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9609 Medical Center Drive
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Via email to jim.knabb@nih.gov

Re: Prospective Grant of Exclusive Patent License in CD19/CD22 CAR Therapies to CJ Healthcare

Dear Dr. Knabb:

Knowledge Ecology International (KEI), Union for Affordable Cancer Treatment, Public Citizen, Social Security Works, Health GAP (Global Access Project), Professor Brook K. Baker, and Clare Love are writing to comment on "Prospective Grant of an Exclusive Patent License: Development and Commercialization of CD19/CD22 Chimeric Antigen Receptor (CAR) Therapies for the Treatment of B-Cell Malignancies[.]" 85 FR 328.¹

The license concerns two CAR therapies that were developed at the National Cancer Institute (NCI) and treat relapsed B-cell acute lymphoblastic leukemia (ALL)—the leading cause of cancer death in children²—and other hematological cancers. Clinical research that contributed to the cell therapies was sponsored by the National Institutes of Health (NIH) and pediatric cancer charities. The first therapy is being tested in three Phase I clinical trials, one conducted by the NIH, and the other two by the Stanford Cancer Institute with funding from the NIH and the California Institute of Regenerative Medicine (CIRM). Early results have been promising.

The NIH is proposing to license the inventions to CJ Healthcare Corp., a large, Korea-based company known for marketing the country's "No.1 Anti-hangover drink."³

¹ 85 Fed. Reg. 328, available at <https://www.federalregister.gov/documents/2020/01/03/2019-28356/prospective-grant-of-an-exclusive-patent-license-development-and-commercialization-of-cd19cd22>.

² <https://www.fda.gov/media/107962/download>.

³ <http://www.cjp.co.kr/eng/brand/condition.asp>.



It is our understanding that Kids v. Cancer, a US-based charity, is also interested in bringing the invention to practical application, and that this effort is supported by Crystal Mackall, the Ernest and Amelia Gallo Family Professor of Pediatrics and Medicine at Stanford University, and until 2016, the Chief of the Pediatric Oncology Branch (POB) at the NCI. Mackall is one of the inventors of the cell therapies and is overseeing the two Stanford clinical trials.

We note the Bayh-Dole Act has a preference for US-based manufacturers and small businesses. 35 U.S.C. § 209(b)-(c). The prospective licensee is neither small nor based in the US.

We object to the license unless the NIH performs the analysis required by the Bayh-Dole Act. Under that statute, a federal agency may not license a government-owned technology on an exclusive basis unless “granting the license is a reasonable and necessary incentive to . . . call forth the investment capital and expenditures needed to bring the invention to practical application[.]” and the “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)(1)-(2).

We are concerned that the NIH has not undertaken the appropriate analysis to determine if an exclusive license is required, and, perhaps more important, if exclusivity is necessary, the proper limitations on the scope of rights. A license that is appropriate in scope will limit the restrictions on competition that an exclusive license imposes and will ensure that the benefits of the inventions are “available to the public on reasonable terms,” a requirement included in the statutory definition of “practical application” of an invention.⁴

The NIH is also required by 40 U.S.C. § 559 to seek the advice of the Attorney General with respect to antitrust law before licensing government-owned inventions.

⁴ “The term ‘practical application’ means to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms.” 35 U.S.C. § 201(f).

In the event that the NIH grants the license we urge that it incorporate provisions designed to safeguard the public interest and promote the policy objectives of the Bayh-Dole Act and the Public Health Service (PHS) Technology Transfer Policy Manual.

Background

The Inventions

Two inventions are covered by the license: E-016-2015: “Chimeric Antigen Receptor Targeting both CD19 and CD22” and E-017-2017: “CD19/CD22 Bicistronic CAR Targeting Human B-Cell Malignancies.”

The CAR therapies are the culmination of years of research at the NCI, and their development was funded by federal and state funds and two cancer charities.

