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December 17, 2024

Re: Prospective Grant of an Exclusive Patent License: Vaccine Augmented Tumor Infiltrating Lymphocytes for the Treatment of Cancer (89 FR 95224)

Dear Dr. Green:

Knowledge Ecology International (KEI) would like to offer the following comments regarding the "Prospective Grant of an Exclusive Patent License: Vaccine Augmented Tumor Infiltrating Lymphocytes for the Treatment of Cancer" (89 FR 95224) to Iovance Biotherapeutics, Inc. (Iovance).

Iovance has had an ongoing relationship with the NIH, beginning in 2011 with a CRADA agreement (under Lion Biotechnologies, Inc. the company name at the time), and then with an exclusive license first executed in 2015 that was amended several times. One of those license amendments was in 2021, for which KEI provided comments.[1] The technology that Iovance licensed from the NIH has become the FDA-approved cell therapy, Amtagvi.[2]

Amtagvi is a cell therapy for the treatment of advanced melanoma that was approved by the FDA in February 2024. The lengthy press release from Iovance announcing Amtagvi's approval (currently a large banner on their website) makes no mention of the license from NCI nor the NIH's involvement at all with the technology.[3] Amtagvi was introduced at a wholesale acquisition cost of $515,000.[4]

Noting Amtagvi's high list price, the NIH must ensure that the instant exclusive license includes terms that ensure the resultant product is available to the public on an affordable and equitable basis. KEI urges the NIH to include terms concerning the following, in order to protect patients' access to products related to the technology to be licensed.

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[1] https://www.keionline.org/35632
[2] https://www.techtransfer.nih.gov/reports/hhs-license-based-vaccines-therapeutics
[3] https://ir.iovance.com/news-releases/news-release-details/iovances-amtagvitm-lifileucel-receives-us-fda-accelerated
[4] https://www.reuters.com/business/healthcare-pharmaceuticals/us-fda-grants-accelerated-approval-iovances-skin-cancer-cell-therapy-2024-02-16/

Access in Developing Countries

The Federal Register notice states that the intended geographic scope of the exclusive license "may be "worldwide"". How has the NIH determined that a "worldwide" geographic scope is necessary to induce investment in this technology? For example, in the CRADA and license agreements concerning Iovance's Amtagvi, are there reporting requirements that have indicated that developing country markets are a key part of their revenue stream? We strongly urge the NIH to assess the impact of a "worldwide" geographic scope for this (and all) exclusive license and also urge the NIH to include in this license terms that ensure affordable access to patients in developing countries.

As cited in the United States Public Health Service Technology Transfer Policy Manual, Chapter No. 300, dated 12/08/2010, "PHS seeks to promote commercial development of inventions in a way that provides broad accessibility for developing countries." NIH must include terms that implement this policy such as limiting the exclusivity in countries with average incomes less than one-third of the United States.

Additionally, NIH should retain a right to grant the WHO, the Medicines Patent Pool, or other governments the right to use the patent rights in procuring the medical technology from competitive suppliers, including technology transfer, in low- and middle-income countries (LMICs). This authority should be exercised when HHS or the WHO determines that people in these markets lack sufficient access to the required medical technology.

Price Gouging

Additionally, US patients should not pay more for the treatment than those in other high income countries. Any resultant treatment 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.

Companies will enter into agreements with terms on this issue - recently HHS entered into an agreement with Regeneron for a COVID-19 treatment with a reasonable pricing clause, and similar international reference pricing clauses have been included in contracts with companies such as Sanofi, Moderna, and Pfizer. Attached is an ANNEX on Pricing Clauses in U.S. Government Contracts for COVID-19 Products citing examples of agreements.

Technology Transfer

The license should include a requirement that the licensee provide manufacturing know-how and regulatory marketing and/or data rights to the NIH or any entity designated by the NIH, in the event that the NIH determines that the price in the United States is excessive, and or in order to expand access to treatments in developing countries that do not have sufficient or reasonably priced access.

Transparency

In 2019, the United States endorsed the adoption of the World Health Assembly (WHA) Resolution 72.8, titled “Improving the transparency of markets for medicines, vaccines and other health products.” In this license, the NIH should incorporate, to the extent possible, transparency norms that meet or exceed the standards outlined in WHA72.8. For example, the license should require the reporting of the costs of clinical trials and the amount of any public sector subsidies in the development of the treatment, including those in addition to direct financial payments, such the U.S. Orphan Drug Tax Credit.

