the treatment of any NY-ESO-1 expressing cancers"

[50] *See* Kite Pharma, Inc.'s Amended Answer and Countercl. para. 19, *Juno Therapeutics, Inc. et al. v. Kite Pharma, Inc.*, No. CV 17-7639-SJO-KSX (C.D. Cal. March 29, 2018).
[51] https://www.sec.gov/Archives/edgar/data/1510580/000156459016013699/kite-10k_20151231.htm
[52] For more information about the NIH-Kite CRADAs, *see* Table 5, Appendix.
[53] For a list of all notices of proposed exclusive licenses to Kite, *see* Table 4, Appendix.
[54] https://www.sec.gov/Archives/edgar/data/1510580/000156459015010571/kite-10q_20150930.htm

	life of patent[55]	
June 2, 2014	Exclusive, worldwide, life of patent.[56]	"TCR-based product candidates that target the NY-ESO-1 antigen for the treatment of any NY-ESO-1 expressing cancers"
December 31, 2014	Exclusive, worldwide, life of patent[57]	"TCR-based product candidates that target HPV antigens E6 and E7 of the HPV subtype 16"
October 1, 2015	Exclusive, worldwide, life of patent[58]	"TCR-based product candidates directed against MAGE A3 and A3/A6 antigens for the treatment of tumors expressing MAGE"
July 2016	Exclusive, worldwide, term not stated[59]	"Fully human anti-CD19 chimeric antigen receptor-based product candidate directed against B-cell malignancies"
September 2016	Exclusive, worldwide, term not stated[60]	"T-cell receptor (TCR) based product candidates for the treatment of tumors expressing mutated KRAS antigens"

Gilead's Market Concentration of Gene Therapies to Treat Hematological Cancers

Gilead has acquired vast rights in CAR T and other gene therapies to treat hematological cancers. It lists the following product candidates as part of its technology suite:

Excerpt from Gilead's 2018 SEC 10-k Filing

Product Candidates for the Treatment of Hematology/Oncology

[55] https://www.sec.gov/Archives/edgar/data/1510580/000156459015010571/kite-10q_20150930.htm.
[56] https://www.sec.gov/Archives/edgar/data/1510580/000156459016013699/kite-10k_20151231.htm.
[57] https://www.sec.gov/Archives/edgar/data/1510580/000151058017000011/kite10q6-30x17.htm.
[58] https://www.sec.gov/Archives/edgar/data/1510580/000151058017000011/kite10q6-30x17.htm.
[59] https://www.biospace.com/article/releases/kite-pharma-announces-exclusive-license-with-nih-for-fully-human-anti-cd19-chimeric-antigen-receptor-car-product-candidate-to-treat-b-cell-malignanc/.
[60] https://www.biospace.com/article/releases/kite-pharma-announces-exclusive-license-with-nih-for-multiple-neoantigen-directed-t-cell-receptor-tcr-product-candidates-to-treat-solid-tumors-expre/.

Product Candidates	Description
Products in Phase 3	
Axicabtagene ciloleucel	Axicabtagene ciloleucel is being evaluated for the treatment of second line diffuse large B-cell lymphoma (DLBCL).
Products in Phase 2	
Axicabtagene ciloleucel	Axicabtagene ciloleucel is being evaluated for the treatment of indolent non-Hodgkin lymphoma. Axicabtagene ciloleucel is also being evaluated for the treatment of DLBCL in combination with anti-PD-L1 mAB and first line DLBCL.
Tirabrutinib	Tirabrutinib, a BTK inhibitor, is being evaluated for the treatment of B-cell malignancies.
KTE-X19	KTE-X19, a CAR T cell therapy, is being evaluated for the treatment of mantle cell lymphoma and adult and pediatric acute lymphoblastic leukemia.
Products in Phase 1	
KITE-718	KITE-718, a MAGE A3/A6, is being evaluated for the treatment of solid tumors.

Consequences of Undue Market Concentration

Undue market concentration will have negative consequences for American cancer patients and taxpayers, employers, and others who pay for such treatments.

The two CAR therapies to receive FDA approval, Yescarta and Kymriah, start at $373,000 and $475,000, respectively, and those prices are exclusive of hospital costs.

The high launch prices of CAR therapies provide a compelling reason not to grant further market concentration in these products to a company like Gilead.

Price and market exclusivity are directly linked: According to healthcare policy experts, "[t]he most important factor that allows manufacturers to set high drug prices for brand-name drugs is market exclusivity[.]"[61]

Evidence of Gilead's own price-setting strategies confirms this statement.

Gilead's pricing strategy for Sovaldi was more focused on maximizing revenue through expanding its market share than it was on broadening patient access, according to a 2015 Senate Finance Committee investigation, which concluded as follows:

[61] Kesselheim, et al.,*The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform*, JAMA, August 23, 2016.

