March 23, 2023

Xavier Becerra
Secretary
Department of Health & Human Services
Washington, DC

Via Email: xavier.becerra@hhs.gov

Re: Appeal of NIH decision to reject petition that HHS use Federal rights in patents on Xtandi to address pricing discrimination against US cancer patients

Dear Secretary Becerra:

The undersigned petitioners hereby appeal the March 21, 2023 decision by the National Institutes of Health (NIH), acting on your behalf, to reject our petition asking the Department of Health and Human Services (HHS) to use its rights in patents on the prostate cancer drug Xtandi in order to enable generic competition to lower the price.

Our petition to HHS was filed on November 18, 2021, by prostate cancer patients Clare Love and Robert Sachs, and later joined by prostate cancer patient Eric Sawyer, and Universities Allied for Essential Medicines (UAEM). The November 18, 2021 petition followed an earlier petition filed with the Department of Defense (DoD) on February 4, 2019, by Love and prostate cancer patient David Reed that Robert Sachs subsequently joined. If you consider both of these requests together, a petition to exercise the government's march-in or other rights in the Xtandi patents has been pending before the federal government for more than four years. The HHS petition was filed 16 months ago.

The petitions were filed with the DoD and HHS instead of the NIH because the NIH has repeatedly demonstrated its unwillingness to even acknowledge that the Bayh-Dole Act includes an obligation to make products invented with federal funds "available to the public on reasonable terms." This is demonstrated by a track record of dismissing multiple requests to use the government's Bayh-Dole safeguard to address pricing abuses and access restrictions, including those concerning the federal government's march-in rights under 35 USC § 203, and the federal government's global royalty-free license, under 35 USC § 202(c)(4). There are also extensive email records between Mark Rohrbaugh, currently NIH Special Advisor for Technology Transfer who is a long-time agency official, and lobbyists for drug companies and university rights holders, obtained through Freedom of Information Act requests, which not only express opposition to any safeguards regarding unreasonable pricing but organize public relations efforts against using a march-in request to address the pricing of products.

HHS chose to assign to the NIH the evaluation of our petition regarding Xtandi. We request HHS to consider this appeal directly, and not assign NIH to review its own decision. The latter would be tantamount to no review at all.

The petition focused on a single issue: the reasonableness of charging US cancer patients 3 to 6 times more than residents of other high-income countries for the drug Xtandi. There is no dispute

about the following facts: Xtandi was invented on grants from the US Army and the NIH at UCLA, a public university. The patents were licensed eventually to Astellas, a Japanese drug company, with a partnership share now held by Pfizer, following its 2016 $14 billion acquisition of Medivation, UCLA's original licensee, that occurred just after the NIH rejected an earlier march-in request on Xtandi. The prices in the United States have consistently been far higher than the prices in other high-income countries.

The legal basis for a march-in case to address this price discrimination against US residents was the obligation in 35 USC § 203(a)(1) that the patent holder takes "effective steps to achieve practical application of the subject invention in such field of use."

As the NIH is well aware, "practical application" is defined in the statute, as follows:

> 35 U.S. Code § 201 - Definitions
>
> (f) The term "practical application" means to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms.

The central issue in the case has always been about the last seven words in the definition: "available to the public on reasonable terms."

The staff of the NIH have repeatedly ignored these critical seven words, the most recent example being the March 21, 2023 letter from Acting NIH Director Lawrence A. Tabak, D.D.S., Ph.D. which misleadingly described the practical application issue as follows:

> . . . practical application is evidenced by the "manufacture, practice, and operation" of the invention and the invention's "availability to and use by the public…." Astellas, the maker of Xtandi, estimates that more than 200,000 patients were treated with Xtandi from 2012 to 2021. /10/ Therefore, the patent owner, the University of California, does not fail the requirement for bringing Xtandi to practical application, as the drug is manufactured and on the market in the manner of other prescription drugs. NIH has reviewed the information submitted by the current petitioners, which is substantially the same as that submitted in 2016, and reached the conclusion that Xtandi is still widely available as a prescription drug.
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> 10 Estimate based on Astellas sales and use data from September 2012 to June 2021. www.Xtandi.com

Absent from the letter is any mention of "reasonable terms" or the price for which Xtandi is sold in the U.S. The quotes from Dr. Tabaks' letter do not track the statute or the regulations on march-in rights, and specifically, omit the central issue in the case, that the patent holder must make the product "available to the public on reasonable terms." This blatant omission cannot and should not be ignored.

Clearly, this is a case about “reasonable terms” and the question is: can a company charge US cancer patients 3 to 6 times more than they charge residents of other high-income countries, for a drug invented on US federal government grants? The NIH letter does not once use the words “reasonable” or “terms.” The NIH justifies the rejection of the petition on the grounds that Astellas and Pfizer are selling the product and it is “widely available as a prescription drug,” an issue that, of course, was never in dispute. However, never did NIH even address the reasonableness of that price discrimination. Nonetheless, one could reasonably ask *how* widely available is the drug, given the restrictive nature of formularies for drugs as expensive as Xtandi? In any case, the Bayh-Dole Act does not set “availability” by itself as a standard.

NIH’s March 21, 2023 letter effectively declares that drug prices are irrelevant, and more specifically, that price discrimination against US cancer patients is irrelevant. This whole case is about price discrimination, and the NIH’s only acknowledgment of this was to say “Understandably, members of the public are concerned that the prices they pay are higher than those in other high-income countries.” After 16 months of foot dragging and repeated assurances by NIH that our petition was being “carefully considered,” petitioners deserve an unbiased legal determination based upon the facts and the issue presented in our petition. However, never did NIH even discuss the reasonableness of that price discrimination, in the context of the Bayh-Dole statutory obligation for patent holders to make inventions based upon taxpayer-funded discoveries “available to the public on reasonable terms.”

