February 5, 2024

Via electronic submission to: regulations.gov

Mojdeh Bahar
Associate Director for Innovation and Industry Services
National Institute of Standards and Technology
100 Bureau Drive, Gaithersburg, MD 20899

Re: *Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights* (NIST–2023–0008)

Dear Ms. Mojdeh Bahar:

The Alliance for Regenerative Medicine ("ARM") appreciates the opportunity to respond to the solicitation by the National Institute of Standards and Technology ("NIST") for comments on the *Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights*, which reviews the factors that an agency may consider when deciding whether to exercise march-in rights (the "Draft Framework"), about which we have serious concerns.

ARM is the leading international advocacy organization that champions the benefits of engineered cell and gene therapies ("CGTs") for patients, healthcare systems, and society. We promote legislative, regulatory, manufacturing and reimbursement initiatives to advance this innovative and transformative sector. As a community, ARM builds the future of medicine by convening the sector, facilitating influential exchanges on policies and practices, and advancing the narrative with data and analysis. We actively engage key stakeholders to enable the development of advanced therapies and to modernize healthcare systems so that patients benefit from these durable, potentially curative treatments. As the global voice of the sector, we represent more than 400 members across 25 countries, including emerging and established biotechnology companies, academic and medical research institutions, and patient organizations. CGTs offer the promise of significant patient benefit across a broad range of diseases, including rare genetic conditions, acquired diseases, and cancers. These treatments are helping thousands of patients worldwide, many of whom have no other viable treatment options. These transformative therapies are much more complex to develop, validate, manufacture, and review than traditional therapeutics and even biologics. To date, the Food and Drug Administration (FDA) has approved ten gene therapies for rare genetic diseases and six CAR-T cell therapies for various blood cancer indications. As the promise of CGTs continues to come into focus, the pipeline for both rare and widely prevalent diseases is accelerating. In the past year, therapies for Duchenne muscular dystrophy and hemophilia A, as well as a cell

therapy for type 1 diabetes have recently received regulatory approval, as have two gene therapies for sickle cell disease (SCD)—a debilitating disease that overwhelmingly affects people of African descent.[1]

ARM submits these comments to address our concerns that the Draft Framework's inclusion of pricing as a consideration for when an agency may exercise so-called march-in rights is contrary to the history, legal framework, and policy objectives of the Bayh-Dole Act. In addition, the proposed framework's use of pricing as a factor would chill innovation, including the development of critical and innovative CGTs, and push industry overseas. This threatens the role of the United States as the global leader in therapeutic discovery.

History of Bayh-Dole Act

More than forty years ago, the Bayh-Dole Act reformed the treatment of intellectual property developed from federally funded research. The Bayh-Dole Act established a system whereby small businesses, non-profit organizations, and academic institutions could own any patents resulting from their inventions and could license those patents to private entities for commercial use, thereby incentivizing commercialization of federally funded inventions and making more discoveries available to the public. The Bayh-Dole Act helped channel federal funds into scientific discoveries by materializing novel concepts into clinical realities through significant private investment, thereby unlocking the benefits of pharmaceutical innovation and maximizing the value of government investment in scientific discovery.[2] In the late 1970s, companies headquartered in Europe introduced more than twice as many new drugs as U.S. companies.[3] The passage of the Bayh-Dole Act has since helped to spur the reversal of that trend. Today, more than half of new drugs worldwide are invented in the U.S.[4] Within the CGT sector, the Bayh-Dole Act bolstered U.S. innovation and pioneered the availability of many therapies that otherwise would have remained theoretical in nature. NIST has previously recognized that "[t]he U.S. innovation system is substantially fueled by the discoveries and

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[1] *See* Data & Statistics on Sickle Cell Disease, Centers for Disease Control and Prevention, July 2023, *available at*: https://www.cdc.gov/ncbddd/sicklecell/data.html#:~:text=SCD%20affects%20approximately%20100%2C000%20A

[2] Private investment in the biopharmaceutical sector has been reported at nearly $130 billion. See U.S. Investments in Medical and Health Research and Development 2013–2018, at 7 (Research America, 2019), ttps://www.researchamerica.org/wp-content/uploads/2022/09/InvestmentReport2019_Fnl.pdf. This private investment is nearly triple the amount of annual public funding of $43 billion of R&D in healthcare innovations. *Id.* at 8. It is estimated that the cost of research and development for a new drug is now approximately $2.3 billion. See https://www2.deloitte.com/us/en/pages/about-deloitte/articles/press-releases/deloittes-thirteenth-annual-pharmaceutical-innovation-report-pharma-r-and-d-return-on-investment-falls-in-post-pandemic-market.html .