Conclusion

It is critical that the NIH ensures that the terms of this license promote the public interest in the invention and protect patients’ equitable access to the technology, should it come to market. KEI therefore requests that the license incorporates the provisions listed above in order to achieve those goals.

Sincerely,
Claire Cassedy
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Knowledge Ecology International

ANNEX Pricing Clauses in U.S. Government Contracts for COVID-19 Products

In 2020 and 2021, several U.S. government contracts for the development of COVID 19 vaccines, therapeutics, diagnostic tests and other related products included provisions on pricing. Some contracts include a most favored nation pricing clause that specifically requires the company to provide the U.S. government with "a price lower" than the price offered to any centralized federal authority that is "a member of the Group of Seven plus Switzerland." The non-US members of the G7 are Canada, France, Germany, Italy, Japan, the United Kingdom.

Table A1, U.S. Government COVID-19 Contracts Containing Reference Price Constraints on Resultant Products

Contractor, Agency, and Contract Number	Subject	Page Located	Reference Price Term Excerpt
Most Favored Nation Clauses			
Eli Lilly The Army W911QY21D0012 P0002 April 7, 2021	Monoclonal Antibody Treatment Production	7-8	**"H. 7 Sales to Covered Nations** (i) Due to the exceptional and unprecedented nature of the COVID-19 threat to global public health, as well as the investments made towards the development of a safe and effective therapeutic against COVID-19, Lilly agrees that it will not at any time prior to 30 September 2021 sell any COVID-19 bamlanivimab/etesevimab combination therapeutic supplied directly to the Government under this Agreement to any centralized federal authority (i.e., federal government or equivalent) of a nation that is a member of the Group of Seven plus Switzerland ('Covered Nation') at a lower price than the prices set forth in this contract. . . . "
Eli Lilly The Army W911QY21C0016 October 26, 2020	Monoclonal Antibody Treatment Production	18	"**H.7 Sales to Covered Nations** (i) Due to the exceptional and unprecedented nature of the COVID-19 threat to global public health, as well as the investments made towards the development of a safe and effective therapeutic against COVID-19, Lilly agrees that it will not at any time prior to 30 June 2021 sell any COVID-19 therapeutic supplied directly to the Government under this Agreement to any centralized federal authority (i.e., federal government or equivalent) of a nation that is a member of the Group of Seven plus Switzerland ('Covered Nation') at a lower price than the prices set forth in this contract. . . ."
Merck Sharp & Dohme The Army W911QY21C0031 June 7, 2021	Therapeutic Development	21	H.7. Fully redacted including the title
Pfizer The Army W58P0522C0001	Paxlovid Purchase Agreement	33	**H.7 Most Favored Nation Clause** (a) If, at any time prior to, or during, the base term and any

