

Prostate Cancer Patients!"Response to Astellas Pharma's Claims About Price of

Xtandi February 23, 2022

Dear Secretary Becerra and Acting Director Tabak:

The undersigned Xtandi march-in petitioners (#Xtandi petitioners") recently became aware of a February 9, 2022 #Statement on the Bayh-Dole Act and Xtandi issued by Astellas Pharma U.S., Inc., a wholly owned subsidiary of the Japanese pharmaceutical company of the same name. Had the statement been served to Xtandi petitioners, we would have responded sooner. Regrettably, the NIH's review process to determine whether to grant a march-in hearing on our petition is being conducted without participation by ourselves or the public, and NIH has yet to implement procedures to ensure transparency and fairness as recommended in a February 4, 2022 letter submitted by counsel for Eric Sawyer.

Since it was issued to the media, we have to assume Astellas!"[February 9 statement](#) has been provided to HHS and the NIH, along with other information unknown to petitioners.

Based upon emails that NIH recently released to Knowledge Ecology International (KEI) pursuant to a FOIA request, we've also become aware that the Bayh-Dole Coalition, a lobbying group representing PhRMA and patent holders, has a back channel for communications with Mark Rohrbaugh, NIH's Special Advisor for Technology Transfer. None of the email communications were on the public record . Given Mr. Rohrbaugh's previous involvement in decisions pertaining to march-in petitions, and efforts to eliminate #reasonable pricing" provisions from exclusive licensing agreements as advocated by the Bayh Dole Coalition, we are deeply concerned about any involvement he may have in deciding whether to grant our petition. For this additional and troubling reason, it's imperative that the Xtandi petition receive a full public hearing before an unbiased fact-finder.

Having now reviewed Astellas!"statement, we wish to offer the following comments. As a general response, however, we note that the accuracy and relevance of Astellas!"claims should be determined in an evidentiary hearing where both sides in the dispute can provide evidence, arguments and rebuttal.

As you are aware, the Xtandi petition raises a singular issue: whether a taxpayer-funded invention is available to the U.S. public on reasonable terms when it is priced three to six times higher in the United States than in other high-income countries. Based upon HHS's and NIH's prior commitments to give #due consideration" to march-in petitions, we feel that any decision in this matter needs, at a minimum, to address this fundamental question.

Astellas offers two separate defenses of its extraordinarily aggressively price discrimination against U.S. residents: a domestic therapeutic reference pricing argument, and claims about relative contributions to the R&D for Xtandi. We address each of these two issues below.

1. Domestic therapeutic reference pricing is not an appropriate standard when U.S. prices are themselves unjustifiably high, and when the U.S. government funds the discovery and early development of a drug.

The first defense put forth by Astellas is to argue that the price for Xtandi is reasonable because, #Xtandi is priced in line with other oral therapies for prostate cancer available in the

U.S. today.” This hollowness of this domestic therapeutic reference price argument are assumptions that the prices themselves are reasonable, and that the role of the federal government in funding the inventions is irrelevant. In the statement Astellas offers no evidence to support either of these assumptions, and also ignores the core basis for the petitioners’ actual petition, namely price discrimination against U.S. residents based upon what Astellas itself charges for Xtandi in other high income countries.

On the issue of the reasonableness of comparative domestic prices, the NIH should note that the President of the United States, the Vice President, the Secretary of HHS, and numerous members of Congress have repeatedly issued public statements that the prices of drugs in the United States are too high, often terming them as #unfair,” #exorbitant.” or #abusive”.

For the NIH to accept the standard put forth by Astellas, it would have to find that the prices cited as domestic reference prices are themselves reasonable, and that the government funding of the inventions should be irrelevant in evaluating prices and that the petitioners’ complaint of price discrimination against U.S. residents is irrelevant, and thus in line with NIH policy. This would put the NIH at odds with Presidential Executive Order 13948 of September 13, 2020, titled #Lowering Drug Prices by Putting America First”; the core principles in the drug pricing proposals in the Build Back Better legislation President Biden has championed; and Secretary Becerra’s September 9, 2021 report, the #Comprehensive Plan for Addressing High Drug Prices: A Report in Response to the Executive Order on Competition in the American Economy.” For example, HHS’s report on drug pricing clearly states:

#Americans pay too much for prescription drugs. We pay the highest prices in the world, which leads to higher spending. Higher spending puts pressure on private and government payers to raise premiums or make benefits less generous. Lack of affordable access to prescription drugs and other health care services leads to worse health outcomes. Patients in other comparable countries regularly pay substantially less for prescription drugs than Americans.”