Between 2012 and 2014, scientists at the POB tested an anti-CD19 CAR cell therapy in children and young adults with relapsed or refractory B-ALL. They found the treatment to be safe and effective in treating the disease.⁵ The clinical trial, NCT01593696, was supported by the NIH and a grant from the St. Baldrick’s Foundation, a charity dedicated to pediatric cancer research.⁶

Despite the promising results, some of the patients treated with the therapy eventually relapse, and a large percentage of those relapses are due to “loss of the CD19 target[.]”⁷ The NCI scientists wondered whether there might be another surface protein to target in order to overcome that resistance.⁸ They “developed a novel CAR T-cell targeting CD22 to test this idea.”⁹

In December of 2014, the scientists began investigating the anti-CD22 CAR therapy in pediatric patients and young adults in the clinical trial NCT02315612, “Anti-CD22 Chimeric Receptor T Cells in Pediatric and Young Adults With Recurrent or Refractory CD22-expressing B Cell

⁵ Lee, et al., “T cells expressing CD19 chimeric antigen receptors for acute lymphoblastic leukaemia in children and young adults: a phase 1 dose-escalation trial,” *The Lancet*, October 12, 2014, doi:[https://doi.org/10.1016/S0140-6736\(14\)61403-3](https://doi.org/10.1016/S0140-6736(14)61403-3).

⁶ <https://www.stbaldricks.org/>.

⁷ Fry, Terry J et al., “CD22-targeted CAR T cells induce remission in B-ALL that is naive or resistant to CD19-targeted CAR immunotherapy,” *Nature medicine* vol. 24,1 (2018): 20-28. doi:10.1038/nm.4441.

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<http://med.stanford.edu/news/all-news/2017/11/clinical-trial-suggests-new-cell-therapy-for-relapsed-leukemia-patients.html>.

⁹

<http://med.stanford.edu/news/all-news/2017/11/clinical-trial-suggests-new-cell-therapy-for-relapsed-leukemia-patients.html>.

Malignancies.”¹⁰ The treatment was found to be equally effective as the anti-CD19 CAR T-cells in eliminating ALL,¹¹ and it led to remission in patients who had relapsed after the anti-CD19 therapy.¹² NCT02315612 was supported by the Intramural Research Program at the NIH and two cancer charities—the St. Baldrick’s Foundation and Stand Up To Cancer.¹³

After the anti-22 CAR therapy demonstrated the same potential for relapse,¹⁴ however, the researchers began to contemplate whether a CAR therapy could be developed to target both the CD19 and CD22 surface proteins at the same time.¹⁵ This led to the conception of the instant inventions, the first of which, a bispecific CD19/CD22 CAR therapy, is being tested in three clinical trials—NCT03448393, NCT03241940, and NCT03233854.¹⁶ The second invention, a bicistronic CD19/CD22 CAR therapy, has had positive results in a xenograft study.¹⁷

The Prospective Licensee

The prospective licensee, CJ Healthcare, was formed in South Korea in 1984.¹⁸ It was bought by Korea Kolmar in February 2018 for \$1.2 billion.¹⁹ CJ Healthcare makes South Korea’s most popular anti-hangover drink, Condition.²⁰ It has 1476 employees.²¹

Proposed Scope of the License

According to the Federal Register, the field of use for the license may be limited to:

¹⁰ Fry, Terry J et al., “CD22-targeted CAR T cells induce remission in B-ALL that is naive or resistant to CD19-targeted CAR immunotherapy,” *Nature medicine* vol. 24,1 (2018): 20-28. doi:10.1038/nm.4441.

¹¹ <https://ccr.cancer.gov/news/milestones-2018/article/car-ts-for-leukemia>.

¹²

<https://ccr.cancer.gov/news/article/phase-I-clinical-trial-will-test-multi-targeted-immunotherapy-in-common-childhood-cancer>.

¹³ Fry, Terry J et al., “CD22-targeted CAR T cells induce remission in B-ALL that is naive or resistant to CD19-targeted CAR immunotherapy,” *Nature medicine* vol. 24,1 (2018): 20-28. doi:10.1038/nm.4441.

¹⁴ Qin, Haiying et al. “Novel CD19/CD22 Bicistronic Chimeric Antigen Receptors Outperform Single or Bivalent Cars in Eradicating CD19+CD22+, CD19-, and CD22- Pre-B Leukemia.” (2017).