Contractor, Agency, and Contract Number	Subject	Page Located	Reference Price Term Excerpt
November 17, 2021			exercised options of this contract, Contractor enters into any agreement with a Covered Nation under which the Covered Nation commits to purchase (i) the same or a lesser volume of Product than the U.S. Government commits to purchase (ii) at a price lower than the price the U.S. Government is obligated to pay for Product under this contract, Contractor shall provide notice of such lower price to the U.S. Government within 30 days of the execution of the Contractor-Covered Nation agreement and the U.S. Government may elect, at its discretion, to receive the benefit of this provision and purchase the Product at that lower price.
Sanofi The Army W15QKN1691002; MCDC2011-005 July 30, 2020	Vaccine R&D and Production	28	"**5.1 Most Favored Nation Clause** (i) Due to the exceptional and unprecedented nature of the COVID-19 threat to global public health and in recognition of the long historical partnership between the U.S. Government and Sanofi Pasteur working on global pandemic solutions, as well as the investments made towards the development of a safe and effective vaccine against COVID-19, Sanofi Pasteur agrees that it will not sell any COVID-19 vaccine licensed under this Agreement to any nation that is a member of the Group of Seven plus Switzerland ('Covered Nation') at a price that is more favorable than those set forth in this Project Agreement."
Most Favored Customer Clauses			
ANP Technologies, Inc. The Army W911QY20D0019 May 29, 2020	Development and Production of a Diagnostic	11	"MOST FAVORED CUSTOMER H.1 Most Favored Customer Awardee agrees that during the term of this contract and for a period of 5 years thereafter, that it shall not offer, sell or otherwise provide the production model of the CLIN 0001 end items (for the avoidance of doubt, CLIN 0001 end items in this clause shall mean a finished good of like material, like quality, to be used in a similar applications, and shall not include more general products to any entity at a price lower than that offered to the DoD. In the event that Awardee sells the production model at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the Contracting Officer in writing of the lower price. For prior purchases, the Awardee shall reimburse the DoD, the difference between the lower price sold to the other customer(s) and the price sold to the DoD multiplied by the number of items sold. Such reimbursement shall occur within thirty days (30) of the Awardee discovering that the lower price was given to another customer. Notwithstanding the foregoing, the Parties may agree to apply the difference in price paid by the other customer(s) and DoD into additional quantities required by the DoD."
AstraZeneca The Army W911QY2190001 October 9, 2020	Monoclonal Antibody Treatment R&D and Production	32	**ARTICLE 9. Most Favored Customer** A. In the event that the Parties agree to a follow-on production pursuant to 10 U.S.C. § 2371b, Awardee agrees that it shall sell to the U.S. Government the first million

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			doses of AZD7442 at a price of [REDACTED]. Any additional doses will be sold to the U.S. Government at a price to be negotiated and agreed by the Parties. B. If Awardee develops a like product (commercialized version or derivative of the production model of the Prototype) with similar capability and intended application, but at a lower unit price ("Like Product") regardless of quantity, Awardee shall make the U.S. Government aware of that similar product and the technical and price differences between that product and the Prototype. Such notification shall be made to the OTAO in writing, of which email is an acceptable form, within [REDACTED] of such offering.
Emergent BioSolutions Canada Inc. The Army W911QY2090013 June 24, 2020	Post-exposure Prophylaxis (PEP) Development	16	"**ARTICLE 9. Most Favored Customer** A. Awardee agrees that it shall not offer, sell, or otherwise provide the production model of the Prototype to any entity at a price lower than it offered to the DoD. In the event that Awardee sells the production model of the Prototype at a lower unit price than that price sold to the DoD, Awardee shall reimburse the DoD, the difference between the lower price sold to the other customer (S) and the price sold to the DoD multiplied by the number of items sold . . . ."
Immunome, Inc. The Army W911QY2090019 July 3, 2020	"research and development of a standardizable and scalable [REDACTED] comprised of [REDACTED] antibodies [REDACTED] . . . ."	16	"**ARTICLE 9. Most Favored Customer** A. Awardee agrees that it shall not offer, sell or otherwise provide the production model of the Prototype to any entity at a lower price than that offered to the DoD. In the event that Awardee sells the production model of the Prototype at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the OTAO in writing of the lower price. . . ."
Inovio Pharmaceuticals, Inc. The Army W911QY2090016 June 22, 2020	Vaccine Delivery Device Development	17	"**ARTICLE 9. Most Favored Customer** A. For a period of six (6) years from the Effective Date, Awardee agrees that it shall not offer, sell or otherwise provide the production model of the Prototype to any entity at a price lower than that offered to the DoD. In the event that Awardee sells the production model of the Prototype at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the OTAO in writing of the lower price. . . ."
Maxim Biomedical, Inc. The Army W911QY20D0018 May 11, 2020	Diagnostic Production	10	**"H.1 Most Favored Customer** A. Awardee agrees that during the term of this contract and for a period of 5 years thereafter, that it shall not offer, sell or otherwise provide the production model of the CLIN 0001 end items (for the avoidance of doubt, CLIN 0001 end items in this clause shall mean a finished good of like material, like quality, to be used in a similar applications, and shall not include more general products to any entity at a price lower than that offered to the DoD. In the event that Awardee sells the production model at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the Contracting Officer in writing of the lower price. . . ."

