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Michael Shmilovich, Esq.,
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RE: Prospective Grant of Exclusive Patent License: Treatment of Type 1 Diabetes and its Comorbidities, 83 FR 38707 (https://www.federalregister.gov/d/2018-16836), to Inversago Pharma, a firm headquartered in Canada.

Dear Michael Shmilovich, Esq.:

Knowledge Ecology International (KEI) and T1International jointly provide the following comments on the prospective grant of an exclusive patent license for human therapeutics for type 1 diabetes to a Montreal-based company called Inversago Pharma, Inc., as noticed on August 7, 2018 in the Federal Register (83 FR 38707).

KEI is a non-profit organization with offices in Washington, DC and Geneva, Switzerland, that focuses on the management of knowledge goods, including medical inventions. KEI is focused on improving innovation for and access to new medical technologies. Our comments to the NIH in this and in several other matters often focus on the responsibility of the NIH to ensure that subject inventions are available to the public on reasonable terms, and that exclusive rights are limited to those that are reasonably necessary to induce the investments needed to bring the invention to practical application. KEI is concerned about the impact of high prices on the affordability of and access to medical treatments, both in the United States and for vulnerable populations in developing countries.

T1International is a non-profit run by people with and impacted by type 1 diabetes, for people with type 1 diabetes. T1International is active around the world in efforts to fight against high prices for insulin and other treatments essential for persons living with type 1 diabetes.

According to the notice published in the Federal Register, the prospective exclusive patent license territory, “will be granted worldwide and in a field of use not broader than human therapeutics for type I diabetes and its comorbidities diabetic nephropathy, chronic kidney disease, diabetic retinopathy, and peripheral and autonomic neuropathy.”

Inversago Pharma, Inc. is a company located in Canada, that is “focused on the development of peripherally-restricted CB1 receptor (CB1) inverse agonists for the treatment of Prader-Willi Syndrome, type 1 diabetes and metabolic disorders in general,” according to the description

provided on the Inversago website.[1] This company has several investigational drugs in their pipeline targeting four indications, but only one of those investigational drugs (for Prader-Willi Syndrome) has reached preclinical stage.[2]

Based on information provided in the Inversago website[3] and the Federal Register notice 80 FR 66015 from October 28, 2015[4], Inversago already holds a license (which was executed[5]) to several NIH-owned inventions related to "CB1 receptor mediating compounds."

NIH scientist George Kunos appears as an inventor in the published applications or issued patents listed in that October 28, 2015 Federal Register notice, as well as in the published or issued patents cited in the 2018 notice.

The geographical scope for the license in the 2015 notice was "worldwide" and the field of use was for the development of therapeutics for "obesity, type 2 diabetes, fatty liver disease and liver fibrosis in humans."[6]

The new exclusive license the NIH proposes for Inversago does two things. First, the NIH will effectively expand the field of use for all of the patents noticed by the NIH in 2015, so that the inventions can be used to treat type 1 diabetes. Second, the NIH includes several new granted patents or patent applications, which will also be licensed to treat type 1 diabetes.

In July 25, 2018, Inversago Pharma Inc announced that it had secured $7 million in financing "to pursue its development plan and advance its CB1 platform as a potent treatment for targeted diseases," including Prader-Willi Syndrome (PWS) and type 1 diabetes.[7] Development of human therapeutics for type 1 diabetes based on CB1 is presumably outside of the field of use of the exclusive NIH license Inversago currently holds.

Inversago notes on its website that the technology for which it had secured $7 million in financing was "based on the work by CB1 world expert George Kunos" at the NIH.[8]

The Federal Register notice 83 FR 38707 published on August 7, 2018 makes no reference to the previous exclusive license agreement executed between Inversago and the NIH. To the general public, the connection between the license agreement noticed in 2015 and executed in

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[1] https://web.archive.org/web/20180817175917/https://inversago.com/en/approach/
[2] https://web.archive.org/web/20180727110313/https://inversago.com/en/our-pipeline/
[3] https://web.archive.org/web/20180817175003/https://inversago.com/en/news-and-events/
[4] https://www.federalregister.gov/d/2015-27454
[5] The exclusive license agreement between Inversago Pharma Inc and the NIH, described in the notice 80 FR 66015, was executed on April 26, 2016, according to the company's website: https://web.archive.org/web/20180817175003/https://inversago.com/en/news-and-events/
[6] https://www.federalregister.gov/d/2015-27454
[7] https://web.archive.org/web/20180817175003/https://inversago.com/en/news-and-events/
[8] https://web.archive.org/web/20180817175003/https://inversago.com/en/news-and-events/

2016 and the prospective exclusive license noticed in 83 FR 38707 should have been made more clear, in the new notice published by the NIH.