<https://www.semanticscholar.org/paper/Novel-CD19%2FCD22-Bicistronic-Chimeric-Antigen-Single-Qin-Nguyen/95997194cbbd89442ca4aafc73b3c6df76bc9e05>.

¹⁵

<https://www.med.stanford.edu/news/all-news/2017/11/clinical-trial-suggests-new-cell-therapy-for-relapsed-leukemia-patients.html>.

¹⁶ Qin, Haiying et al. “Preclinical Development of Bivalent Chimeric Antigen Receptors Targeting Both CD19 and CD22.” *Molecular therapy oncolytics* vol. 11 127-137. 6 Nov. 2018, doi:10.1016/j.omto.2018.10.006.

¹⁷ <https://www.ott.nih.gov/technology/e-017-2017>.

¹⁸ <http://www.cjp.co.kr/eng/company/history.asp>.

¹⁹

<https://www.reuters.com/article/us-cj-healthcare-m-a-korea-kolmar/korea-kolmar-buying-cj-healthcare-for-1-2-billion-shares-soar-idUSKCN1G50W8>.

²⁰ *Id.*

²¹ <https://www.bloomberg.com/profile/company/1239226D:KS>.

Treatment of B cell malignancies using autologously-derived, lentiviral vector transduced, T cells expressing chimeric antigen receptor(s) (CAR) dual specific for CD19 and CD22, utilizing the anti-CD19 antigen binding domain of the FM63 antibody and the anti-CD22 antigen binding domain of the M971 antibody.²²

The proposed territorial reach of the license is “worldwide.”²³

Argument

1. CJ Healthcare may not be the most appropriate choice of licensee, and the NIH should take all reasonable measures to grant the license to an entity that will commit to manufacturing any product embodying the inventions in the United States and to developing the inventions’ pediatric indications.

We have questions regarding the suitability of CJ Healthcare to develop this technology.

One important question concerns the use of the inventions for pediatric indications. If CJ Healthcare is not committed to investing in the development of the technology for both adult and pediatric patients, another licensee may be more appropriate.

As we have noted, CJ Healthcare does not appear to satisfy a preference for licensing federally-owned inventions to small businesses and US companies. The company is not a small business. It has nearly 1500 employees and was recently acquired by Korea Kolmar, a firm which describes itself as “the biggest Korean Pharmaceutical contract manufacturer.”²⁴

Another issue that is not very clear concerns the location of the cell manufacturing. Will CJ Healthcare/Kolmar manufacture the CAR T-cells in the United States? CJ Healthcare’s website lists the location of its manufacturing plants, and none are in the US.²⁵ KEI asked Jim Knabb, the point of contact for the license, whether “CJ Healthcare agreed to substantially manufacture any product embodying the inventions in the United States[.]” He responded that “CJ is aware of the requirements under 37 CFR 404.5(a)(2) and abide by the requirements thereunder.” This statement does not fully clarify the issue, however, because licensees may obtain waivers for the US manufacturing requirement.

If CJ Healthcare does not have the capacity to manufacture the CAR T-cells in the United States, the NIH should at least ensure that the company is capable of bringing the invention to

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<https://www.federalregister.gov/documents/2020/01/03/2019-28356/prospective-grant-of-an-exclusive-patent-license-development-and-commercialization-of-cd19cd22>.

²³ *Id.*

²⁴ <http://www.kolmarpharm.co.kr/eng/>.

²⁵ http://www.cjp.co.kr/eng/company/production_facility/osong_workplace.asp.

practical application here. CJ Healthcare's website describes how the firm strives to become "a global No.1 pharmaceutical player in the global market" by "expanding the exports to Japan, Southeast Asia, Central and South America, and Europe," but does not mention US exports.²⁶

Additionally, we have concerns about Korea Kolmar's manufacturing record.²⁷ In 2018, the FDA sent Korea Kolmar a warning letter "summariz[ing] significant violations of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals."²⁸ The letter was based on a September 2017 inspection of Kolmar's drug manufacturing facility in which the investigator observed violations such as (1) improper handling of irregular test results and (2) tearing up and discarding documents and records. According to the letter, Kolmar admitted to the FDA that its staff were inadequately trained in cGMP-compliant procedures. The letter concluded by warning Korea Kolmar that the "FDA may withhold approval of any new applications or supplements listing your firm as a drug manufacturer."²⁹

Korea Kolmar has also been the subject of at least two FDA import alerts,³⁰ meaning that the FDA has enough evidence to allow for Detention Without Physical Examination (DWPE) of products that appear to be in violation of the FDA's laws and regulations.

