

Jim Knabb
Senior Technology Transfer Manager
NCI Technology Transfer Center
National Cancer Institute
National Institutes of Health
Email: jim.knabb@nih.gov

July 9, 2021

Re: Prospective Grant of an Exclusive Patent License: Development and Commercialization of Monospecific CD22 Chimeric Antigen Receptor (CAR) Therapies for the Treatment of B-Cell Malignancies ([86 FR 33326](#))

Dear Jim Knabb:

Knowledge Ecology International (KEI) and the Union for Affordable Cancer Treatment (UACT) offer the following comments regarding the “Prospective Grant of an Exclusive Patent License: Development and Commercialization of Monospecific CD22 Chimeric Antigen Receptor (CAR) Therapies for the Treatment of B-Cell Malignancies” (86 FR 33326) to Syncopation Life Sciences Inc., (Syncopation), which is located in Palo Alto, California (website: <https://syncopationlife.com>).

Why the NIH would make this license exclusive, at least for the proposed field of use, which includes a CAR T that is already in clinical trials, and according to notice, “has shown early promise in clinical trials for ALL and NHL” is not obvious.

The NIH funded and controls the inventions and the know-how to provide a CAR T treatment that is already in a trial with a projected enrollment comparable to or larger than all but one of the current FDA approved CAR T treatments.

The NIH seems to currently have the ability to register the CAR Treatment in trial [NCT02315612](#), “Anti-CD22 Chimeric Receptor T Cells in Pediatric and Young Adults With Recurrent or Refractory CD22-expressing B Cell Malignancies,” and (1) avoid the granting to one company of seven years of exclusivity under the Orphan Drug Act, (2) avoid privatizing 12 years of exclusive rights in regulatory test data, (3) avoid granting a priority review voucher to distort regulatory approvals, and (4) could provide technology transfer and open licensing of the inventions throughout the world, making the treatment a global public good.

Instead, the NIH is proposing to privatize its inventions and the potential orphan and test data rights, so that a single firm has a global monopoly on a promising treatment for pediatric cancers, knowing that every other CAR T treatment has been priced from \$373,000 to \$438,000, with massive global inequality of access.

In the present case, the NIH has an applicant that includes as one of its founders, Nancy Goodman, who is best known for her efforts to lobby the US Congress to create a pediatric priority review voucher. Now Goodman and her colleagues stand to be beneficiaries of the waivers, which have in recent years traded for approximately \$100 million, if the applicants are successful in registering the treatment, even if this is based upon the evidence from the NIH funded run trial.

The Federal Register notice does not provide the rationale for the granting of exclusive patent rights. Even if the NIH wants Syncopation to have incentives to invest in the further commercialization of the NIH's CAR T treatment, to grant exclusive rights in patents, let alone life of patent terms and global rights is not required. Even without exclusive rights to the patents or the regulatory test data, Syncopation would earn a valuable pediatric priority review voucher (a fact well known to Nancy Goodman and everyone else developing similar treatments), worth perhaps \$100 million, and seven years of exclusive rights under the Orphan Drug Act, not to mention even longer orphan exclusivities in the European Union.

If the NIH decides to give exclusive rights in the NIH's patented inventions and/or the NIH's regulatory test data, surely the NIH has ample leverage to obtain terms that limit the negative impacts of a legal monopoly on a cancer treatment. At least two persons/entities involved in Syncopation should be open to provisions which provide protections to the public as regards pricing and access. Nancy Goodman comes to the company from a non-profit patient advocacy charity. One of the three listed investors, Emerson Collective works with Laurene Powell Jobs, and includes in its mission impact investing, philanthropy and advocacy, "in pursuit of a more equal and just America." If the NIH is not exploring ways to protect access and affordability in the licenses, it is because the NIH is indifferent to vast inequality of access globally or the costs its actions impose on health systems and families.

