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March 30, 2021

**Re: Prospective Grant of an Exclusive Patent License: Development, Production, and Commercialization of Ebola Neutralizing Single Monoclonal Antibody for the Treatment of Ebola Virus Disease in Humans ([86 FR 14331](#))**

Dear Daniel Lee, J.D.:

Knowledge Ecology International (KEI) would like to offer the following comments regarding the “Prospective Grant of an Exclusive Patent License: Development, Production, and Commercialization of Ebola Neutralizing Single Monoclonal Antibody for the Treatment of Ebola Virus Disease in Humans,” to Ridgeback Therapeutics, L.P. located in Miami, Florida.

The geographic scope of the license is worldwide, and the field of use conveys the rights to the, “development, production, and commercialization of Ebola neutralizing monoclonal antibody mAb114, as a single antibody not in combination with other monoclonal antibodies, for the treatment of Ebola virus disease in humans.”

According to the *Federal Register (FR)* notice, the invention the NIH intends to license is E-045-2015, titled “Neutralizing Antibodies to Ebolavirus Glycoprotein and Their Use.” The National Institutes of Health (NIH) Office of Technology Transfer (OTT) website publishes abstracts for NIH-owned inventions, and the abstract for E-045-2015 at the OTT webpage is titled, “Human-derived Monoclonal Antibody for Treatment of Ebola Virus Infection”. The OTT abstract for E-045-2015 calls the invention, “mAb114”.

It is unclear from the Federal Register Notice whether the invention the NIH is currently proposing licensing to Ridgeback is identical to mAb114 or if it is a companion technology. The patent and patent application numbers in the E-045-2015 abstract for the OTT website do not match the numbers listed in the *Federal Register* notice.

There are, however, several reasons to think that the inventions are the same. First, a patent that is listed in the E-045-2015 abstract at the OTT website is titled, “Neutralizing antibodies to

Ebola virus glycoprotein and their use” -- the same title used in the *FR* notice. Second, the inventors listed in the patents on the E-045-2015 abstract match the inventors of mAb114.

According to a January 24, 2019 press release issued by the National Institute of Allergy and Infectious Diseases (NIAID), mAb114 was invented by the NIAID and the Army in conjunction with Institute for Research in Biomedicine, and the NIAID subsequently licensed mAb114 to Ridgeback.<sup>1</sup> Given the connections between the invention as described in the *FR* notice and the description in the OTT invention abstract, it appears that the invention the NIH is proposing licensing to Ridgeback is in fact mAb114. Assuming this is the case, it is unclear why the NIH is publishing the *Federal Register* notice now. If the NIH failed to notify the public before executing an exclusive license to Ridgeback in this invention in 2019, then that license is void for failure to comply with the notice and comment requirements at 35 U.S.C. § 209(e), which cannot be performed retroactively.

The January 24, 2019 press release states further that at the time of the release mAb114 was in two clinical trials: NCT03478891 and NCT03719586. The first clinical trial listed in the press release was a Phase 1 trial of mAb114 consisting of 19 patients. It was conducted by the NIH at its Clinical Center in Bethesda, Maryland. A paper reporting results on the trial states that none of the patients treated with mAb114 suffered serious side effects from the treatment.<sup>2</sup> The second is a completed Phase 2/3 trial which investigated four treatments, including mAb 114, in 1044 participants. This trial was conducted in the Congo but was administered and funded by NIAID. A paper reporting the results of the Phase 2/3 trial states that mAb114 was more effective in treating Ebola than other treatments investigated in the study.<sup>3</sup>

Ridgeback was awarded two grants from the Assistant Secretary of Preparedness and Response to develop mAb114: Contract No. 75A50120C00009, wherein Ridgeback can be reimbursed up to \$153,663,387.24 for “CMC efforts for mAb114 for the Development and Treatment of Ebola”, and 75A50119C00059, wherein Ridgeback was awarded \$13,988,547 for “Additional in-scope work for CMC efforts for mAb114 development for the treatment of Ebola”. Under these two contracts, Ridgeback could earn up to \$168 million for developing mAb114.

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<sup>1</sup> <https://www.niaid.nih.gov/news-events/investigational-monoclonal-antibody-treat-ebola-safe-adults>

<sup>2</sup> Gaudinski MR, Coates EE, Novik L, Widge A, Houser KV, Burch E, Holman LA, Gordon IJ, Chen GL, Carter C, Nason M, Sitar S, Yamshchikov G, Berkowitz N, Andrews C, Vazquez S, Laurencot C, Misasi J, Arnold F, Carlton K, Lawlor H, Gall J, Bailer RT, McDermott A, Capparelli E, Koup RA, Mascola JR, Graham BS, Sullivan NJ, Ledgerwood JE; VRC 608 Study team. Safety, tolerability, pharmacokinetics, and immunogenicity of the therapeutic monoclonal antibody mAb114 targeting Ebola virus glycoprotein (VRC 608): an open-label phase 1 study. *Lancet*. 2019 Mar 2;393(10174):889-898. doi: 10.1016/S0140-6736(19)30036-4. Epub 2019 Jan 24. Erratum in: *Lancet*. 2020 May 30;395(10238):1694. PMID: 30686586; PMCID: PMC6436835.