[3] *See* Stephen Ezell The Bayh-Dole Act's Vital Importance to the U.S. Life Sciences Innovation System (March 2019), available at https://itif.org/publications/2019/03/04/bayh-dole-acts-vital-importance-us-life-sciences-innovation-system/

[4] *See* Yali Friedman, Where Are Drugs Invented, and Why Does It Matter?, 16 ACS MEDICINAL CHEMISTRY LETTERS 589, 590 (May 2017), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5467189/#.

inventions arising from federally funded R&D at the Nation's universities, research institutes, and Federal Laboratories."[5]

Since the passage of the Bayh-Dole Act, more than 200 new medicines, including cell and gene therapies used to treat fatal diseases such as hemophilia and cancer, have been commercialized through effective collaboration between academic and industry researchers.[6] These developments have brought substantial benefits to research entities, commercial partners, and the public. By incentivizing partnerships between academic research institutions and commercial developers, the Bayh-Dole Act also allowed universities to generate substantial licensing revenue that could in turn be redirected to new research efforts and discoveries. The Act also provided certain rights for the federal government with respect to federally funded inventions, including the right to "march-in" under certain circumstances to require the contractor (or its licensee or assignee) to grant a license for a federally funded invention in any field of use to a responsible applicant "upon terms that are reasonable under the circumstances," or, if the contractor/licensee/assignee refuses to do so, grant itself such a license. However, this march-in right is not absolute. Instead, the Bayh-Dole Act allows the agency that entered into the funding agreement to exercise this march-in authority under only one of four specified circumstances where the innovation would not otherwise reach the U.S. market.[7] To date, no agency has ever exercised this march-in authority.

Use of Drug Pricing as a Factor for March-in is Inconsistent with the History, Legal Framework, and Policy Objectives of the Bayh-Dole Act.

The Draft Framework states that, with respect to the statutory criterion concerning whether the contractor or assignee has not taken steps to achieve practical application, for commercialized products where "the price or other terms at which the product is currently offered to the public are not reasonable, agencies may need to further assess whether march-in is warranted."[8] The Draft Framework further indicates that for a product that is being commercialized, the agency may ask: "Has the contractor or licensee made the product available only to a narrow set of consumers or customers because of high pricing or other

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[5] *See* NIST Special Publication 1234, Return on Investment Initiative for Unleashing American Innovation (April 2019), available at https://nvlpubs.nist.gov/nistpubs/SpecialPublications/NIST.SP.1234.pdf

[6] *See* AUTM, Technology Transfer Infographic (2018), *available at* https://autm.net/AUTM/media/Surveys-Tools/Documents/AUTM_FY2018_Infographic.pdf

[7] These circumstances include: action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use; action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees; action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or action is necessary because the agreement required by section 204 [generally requiring manufacturing in the United States] has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204. *See* 35 U.S.C § 203.

[8] *See* NIST, Request for Information Regarding the Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights (Dec. 8, 2023), *available at* https://public-inspection.federalregister.gov/2023-26930.pdf.

extenuating factors? Has the contractor or licensee provided any justification for the product's price or background on any extenuating factors which might be unreasonably limiting availability of the subject invention to consumers or customers?"

However, nowhere in the statutory text of the Bayh-Dole Act is any mention of pricing as a factor that can be considered in determining whether a product is reasonably available to the public, nor is there any explicit mention of a "reasonable price."

Consistently, the National Institutes of Health ("NIH") has rejected past calls to grant agencies march-in rights on the basis of drug pricing.[9] NIH has stated previously that it "agrees . . . that the extraordinary remedy of march-in is not an appropriate means of controlling prices. The issue of drug pricing has global implications and, thus, is appropriately left for Congress to address legislatively."[10] As recently as 2023, NIH denied a petition for march-in authority concerning the cancer drug Xtandi on the grounds of inappropriate pricing.[11]

Further, the co-authors of the Bayh-Dole Act, Senators Birch Bayh and Bob Dole, confirmed that exercising march-in rights on the basis of pricing considerations was never part of the intent of the Bayh-Dole Act. More than twenty years ago, two academics published a law review article and an op-ed arguing that march-in rights could be used as a price-control mechanism for drugs that arose from federally funded inventions.[12] The Senators responded that they never intended for agencies to exercise march-in rights based on pricing:

> *Bayh-Dole did not intend that the government set prices on resulting products. The law makes no reference to a reasonable price that should be dictated by the government. This omission was intentional; the primary purpose of the act was to entice the private sector to seek public-private research collaboration rather than focusing on its own proprietary research.*[13]

The use of pricing as a criterion for determining whether to exercise march-in rights, as outlined in the Draft Framework, is inconsistent with the history and legal framework of Bayh-Dole,

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[9] *See, e.g.*, National Institutes of Health Office of the Director, In the Case of Norvir® Manufactured by Abbott Laboratories, Inc. (July 29, 2004), available at https://www.essentialinventions.org/docs/usa-ritonavir/zerhouni29jul04.pdf.

[10] *Id.*

[11] *See* Letter from Lawrence Tabak, Performing the Duties of NIH Director, to Robert Sachs and Clare Love (Mar. 21, 2023), *available at* https://www.keionline.org/wp-content/uploads/NIH-rejection-Xtandi-marchin-12march2023.pdf.

