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Via email: david.lambertson@nih.gov

Re: 84 FR 33270, Prospective Grant of an Exclusive Patent License: Allogeneic Therapy Using Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20; and 84 FR 33272, Prospective Grant of an Exclusive Patent License: Autologus Therapy Using Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20, to Kite Pharma, Inc. located in Santa Monica, CA.

Dear Dr. Lambertson:

Knowledge Ecology International (KEI), Social Security Works (SSW), Union for Affordable Cancer Treatment (UACT), Universities Allied for Essential Medicines (UAEM) and Clare Love, a cancer patient, are writing to provide comments on the prospective grant of exclusive patent licenses concerning allogeneic and autologous therapies using bicistronic chimeric antigen receptors (CARs) targeting CD19 and CD20, to Kite Pharma, Inc. ("Kite") located in Santa Monica, CA.

The license should be rejected on the grounds that it is anticompetitive

The license appears to give Gilead/Kite exclusive rights on two patented inventions that would provide treatments directly in competition with other patented inventions the National Institutes of Health (NIH) has already licensed to Gilead, including those involving CAR technologies for the treatment for the exact same diseases as earlier licenses. As far as we can determine, the NIH has failed to request the advice of the Attorney General regarding the competition issues, as is required by 40 U.S.C. § 559.

Since 2012, the NIH has entered into several Cooperative Research and Development Agreements (CRADAs) and exclusive licenses with Gilead relating to CAR technologies. The close relationship between the NIH and Gilead/Kite officials was explored in a front page story in the New York Times on December 19, 2019, by Matt Richtel and Andrew Pollack, titled: Public Labors, Corporate Gains: Harnessing the U.S. Taxpayer to Fight Cancer and Make Profits.[1]

The Gilead/Kite CAR T treatment Yescarta was licensed from the NIH, and approved by the US Food and Drug Administration (FDA) “for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.”[2]

[1] https://www.nytimes.com/2016/12/19/health/harnessing-the-us-taxpayer-to-fight-cancer-and-make-profits.html
[2] https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/yescarta-axicabtagene-ciloleucel

In 2017, the NIH proposed a broad license[3] to Gilead/Kite for CD30 chimeric antigen receptor (CAR)-based immunotherapy using autologous T-cells, for the treatment of:

- 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).

In the current case, the NIH is proposing two more exclusive licenses to Gilead/Kite for CAR technologies.

The Federal Register (FR) notice indicates the field of use for the new technologies as:

> "The development, production and commercialization of an anti-CD19 anti-CD20 dual targeting chimeric antigen receptor (CAR)-based immunotherapy . . . where the CAR has at least:
>
> (1) A dual antigen specificity;
> (2) the complementary determining region (CDR) sequences of the anti-CD19 antibody known as Hu19;
> (3) the complementary determining region (CDR) sequences of the anti-CD20 antibody known as 2.1.2; and
> (4) a T cell signaling domain;
>
> for the treatment of B-cell derived human cancers."
>
> This technology discloses the development of chimeric antigen receptors that recognize both the CD19 and CD20 cell surface proteins. 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).

The field of use is for a range of B-cell derived human cancers and overlaps with the diseases covered in the previous licenses to Gilead/Kite.

By providing a life-of-patent license to Gilead/Kite for this new technology, the NIH is foreclosing the opportunity for competition with Gilead, by one or more companies.

[3] https://www.federalregister.gov/d/2017-27416

We question the presumption that this technology, which has not even been published yet, and for which a patent has yet to be granted, needs to be licensed on an exclusive basis.

We note that Gilead/Kite received 7 years of Orphan Drug exclusivity for Yescarta, and Novartis received 7 years of Orphan Drug exclusivity for Kymriah, in addition to 12 years of test data protection. So the proposed grant of two exclusive licenses on these technologies appears a gratuitous award of a monopoly on publicly-funded research to Gilead/Kite, the firm that has already benefited enormously from previous federal licenses. Note that Kite's Yescarta CAR T therapy benefited from an NIH CRADA and exclusive licenses, and the company was sold to Gilead for $11.8 billion, based primarily on the NIH-licensed technology.

In the first six quarters since its initial approval, despite massive challenges in securing third party reimbursements for a new technology and a very slow European launch, Yescarta has earned $366 million, including $96 million in the first three months of 2019.

