Recent Bayh-Dole Act News: Comments on the Draft Framework; HHS Refuses to March-In on Xtandi; and Delayed Contracting Doesn't Avoid Bayh-Dole

U.S. universities and academic institutions rely heavily on federal grants to fund their research and generate innovations in life sciences. Universities often out-license patents protecting inventions created using federal funding to private companies including many startups. Hundreds of drugs have been developed by collaboration between universities and private industry. The Bayh-Dole Act of 1980 governs the use of federal grants and ownership of inventions and intellectual property generated from the sponsored research. In exchange for federal support, recipients agree to grant the federal government a non-exclusive license to resulting patents covering any inventions supported by the grant. Further, the government retains the right to "march-in" and grant third parties licenses under certain circumstances.

Proposed Updates to Exercise of March-In Rights

On December 7, 2023, the National Institute of Standards and Technology (NIST) released a **draft framework** attempting to clarify the circumstances under which the U.S. federal government can "march-in" and grant licenses to third parties for inventions supported by federal grants. We originally wrote about the proposed guidance on "march-in" rights and provided Q & A **here**. To date, the government has never exercised such "march-in" rights.

Public comments to the draft framework were due by February 6, 2024. Evidencing the potential impact on the dynamics in the U.S. life sciences startup ecosystem, 51,873 public comments were submitted by the deadline. As of February 12, 2024, there were **672 posted comments**. Of these, those in opposition of the proposed framework expressed concerns that it would disincentivize entrepreneurship and innovations, countering the original purpose of the Bayh-dole Act.

- Howard Dean, former governor of Vermont, stated that "the framework put forward on December 8 will have little – if any – impact on the prices consumers pay for medicines, but will negatively impact the private sector's willingness to commercialize federally supported technologies, across all industries. … even if marching in on the basis of price were authorized by the law, which is not, the NIH's long-held contention that prices would not be impacted is correct. The truth is that most medicines are protected by a number of different patents, very few of which are Bayh-Dole subject inventions."

- Biotechnology Industry Organization (BIO) commented that "[t]he suggestions in the draft framework that agencies use the march-in authority to regulate the pricing of successfully commercialized products, particularly complex products like biopharmaceutical products, is not only inconsistent with the statute, it is unrealistic. In the biopharmaceutical sector, for

example, patents on inventions supported by federal funding only infrequently have a connection to a finished, marketed biopharmaceutical product, and when they do, that connection is usually attenuated. … One study estimates that 'biotechnology companies invest $100 in development for every $1 the government invests in research that leads to an innovation.'"

- The National Venture Capital Association (NVCA) commented that "NIST's guidance would unavoidably deter VCs from investing in inventions arising from federally funded research—directly contrary to the innovation environment the Act meant to foster. The increased risk directly disrupts existing investors' reliance interests. And it further makes any future technologies backed by federal funds potentially toxic for VC investment. This outcome 'frustrate[s] the policy that Congress sought to implement' through the Bayh-Dole Act—that is, to encourage private investment in government-funded inventions."