A second justification used to reject the petition is that a march-in proceeding would be “lengthy” relative to the remaining patent life and would not be “an effective means of lowering the price of the drug.”

> “In addition, given the remaining patent life and the lengthy administrative process involved for a march-in proceeding, NIH does not believe that use of the march-in authority would be an effective means of lowering the price of the drug.”

It is ironic that our petition, first filed in 2019 and later filed in 2021, is considered not timely, in March 2023, by an agency that promised a decision more than a year ago. But has the opportunity for government action actually run out on the Xtandi monopoly? The FDA Orange Book patents on Xtandi expire in 2027, four years from now, and every year of monopoly pricing is not only worth billions to Astellas and Pfizer, but more importantly imposes high costs and restricted access to a life extending treatment for many advanced prostate cancer patients.

The ‘clock has run” argument might have some weight if NIH had not totally ignored the federal government’s parallel authority, cited by petitioners, to use its royalty-free rights in the patents under 35 USC § 202(c)(4), which gives the US government a “paid-up license to practice or have practiced for or on behalf of the United States any subject invention throughout the world.” This license, which does not even require the payment of royalties to Astellas, gives the US government the legal ability to authorize a generic version of Xtandi at any time, the only issue being a question of the breadth of the authorization. If the authorization is extended to Medicare and Medicaid, and put on the Federal Supply Schedule (FSS), it would have a rapid impact on Xtandi’s price in the United States. This gives HHS tremendous leverage, and makes the combination of rights, march-in under §203 or the royalty-free license under § 202, a powerful tool to address this clear abuse in

pricing in the near term. Curiously, HHS fails to use all the tools currently available to it while at the same time the Biden Administration publicly decries the excessive cost of prescription drugs in the U.S.

It is particularly offensive that NIH has been unwilling to even consider the overriding legal issue presented by our petition, and conveys disrespect for us as American citizens exercising legitimate rights while insulting the intelligence of anyone who has followed this issue. As noted in a separate HHS press release, also dated March 21, 2023, more than 80,000 persons had provided comments in a related 2021 rulemaking proceeding on Bayh-Dole regulations, on the very topic of the definition of "practical application." This is not some minor technical issue. The overwhelming majority of those opposed eliminating the Bayh-Dole Act's "reasonable terms" protection. The requirement that patent holders make products "available to the public on reasonable terms" was and is a widely discussed topic and of course is one of the subjects of the Presidential Executive Order 14036 on Competition cited by NIH. And yet, NIH cited the Executive Order while rejecting our petition on the grounds that mere availability at any price satisfies the definition of practical application, a position at odds with the Executive Order.

There are now four companies that have filed ANDA applications for enzalutamide, two of which have received tentative approval from the FDA. To act as if the federal government is powerless to address this abusive price discrimination against US residents is appalling and a dereliction of our Government's duty to enforce the terms of patents arising out of taxpayer-funded discoveries.

In considering the appeal, we ask HHS to also include in its review the evidence and analysis included in the memorandum in support of the petition to HHS to exercise the march-in or paid up royalty right in patents on the prostate drug Xtandi, which was submitted to HHS and NIH on January 25, 2022. (See:https://www.keionline.org/xtandidocs/xtandi-25jan2022.pdf) Among other things, this memorandum provides:

- Table 1, a review of "Prices of 40 mg capsules of Xtandi in 16 high income countries compared to FSS, Medicaid, Medicare Part D, Drugs.Com coupon, AWP and WAC prices.
- Table 2, a review of the annual cost of Xtandi for patients in the United States and eight high income countries with large economies, and the ratio of the cost to GNI per capita in each of the countries.
- Evidence of restrictive placement of Xtandi on US formularies.
- Table A1, A list of recent U.S. government COVID-19 contracts that contain a reference price constraints on resultant products.

HHS is also asked to take note of our letter of February 3, 2022 to you and Acting NIH Director Dr. Tabak providing information on a contract between the Army and Pfizer (W58P0522C0001) to purchase the Covid-19 treatment Paxlovid that contains a most favored nation clause requiring that if Pfizer charges a "Covered Nation" a lower price than it charged the United States for Paxlovid, then Pfizer must offer that lower price to the United States. The clause, located at section H.7 of the contract, states that if the government accepts the lower price, the contract is thereby amended to reflect the lesser cost. A "Covered Nation" is Canada, France, Germany, Italy, Japan, the United Kingdom, the United States, or Switzerland. The terms of this contract are a more strict international reference pricing standard than we had endorsed.

We also ask HHS to reflect on the recommendation of 19 organizations that wrote to HHS on November 19, 2022 seeking to create a narrow standard to justify granting our petition. They suggested that the federal government consider that an international reference pricing cap on prices is appropriate, without prejudice to other cases with different facts, when a product meets each of these standards,

(1) the product is for a non rare disease
(2) the product has already generated very large revenues
(3) the government funded all of the primary patented inventions and
(4) the pricing disparities are enormous,

Given the government's unnecessarily long delays reviewing these petitions, which the NIH has now invoked as one of its excuses to reject our petition, we respectfully request HHS decide our appeal within 30 days. We realize this may be an ambitious timetable but for tens of thousands of American men living with advanced prostate cancer, every month truly matters when it comes to their lives and the availability "on reasonable terms" of life-extending drugs like enzalutamide. We also request you appoint as the reviewing authority an impartial HHS official not involved in preparing the March 21 NIH decision.

Sincerely,

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