Yescarta and Kymriah Sales in millions of USD

	2019Q1	2018Q4	2018Q3	2018Q2	2018Q1	2017Q4
Yescarta	$96	$80	$75	$68	$40	$7
Kymriah	$45	$28	$20	$16	$12	$7
Sources	https://www.sec.gov/Archives/edgar/data/882095/000088209519000014/q119form10-q.htm https://www.sec.gov/Archives/edgar/data/882095/000088209518000015/q118form10-q.htm https://www.sec.gov/Archives/edgar/data/882095/000088209518000022/q218form10-q.htm https://www.sec.gov/Archives/edgar/data/882095/000088209518000029/q318form10-q.htm https://www.sec.gov/Archives/edgar/data/882095/000088209519000006/a2018form10-k.htm https://www.novartis.com/sites/www.novartis.com/files/q1-2019-media-release-en.pdf https://www.novartis.com/sites/www.novartis.com/files/q1-2018-media-release-en.pdf https://www.novartis.com/sites/www.novartis.com/files/2018-10-interim-financial-report-en.pdf https://www.novartis.com/sites/www.novartis.com/files/q4-2018-media-release-en.pdf https://www.sec.gov/Archives/edgar/data/1114448/000137036819000002/a19013020f.htm					

The first two CAR T treatments (Kymriah and Yescarta) were approved by the US FDA on the basis of evidence from 63[4] and about 100 patents[5], respectively. The per patient costs of such trials was estimated by Professor Carl June at roughly $150,000 per patient, making the trial costs trivial ($10 to $15 million), relative to revenues, even with adjustments for trial failures, and the challenges of securing reimbursements for a novel technology that has a price tag roughly 60 percent higher than the cost of buying a house,[6] a purchase often financed over 30 years.

The NIH license of yet another B-cell CAR T treatment to Gilead/Kite for the treatment of hematological malignancies will increase concentration, and protect Yescarta and Kymriah from

[4] https://www.fda.gov/news-events/press-announcements/fda-approval-brings-first-gene-therapy-united-states

[5] https://www.fda.gov/news-events/press-announcements/fda-approves-car-t-cell-therapy-treat-adults-certain-types-large-b-cell-lymphoma

[6] https://www.zillow.com/home-values/

price competition at a time when the new cell- and gene-therapies present emerging threats to health care budgets, and the high prices for treatments, which have nothing to do with R&D or cell manufacturing costs, are associated with rationing.

The license should be rejected on the grounds that it lacks sufficient safeguards for the public.

The NIH is highly secretive about its licensing practices, but as far as we can tell from Dr. Francis Collins' public statements and the frequent feedback we get from NIH licensing officials, the NIH is opposed to placing any conditions on the pricing of treatments, makes no effort to limit the years of exclusivity on licenses, and does nothing to ensure access in developing countries. For these reasons alone, we oppose the grant of the exclusive license, as a violation of the requirements to make inventions "available to the public on reasonable terms" [35 U.S.C. § 201(f)], to limit the scope of rights to that which is reasonably necessary [35 U.S.C. § 209], to avoid unreasonable use of inventions (35 U.S.C. § 200), and to implement patent rights in a manner "to protect public health and, in particular, to promote access to medicines for all" [2001 WTO Doha Declaration on TRIPS and Public Health].

The NIH has also opposed efforts to promote more transparency of the value chain for biomedical inventions, which runs counter to the objectives of the World Health Assembly resolution WHA72.8, "Improving the transparency of markets for medicines, vaccines, and other health products," adopted on May 28, 2019, with strong support of the U.S. government.[7]

The license should be rejected on the grounds that the process lacks transparency.

The NIH is licensing the exclusive rights to a patent application that has never been published.

The NIH refused to provide information about what it has spent on R&D for the licensed technology, what it costs to manufacture the cells for the licensed technology, and what the NIH has spent on previous CAR T trials, all highly relevant facts for deciding if an exclusive license is justified and what the term of exclusivity should be.

The NIH's lack of response to requests for information.

On July 12, 2019, Claire Cassedy from KEI sent you an email with ten questions about the two proposed exclusive licenses. You replied to this email on July 16, 2016, referring only to three of the ten questions raised, and failed to address the remaining questions of her July 12, 2019,

[7] http://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_R8-en.pdf

email. On July 16, 2019, KEI Director James Love sent you an additional email noting that failing to address the questions raised was withholding information that we need to comment on the proposed license. You did not respond to the July 16, 2019 email by James Love. Attached herein are the two emails we sent you, and your July 16, 2019 response.

The NIH should comply with 40 U.S.C. § 559, which is not preempted by the Bayh-Dole Act.

At the appropriate time in the licensing process, we expect the NIH to obtain advice from the Attorney General (as is required under 40 U.S.C. § 559) to determine if the "disposal to a private interest would tend to create or maintain a situation inconsistent with antitrust law."

The Bayh-Dole Act provides that "[n]othing in this chapter shall be deemed to convey to any person immunity from civil or criminal liability, or to create any defenses to actions, under any antitrust law[.]" 35 U.S.C. § 211.