As noted in a separate communication in this proceeding, Pfizer (which partnered with Astellas to market Xtandi in the U.S.) agreed to give the United States government its #most favored nation” price for Paxlovid, a treatment for COVID-19. Pfizer and the U.S. government defined this price as the lowest price in the G7 countries plus Switzerland. The Paxlovid contract, and several similar contracts recently signed in connection with the COVID-19 response, illustrate the willingness of industry to protect U.S. residents against adverse price discrimination.

2. Astellas seeks to minimize the value of the federal government’s financial support for the research and development of Xtandi, and to exaggerate its own contribution.

According to its February 9th statement, Astellas #invested more than \$1.4 billion to date in research and development efforts for Xtandi,” while listing the federal contribution at \$0.5

million. Astellas argues that this allegedly huge disparity should justify its price discrimination against U.S. residents, including its average wholesale price for Xtandi in January, 2022 of \$189,000 per year.

Industry R&D outlays

The Astellas statement about the company’s outlays on research and development #to date” provide no detail of what was claimed, or when the outlays took place. The most widely cited studies of drug development costs for a new molecular entity distinguish between the R&D outlays through FDA approval, and expenditures on trials after approval. Professors Joseph

DiMasi and Hansen Grabowski's widely quoted 2016 paper estimates the costs of clinical trials through approval at \$339.3 million (J.A. DiMasi et al. / Journal of Health Economics 47 (2016) 20–33). This is a significant number, but far less than the \$1.4 billion figure the Astellas has proposed be considered.

Any outlays on trials that were incurred after FDA approval came after Xtandi was already generating sales revenues, which have now exceeded \$20 billion.

If, however, Astellas and partner R&D costs are to be considered as a justification for price discrimination against U.S. residents - and we do not think they are relevant to the disparity between what Astellas charges American consumers versus those in other wealthy countries - we ask that Astellas provide the enrollment and costs of each clinical trial cited in the FDA medical review for the approval of Xtandi, as well as the costs of any other clinical trials on Xtandi, through the August 2012 FDA approval date. Having data on enrollment and outlays by trial makes it possible to evaluate the risk-adjusted costs and the reasonableness of the Astellas assertions, given available third party evidence and records obtained by Knowledge Ecology International (KEI) under FOIA of trial costs.

In order to provide additional evidence of the need to more critically evaluate the Astellas assertion on R&D costs, we refer you to a recent FOIA record from the University of Texas Southwestern Medical Center (#UT Southwestern"), regarding the cost of the Phase 3 clinical trial NCT00974311, #Safety and Efficacy Study of MDV3100 in Patients With Castration Resistant Prostate Cancer Who Have Been Previously Treated With Docetaxel-based Chemotherapy (AFFIRM)." This record shows that UT Southwestern was paid \$16,701 per patient for the trial. There were 1,199 patients in the trial, in 249 study locations. If the UT Southwestern figure was applied to all of the 1,199 patients, the payments would be just over \$20 million. Astellas may certainly have evidence that the trial costs were indeed higher but this record illustrates clearly why transparency is important, and why decisions should not be based upon vague drug company press releases. UT Southwestern was not the only location where Xtandi trials were conducted; Astellas partnered with a number of universities to conduct the trials. Other records disclosing the budgets and outlays on the trials exist and should be shared by Astellas, since it placed this information at issue.

Federal government outlays

Astellas next draws a comparison between its supposed contribution to the development of Xtandi and that of the U.S. Government's—a comparison that lacks specifics of evidentiary value. At the outset, we note that the Bayh-Dole Act makes any invention #conceived or first

actually reduced to practice in the performance of work under a funding agreement" a #subject invention." 35 U.S.C. § 201(e). Since all patents associated with Xtandi acknowledge government support, the government is authorized to march-in on those patents when Xtandi is not made #available to the public on reasonable terms." 35 U.S.C. §§ 203(a)(1), 201(f).

Petitioners need not demonstrate that the government paid a specific amount to Xtandi's development for this remedy to apply. However, to the extent that the federal government's contributions to the development of enzalutamide are relevant, Astellas has deliberately and wrongfully minimized the federal government's role.