<sup>3</sup> Camara M, Kojan R, Walker R, Dighero-Kemp B, Cao H, Mukumbayi P, Mbala-Kingebeni P, Ahuka S, Albert S, Bonnett T, Crozier I, Duvenhage M, Proffitt C, Teitelbaum M, Moench T, Aboulhab J, Barrett K, Cahill K, Cone K, Eckes R, Hensley L, Herpin B, Higgs E, Ledgerwood J, Pierson J, Smolskis M, Sow Y, Tierney J, Sivapalasingam S, Holman W, Gettinger N, Vallée D, Nordwall J; PALM Consortium Study Team. A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics. *N Engl J Med*. 2019 Dec 12;381(24):2293-2303. doi: 10.1056/NEJMoa1910993. Epub 2019 Nov 27. PMID: 31774950.

In addition to the direct monetary support from ASPR/BARDA, the NIH granted Ridgeback the rights in Phase 1 clinical trial data needed to support an application for FDA approval of mAb114, rights that may be worth \$100,000,000. In September of 2020, NIAID told KEI the following regarding mAb114 clinical trial data via email:

“NIAID filed two INDs related to mAb114 – one for the Phase 1 clinical trial of mAb114 and one for the PALM clinical trial in which the efficacy of mAb114, ZMapp, Remdesivir, and REGN-EB3 was evaluated. To enable expedited review of the BLA for mAb114 by the FDA, NIAID transferred the Phase 1 IND to Ridgeback Biotherapeutics. NIAID received no consideration for this transfer, and it was not conveyed under a license agreement. The transfer will accelerate access to this important therapeutic, enabling effective responses to ongoing Ebola outbreaks in Africa. NIAID remains the sponsor of the PALM clinical trial, and the data from this clinical trial has been shared with all of companies that supplied study products for this clinical trial.”

The NIH received nothing for transferring Phase 1 clinical data to Ridgeback, which not only could be described as “expediting approval of the treatment,” but also as granting Ridgeback a 12 year FDA regulatory monopoly on the test data. The NIH could have retained the rights in the data, allowing the government to obtain generic or biosimilar versions of the drug from third parties, particularly since the NIH has the manufacturing know-how for the drug, instead of gifting Ridgeback with a 12 year monopoly on the government’s own clinical trial data. One consequence of the series of transactions with Ridgeback is that the company was able to obtain a considerable commercial advantage in providing the US government with a drug that the US government itself invented and developed. Another consequence is that on December 21, 2020, the FDA determined that Ridgeback was [able to claim](#) a material threat medical countermeasure priority review voucher (PRV), as provided under section 565A of the Federal Food, Drug and Cosmetic Act (FDCA), assigned a tracking number, PRV BLA 761172, for the registration of Ebanga (ansuvimab-zykl, formerly referred to as mAb114).

It is not clear why the NIH proposes giving Ridgeback an exclusive license in mAb114 if the company already holds a license in the treatment. It is possible that the current license is non-exclusive, and that the NIH and Ridgeback desire to make it exclusive, which would make it more difficult for competitors to supply less expensive biosimilar versions.

Considering the government’s investment in mAb114, Ridgeback’s license in the technical data, the FDA approval of mAb114, and the priority review voucher claimed by Ridgeback for mAb114, we do not believe that the criteria for granting an exclusive license in the treatment are met. KEI opposes the grant of this exclusive license. The justification for an exclusive license in a federally-owned invention is to provide the incentive that is reasonably necessary for bringing an invention to market. 35 U.S.C. § 209(a)(1). Based upon a Ridgeback press release published in December of 2020, mAb114 is already at market because it has been granted FDA approval.

When granting exclusive patent licenses to federally-owned inventions, the NIH may only grant an exclusive license when exclusivity is a necessary incentive and must limit the scope of patent licenses, including the period of exclusivity, to that which is reasonable and necessary. 35 U.S.C. §209(a)(2). An invention requires a significantly lower level of incentives to induce commercialization when clinical trials are already completed and/or underway, the prospective licensee already has a license to clinical trial data, and the licensee will be reimbursed up to \$150 million on its expenditures to bring the invention to market. If it is the case that the invention that the NIH is proposing licensing on an exclusive basis to Ridgeback has already received FDA approval, then an exclusive license is not a reasonable and necessary incentive.

If the NIH chooses to ignore the requirements of 35 U.S.C. 209, and grant an exclusive license, KEI asks the NIH to include the following considerations and provisions in the terms of these licenses.

### ***Transparency***

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

**Acknowledgement of federal funding - publication and publicity.** The licensee should be required to include, when issuing statements, press releases, and other documents describing the development of any product that includes the licensed inventions, a statement that describes the role of the licensed inventions and the total and proportionate contribution of federal funding to the research and development performed to bring the inventions to market.

**Additional transparency issues.** The license should have provisions that give effect to the transparency norms set out in WHA72.8 “Improving the transparency of markets for medicines, vaccines, and other health products”, a resolution enthusiastically supported by HHS in 2019.

### ***Additional Provisions to Protect the Public Interest***

**Global registration and affordability.** The licenses should require the licensee to disclose the steps that each 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.

**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.

### ***Conclusion***

This license appears to completely ignore the restrictions on 35 U.S.C. § 209, which restrict the use of an exclusive license unless the exclusivity is a reasonably necessary incentive to call forth the investment capital and expenditures needed to bring the invention to practical application. The government has funded the development of the treatment, granted exclusive rights in test data to Ridgeback for no consideration, and the product already registered with the FDA, generating an additional windfall to Ridgeback by the granting of a valuable priority review voucher. We strongly oppose the grant of an exclusive license to Ridgeback for this invention.

Please notify us if and when a license is granted, so we can request a copy under the Freedom of Information Act.

Sincerely,

Claire Cassedy

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Knowledge Ecology International