The Bayh-Dole Act sets out the areas where the statute "shall take precedence over any other Act which would require a disposition of rights in subject inventions[,]" 35 U.S.C. § 210, and mentions 21 separate statutes, but does not include 40 U.S.C. § 559.

Kite Pharma

According to the Federal Register notice, the prospective licensee is Kite Pharma, located in Santa Monica, CA. Kite Pharma was purchased by Gilead Sciences ("Gilead") in October 2017 for $11.9 billion and is now a wholly-owned subsidiary of Gilead.[8]

In October 18, 2017, the Food and Drug Administration (FDA) approved Yescarta, a cell therapy marketed by Kite/Gilead indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma.[9] At launch, Kite/Gilead set the price for Yescarta at $373,000 for a course of treatment. The federal agency contract V797D-70252,[10] signed between the U.S. Veterans Affairs (VA) and Gilead, has a Federal Supply Schedule price for Yescarta of $373,000 as of July 15, 2019.[11] According to the same contract V797D-70252, the Big4 price for Yescarta is $284,904.52. In both cases, the "price stop date" is September 29, 2022.

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[8] https://www.gilead.com/news-and-press/press-room/press-releases/2017/8/gilead-sciences-to-acquire-kite-pharma-for-119-billion

[9] https://www.fda.gov/media/108458/download

[10] https://www.vendorportal.ecms.va.gov/nac/Search/Details/V797D-70252

[11] A list of all VA prices, including for Yescarta, is available here: https://www.va.gov/opal/nac/fss/pharmPrices.asp

Intellectual property to be licensed

Both Federal Register notices 84 FR 33270 and 84 FR 33272 cite one provisional patent application filed in the U.S.: 62/732,263, entitled “Bicistronic Chimeric Antigen Receptors Targeting CD19 and CD20 and Their Uses”; and have a catchall phrase suggesting that the proposed license could also cover “[...] U.S. and foreign patent applications claiming priority to the aforementioned application.”

We searched the cited provisional patent application using the USPTO Public Patent Application Information Retrieval (PAIR) system and the Patent Application Full Text and Image Database (AppFT). This search returned zero results. We note that the USPTO normally does not publish these types of applications, pursuant to 35 U.S.C. § 122. In order to have a clear understanding of the intellectual property that will be covered in the license we have to be able to read the patent claims. Not being able to scrutinize this document prior to the deadline established in the Federal Register notice undermines our ability to understand and comment on whether the proposed license is “a reasonable and necessary incentive” as provided under 35 U.S.C. § 209, and the extent that the license creates unwanted market concentration for B-Cell CAR therapies.

The field of use described in the Federal Register notice 84 FR 33270 is as follows:

> “The development, production and commercialization of an anti-CD19 anti-CD20 dual targeting chimeric antigen receptor (CAR)-based immunotherapy using allogeneic (where the donor and the recipient are different) immune cells, wherein the genome editing is meditated only by zinc-finger nucleases, and where the CAR has at least:
>
> (1) A dual antigen specificity;
>
> (2) the complementary determining region (CDR) sequences of the anti-CD19 antibody known as Hu19;
>
> (3) the complementary determining region (CDR) sequences of the anti-CD20 antibody known as 2.1.2; and
>
> (4) a T cell signaling domain;
>
> for the treatment of B-cell derived human cancers.”

The field of use described in the Federal Register notice 84 FR 33272 is as follows:

> “The development, production and commercialization of an anti-CD19 anti-CD20 dual targeting chimeric antigen receptor (CAR)-based immunotherapy using autologous (meaning one individual is both the donor and the recipient) immune cells transfected with either a viral or non-viral vector, wherein the vector expresses a CAR having at least:
>
> (1) A dual antigen specificity;
>
> (2) the complementary determining region (CDR) sequences of the anti-CD19 antibody known as Hu19;
>
> (3) the complementary determining region (CDR) sequences of the anti-CD20 antibody known as 2.1.2; and
>
> (4) a T cell signaling domain;
>
> for the treatment of B-cell derived human cancers.”

The field of use proposed in the Federal Register notice 84 FR 33270 relates to a CAR-based immunotherapy using **allogeneic (where the donor and the recipient are different)** immune cells, wherein the genome editing is mediated only by zinc-finger nucleases. The field of use described in the Federal Register notice 84 FR 33272 relates to a CAR-based immunotherapy using **autologous (meaning one individual is both the donor and the recipient)** immune cells transfected with either a viral or non-viral vector.

