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Via Email: vidita.choudhry@nih.gov

Re: Prospective Grant of an Exclusive Patent License: Antibody-Based Therapy for the Treatment of CD20 Expressing Lymphomas, 85 FR 31193, to the firm, Retargeted Therapeutics

Dear Dr. Choudry:

Knowledge Ecology International (KEI) and the Union for Affordable Cancer Treatment (UACT) are writing to comment on the "Prospective Grant of an Exclusive Patent License: Antibody-Based Therapy for the Treatment of CD20 Expressing Lymphomas" to "Retargeted Therapeutics, a corporation incorporated under the laws of the state of Delaware," as described in the Federal Register notice located at 85 FR 31193 ("the notice").[1]

The inventions were supported by funding from U.S. taxpayers, with the aim to make certain monoclonal antibody treatments more effective in combating B-cell lymphomas.

To grant the license, the National Institutes of Health (NIH) must determine that it serves the public interest, that exclusivity is necessary to incentivize a company to commercialize the invention, and that the scope of the license is not broader than necessary. The NIH must also seek the antitrust advice of the U.S. Attorney General before executing the license.

We are concerned that the process for the proposed license lacks transparency, and that the license will not serve the public interest.

[1] 85 Fed. Reg. 31193 (May 22, 2020), available at https://www.federalregister.gov/documents/2020/05/22/2020-11036/prospective-grant-of-an-exclusive-patent-license-antibody-based-therapy-for-the-treatment-of-cd20.

According to the FR notice, Retargeted Therapeutics is incorporated in Delaware. But there is no evidence of such registration in the state's online business records. Even more puzzling, the company that the NIH has chosen for an exclusive license does maintain a website.

The NIH has not responded to several questions about the license.

Based upon the NIH's prior approach toward its technology transfer responsibilities under the Bayh-Dole Act and its other legal duties, we are concerned that the NIH has not engaged in the type of economic analysis required by 35 U.S.C. § 209(a), and it is our assumption that the NIH has failed to seek the advice of the U.S. Attorney General, as is required by statute.

It is especially difficult to comment on a license when the terms of the license are not disclosed by the NIH, and the company is a ghost.

Background

The Inventions

The proposed license covers seven patents or patent applications, all titled, "Antibody Targeting Cell Surface Deposited Complement Protein 3d and Use Thereof."[2]

The patent filing dates range from January 8, 2014 to December 9, 2019, roughly seven months ago.

Four of the patent applications are in the United States, including one that was granted on July 31, 2018, and three that are still pending. There is one patent application pending in Canada, one application to the WIPO PCT, and one application to the EPO, which was granted on September 18, 2019.

NIH ref No.	Title	Patent application No.	Filing date	Issue date	Issued patent No.
E-758-2013-0-US-01	Antibody Targeting Cell Surface Deposited Complement Protein C3d and Use Thereof	61/924,967	Jan 8, 2014		
E-758-2013-1-PCT-01	Antibody Targeting Cell Surface Deposited Complement Protein C3d and Use Thereof	PCT/US2015/010620	Jan 8, 2015		
E-758-2013-1-US-02	Antibody Targeting Cell Surface Deposited Complement Protein C3d and Use Thereof	15/110,577	Jul 8, 2016	Jul 31, 2018	10,035,848
E-758-2013—1-CA-03	Antibody Targeting Cell Surface Deposited Complement Protein C3d and Use Thereof	2936346	Jan 8, 2015		

[2] *Id.*

E-758-2013-1-EP-04	Antibody Targeting Cell Surface Deposited Complement Protein C3d and Use Thereof	15701442.4	Jan 8, 2015	Sep 18, 2019	3092252
E-758-2013-1-US-05	Antibody Targeting Cell Surface Deposited Complement Protein C3d and Use Thereof	16/047,929	Jul 27, 2018		
E-025-2019-0-US-01	Antibody Targeting Cell Surface Deposited Complement Protein C3d and Use Thereof	62/945,569	Dec 9, 2019		

U.S. Patent No. 10,035,848, (the "'848 patent") was issued on July 31, 2018. The inventors listed on the '848 patent are Adrian Wiestner, Martin Skarynski, Margaret Lindorfer, Ronald Taylor, Christoph Rader, and Berengere Vire.[3] According to the USPTO publication, the '848 patent is co-assigned to the University of Virginia Patent Foundation, but the notice fails to mention this or to explain the role of the University of Virginia Patent Foundation in the proposed license. The patent text contains the following statement of "Government Interests":

> This invention was made with Government support under project number 1ZIHL006070-03 by the National Institutes of Health, National Heart, Lung, and Blood Institute. The Government has certain rights in the invention.[4]

1ZIAHL006070-03 is a Fiscal Year 2012 intramural grant from the National Heart, Lung, and Blood Institute (NHLBI) for $482,780. The principal investigator for the project is Dr. Adrian Wiestner.