Kids v. Cancer, a nonprofit organization dedicated to promoting pediatric cancer research,³¹ has expressed interest in securing a commercial partner to develop the technology. If, in fact, Crystal Mackall is supporting the Kids v. Cancer proposal, the NIH should give considerable weight to the capacity of Kids v. Cancer to develop the technology, especially considering the charity's mission of ending cancer in children.

We have had discussions with Kids v. Cancer, and it was open to the notion that the license should be consistent with the PHS policy of promoting access in developing countries. If Kids v. Cancer obtains a license, we believe discussions over the affordability in reasonable pricing for the United States will be possible, although we have no assurances that concessions in this area will be forthcoming.

²⁶ http://www.cjp.co.kr/eng/business/global_business.asp.

²⁷

<https://www.fiercepharma.com/manufacturing/fda-hits-cdmo-korea-kolmar-warning-letter-over-manufacturing-issues>.

²⁸

<https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/kolmar-korea-co-ltd-542511-05182018>.

²⁹ *Id.*

³⁰

<https://search.usa.gov/search?utf8=%E2%9C%93&affiliate=fdaimportalertssearch&query=Korea+Kolmar+%&commit=Search>.

³¹ <https://www.kidsvcancer.org/about-us/>.

2. The NIH has not demonstrated that it properly evaluated the necessity of granting an exclusive license.

We are also concerned that the NIH has not given adequate consideration to whether an exclusive license is necessary for this technology.

A federal agency may not grant an exclusive license in government-owned technology unless “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).

As the NIH has acknowledged, “[t]he value of patent commercialization licenses are not uniform and depend on many factors[.]”³² The factors to be considered when determining the necessary incentive under 35 U.S.C. § 209(a)(1) include, but are not limited to, the following:

1. The development stage of the technology and government’s investment in R&D;
2. The costs of financing research and development and bringing the invention to market, including clinical trial costs (and the extent to which those costs may be covered by the Orphan Drug Tax Credit, Research Credit, or reimbursement by health insurance or other subsidies); and
3. The existence of regulatory incentives such as test data protection, Orphan Drug exclusivity and the award of one or more priority review vouchers (PRVs).

It is our understanding that the NIH has not undertaken a serious evaluation of the factors listed above, relating to practical application of the inventions, in order to evaluate whether or not an exclusive license was a “reasonable and necessary incentive.”

KEI asked Dr. Knabb how the NIH determined that exclusivity was warranted. He referred KEI to his answers in relation to an earlier prospective exclusive patent license in the same technology, to a company called Lyell Immunopharma.³³

With respect to that license, Dr. Knabb stated that [t]he grant of exclusivity to the

³² Mark L. Rohrbaugh, “NIH: Moving Research from the Bench to the Bedside, Testimony before the House Committee on Energy and Commerce, Subcommittee on Health,” July 10, 2003, available at <https://www.govinfo.gov/content/pkg/CHRG-108hhrg88429/html/CHRG-108hhrg88429.htm>.

³³

<https://www.federalregister.gov/documents/2019/08/20/2019-17866/prospective-grant-of-an-exclusive-patent-license-development-and-commercialization-of-cd19cd22>. KEI asked Dr. Knabb what happened to the proposed license to Lyell Immunopharma, and he did not answer. Because the NIH is proposing to license the technology exclusively to CJ Healthcare, however, it can safely be assumed that the agreement with Lyell was never executed.

Government-owned intellectual property seeks to fulfill the Government's interest in promoting the public health and public access to therapeutics."³⁴ That analysis misses the point.