Geographic scope

According to both Federal Register notices 84 FR 33270 and 84 FR 33272, the territory of the proposed license “may be worldwide.” Since the provisional application was filed September 17, 2018, it is still within the deadline to start direct national filings claiming the priority of the application 62/732,263 under the Paris Convention and to start a PCT procedure. As we understand it, the catchall phrase “[...] U.S. and foreign patent applications claiming priority to the aforementioned application” means that the proposed licenses could cover all subsequent applications claiming the priority of the U.S. provisional application 62/732,263, including a PCT international application. This means that the geographical scope of the licenses could potentially cover a large number of countries, including nearly all developing countries. The Federal Register notice fails to clarify in which countries the NIH intends to claim the priority of the provisional application 62/732,263, despite the fact that a number of public health groups have raised questions about the geographic scope in NIH licensing practices, including in particular the use of exclusive licenses for developing countries, in previous license comment periods.

The lack of transparency and specificity of the geographic scope of this proposed licenses makes it impossible to evaluate whether their scope complies with the requirements provided under 35 U.S. C. § 209, or if the licenses will be consistent with the policies set out in the "United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy," which states that "PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries."

Technology

The two proposed licenses describe the technology in question as follows:

> "This technology discloses the development of chimeric antigen receptors that recognize both the CD19 and CD20 cell surface proteins. 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). Although the FDA has recently approved CAR-based therapies which target only CD19 (Yescarta, Kymriah), tumors are capable of undergoing tumor antigen escape (the downregulation of target antigen expression on tumor cells), which results in gradual resistance to "single target therapies." As a result, patients receiving single target CAR therapies are susceptible to relapse. This has prompted investigators to pursue dual targeting CAR therapies to provide as a means of overcoming tumor antigen escape, thereby providing a more comprehensive therapeutic alternative. The development of a new therapeutic targeting both CD19 and CD20 will benefit public health by offering up an improved treatment for patients that would otherwise be subject to relapse due to tumor antigen escape."

Antigen loss is a major barrier to CAR T therapies. According to Robbie Majzner and Crystal Mackall, "[e]merging data from chimeric antigen receptor (CAR) T-cell trials in B-cell malignancies demonstrate that a common mechanism of resistance to this novel class of therapeutics is the emergence of tumors with loss or downregulation of the target antigen."[12] They continue suggesting that "[a]ntigen loss or antigen-low escape is likely to emerge as an even greater barrier to success in solid tumors, which manifest greater heterogeneity in target antigen expression."[13] Robbie Majzner and Crystal Mackall then conclude the following:

> "Clinical experience with B-cell malignancies has demonstrated that CAR T cells have the potential to alter the landscape of cancer immunotherapy. However, the emergence of antigen-negative and antigen-low tumor variants has shown that, like all anticancer agents, CARs are likely to require combinatorial approaches to bring about cures in a high fraction of patients. Whereas in hematologic malignancies, lineage-derived antigens are expressed at high levels and can be efficiently targeted by CARs, in solid tumors

[12] http://cancerdiscovery.aacrjournals.org/content/8/10/1219.long
[13] http://cancerdiscovery.aacrjournals.org/content/8/10/1219.long

> most viable antigens are expressed at lower levels and more heterogeneously. Reengineering CARs for multispecificity and activity at lower levels of antigen will be an area of important research as the community attempts to enhance the potency of CAR T cells and the breadth of diseases for which they can provide clinically meaningful effects."[14]

According to Nirav N. Shah, Theresa Maatman, Parameswaran Hari, and Bryon Johnson:

> "One obvious way to combat the problem of antigen loss following CAR-T cell therapy is by targeting more than one antigen receptor. This can be accomplished by 1 of 4 different approaches: (a) Generate 2 or more cell populations expressing different CARs and infuse them together or sequentially (coadministration); (b) Use a bicistronic vector that encodes 2 different CARs on the same cell; (c) Simultaneously engineer T cells with 2 different CAR constructs (cotransduction), which will generate three CAR-T subsets consisting of dual and single CARexpressing cells; or (d) Encode 2 CARs on the same chimeric protein using a single vector (i.e., bi-specific or tandem CARs) (Figure 2). These different approaches are highlighted in a recent review article by Majzner and Mackall (16)."[15]

Based on the description provided in the Federal Register notices and our own research, our understanding is that the technology covered in the proposed license is a bicistronic construct for a CAR that targets both CD19 and CD20. This bicistronic construct can express two CARs from a single vector, thereby allowing for a more efficient transfection of T cells.

Proposed safeguards for license

In the event that the NIH decides to grant these exclusive licenses, we ask that the following safeguards be placed on the licenses.