- Multiple universities submitted comments, some noting that Bayh-Dole works well in its current form. The **University of North Carolina – Chapel Hill** commented that "[t]he Bayh-Dole Act is legislation that works extremely well, and no changes to the Act are necessary. In fact, the use of march-in rights as described in the Draft Guidelines would represent a huge step backwards and threaten to undermine the positive effects of the Act." **Ann Arbor SPARK** commented that "[t]he framework changes you are proposing are unnecessary. They increase uncertainty and undermine a proven policy framework. They will have a detrimental and destabilizing effect on university research commercialization and startup company formation." Several universities raised concerns regarding negative effects on their ability to commercialize university research. **Cornell University** noted that "[t]he risk of price-based march-in rights will discourage potential licensees, disincentivize the commercialization of federally funded inventions, and decrease the likelihood of university technology adoption. This will likely lead to the scenario where new products, particularly new drugs, will no longer be based on the technologies of federally funded intellectual property to the detriment of the U.S. economy, consumers, and U.S. global competitiveness. This would have a negative impact on Cornell's technology transfer enterprise, …" **Yale University** likewise commented that "[t]he shift of final control of licensing away from universities would have significant adverse effects on universities' efforts in knowledge transfer. Exercising march-in rights to issue a non-exclusive license is tantamount to breaking a patent, and the knowledge that an agency could take such action would erode investors' confidence in the value of the intellectual property embodied in the patent. Entrepreneurs and investors would be reluctant to make the considerable investment required to bring university inventions to market if they knew that federal agencies could issue non-exclusive licenses to competitors at any time. No private entity would expect to attract investors on such terms, and it is unrealistic to expect that the proposed march-in framework could be adopted without undermining the efficacy of the Bayh-Dole Act." The **University of Texas System** commented on the potential effects on faculty: "[i]f this proposal is enacted, there is substantial concern that faculty will become less interested in the commercial process overall, adversely impacting businesses and start-ups across the state that seek to partner with their local institutions. … Faculty who want to see their research developed and translated into public benefit will be incentivized to leave our universities for industry, depriving our students of important learning and research opportunities."

Many of the comments were from individuals in support of the proposed framework. The Federal Trade Commission also submitted comments in support, arguing amongst other things that "price may be an appropriate basis for marching in." Knowledge Ecology International (a filer of multiple

petitions for march-in) was likewise pleased to see price as a basis for march-in, but commented that "on the issue of standards for unreasonable pricing, the draft guidance gets a failing grade."

Xtandi® Decision

On February 5, 2024, the U.S. Department of Health and Human Services (HHS) **affirmed** the National Health Institute's (NIH) decision not to exercise march-in rights with respect to Xtandi® (enzalutamide). The NIH's original decision was issued in **March 2023** in response to a petition by several cancer patients. NIH stated that Xtandi was widely available to the public. Further, NIH noted that the remaining patent life and the lengthy administrative process involved for a march-in proceeding weighed against any attempt to exercise its march-in rights.

University of South Florida Board of Trustees v. U.S.

The Federal Circuit recently upheld the government's royalty-free license to a patent resulting from government sponsored research. The ***University of South Florida Board of Trustees v. United States***, decided on February 9, 2024, involved the issue of whether the government held a royalty-free patent license over certain Alzheimer's disease research funded by a NIH grant if the inventions were created prior to a sub-contractor funding agreement. In this case, the grant covered experiments to reduce the claimed invention to practice (i.e., production of transgenic mice and recognition that the mice worked for their intended purpose). Mayo, the grantee, agreed to cover the cost of certain research conducted at UCSF (the subcontractor). The Mayo/UCSF contract was actually executed after UCSF's work was begun. The Federal Circuit ruled that the license to the government can be retroactively applied because the statutory language broadly covers work done before the contract if the work was eventually paid for by the federal funding. Per the Federal Circuit, "what occurred here is not an uncommon fact pattern in government funding of research conducted in part by non-grantee members of a consortium called for in a government grant. Specifically, the record makes clear that subcontracts are commonly not executed until sometime after the grant is awarded, yet the grant-covered work proceeds without waiting for the inking of a subcontract."

This case is a good reminder that (1) Bayh-Dole kicks in even when the funds are only supporting reducing a prior-made invention to practice, and (2) it does not matter when the contract is executed; if federal monies are used, Bayh-Dole kicks in.

A Joint Research Pitfall – Soon to be Resolved?

Innovators in life sciences at companies and universities often collaborate and conduct research under a joint research agreement (JRA). The Cooperative Research and Technology Enhancement Act of 2004 (the "CREATE Act") was enacted to promote collaboration and cooperative research between different entities. The United States Patent and Trademark Office ("USPTO") recently proposed new rules for filing terminal disclaimers to address a particular issue in the case of JRAs.