The Federal Register notice disclosing the invention as available for licensing, 83 FR 51969, states that the technology was invented by researchers at NIH and the

[3] http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&u=%2Fnetahtml%2FPTO%2Fsearch-adv.htm&r=1&f=G&l=50&d=PTXT&p=1&S1=10,035,848&OS=10,035,848&RS=10,035,848.

[4] *Id.*

University of Virginia School of Medicine.[5] It also states that the publication, "A CD19/CD3 bispecific antibody for effective immunotherapy of chronic lymphocytic leukemia in the ibrutinib era,"[6] is relevant to the invention. That article lists, as support, the intramural program at NHLBI and NIH Grant No. R01 CA181258, a grant to Christoph Rader from 2014 to 2018 for a total of $1,985,775.

Scope of the License

The proposed territorial reach of the license is worldwide, and the "fields of use that may be limited to use of anti-C3d monoclonal antibodies (mAbs) to potentiate anti-tumor activity of anti-CD20 mAbs for the treatment of B-cell lymphomas."[7] The proposed fields of use appear to be commensurate with the claims in the '848 patent. The notice does not state the proposed term of exclusivity.

The Prospective Licensee

The prospective licensee, Retargeted Therapeutics, does not maintain a website and is not incorporated in the state of Delaware, according to Delaware's online business records. KEI searched the terms "Retargeted Therapeutics" and "Retargeted" in the "Entity Name" field at the Delaware Department of State: Division of Corporations website (https://icis.corp.delaware.gov/ecorp/entitysearch/namesearch.aspx), and no results were returned.

Discussion

1. The prospective licensee, Retargeted Therapeutics, is a Ghost.

Retargeted Therapeutics is not listed in the Delaware Division of Corporations public database as a company incorporated in Delaware, and more importantly, does not have any public presence, and has no history of commercializing inventions.

In order to grant an exclusive patent license, the NIH must find, among other requirements, "that the public will be served by the granting of the license, as indicated by *the applicant's intentions, plans, and ability to bring the invention to practical application* or otherwise promote the invention's utilization by the public." 35 U.S.C. § 209(a)(2)(emphasis added). Achieving "practical application" requires making an invention available to the public "*on reasonable terms*." 35 U.S.C. § 201(f)(emphasis added).

[5] 83 Fed. Reg. 51969 (Oct. 15, 2018), available at https://www.govinfo.gov/content/pkg/FR-2018-10-15/pdf/2018-22359.pdf.
[6] Robinson HR, Qi J, Cook EM, et al. *A CD19/CD3 bispecific antibody for effective immunotherapy of chronic lymphocytic leukemia in the ibrutinib era.* Blood. 2018;132(5):521-532. doi:10.1182/blood-2018-02-830992.
[7] 85 FR 31193.

The Federal Register Notice for the proposed license states that Retargeted Therapeutics is incorporated in Delaware. As noted above, KEI searched the online business records of Delaware, and no business of the name Retargeted Therapeutics or containing "Retargeted" is registered to conduct business or incorporated in Delaware. In addition, Retargeted Therapeutics does not maintain a website or any sort of social media presence. Because of the lack of any publicly available information about Retargeted Therapeutics, it is impossible to determine whether the company has the capacity to develop the invention into a product that is beneficial to cancer patients, let alone whether it will commit to making the technology available to the public on reasonable terms.

KEI emailed Dr. Vidita Choudry, the point of contact for the license, the question: "How can the public be assured that a non-registered, non-entity with no public presence and no history of commercializing inventions will use this invention in a way that is beneficial to the public?" She did not answer prior to 5 p.m. on the close of the comment period. KEI called Dr. Choudry at 3 p.m. on June 8, 2020, and asked her for the names of the principal officers of Retargeted Therapeutics. She would not answer, repeatedly stating that she would respond to KEI's email "in due time," even after KEI pointed out that the comment period would close that same day. KEI sent a follow-up email, asking for the identities of Retargeted's principal officers, and explaining that the information is not available online. She did not respond prior to 5 p.m. on the close of the comment period. KEI also asked Dr. Wiestner, one of the inventors of the technology, for the names of the principal officers of Retargeted Therapeutics. He did not respond prior to 5 p.m. on the close of the comment period, either.

2. We believe that NIH has not meaningfully evaluated whether the scope of exclusivity is not broader than necessary.

The grant of a monopoly on a federally funded invention is subject to restrictions in the Bayh-Dole, and in particular, when the invention is owned or partly owned by the federal government.