Granting exclusive rights in a valuable cancer treatment will always increase the likelihood that a firm will agree to commercialize the invention. The question is whether exclusivity is necessary, and that can only be answered in the affirmative when no other qualified commercial partner would agree to develop the technology on a non-exclusive or co-exclusive basis.

An analysis of the relevant factors shows that the subject inventions are valuable technologies.

Stage of Development

Exclusive license terms may be justified where a patented invention is merely a gleam in the eye of an NIH scientist. The subject inventions, however, are more advanced. The first invention has successfully completed the riskiest stages of R&D—basic and preclinical research—and is being investigated in three clinical trials: NCT03448393, NCT03241940, and NCT03233854. The second invention has had positive results in a xenograft study.

The inventions' development stages are described in greater detail below.

The First Invention - A Bispecific CAR Construct

As noted, the first invention covered by the license, a bispecific CAR therapy, is being investigated in three clinical trials. All three clinical trials are Phase 1 - the riskiest stage of clinical trial testing in the FDA approval process. All were supported by government funds.

The first trial listed, NCT03448393, is being conducted at the NIH Clinical Center in Bethesda, Maryland. The second trial, NCT03241940, is being conducted at Stanford and is funded by NIH Grant No. P30CA124435. The third, NCT03233854, is being conducted at Stanford and is funded by an \$11 million grant from CIRM.

NCT03448393, "CD19/CD22 Chimeric Antigen Receptor (CAR) T Cells in Children and Young Adults With Recurrent or Refractory CD19/CD22-expressing B Cell Malignancies"

Size: 89 Participants

Start Date: March 26, 2018

Primary Completion Date: December 1, 2021

Sponsor: NCI/NIH

Principal Investigator: Nirali Shah

Grant: 1ZIABC011823 (NIH Intramural Grant)

³⁴ Attachment A.

NCT03241940, “Phase I Dose Escalation Study of CD19/CD22 Chimeric Antigen Receptor (CAR) T Cells in Children and Young Adults With Recurrent or Refractory B Cell Malignancies”

Size: 50 Participants

Start Date: October 20, 2017

Primary Completion Date: August 1, 2025

Sponsor: Stanford Cancer Institute

Principal Investigator: Crystal Mackall

Grant: P30CA124435 (NIH Extramural Grant)

NCT03233854, “Phase I CD19/CD22 Chimeric Antigen Receptor(CAR) T Cells in Adults With Recurrent/Refractory B Cell Malignancies”

Size: 57 Participants

Start Date: September 1, 2017

Primary Completion Date: September 1, 2025

Sponsor: Crystal Mackall, MD, CIRM

Principal Investigator: David Miklos (Stanford University)

Grant: CIRM Grant CLIN2-10846 - \$11,034,982

The therapy has been tested at Stanford in 12 patients—five with Diffuse Large B-Cell Lymphoma (DLBCL) and six with ALL—and had “impressive results.”³⁵ Leah Hoffman, the point of contact for the intramural trial, confirmed that the NIH has begun testing the invention in pediatric subjects. KEI requested additional information about the status of the NIH trial from the principal investigator, Nirali Shah, but as of the date of these comments, she has not responded.

The fact that the federal government and state of California are funding these trials, including one conducted on the NIH campus by NCI employees, indicates that these inventions have a higher likelihood of success than technologies licensed at earlier, riskier stages of development.

The Second Invention - A Bicistronic CAR Construct

The NIH abstract for the second invention, a bicistronic CAR T-cell therapy, describes its development stage as “Pre-clinical (in vivo)[.]”³⁶ It notes that the treatment “eradicated ALL in a xenograft model derived from a patient with relapse following CD19-directed therapy[.]”³⁷

Federal Funding

³⁵ Crystal Mackall, “Future Development of CAR T Cells for Pediatric Malignancies,” 7th ACCELERATE Pediatric Oncology Conference Feb 2019, Brussels, available at

<https://www.accelerate-platform.org/wp-content/uploads/sites/4/2019/03/2.-Crystal-Mackall.pdf>.

³⁶ <https://www.otc.nih.gov/technology/e-017-2017>.