If the amount and economic value of the federal government's grants are to be evaluated, it would require more specific information on the grants that are included, which can be contrasted with federal support not included by Astellas in its statement. We also note that grants directly related to enzalutamide were part of much larger federal grant programs for prostate cancer.

According to a February 15, 2022 review by KEI (available here: <https://www.keionline.org/37384>), the US Department of Defense's Congressionally Directed Medical Research Program (CDMRP) outlays on prostate cancer research were more than \$2 billion by fiscal year 2021, and averaged \$84 million per year from fiscal year 2000 to 2007. Also, a search of NIH RePORTER using the keyword #prostate" identifies more than \$11 billion in grants, including grant totals of \$200 million to \$500 million per year from fiscal years 2000 to 2007. The funding for the NIH grant listed on the Xtandi patent, from 2000 to 2012 (the year Xtandi was approved by the FDA), was \$18 million. Charles Sawyers, the lead inventor on the Xtandi patents, is listed as the principal investigator for \$27.7 million in NIH-funded projects and \$8.3 million in subprojects, beginning in 1985. Michael Jung, another of the Xtandi inventors, was the principal investigator for 42 NIH grants involving \$5.99 million. Academic studies such as the DiMasi study cited above, have placed the risk-adjusted value of pre-clinical investments at more than \$1 billion, and at 40 to 67 percent of the total risk-adjusted costs of drug development.

As KEI notes in the above-cited review, #Like the industry, the government places a lot of bets in medical research, in hopes that some will come through. The Astellas statement misleadingly understates the government's role."

This is yet another reason why a march-in hearing conducted by an impartial finder of facts with participation by all stakeholders is essential to creating an evidentiary record upon which NIH can make an informed objective decision.

Without a hearing on the request to use the federal government's march-in or government use rights, it is also impossible to verify Astellas'"claims concerning Medicare and private insurance users!"out-of-pocket expenses. The same can be said for Astellas!"patient assistance claims.

In

its statement Astellas asserts that Medicare Part D patients!"average out-of-pocket expense is \$226.40/month or about \$2,700 annually and those with private insurance about \$254.88/month or \$3,000 annually. Even if substantiated, use of average costs obscures the range and distribution of prostate cancer patients!"out-of-pocket expenses for Xtandi, which includes more than \$10,000/year in some documented cases. Also not addressed in Astellas!"statement is the number of prostate cancer patients whose insurance carriers have not approved use of Xtandi and instead directed them to less efficacious oral therapies, a practice sometimes described as step therapy.

If Astellas seeks to justify U.S. patient co-payments as a defense for discriminatory pricing against U.S. residents, then these claims also should be subject to transparency and examination by the prostate cancer patient petitioners.

Finally, it should be pointed out that Astellas's argument about #preserving an environment that enables U.S. pharmaceutical companies to continue to invest in innovative research on behalf of patients" is a red herring. The fundamental policy question the Xtandi petition raises is whether pharmaceutical companies whose patent rights are based upon discoveries funded by U.S. taxpayers are granted license to discriminate against and charge American consumers substantially more than residents of any other high income country when commercializing the taxpayer-funded discoveries. If U.S. taxpayers did not pay for the invention of enzalutamide, the petition would not have been filed and the Bayh-Dole remedies would not be available.

Petitioners have benefited from and strongly support U.S. government funding of scientific

research, as have the companies who have profited financially from commercializing such research. The Bayh-Dole Act requires funding agencies to obtain the rights necessary to protect the public from unreasonable use of inventions, (35 U.S.C. § 200) and requires companies to make the benefits #available to the public on reasonable terms.” Id. § 201(f). Prostate cancer patients and anyone who pays for prostate cancer drugs in the United States are #the public,” and the price for Xtandi in the United States -three to six times what it charges patients in other high income countries - is not reasonable for a product invented on federal grants. We urge HHS and the NIH to grant the Xtandi petitioners a hearing so that our claim that this gross price discrimination against U.S. residents warrants exercise of the federal government’s march-in and government use rights can be fairly evaluated. The hearing should be a proceeding with a transparent record and full participation by all stakeholders. Any less due process would be an affront to U.S. prostate cancer patients and taxpayers.

Respectfully submitted,

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