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Re: Prospective Grant of Exclusive Patent License: The Development of a Bispecific, Biparatopic Antibody-Drug Conjugate to GPC3 for the Treatment of Human Liver Cancers to Salubris Biotherapuetics, Inc.

Document Citation:, 82 FR 36808

Dear Dr. Lambertson,

We are writing regarding the notice published in the federal register, regarding a proposed exclusive worldwide license on a portfolio of patents relating to a bispecific, biparatopic antibody-drug conjugate (ADC) having: (1) The CDR sequences of both the hYP7 and HN3 anti-GPC3 monoclonal antibodies; and (2) a microtubule inhibitor payload including, but not limited to, auristatin and mertansine; for the treatment of human liver cancer.

KEI offers the following observations on the potential medical benefits of the technology.

Therapeutic antibodies have revolutionized therapy for cancer and autoimmune diseases. First monoclonal antibodies were used to target a single epitope on malignant cells, or harmful protein. Antibodies were then rendered more potent by conjugating cytotoxic molecules to them. As our understanding of the immune system is improving, we can now use antibodies to activate our lymphocytes against tumor cells. Breakthroughs in recombinant DNA technology and sequencing have enabled scientists to design multispecific antibodies that can target more than one epitope on the same or different antigen. This new generation of antibodies are effectively multi-tools with each Fv performing a different function. For example, bispecific antibodies can on one hand bind to receptors overexpressed on tumor cells and also increase

internalization (for drug delivery) or trigger cell death. Some bispecific antibodies, such as BiTEs, can link effector T-cells to cancer cells. The considered license describes two paratopes that could be engineered within one antibody to target liver cancer cells. Not only would this improve the specificity of the antibody drug conjugate, but it could also inhibit growth in these cancer cells. Many bispecific antibodies are already in clinical trials and several are already on the market. The versatility of these next generation antibodies makes them highly effective therapeutic agents.

According to the Federal Register notice, the license is to Salubris Biotherapeutics, Inc. (Salubris), located in Gaithersburg, Maryland.

We have seven questions about the proposed license:

> Question 1. Is Salubris Biotherapeutics Inc. a subsidiary of Shenzhen Salubris Pharmaceuticals, a Chinese company headed by the billionaire Ye Chenghai, headquartered in Futian District, Shenzhen, Guangdong? (http://www.salubris.cn/ch/)
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> Question 2. What is the term of the proposed license?
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> Question 3. What is the proposed royalty on the license?
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> Question 4. How much money did the NIH or other federal agencies spend to develop this technology?
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> Question 5. Will the NIH or any other federal agency be subsidizing the future development of this technology in any way, and if so, how?
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> Question 6. What terms have the NIH included in the license to ensure that a product based upon the patented invention will be "available to the public on reasonable terms," as is required by the Bayh-Dole Act?
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> Question 7. Did the NIH undertake any economic analysis to ensure that the terms of the license are consistent with the requirements of 35 USC 209, particularly as regards to ensuring "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application"?

Reserving the right to ask additional questions or make additional comments, KEI proposing the following issues be addressed in any license agreement:

1) [The party obtaining the license] agrees to disclose the steps it will take to enable the registration and availability of the product at an affordable price in every county with a demonstrated need, 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; and

2) [The party obtaining the license] agrees to make the product available to the public in the U.S. at publicly disclosed prices no higher than the median price charged in Canada plus the seven countries with the largest GDP, which have per capita incomes of at least half that of the U.S.

3) [The party obtaining the license] agrees to make a available a report every year that will be made available to the public, waiving all claims of confidentiality, that provides the following information:

a) Outlays on R&D spending on products the use the licensed invention, including separately spending on each clinical trial separately,
b) The average and marginal costs of manufacturing products based upon the licensed invention,
c) The total number of units and revenue of sales in every country where the product is registered and sold,
d) The royalties paid in that period to the NIH for use of the invention,
e) Any subsidies for R&D received from any government or charity, or any tax credits relating to the development and distribution of the products.
f) All outlays relating to marketing the product,
g) All outlays relating to legal issue or governmental affairs, including lobbying activities.

4) [The party obtaining the license] agrees to make available the following to any generic drug manufacturer seeking marketing approval for any small molecule and biologic product in any OECD country or for WHO prequalification for any biologic drug or vaccine:

a) Materials:,
i) Cellular clones and hybridoma stocks
ii) Plasmids, plasmid maps, and sequences of antibody complementarity determining regions (CDR)
iii) Physicochemical/ biophysical characterization
b) Methods:
i) Growth conditions and protocols
ii) Attenuation or inactivation protocols
iii) Extraction and purification protocols
iv) Synthetic work-up and schemes
c) sufficient quantities of the approved medication for a generic developer's testing; and to

d) allow the developer to join, a single, shared system of elements to assure safe use (ETASU) of the medication.

In previous comments, the NIH has rejected our proposals on transparency, citing 35 USC 209(f) as the rationale. This statute reads as follows:

> (f) Plan.—No Federal agency shall grant any license under a patent or patent application on a federally owned invention unless the person requesting the license has supplied the agency with a plan for development or marketing of the invention, except that any such plan shall be treated by the Federal agency as commercial and financial information obtained from a person and privileged and confidential and not subject to disclosure under section 552 of title 5.

KEI notes that 35 USC 209(f) only relates to "a plan for development or marketing of the invention" that is provided to an agency during negotiations on a license. That is different from reports that a license holder can and should make to provide the public with information on how a drug company invests in and markets a product under an exclusive license, the subsidies involved in that development, or the know-how and materials that are shared in order to make generic markets more competitive once the exclusive term of the license concludes.

Sincerely,

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