Terminal disclaimers can be filed to overcome obviousness-type double patenting rejections. Under the current rules, parties to a JRA can only file a terminal disclaimer if certain circumstances are met. Under the CREATE Act, two patent applications of different ownership are considered commonly owned if an invention at issue was made pursuant to a joint research agreement, the invention is within the scope of the agreement, and the parties to the agreement are the applicants of the application. Even if these requirements are met, a terminal disclaimer can only be filed if the patent or patent application referenced in the double patenting rejection is prior art.

Under current practice, for example, if a company and a university collaborate under a JRA and file two patent applications of different ownership (e.g., one solely owned and the other co-owned) on the same day so that one is not prior art to the other, a terminal disclaimer cannot be filed. In that case, a petition must be filed and granted to waive the requirement.

The USPTO proposed changes to allow an applicant to file a terminal disclaimer even if the referenced patent or application is not prior art without the need to file the petition. These changes, if implemented, will facilitate the management of a patent portfolio subject to a JRA.

Orange Book Listable?

 When submitting a new drug application ("NDA") with the FDA, an applicant (or branded company) is required to file a list of patents that cover the drug product. These patents will be listed in the FDA's Orange Book upon approval of the drug for commercial sale. Patents that are eligible to be listed in the Orange Book are patents that have claims that cover the drug substance (active ingredient), the drug product (formulation and composition), or the approved method of use.

What patents can't be listed in the Orange Book?

Patents that have claims directed to the process or manufacture of the drug substance, to the packaging of the drug product, or to metabolites or intermediates of the drug substance are not eligible to be listed in the Orange Book.

Why pursue patents that are Orange Book listable?

Competitors seeking to market a generic version of the drug must certify for each patent claiming the drug or the approved use of the drug that (i) such patent information has not been filed; (ii) the patent has expired; (iii) the date the patent will expire; or *(iv) the patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted.* Filing a paragraph IV certification can constitute an act of patent infringement and the generic company can be sued before even selling the generic version of the drug. If the branded company files the suit within 45 days of the notice of filing the certification, the FDA will postpone the generic drug approval for 30 months. During this 30 month period, the branded company and the generic competitor can litigate the patent dispute while the generic drug is barred from entering the market. If all patents are held invalid or not infringed, the FDA can proceed to approve the generic drug even if the 30 month period has not yet concluded.

The Purple Book and The Orange Book – When do Patents Expire and Regulatory Exclusivities end for FDA Approved Products?

The Food and Drug Administration (FDA) maintains two searchable online databases for approved products: the **Purple Book** (approved licensed biological products) and the **Orange Book** (approved drug products). The Orange Book provides details about an approved drug product, including the patents covering the approved drug product and the expiration dates of the patents and regulatory exclusivities, leaving investors, competitors, and the public in the dark as to when an approved biological product falls into the public domain.

For example, Sunosi® (solriamfetol hydrochloride) is a small molecule drug developed by Jazz Pharmaceuticals and was approved by the FDA on June 17, 2019 for the treatment of excessive sleepiness in adult patients with narcolepsy or obstructive sleep apnea. The NDA (new drug application) number, patents covering the product, the expiration dates of the patents, and regulatory exclusivity data are provided in the Orange Book.

Contrast this with Evenity® (romosozumab-aqqg), Amgen's monoclonal antibody approved for the treatment of osteoporosis in postmenopausal women at high risk for fracture. The Purple Book provides the approval date, proprietary name and generic name, BLA (biologics license application) number and type, date of first licensure, and a link to the product label. However, the Purple Book does not list the patents covering the product or regulatory exclusivity information. Thus, unlike patent litigation involving generic approvals for small molecule drugs, where the patents that will be involved are predictable based on the Orange Book listings, the patents that will be involved in

litigation over a biosimilar approval are typically revealed for the first time during the litigation itself.