³⁷ *Id.*

The NIH should consider the federal government's investment in developing a patented invention when negotiating an exclusive license in the technology, because it impacts the value of the invention and the reasonableness of granting broad exclusive rights.

The NIH would not disclose how much money the government has allocated toward developing the inventions, but we can make an estimate using data provided by CIRM.

CIRM reports on its website that the grant award for NCT03233854 was \$11,034,982. Dividing \$11,034,982 by the number of subjects enrolled, 57, we arrive at an per-patient cost of \$193,596. Multiplying that figure by the number of patients enrolled in the two NIH-sponsored trials—139—we estimate the federal government is investing \$27 million to the invention's clinical research.

KEI asked Dr. Knabb what the NIH has spent on the invention's research and development, and he declined to answer. Of course, the NIH knows what its own trials costs, and we would appreciate if the NIH could share this information so that we do not have to make estimates.

Regulatory Incentives

The subject inventions will likely qualify for valuable regulatory incentives, which must be taken into consideration when determining the "necessary incentive."

The first two CAR therapy approvals, for Yescarta and Kymriah, were granted orphan designation, breakthrough therapy designation, and priority review. Orphan drug designation confers 12 years market exclusivity for certain indications, as well as 12 year of test data protection on all indications, and a 25 percent tax credit on R&D costs, as well as other benefits.

Breakthrough therapy and priority review designations expedite the FDA approval process, reducing the time and thus expense of bringing an invention to market. The subject inventions are likely to qualify for such incentives. Since 2014, the FDA has granted at least five treatments an Orphan designation for DLCBL, one of the indications in this license.

Generic Name	Orphan Designation	Designation Date	Designation Status
blinatumomab	Treatment of diffuse large B-cell lymphoma	07/06/2017	Designated
C24H28N8O7S2	Treatment of diffuse large B-cell lymphoma	04/02/2015	Designated
Valproic acid	Treatment of diffuse large B-cell lymphoma	03/30/2017	Designated
tisagenlecleucel-T (Kymriah)	Treatment of diffuse large B-cell lymphoma	02/03/2015	Designated
axicabtagene ciloleucel (Yescarta)	Treatment of diffuse large B-cell lymphoma	03/27/2014	Designated

Kymriah earned Novartis a priority review voucher for its indications in B-cell precursor ALL that is refractory or in second or later relapse—another of the indications of the subject therapy.³⁸

On March 18, 2019, GW Pharmaceuticals announced it had sold a pediatric PRV for \$105 million.³⁹

2. The NIH has not demonstrated that it properly analyzed whether the scope of rights in this license will not be greater than reasonably necessary to induce the investment needed to commercialize the inventions.

Under 35 U.S.C. § 209(a)(2), the scope of an exclusive license must “not [be] greater than reasonably necessary to provide the incentive for bringing the invention to practical application[.]” The scope of an exclusive patent license may vary in terms of the period of exclusivity, territorial reach, and field of use, among other parameters.

The term of exclusivity is the most important aspect of the scope of an exclusive patent license because it determines the length of time that a licensee may claim a monopoly on a government-owned technology. This is an issue that warrants serious consideration, especially in the area of life-saving medicines, where exorbitant prices can mean life or death.

KEI asked Dr. Knabb how “the NIH [plans to limit the scope of the license to not broader than the necessary incentive.” Once again, he referred KEI to his statements regarding the prospective license to Lyell Immunopharma. There, he did not answer KEI’s questions about the duration of the license, stating that it was “not yet [] negotiated and would be business confidential[.]”⁴⁰

It appears, however, that the NIH always grants exclusive licenses for life-of-patent in gene and cell therapies such as the instant inventions.⁴¹ Dr. Mark Rohrbaugh, Special Advisor for Technology Transfer to the NIH Deputy Director for Intramural Research, stated in a letter to KEI that the NIH grants exclusive, life-of-patent licenses in cell and gene therapies because no company will commercialize them without such rights. This policy or practice violates Section 209, which requires that federal agencies negotiate exclusive licenses on a case-by-case basis, and mandates that the scope of a license in federally-owned inventions is limited to the necessary incentive.