We are concerned that the NIH likely has not properly considered the scope of rights in the exclusive license is not broader than necessary, for example, as regards the number of years of exclusivity.

Nonexclusive licenses are preferred.[8] The NIH may grant an exclusive or partially exclusive license only when "granting the license is a reasonable and necessary incentive to—call forth

[8] PHS, *Policy for Making Determines Regarding the Grant of Exclusive or Partially Exclusive Commercialization*, United States Public Health Service Technology Transfer Policy Manual Chapter No. 305 (June 20, 2013), available at https://www.ott.nih.gov/sites/default/files/documents/policy/pdfs/305-policy.pdf.

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).

If the NIH determines that exclusivity is a necessary incentive, it must also ensure that the scope of the license is not broader than needed. *See* 35 U.S.C. § 209(a)(2)(requiring that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application, as proposed by the applicant, or otherwise to promote the invention's utilization by the public[.]").

KEI emailed Dr. Choudhry a list of questions about the license and the NIH's analysis. Among other questions, KEI asked how the NIH determined that exclusivity is a necessary incentive and that the scope of the license does not exceed the incentive needed. She did not respond prior to the close of the comment period.

Based on the NIH's previous statements regarding exclusive patent licenses, we can assume that it did not perform the analysis required by 35 U.S.C. § 209(a)(1)-(2). KEI has raised two main issues with respect to exclusivity and the scope of proposed licenses: whether the NIH performed any economic analysis of the necessity of exclusivity and whether it considered limiting the scope of exclusivity to shorter than life of patent. The NIH answered both questions in the negative in the past, stating that for early stage therapeutics there is no demand for non-exclusive licenses, and that more controversially, that companies will not commit to commercializing an invention unless they are granted exclusivity for life of patent.[9] We have also asked whether the NIH has considered limiting exclusivity to high-income countries, or to non-US markets, but have not received a response to that inquiry, even though there is ample evidence that companies develop therapies with exclusivity limited to only one country, or some countries. For example, it is not uncommon for a company to expect exclusivity only in the United States, or only in European markets, even when inventions were not subsidized by the federal government.

The NIH's across-the-board assumptions about the necessary incentive do not satisfy its obligations under the Bayh-Dole Act. As the NIH has recognized, every invention is different and has unique commercial value. 35 U.S.C. § 209(a) requires a case-specific analysis. Specifically, in order to conclude that an exclusive license is necessary and that the scope of the license is not broader than necessary, some analysis must be undertaken, including, for example, consideration of the other types of incentives provided by law, such as test data protection, Orphan Drug exclusivity, etc., and the likely case that the developer can bring other patented inventions into the project, for which exclusivity exists. The NIH must also consider the possibility that a license for shorter than life of patent will be adequate to incentivize a company to commercialize a federally-owned invention, as it has done with numerous products for the treatment of cancer, including cases where products were only protected by five years

[9] Letter from Mark Rohrbaugh, Ph.D., J.D., NIH Special Advisor for Technology Transfer, to KEI (Nov. 26, 2019)(on file with KEI).

of exclusive rights in regulatory test data, with no patents. If the NIH did not investigate the possibility of granting a non exclusive or co-exclusive license, limiting the term of the proposed license, or otherwise limiting the terms, such as granting exclusivity only to non-US high income countries, it has not satisfied its obligations under 35 U.S.C. § 209(a)(1)-(2).

3. 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 because the NIH has not first obtained the antitrust advice of the United States Attorney General before disposing of government-owned property.

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).

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."

KEI asked Dr. Choudry whether the NIH requested the advice of the U.S. Attorney General concerning the licenses. Dr. Choudry 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.

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.

4. 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 license implements 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. **Geographic scope of exclusivity.** If the NIH decides to grant exclusive rights to the subject inventions, it should limit exclusivity to the European Union, Japan and other high-income countries, but not the United States, so that countries that did not fund the R&D underlying the inventions would bear the costs of the exclusivity, while the US residents would not. The NIH should also limit exclusivity in moderate and lower income countries, where the monopoly is likely to have an adverse impact on access with almost no benefit in terms of the incentives for the company.

2. **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.

3. **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.”

4. **Global registration and affordability.** The license should require Retargeted Therapeutics 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.

5. **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.

6. **Years of exclusivity.** We propose the license reduces 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[.]"

7. **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

We object to the proposed license to Retargeted Therapeutics for the reasons stated herein. In the event that the NIH grants the license, we ask that it incorporates the provisions listed above, which are designed to protect the public interest in the licensed technologies and to

accomplish the policies outlined in the PHS Technology Transfer Manual and Section 200 of the Bayh-Dole Act.

Sincerely,

Knowledge Ecology International
Union for Affordable Cancer Treatment