1. **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. To evaluate this proposal, the NIH should require Gilead/Kite to publicly disclose the prices that it charges on its existing products for cancer, HIV and Hepatitis C Virus in the United States and in the seven reference countries, to establish if Gilead is charging U.S. residents more than in the other high income countries for the cell therapies and drugs for HIV and HV, that were developed with federal support.

[14] http://cancerdiscovery.aacrjournals.org/content/8/10/1219.long
[15] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6423158/pdf/fonc-09-00146.pdf

2. **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 developing countries. If the NIH rejects this suggestion, it needs to provide some mechanism giving effect to the policy objective in the "United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy," which states the following: "PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries."

3. **Global registration and affordability.** The license should require Kite/Gilead to disclose the steps it 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.

4. **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.

5. **Years of exclusivity.** We propose the license reduce the years of exclusivity when revenues are large. The NIH has many options, including by providing an option for non-exclusive licensing, such as was done in the ddI case. We propose that the 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 license 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."

6. **Transparency of R&D outlays.** The licensee 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 will note that this is not a request to see a company business plan or license application. We are asking that going forward the company 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.

Sincerely,

Knowledge Ecology International (KEI)
Social Security Watch (SSW)
Universities Allied for Essential Medicines (UAEM)
Union for Affordable Cancer Treatment (UACT)
Clare Love

ANNEX - Previous Gilead/Kite Licenses

Previously proposed licenses to Kite Pharma

Several previous exclusive licenses proposed by the NIH have Kite Pharma as the prospective licensee. All of these previous licenses appear to cover inventions related to cell therapies. In the Federal Register notices the NIH failed to mention these previous exclusive licenses, whether they have been executed, or whether they have any relation to the proposed license.

Previous Federal Register notices listing Kite Pharma, Inc. as the prospective licensee

Date	Notice title and URL
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
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

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
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
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
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
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

KEI has filed comments on several proposed licenses to Kite Pharma.[16]

The NIH has executed several licenses with Kite Pharma. For example, in a form filed with the Securities and Exchange Commission (SEC) on June 17, 2014, Kite Pharma disclosed a May 22, 2014 license from the NIH that covered the PCT procedure PCT/US13/042162 and apparently another patent document whose number is redacted.[17] The Federal Register notice 79 FR 16347 published March 25, 2014, described a proposed exclusive license to Kite Pharma, and listed two patent documents: U.S. Provisional Patent Application No. 61/650,020; and PCT Application No. PCT/US13/042162, the same PCT document covered in the license disclosed on June 17, 2014, by Kite Pharma to the SEC.[18]

[16] See: https://www.keionline.org/23177, https://www.keionline.org/26686

[17] https://content.edgar-online.com/ExternalLink/EDGAR/0001193125-14-239257.html?hash=86559f49106fc5339d18e3d6f40ebab76d0c8488bd9dbc858d4ce87ba9380ec5&dest=D705296DEX1017_HTM#D705296DEX1017_HTM

[18] https://www.federalregister.gov/d/2014-06412

Kite Pharma has also disclosed a September 28, 2015 exclusive license with the NIH covering eleven patent documents related to “T Cell Receptors Recognizing HLA-A1- or HLA-CW7-Restricted Mage.”[19] One of the patent documents listed in that exclusive license is PCT/US13/059608, which was also listed in the Federal Register notice 79 FR 62169, published on October 16, 2014, which describes a proposed exclusive license to Kite Pharma.[20]

This is not a comprehensive list of all the licenses executed between the NIH and Kite Pharma.

We are aware of three 10-K forms and one amendment filed by Kite Pharma before the SEC between 2015 and 2017, prior to being acquired by Gilead. In these filings, Kite described several licenses with the NIH. Below is a table containing links to the 10-K filings available at the SEC website, and excerpts of these 10-K filings where Kite Pharma reference executed licenses follow below the sections regarding CRADAs Kite has entered with the NIH.

Filing	Date	URL
10-K	2/28/2017	https://www.sec.gov/Archives/edgar/data/1510580/000151058017000003/kite20161231-10k.htm
10-K/A	6/28/2016	https://www.sec.gov/Archives/edgar/data/1510580/000119312516634919/d391716d10ka.htm
10-K	2/29/2016	https://www.sec.gov/Archives/edgar/data/1510580/000156459016013699/kite-10k_20151231.htm
10-K	3/26/2015	https://www.sec.gov/Archives/edgar/data/1510580/000156459015001985/kite-10k_20141231.htm

CRADAs signed between Kite Pharma and the NIH

Kite Pharma has also signed Cooperative Research and Development Agreements (CRADAs) with the NIH. Below is a description of one of these CRADAs, based on a 10-K form filed by Kite Pharma before the SEC.