Discussion

Syncopation was incorporated in California only two months ago, in May 2021. Among the three founders listed is Nancy Goodman, who is better known to some for her charity [Kids v Cancer](#), and her role in lobbying for the pediatric priority review voucher. She is married to Michael Froman, the former United States Trade Representative. The other two founders of Syncopation are two Stanford scientists, Crystal Mackall, and Robbie Majzner. Mackall is listed as the principal investigator in \$52 million of NIH/NCI grants.

The technology is to be licensed on a worldwide basis, for the:

"Development, manufacture and commercialization of chimeric antigen receptor T cell (CAR-T) immunotherapies (both autologous and allogeneically derived) for the treatment of B cell malignancies that express CD22 wherein:

1. The T cells are engineered to be monospecific for CD22; and
2. The chimeric antigen receptor is specific for CD22 via the m971 scFv”.

This technology discloses CAR therapies that target CD22 by utilizing the anti-CD22 binder known as m971. CD22 is expressed on the surface of B cells in B cell malignancies and CD22-targeting CAR-T has shown early promise in clinical trials for ALL [acute lymphoblastic leukemia] and NHL [Non-Hodgkin's lymphoma].”

The investors in the company include three firms: Samsara Biocapital, Red Tree Venture Capital, and Emerson Collective. Emerson Collective works with Laurene Powell Jobs, and includes in its mission impact investing, philanthropy and advocacy, “in pursuit of a more equal and just America.”

We have previously expressed our concerns to Nancy Goodman about the lack of access to the new cell therapies in developing countries, in the context of our opposition to the January 2020 proposed exclusive license for a similar technology to CJ Healthcare, (“CJ”) ([86 FR 33326](#); <https://www.keionline.org/32158>). At the time, Goodman was considering a competing license proposal, and we asked if she would agree to any limitations on the geographic scope of the licenses in lower income countries, or on price discrimination against U.S. residents. At the time we did not have an answer to those questions, but today, these are issues that need to be raised and some questions answered.

As noted in the Federal Register notice, the technology to be licensed has already entered into clinical trials by the NIH for two possible indications (ALL and NHL). It is our understanding that this includes trial [NCT02315612](#), Anti-CD22 Chimeric Receptor T Cells in Pediatric and Young Adults With Recurrent or Refractory CD22-expressing B Cell Malignancies. The trial has a projected enrollment of 208 participants and is funded by U.S. taxpayers. For context, consider the following.

- The safety and efficacy of Kymriah were demonstrated in one multicenter clinical trial of 63 pediatric and young adult patients with relapsed or refractory B-cell precursor ALL.
- For Yescarta, the primary efficacy analysis involved 81 patients.
- The clinical review team’s recommendation for accelerated approval of Tecartus for the treatment of adults with relapsed or refractory (r/r) mantle cell lymphoma (MCL) is based on the clinical study ZUMA-2, which included 82 patients.
- Breyanzi’s approval was based upon evidence from 268 treated patients.
- The approval of Abecma was based upon evidence from 140 enrolled patients.

We ask the NIH to consider several measures in an exclusive license to protect the public interest.

Ensuring global access

Given the vast global inequality in access to cell therapies, the NIH should ensure that the exclusive license does 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.”

Prohibition against prices that discriminate against US residents

Any license should ensure that U.S. residents are not asked to pay prices that exceed the median price from the seven economies of the largest GDP and at least 50 percent of U.S. per capita income. The per capita income can be based upon the World Bank’s Atlas method.

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 Syncopation 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 licensees 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 LMICs, upon a finding by HHS or the WHO that people in these markets do not have sufficient access to the medical technology.

Conclusion

In the event that the NIH grants an exclusive license, the restrictions and safeguards in 35 USC 209 are intended to protect the public. The NIH needs to demonstrate that the license includes measures to insure transparency and access, and avoids unnecessary fiscal toxicity.

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

Sincerely,

Knowledge Ecology International
Union for Affordable Cancer Treatment