[12] *See* Peter S. Arno & Michael H. Davis, *Why Don't We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed Upon Patents Deriving in Whole or in Part from Federally Funded Research*, 75 Tul. L. Rev. 631 (2001); *see also* Peter Arno & Michael Davis, *Paying Twice For the Same Drugs*, Washington Post (Mar. 27, 2002), available at: https://www.washingtonpost.com/archive/opinions/2002/03/27/paying-twice-for-the-same-drugs/c031aa41-caaf-450d-a95f-c072f6998931/

[13] *See* Birch Bayh & Bob Dole, *Our Law Helps Patients Get New Drugs Sooner*, Washington Post (Apr. 11, 2002), available at https://www.washingtonpost.com/archive/opinions/2002/04/11/our-law-helps-patients-get-new-drugs-sooner/d814d22a-6e63-4f06-8da3-d9698552fa24/.

which has never permitted the exercise of march-in rights merely because critics object to the price of a commercialized product arising in part from federal funding of an invention. Moreover, it is wholly at odds with the intent of the original drafters of the law and threatens to undercut successful legislation that has encouraged the development and commercialization of hundreds of new medicines over the past forty years.

The Draft Framework Poses Harms to Future U.S. Innovation.

Allowing pricing to be a basis for the exercise of march-in rights would harm innovation by corroding the incentives to translate federally funded inventions to the marketplace to improve available treatments for patients and contribute to the growth of the U.S. economy. The possibility that march-in rights would discourage current and future licensees from making further investments in commercializing federally funded inventions is not speculative.

Determining whether to license and invest in new technologies is a risky endeavor. Universities and other research institutions typically generate inventions and license them at early stages of the discovery, long before the promise of these inventions can be realized commercially. Licensees must consider many areas of risk, including the time and cost of development, the financial risk of failure, marketing budgets, the size of the patient population, competing therapies, and the price of a product. To date, the Bayh-Dole Act has successfully incentivized many private sector companies, including numerous start-ups, to license and attempt to commercialize new therapies. The possibility of the government exercising march-in rights for a commercialized product based on pricing intensifies the risks for companies interested in licensing and lowers their incentives to innovate. If private companies become hesitant to license federally funded technology, progress toward developing a robust pipeline of critical therapeutics would begin to erode. Furthermore, it alters the incentives of the private sector, directing investments in biotechnology advancements abroad rather than in the U.S., thereby reversing decades of U.S. leadership in biopharmaceutical innovation.

Our organization's members are well aware of the scientific discoveries encouraged by the Bayh-Dole Act. There are numerous public-private partnerships in the CGT market that have been fostered by the incentive framework established by this statute. Amongst these partnerships are bureaucratic entities such as the Foundation for the NIH's Accelerating Medicines Partnership Bespoke Gene Therapy Consortium,[14] which brings together partners from the public, private, and non-profit sectors to foster development of gene therapies intended to treat rare genetic diseases, which affect populations too small for viable commercial development; the National Institute for Innovation in Manufacturing Biopharmaceuticals' Viral Vector Manufacturing and Analytics Program,[15] which seeks to create a shared-access platform for the technical development, manufacturing, and characterization of

[14] *See* Foundation for the NIH's Accelerating Medicines Partnership Bespoke Gene Therapy Consortium, https://fnih.org/our-programs/accelerating-medicines-partnership-amp/bespoke-gene-therapy-consortium-bgtc/
[15] *See* National Institute for Innovation in Manufacturing Biopharmaceuticals' Viral Vector Manufacturing and Analytics Program https://www.niimbl.org/projects-programs/viral-vectors/

AAV-based gene therapy vectors; and the NIST Genome Editing Consortium,[16] which addresses the measurements and standards needed to increase confidence and lower the risk of utilizing genome editing technologies in research and commercial products. These partnerships are critical in sustaining continued access to innovation.

The resulting harm to innovation this Draft Framework evokes is a particularly important consideration in the context of CGTs. While the US remains an international trailblazer in pharmaceutical advances, the CGT sector represents one of the fastest growing and most distinctive clinical advances to modern medicine. CGTs and other regenerative medicines are different from traditional pharmaceuticals. Many CGTs are designed to durably and even permanently address the underlying cause of a disease. Instead of daily doses apportioned over the course of one's condition, CGTs are given in just a few administrations, or even a single dose. Because these therapies can provide significant direct and indirect savings in medical costs over a patient's lifetime, it is essential that pricing is not a deterrent to innovation in this sector for patients in the US who rely these therapies today and in the future.

We thank NIST for its consideration of these comments in evaluating the Draft Framework.

Sincerely,

Erica Cischke, MPH

Vice President, Government Affairs

[16] *See* NIST Genome Editing Consortium, https://www.nist.gov/programs-projects/nist-genome-editing-consortium