Contractor, Agency, and Contract Number	Subject	Page Located	Reference Price Term Excerpt
Murtech, Inc. The Army W911QY20D0017 May 11, 2020	Diagnostic Production	15	**"H.1 Most Favored Customer** A. Awardee agrees that during the term of this contract and for a period of 2 years thereafter, it shall not offer, sell or otherwise provide the production model of the CLIN 0001 end items (herein the 'Items') (for the avoidance of doubt, CLIN 0001 production model end items in this clause shall mean a finished good of like material, like quality, to be used in a similar applications, and shall not include more general products) to any entity at a price lower than that offered to the DoD."
Novavax The Army W911QY20C0077 P0002 June 4, 2020	Vaccine Development and Production	4	"The Contractor shall maintain a most favored customer provision for the product once authorized or licensed by the FDA, such that the Contractor shall not give any entity a better price than the DoD for a period of five (5) years from the award of this contract, limited to customers in the U.S. and purchases made in the U.S to include sale prices as compared to commercial clients with respect to quantity, location of delivery, fundamental differences in deliverable formulation, and material differences in terms and conditions for commercial contracts."
Rigel Pharmaceuticals The Army W911QY2190018 January 29, 2021	Therapeutic Development	29	**ARTICLE 20. Most Favored Customer.** A. In the event that the Parties agree to a follow-on production agreement pursuant to 10 U.S.C. 2371b, Awardee agrees that it shall sell to the U.S. Government up to [REDACTED] treatment courses of TAVALISSE at a price not greater than [REDACTED]. Any additional treatment course will be sold to the U.S. Government at a price to be negotiated and agreed by the Parties. B. If Awardee develops a like product (commercialized version or derivative of the production model of the Prototype) with similar capability and intended application, but at a lower unit price ("Like Product") regardless of quantity, Awardee shall make the DoD aware of that similar product and the technical and price differences between that product and the Prototype. Such notification shall be made to the OTAO in writing, of which email is an acceptable form, within thirty (30) days of such offering.
60 Degrees Pharmaceuticals The Army W911QY2190011 December 4, 2020	Therapeutic Development	16	**Article 9. Most Favored Customer** A. [REDACTED] [REDACTED] C. This Article applies only to products sold in the [REDACTED] related to COVID-19.
Government Preference Clauses			
Becton, Dickson & Company The Army W911SR2030001 July 1, 2020	Needle Production	17	**"9. Government Preference** 9.1 Pricing. During the term of the Agreement, the Recipient agrees that, in the event that it enters into a Group Purchasing Organization (GPO) contract with a Qualifying Third Party (as defined below) with respect to a Qualifying Product (as defined below) with a per unit GPO price lower than that offered for the same Qualifying Product to the Government, the Recipient shall (i) promptly notify the Agreements Officer in writing of the lower price

Contractor, Agency, and Contract Number	Subject	Page Located	Reference Price Term Excerpt
			and (ii) extend the lower price to all future sales of the Qualifying Product to the Government. . . . " For purposes of this section, "Covered Nation" shall mean a nation that is a member of the Group of Seven (Canada, France, Germany, Italy, Japan, the United Kingdom, and the United States) plus Switzerland.
Global Life Sciences Solutions The Army W911NF2130001 October 13, 2020	Expanded Manufacturing and Production Capacity	8	**9. Government Preference** 9.1 [REDACTED] 9.2 [REDACTED] 9.3 [REDACTED]
Retractable Technologies, Inc. HHS W911SR2030004 July 1, 2020	Expansion of Manufacturing Capacity of Needles/Syringes	23	**9. Government Preference** [REDACTED]
SIO2 Medical Products, Inc. The Army W911NF2030003 June 5, 2020	Vaccine Delivery Device R&D	13	"**9. Government Preference** 9.1 Pricing. During the period of performance and the exercised optional availability periods, the Recipient agrees that, in the event that it offers, sells or otherwise provides a Qualifying Product (as defined below) to any Qualifying Third Party (as defined below) at a per unit price lower than that offered for the same Qualifying Product to the Government or a third party purchasing Qualifying Product pursuant to a designation by the Government pursuant to Section 9.2 or 9.3 (an 'MCM Partner'), the Recipient shall (i) promptly notify the Agreements Officer in writing of the lower price and (ii) extend the lower price to all future sales of the Qualifying Product to the Government or an MCM Partner."