³⁸

<https://www.federalregister.gov/documents/2017/09/11/2017-19130/issuance-of-priority-review-voucher-rare-pediatric-disease-product>.

³⁹

<https://www.globenewswire.com/news-release/2019/03/18/1756217/0/en/GW-Pharmaceuticals-plc-Announces-the-Sale-of-Priority-Review-Voucher-for-105M.html>.

⁴⁰ Attachment A.

⁴¹ Attachment B.

3. The NIH was not transparent about the government's financial contribution to the patented inventions, limiting the public's right to comment under 35 U.S.C. § 209(e).

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).

For the public to meaningfully comment on a license, it must have basic information about it. Our ability to comment on the license has been limited by the NIH's refusal to state what it has spent on the relevant clinical trials—an issue that is relevant to whether the grant of exclusivity and scope of the license are reasonable.

When asked how much money NIH has contributed to the development of the subject inventions, Dr. Knabb responded that he “d[id] not have additional information related to the costs, etc. of these clinical trials.” While it may be the case that Dr. Knabb does not personally have such information, someone within NIH should be able to disclose such data.

KEI submitted a request under the Freedom of Information Act (FOIA)⁴² to obtain that information, but its efforts were unsuccessful. The NIH denied KEI's request, stating that it does not have any records of the actual or expected costs of the intramural trials and that the costs of extramural trials can be located online, using RePORTER.⁴³ KEI's FOIA request explained in detail, however, that RePORTER does not contain the records and information sought. KEI submitted an administrative appeal of the denial and is awaiting a response. We note, however, that nothing in the FOIA precludes an agency from providing information to the public voluntarily, in connection with an exclusive patent license for which the notice-and-comment period is typically shorter than the period of time in which the NIH processes and responds to FOIA requests.

4. The NIH apparently has not sought the antitrust advice of the U.S. Attorney General regarding the license, as required by 40 U.S.C. § 559.

We object to the license unless the NIH first obtains the antitrust advice of the United States Attorney General, who confirms that the license would not be anticompetitive.

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).

⁴² NCI 19-133, FOIA Case No. 52838.

⁴³ Attachment C.

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." The statute exempts personal property if the fair market value is less than \$3,000,000, but specifically excludes "a patent, process, technique, or invention" from that exception.

The regulation 41 C.F.R. § 102-75.270 also makes clear the inclusion of patents "irrespective of cost."

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 Dr. Knabb whether the NIH requested the advice of the U.S. Attorney General concerning the licenses. Dr. Knabb did not answer. In the past, the NIH has asserted its position with respect to 40 U.S.C. § 559 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 governed by the Bayh-Dole Act and its regulations.

We disagree.

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

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.

If NIH grants an exclusive license in a federally-owned invention, it is disposing of a government property interest so as to trigger 40 U.S.C. § 559.

5. In the event that the NIH decides to grant the license over our objections, we recommend that the NIH includes a series of provisions designed to safeguard the public interest and ensure that the licenses implement the governing principles listed in the Public Health Service (PHS) technology transfer manual.

In the event that the NIH proceeds with the license, KEI requests that it includes the following provisions to protect the public's interest in the NIH-funded technology:

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.
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 something that will give effect to the policy objective in the "United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, PHS Licensing Policy," which states the following: "PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries."
3. **Global registration and affordability.** The license should require CJ Healthcare 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.

Conclusion

The CAR therapies covered by this license are being developed by NCI and Stanford scientists, with the support of the federal government, cancer charities, and the state of California. As always, the license may not be granted unless it satisfies all of the criteria set forth under 35 U.S.C. § 209(a) and the NIH first obtains the antitrust advice of the US Attorney General. If the NIH proceeds with the license, on the grounds that some exclusivity is required, we request that the years of exclusivity be limited to that which is reasonably necessary, and that the license incorporate the modest safeguards outlined above regarding pricing and affordability, and transparency.

Sincerely,

Knowledge Ecology International
Union for Affordable Cancer Treatment
Public Citizen
Social Security Works
Health GAP (Global Access Project)
Professor Brook K. Baker
Clare Love