> Over the eight months Gilead spent determining the price of Sovaldi, the company repeatedly made clear its primary focus was outmaneuvering potential competitors to ensure its drugs had the greatest share of the market, for the highest price, for the longest period of time.[62]

The report found that Gilead could have made a profit on Sovaldi by charging $55,000 for a 12-week course of treatment, yet chose to charge $84,000, a price that would deliver higher profits but result in fewer patients being treated.[63]

Granting the exclusive licenses to a competitor, rather than to Gilead, would have introduced new competitors into the market, and could have helped bring prices down.

NCI has not articulated a logical rationale for concluding, over our objections, that giving additional rights in CAR to Gilead would be consistent with 35 U.S.C. § 209(a)(4). In its final determinations, NCI considers only two facts: the existence of a single competitor, Novartis, in the relevant market, and the fact that the licenses do not extend to all fields of use.

The NIH's reliance on the existence of one other competitor in the market is misplaced. In NIH's line of reasoning, a license will satisfy 35 U.S.C. § 209(a)(4) so long as there is one other manufacturer of a similar therapy in the same field of use. Yet 35 U.S.C. § 209(a)(4) does not ask whether a license will eliminate all other competitors. Rather, it prohibits an exclusive license that "will tend to *substantially lessen* competition[.]"

If NIH does not consider itself equipped to engage in a legitimate analysis of the potential anticompetitive effects of its licensing decisions, that would provide a compelling reason for it comply with 40 U.S.C. § 559, which requires federal agencies to seek the advice of the U.S. Attorney General when disposing of government property, including intellectual property rights. As a matter of practice, the NIH does not seek out such advice.

5. The NIH's lack of transparency regarding the licenses impeded the public's right to comment.

A federal agency may not grant an exclusive license in government-owned technology without first notifying the public of the prospective license, allowing a minimum 15-day period for the public to comment, and considering all timely submitted comments. 35 U.S.C. § 209(e).

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[62] Senate Finance Committee, *Executive Summary, The Price of Sovaldi and its Impact on the U.S. Healthcare System*, December 2015, available at https://www.finance.senate.gov/imo/media/doc/11%20SFC%20Sovaldi%20Report%20Executive%20Summary.pdf.

[63] S. Rep. No. 114-20, at 20-22 (2015), available at https://www.finance.senate.gov/imo/media/doc/1%20The%20Price%20of%20Sovaldi%20and%20Its%20Impact%20on%20the%20U.S.%20Health%20Care%20System%20(Full%20Report).pdf.

In order for the public to meaningfully participate in the notice-and-comment process, it must have basic information about the licenses. Because the NIH failed to provide sufficient information in its federal register notices, KEI was required to request that information directly from the agency. It did so on July 12, 2019, when KEI Researcher Claire Cassedy emailed Dr. Lambertson a list of 10 questions related to the criteria for granting an exclusive license. The questions addressed issues such as the stage of research and development of the invention, whether any clinical trials were associated with the technology, the duration of the licenses, whether NIH sought the advice of the Attorney General under 40 U.S.C. § 559, and how the NIH would negotiate license terms to ensure access to the resultant products on reasonable terms.[64]

Dr. Lambertson refused to answer seven of the 10 questions, erroneously asserting that the questions "either ha[d] been answered previously or [were] not related to the criteria . . . regarding a decision by a federal agency to grant an exclusive license."[65]

KEI reviewed the NIH's past answers to KEI's questions regarding prospective licenses to determine whether the NIH had answered them previously. It had not. The NIH refused to answer questions about government funding on the basis that it purportedly did not have access to such information or the information was not within its purview. In response to past questions about the duration of a prospective license, the NIH asserted that the term had yet to be negotiated or was confidential. And the NIH has asserted erroneous objections that KEI's questions seek irrelevant information and that the agency is not required to seek the advice of the Attorney General under 40 U.S.C. § 559.

None of the NIH's justifications for its lack of transparency pass muster. KEI's questions bear directly on the criteria governing government licenses of federally-owned technologies. When taxpayers invest tens of billions of dollars annually in biomedical research and development, the NIH should be able to tell the American public how much of its taxpayer dollars are used to finance the development of a particular technology.

The NIH should not promise confidentiality to prospective licensees with respect to licensing terms that bear directly on whether the scope of a license is not greater than reasonably necessary to incentive the commercialization of government-owned technology, a matter on which the public is entitled to comment.

Moreover, licensing terms such as the duration of a license and royalty payments to the NIH are often disclosed by companies such as Kite in their SEC filings. In a 2017 quarterly SEC report, for example, Kite disclosed a number of NIH exclusive licenses that were set to "expire upon expiration of the last patent contained in the licensed patent rights[.]"[66]

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[64] *See* Attachment A.
[65] *See id.*
[66] https://www.sec.gov/Archives/edgar/data/1510580/000151058017000011/kite10q6-30x17.htm.

In any event, when it comes to government licensing of publicly-financed technologies, the public's right to know the terms of the licenses and what the public has spent on the inventions outweighs any private interest in non-disclosure. To maintain that the NIH need not disclose to the public information that is directly relevant to the appropriateness of the licenses would be to render the public's right of comment at 35 U.S.C. § 209(e) a nullity.