Aside from the press release by Inversago stating that the company had secured $7 million in financing, there are no publicly available reports of the efforts or investments done by Inversago to bring into practice the inventions covered in the first license agreement. The NIH has not provided an explanation of whether and how the prospective exclusive license noticed in 83 FR 38707 will expand the existing exclusive license between the NIH and Inversago; nor has it provided an explanation of how the NIH has determined that expanding the exclusive license granted to this company is a reasonable and adequate incentive to induce development, given the existing obligation to bring the inventions to practical application for type 2 diabetes.

KEI and T1International ask the NIH if it is satisfied that Inversago is, in fact, on track to bring the inventions licensed in 2016 to practical application? And if so, what is to be gained by granting an exclusive license to Inversago for use to treat type 1 diabetes? Until the NIH explains this, we oppose creating a monopoly on the NIH-owned inventions for type 1 diabetes.

Here are some additional provisions that we recommend in the event that the NIH does indeed, seek to execute an exclusive license for type 1 diabetes uses, for the patents noticed in 2018.

1. No discrimination against US residents in pricing

We ask that the NIH include language in the proposed exclusive license to ensure that the prices in the U.S. for any drug, vaccine, medical device or other health technology using the inventions are not higher than the median price charged in the seven countries with the largest gross domestic product (GDP), that also have a per capita income of at least 50 percent of the United States, as measured by the World Bank Atlas Method.

We consider this a modest request to protect U.S. residents, who paid for the R&D that created the licensed inventions.

2. Reduce term of exclusivity when revenues are large

In addition to an external reference pricing test, we propose that the exclusivity of the license in the U.S. should be reduced when the global cumulative sales from products or services using the inventions exceed certain benchmarks.

Given the modest cost of acquiring an NIH patented invention, the amount of money the developer needs in sales to justify additional investments in R&D is reduced, as compared to cases where a company developes or acquires the technology from non government sources.

This request is consistent with the statutory requirements of 35 USC § 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.”

One possible implementation of revenue benchmarks is as follows: exclusivity will be reduced by one year for every $500 million in revenue equivalents, earned after the first $1 billion, where revenue equivalent is defined as global cumulative sales plus market entry rewards as well as government grants or tax credits, for the product or products using the invention. However, the NIH could choose different benchmarks, so long as the limits on exclusivity address the requirements of 35 USC 209, that the incentive is “not greater than reasonably necessary.”

3. Developing countries

We are concerned that several NIH-funded inventions are not accessible in developing countries, due to prices that are high and not affordable in markets where per capita incomes are significantly lower than the United States. For this reason, we ask the NIH to limit the exclusivity in the license to countries that have per capita incomes that are at least 30 percent of the United States.

We also ask the NIH to reach out to the Medicines Patent Pool (MPP), in order to enter into an agreement that gives the MPP an option to negotiate non-exclusive open licenses for the inventions in developing countries.

4. Transparency

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 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 USC § 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 market.

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KEI is an award-winning nonprofit organization that works extensively on issues pertaining to access to affordable medicines and related intellectual property concerns. KEI conducts research, writing, and advocacy in the public interest on behalf of patients, taxpayers, and consumers, including on the licensing of federally-funded and/or federally-owned medical technologies, and comments frequently on proposed exclusive licenses by the federal government including those by NIH.

T1International is a non-profit run by people with and impacted by type 1 diabetes for people with type 1 diabetes. T1International believe in a world where everyone with type 1 diabetes – no matter where they live – has everything they need to survive and achieve their dreams. T1International support local communities by giving them the tools they need to stand up for their rights so that access to insulin and type 1 diabetes supplies becomes a reality for all.

Annex:

Patent documents listed in both the 2015 and 2018 Federal Register notices re: Inversago Pharma, Inc.

Application or patent code	HHS Reference number	Filing date	Patent office
61/725,949	E-282-2012-0-US-01	11/13/2012	United States
PCT/US2013/069686	E-282-2012-0-PCT-02	11/13/2013	PCT
14/442,383 issued as 9,765,031	E-282-2012-0-US-03	11/13/2013	United States
2889697	E-282-2012-0-CA-04	04/27/2015	Canada
13802153.0	E-282-2012-0-EP-05	06/01/2015	EPO
3733/DELNP/2015	E-282-2012-0-IN-06	05/01/2015	India
2015-542015	E-282-2012-0-JP-07	05/11/2015	Japan
201380069389.9	E-282-2012-0-CN-08	07/03/2015	China
61/991,333	E-140-2014-0-US-01	05/09/2014	United States
62/171,179	E-282-2012-1-US-01	06/04/2015	United States
PCT/US2015/029946	E-140-2014-0-PCT-02	05/08/2015	PCT