Cooperative Research and Development Agreement with the NCI[21]

“In August 2012, we entered into the CRADA with the U.S. Department of Health and Human Services, as represented by the NCI, for the research and development of

[19] https://www.sec.gov/Archives/edgar/data/1510580/000156459016013699/kite-ex1029_303.htm
[20] https://www.federalregister.gov/d/2014-24502
[21] https://www.sec.gov/Archives/edgar/data/1510580/000156459015001985/kite-10k_20141231.htm Page 18

eACT-based product candidates for the treatment of multiple advanced and metastatic cancer indications. Under the CRADA, the NCI develops and tests, including in Phase 2 and 1-2a clinical trials, multiple CAR- and TCR-based product candidates targeting various antigens such as CD19, SSX2, NY-ESO-1, MAGE, HPV 16 E6 and E7, and EGFRvIII. These activities are conducted through a research plan that we jointly developed with the NCI. On February 24, 2015, we amended the CRADA to expand the research plan to include (1) the research and development of the next generation of TCR-based product candidates that are engineered to recognize neo-antigens, (2) the optimization of new methods to manufacture this next generation of TCR-based product candidates and (3) the advancement of CAR-based product candidates for the treatment of clear cell renal cell carcinoma and TCR-based product candidates for the treatment of certain epithelial tumors such as lung and colorectal cancer."

"Each party individually owns all inventions, data and materials produced solely by its employees in the course of performing the activities under the CRADA. The parties jointly own any inventions and materials that are jointly produced by employees of both parties in the course of performing activities under the CRADA. Subject to certain conditions, this collaboration provides us with an exclusive option to negotiate commercialization licenses from the NIH to intellectual property relating to CAR- and TCR-based product candidates conceived or first reduced to practice in performance of the CRADA research plan. This includes the right to negotiate a license to intellectual property related to CAR- and TCR-based product candidates that are being tested in multiple Phase 1-2a clinical trials that we are funding under the CRADA other than CD19, EGFRvIII, SSX2 and NY-ESO-1, and one product candidate related to a type of MAGE antigen that we are not intending to pursue. We may exercise this right by providing four months written notice after either we receive notice that a patent application covering an invention has been filed, or the date on which we file a patent application for an invention. We then have ten months to negotiate the license with the NIH. These time periods may be extended by the U.S. Public Health Service upon good cause."

"To support the additional research activities under the amended CRADA, our quarterly payments to the NCI increased from $250,000 to $750,000. To the extent we license patent rights relating to an eACT-based product candidate, we will be responsible for all patent-related expenses and fees, past and future, relating to the eACT-based product candidate. In addition, we will be required to supply certain test articles, including peripheral blood lymphocytes, transduced with TCR or CAR, grown and processed under cGMP conditions, suitable for use in clinical trials, where we hold the IND for such clinical trial."

"The CRADA has a five-year term expiring on August 30, 2017. The CRADA may be terminated at any time by mutual written consent. We or NCI may unilaterally terminate

the CRADA for any reason or for no reason at any time by providing written notice at least 60 days before the desired termination date."

Kite Pharma - NIH Licenses Referenced in Kite Pharma SEC 10-K Forms

2013 NIH License Agreement[22]

"Pursuant to a patent license agreement with the NIH, dated April 11, 2013, the Company holds an exclusive, worldwide license to certain intellectual property, including intellectual property related to a CAR-based product candidate that targets the EGFRvIII antigen for the treatment of brain cancer and head and neck cancer, 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. The Company has a co-exclusive license to intellectual property related to these product candidates for the treatment of certain other cancers. The Company may require an additional license relating to the EGFRvIII scFv target binding site from a third-party in order to commercialize a CAR-based product candidate that targets the EGFRvIII antigen."

"Pursuant to the terms of the NIH License, the Company paid the NIH one-time cash payments in the aggregate amount of $200,000. The Company reimbursed the NIH for past patent expenses in the aggregate amount of approximately $58,000, with half of this amount paid during 2013 and the balance paid in May 2014."

"The Company is also required to pay the NIH minimum annual royalties in the amount of $20,000. The first minimum annual royalty payment is payable on the date that is 60 days following the expiration of the 2012 CRADA, and thereafter shall be payable on each January 1st."

"The Company is also required to make performance-based cash payments upon successful completion of clinical and regulatory benchmarks relating to the products covered by the NIH license (the "Licensed Products"). The aggregate potential clinical and regulatory benchmark payments for each Licensed Product are $4.0 million, of which $3.0 million is due only after marketing approval in the United States, Europe, Japan, China or India. The first benchmark payment of $50,000 will be due upon the commencement of the first company sponsored human clinical study of a Licensed Product in the United States."