6. The NIH has not implemented objectives in the PHS Technology Transfer Policy Manual regarding promoting access in developing countries.

The PHS's licensing policy is governed by the following principle, among others:

"PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries."[67]

In our July 29, 2019 comments, we asked that the NIH not grant the licenses unless efforts were made to ensure access in developing countries.[68]

Access to CAR therapies in developing countries is effectively nonexistent today, outside of China. All of the individuals and groups who cosigned the comments and join this appeal believe that governments should license intellectual property in a way that enables more equal access. How we treat patients in low-income countries goes to the character of the people who manage the NIH and its technology transfer offices. There are at least five billion people in the world who live in resource-poor countries, not even counting China, and who have at best extremely unequal access, if any, to the new NIH-funded cell and gene therapies. Someone working in a public institution should see this is a real problem, and one that deserves some actual attention.

We object to any licenses that do not satisfy PHS's governing licensing principle of promoting access in developing countries.

It would be quite simple to at least ask the licensee to provide a plan, made public so there is some accountability, as to how access will be extended to countries with per capita incomes less than 30 percent of the United States. Not even making this part of the negotiation is appalling and inconsistent with PHS's own stated licensing policies.

D. CONCLUSION

For all of the reasons stated above, appellants request that the NIH reverses its decision to proceed with the licenses at issue and reopen the licenses to competitive bidding, unless they

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[67] PHS, *United States Public Health Service Technology Transfer Manual*, Chapter No. 300, PHS Licensing Policy, available at https://www.ott.nih.gov/sites/default/files/documents/policy/pdfs/300-policy.pdf.

[68] *See* Attachment F.

include the public interest safeguards referred to in our submitted comments and the NIH seeks and obtains the antitrust advice from the Attorney General, who confirms that the licenses will not create or maintain a situation inconsistent with federal antitrust laws.

We request a hearing on this appeal.

Sincerely,

Knowledge Ecology International
Social Security Watch
Universities Allied for Essential Medicine
Union for Affordable Cancer Treatment
Clare Love

APPENDIX

Table 3: Yescarta and Kymriah Sales in Millions of U.S. Dollars

	2019 Q1	2018 Q4	2018 Q3	2018 Q2	2018 Q1	2017 Q4
Yescarta	$96	$80	$75	$68	$40	$7
Kymriah	$45	$28	$20	$16	$12	$7

Table 4: Previous Federal Register Notices Listing Kite as Prospective Licensee

Date	Notice Title and URL
01/24/ 2012	"Prospective Grant of Exclusive License: Development of T Cell Receptors and Chimeric Antigen Receptors Into Therapeutics for Adoptive Transfer in Humans To Treat Cancer" Link: https://www.federalregister.gov/d/2012-1383
03/25 2014	"Prospective Grant of Exclusive License: Development of T Cell Receptors for Adoptive Transfer in Humans to Treat Cancer" Link: https://www.federalregister.gov/d/2014-06412
10/16/ 2014	"Prospective Grant of Exclusive License: Development of T Cell Receptors for Adoptive Transfer in Humans To Treat Cancer" Link: https://www.federalregister.gov/d/2014-24502

06/26/ 2015	“Prospective Grant of Exclusive License: The Development of an Anti-CD19 Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancers” Link: https://www.federalregister.gov/d/2015-15657
08/17/ 2016	“Prospective Grant of Exclusive Patent License: Development of T Cell Receptors (TCRs) Targeting the KRAS G12D Mutation for the Treatment of Cancer” Link: https://www.federalregister.gov/d/2016-19549
10/05/ 2016	“Prospective Grant of Exclusive Patent License: Development of Anti-CD70 Chimeric Antigen Receptors for the Treatment of CD70 Expressing Cancers” Link: https://www.federalregister.gov/d/2016-24030
12/20/ 2017	“Prospective Grant of an Exclusive Patent License: The Development of an Anti-CD30 Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer” Link: https://www.federalregister.gov/d/2017-27416

Table 5: Previous CRADAs Between the NIH and Kite

Date	CRADA Title and Number
08/31/ 2012	“Cooperative Research and Development Agreement for the Development of NCI Proprietary Peripheral Blood Autologous T Cell Therapies Using Genetically Modified Peripheral Blood Lymphocytes that Express NCI Proprietary T-cell Receptors and/or Chimeric Antigen Receptors for Use in Immunotherapy for Patients with Metastatic Cancer, Utilizing the Expertise of Kite Pharma in the Development and Manufacturing of Cancer Immunotherapies” Number: C-064-2012/0
06/09/ 2016	“Clinical Development of T Cell Receptor Gene Therapy Targeting HPV-16 E6 and E7 for HPV-Associated Cancers” Number: C-070-2016/0
01/04/ 2016	“Clinical Evaluation of NCI-hCD19-CAR, a CD19-Targeting Chimeric Antigen Receptor (CAR) for the Treatment of B Cell Lymphoma and B cell Leukemia, and the Development of Novel CARs Targeting B Cell Malignancies” Number: C-017-2016/0