[22] https://www.sec.gov/Archives/edgar/data/1510580/000156459016013699/kite-10k_20151231.htm Page 88

"In addition, the Company must also pay the NIH royalties on net sales of Licensed Products at rates in the mid-single digits. The Company is also required to pay NIH benchmark payments based upon aggregate net sales of Licensed Products, which amount will equal up to $7.0 million following aggregate net sales of $1.0 billion. To the extent the Company enters into a sublicensing agreement relating to the Licensed Products, the Company is required to pay the NIH a percentage of all consideration received from a sublicensee, which percentage will decrease based on the stage of development of the Licensed Products at the time of the sublicense. Pursuant to an amendment dated October 1, 2015, any such sublicense payment will be subject to a cap."

"The license will expire upon expiration of the last patent contained in the licensed patent rights, unless terminated earlier. None of the applications included in the NIH licensed patent rights have issued yet. Any patents issuing from these applications will have a base expiration date no earlier than 2031. The NIH may terminate or modify the NIH license in the event of a material breach, including if the Company does not meet certain milestones by certain dates, or upon certain insolvency events that remain uncured following the date that is 90 days following written notice of such breach or insolvency event. The Company may terminate the license, or any portion thereof, at its sole discretion at any time upon 60 days written notice to the NIH. In addition, the NIH has the right to require the Company to sublicense the rights to the product candidates covered by this license upon certain conditions, including if the Company is not reasonably satisfying required health and safety needs or if the Company is not satisfying requirements for public use as specified by federal regulations."

"The expenses recognized under the NIH license were $196,484, $90,000 and $191,200 for the years ended December 31, 2015, 2014 and 2013, respectively."

May 2014 NIH License Agreement[23]

"Pursuant to a patent license agreement with the NIH, dated May 29, 2014, we hold an exclusive, worldwide license to certain intellectual property related to TCR-based product candidates that target the NY-ESO-1 antigen for the treatment of any NY-ESO-1 expressing cancers. As of the date of the license, NY-ESO-1 expressing tumors can be found in the following cancers: sarcoma, urothelial carcinoma, esophageal carcinoma, non-small cell lung cancer, breast carcinoma, ovarian carcinoma, prostate carcinoma, multiple myeloma, hepatocellular carcinoma, gastric cancer, head and neck cancer, pancreatic carcinoma, brain cancer, colorectal carcinoma and melanoma."

[23] https://www.sec.gov/Archives/edgar/data/1510580/000156459015001985/kite-10k_20141231.htm
Pages 19-20

“Pursuant to the terms of this license, we are required to pay the NIH a cash payment in the aggregate amount of $150,000, two-thirds of which was due and paid within sixty days of the date of the agreement and one-third of which will be payable upon the earlier to occur of (1) 18 months from the date of execution of the license and (2) the termination of the license. We also agreed to reimburse the NIH for past patent expenses in the aggregate amount of approximately $30,000.”

“The terms of this license also require us to pay the NIH minimum annual royalties in the amount of $20,000. The first minimum annual royalty payment is payable on the date that is 60 days following the expiration of the CRADA, and thereafter shall be payable on each January 1.”

“We are also required to make performance-based payments upon successful completion of clinical and regulatory benchmarks relating to the licensed products. The aggregate potential benchmark payments are $4.0 million, of which aggregate payments of $3.0 million are due only after marketing approval in the United States or in Europe, Japan, China or India. The first benchmark payment of $50,000 will be due upon the commencement of our first sponsored human clinical study.”

“In addition, we are required to pay the NIH one-time benchmark payments following aggregate net sales of up to $1.0 billion on licensed products. The aggregate potential amount of these benchmark payments is $7.0 million. We must also pay the NIH royalties on net sales of products covered by the license at rates in the mid single digits. To the extent we enter into a sublicensing agreement relating to a licensed product, we are required to pay the NIH a percentage of all consideration received from a sublicensee, which percentage will decrease based on the stage of development of the licensed product at the time of the sublicense. Any such sublicense payments shall be made in lieu of, and not in addition to, benchmark payments, and are subject to certain caps.”

“The license will expire upon expiration of the last patent contained in the licensed patent rights, unless terminated earlier. None of the applications included in the NIH licensed patent rights have issued yet. Any patents issuing from these applications will have a base expiration date no earlier than 2031. The NIH may terminate or modify the NIH license in the event of a material breach, including if we do not meet certain milestones by certain dates, or upon certain insolvency events that remain uncured following the date that is 90 days following written notice of such breach or insolvency event. We may terminate the license, or any portion thereof, at our sole discretion at any time upon 60 days written notice to the NIH. In addition, the NIH has the right to require us to sublicense the rights to the product candidates covered by this license upon certain conditions, including if we are not reasonably satisfying required health and safety needs or if we are not satisfying requirements for public use as specified by federal regulations.”

December 2014 National Institutes of Health ("NIH") License Agreement[24]

"Pursuant to a patent license agreement with the NIH, dated December 31, 2014, the Company holds an exclusive, worldwide license to certain intellectual property related to TCR-based product candidates that target HPV antigens E6 and E7 of the HPV subtype 16."

"Pursuant to the terms of this license, the Company paid the NIH a cash payment in the aggregate amount of $350,000 in February 2015. The Company is required to make performance-based payments upon successful completion of clinical and regulatory benchmarks relating to the licensed products. The aggregate potential benchmark payments for each licensed product are $6.0 million, of which aggregate payments of $5.0 million are due only after marketing approval in the United States or in Europe, Japan, China or India. The first benchmark payment of $50,000 will be due upon the commencement of the Company's first sponsored Phase 1 clinical trial.
In addition, the Company is required to pay the NIH one-time benchmark payments following aggregate net sales of up to $1.0 billion of licensed products. The aggregate potential amount of these benchmark payments is $7.0 million. The Company must also pay the NIH royalties on net sales of products covered by this license at rates in the mid-single digits. To the extent the Company enters into a sublicensing agreement relating to a licensed product, the Company is required to pay the NIH a percentage of all consideration received from a sublicensee, which percentage will decrease based on the stage of development of the licensed product at the time of the sublicense. Any such sublicense payment is subject to a certain cap."

"The license will expire upon expiration of the last patent contained in the licensed patent rights, unless terminated earlier. None of the applications included in the NIH licensed patent rights have issued yet. Any patents issuing from these applications will have a base expiration date no earlier than 2034. The NIH may terminate or modify the license in the event of a material breach, including if the Company does not meet certain milestones by certain dates, or upon certain insolvency events that remain uncured following the date that is 90 days following written notice of such breach or insolvency event. The Company may terminate the license, or any portion thereof, at its sole discretion at any time upon 60 days written notice to the NIH. In addition, the NIH has the right to require the Company to sublicense the rights to the product candidates covered by the license upon certain conditions, including if the Company is not reasonably satisfying required health and safety needs or if the Company is not satisfying requirements for public use as specified by federal regulations."

[24] https://www.sec.gov/Archives/edgar/data/1510580/000151058017000003/kite20161231-10k.htm Pages 89-90

October 2015 NIH License Agreement[25]

"Pursuant to a patent license agreement with the NIH, dated October 1, 2015, the Company holds an exclusive, worldwide license to certain intellectual property related to TCR-based product candidates directed against MAGE A3 and A3/A6 antigens for the treatment of tumors expressing MAGE. Pursuant to the terms of this license, the Company paid the NIH a cash payment in the aggregate amount of $1.2 million in November 2015."

"The Company is also required to make performance-based payments upon successful completion of clinical and regulatory benchmarks relating to the licensed products. The aggregate potential benchmark payments for each licensed product are $8.4 million, of which aggregate payments of $6.0 million are due only after marketing approval in the United States or in Europe, Japan, China or India. Also, a benchmark payment of $150,000 will be due upon the commencement of the Company's first sponsored Phase 1 clinical trial for each licensed product in each indication."

"In addition, the Company is required to pay the NIH one-time benchmark payments following aggregate net sales of up to $1.0 billion of licensed products. The aggregate potential amount of these benchmark payments is $12.0 million. The Company must also pay the NIH royalties on net sales of products covered by this license at rates in the mid-single digits. To the extent the Company enters into a sublicensing agreement relating to a licensed product, the Company is required to pay the NIH a percentage of all consideration received from a sublicensee, which percentage will decrease based on the stage of development of the licensed product at the time of the sublicense. Any such sublicense payment is subject to a certain cap."

"The license will expire upon expiration of the last patent contained in the licensed patent rights, unless terminated earlier. None of the applications included in the NIH licensed patent rights have issued yet. Any patents issuing from these applications will have a base expiration date no earlier than 2032. The NIH may terminate or modify the license in the event of a material breach, including if the Company does not meet certain milestones by certain dates, or upon certain insolvency events that remain uncured following the date that is 90 days following written notice of such breach or insolvency event. The Company may terminate the license, or any portion thereof, at its sole discretion at any time upon 60 days written notice to the NIH. In addition, the NIH has the right to require the Company to sublicense the rights to the product candidates covered by the license upon certain conditions, including if the Company is not

[25] https://www.sec.gov/Archives/edgar/data/1510580/000151058017000003/kite20161231-10k.htm Page 90

reasonably satisfying required health and safety needs or if the Company is not satisfying requirements for public use as specified by federal regulations.”