April 12, 2021

Lloyd J. Austin III
Secretary of Defense
1000 Defense Pentagon
Washington, DC 20301-1000

Re: Request to join march-in petition seeking to remedy excessive and unreasonable prices for Xtandi (INN: enzalutamide)

Dear Secretary Austin:

My name is Robert Sachs. I am battling advanced prostate cancer, and until recently was treated with enzalutamide, a drug marketed by the Japanese pharmaceutical company Astellas (under a license from a company that was acquired by Pfizer) under the trade name Xtandi. I am requesting to join the Xtandi march-in petition by two other prostate cancer patients, Clare Melvin Love, a veteran of the Vietnam War, and David P. Reed, PhD., a computer scientist and former adjunct professor at MIT. That petition requests that the U.S. Army use its rights under 35 USC 203 (march-in rights) to grant licenses to use three patents on inventions that the Army has funded (patents 7709517, 8183274 and 9126941). The Love and Reed petition was filed with former Secretary of the Army Mark Esper on February 4, 2019, and to my knowledge and as far as the original petitioners know, was never acted upon.

In addition to battling prostate cancer for the past six years, I've served since 1998 as a trustee of the Dana-Farber Cancer Institute, one of the pre-eminent academic cancer hospitals and research institutes in the world and am a former board chair of the National Coalition for Cancer Survivorship. While my membership in both organizations has informed my views, I petition you on my own behalf.

Prostate cancer is not a rare disease. The American Cancer society projects 248,530 American men will become prostate cancer patients this year, and 34,130 will die from it. Since 1997, the Department of Defense has funded the "Prostate Cancer Research Program (PCRP)" (https://cdmrp.army.mil/pcrp/). DoD notes that prostate cancer incidence, morbidity, and mortality rates "vary markedly by race and ethnicity, with African American (AA) men experiencing the highest rates in the U.S."

The nature of the dispute

I am attaching a PDF copy of the Love and Reed petition, and will not repeat every part of the case they make. However, I will note that there is no dispute about the basic facts in the case. Xtandi is a drug to treat prostate cancer. As described below, the drug is extremely expensive. The company that sells Xtandi discriminates against U.S. residents, by charging patients in the U.S. the highest prices in the world, by far. Xtandi was invented with grants from the U.S. Army and the NIH, and thus, as a funder of the inventions, the U.S. government has the right to permit generic competition to drive down the prices, in order to remedy an excessive and unreasonable price.

The Army has rights in all three patents

As described in the February 4, 2019 petition by Love and Reed, the lead inventor was Charles Sawyers, who at the time the patents were filed was a researcher at UCLA supported by the DoD Prostate Cancer Research Program (PCRP). And, in addition to funding the inventions, the Department of Defense Prostate Cancer Clinical Trials Consortium also supported a critical early trial.

The U.S. government rights in each patent are declared on the patents, including the fact that the Department of Defense (Army) grant W81XWH-04-1-0129 supported the invention.

1. Patent number 7709517.

Government Interest Statement on patent: "This invention was made with United States Government support under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129. The Government has certain rights in the invention."

2. Patent number 8183274.

Government Interest Statement on patent: "This invention was made with United States Government support under National Institutes of Health SPORE grant number 5 P50 CA092131and Department of Defense (Army) grant number W81XWH-04-1-0129. The Government has certain rights in the invention."

3. Patent number 9126941.

Government Interest Statement on patent: "This invention was made with Government support under Grant No. W81XWH-04-1-0129 awarded by the United States Army, Medical Research and Materiel Command; Grant No. CA092131 awarded by the National Institutes of Health. The Government has certain rights in this invention."

Astellas is charging U.S. residents far more for Xtandi than is the case for residents of any other country

As noted in the 2019 petition, the U.S. average wholesale price (AWP) was $109 for a single 40 mg capsule of Xtandi in 2018. In 15 high-income countries surveyed, the AWP for Xtandi was less than half the U.S. price. In 11 of the 15 countries it was less than one-third and in 6 countries it was less than one-fourth the U.S. price. U.S. taxpayers who funded the early development of Xtandi are now being charged multiple times what citizens of other developed countries must pay.

Action requested

As the son of a now deceased WWII Army-Air Force co-pilot who fought for our country,
I request the Department of Defense take the following actions on the February 4, 2019 petition:

1. Grant a hearing on the march-in petition, and

2. Allow me to join the petitioners and present evidence at the hearing.

If, for some reason, the previous Administration turned down the February 4, 2019 petition, without any public hearing or even notifying the petitioners, then please consider my letter as a new march-in request. President Biden, Vice President Harris and HHS Secretary Becerra have all spoken about the need to curb excessive drug prices. The facts of the Xtandi case offer this opportunity.

Sincerely,

Robert Sachs
Boston, Massachusetts 02115
RSachs@pilothouse.com

CC: Secretary Xavier Becerra, Department of Health and Human Services

ATTACHMENT: February 4, 2019 Clare Love and David Reed March-in Petition Regarding Xtandi (Enzalutamide)

Annex: Excerpts from my comments in a NIST rulemaking proceeding

I have addressed the Xtandi march-in issue recently, in comments regarding a proposed rule by the National Institute of Standards and Technology (NIST) that would impose restrictions on the use of march-in rights when prices are an issue. The regulations were proposed on January 4, 2021, before President Biden took office. About 80,000 persons and groups have opposed the NIST proposed restrictions on march-in rights. My comments to NIST are available on the official docket (https://www.regulations.gov/comment/NIST-2021-0001-9788), and I will quote from those comments in this petition.

Excerpts from comments by Robert Sachs in NIST-2021-0001-9788

> I'm a 72-year-old battling advanced prostate cancer but am by no means unique. Another 1.9 million Americans will be newly diagnosed with cancer this year, among them nearly 250,000 men with prostate cancer.
>
> In addition to battling prostate cancer for the past six years, I've served since 1998 as a trustee of the Dana-Farber Cancer Institute, one of the pre-eminent academic cancer hospitals and research institutes in the world and am a former board chair of the National Coalition for

Cancer Survivorship. Although my board service has informed my views, I submit these comments on my own behalf.

Serving on the Dana-Farber and NCCS boards has given me a much greater appreciation of the vital need for government, industry and philanthropic support for cancer research. Needless to say, ongoing research and future discoveries are likely to save the lives of millions of more diagnosed with cancer. However, I do not believe scientific research and cancer patient interests need be at odds here.

. . .

Along with thousands of other men confronted with the most aggressive forms of prostate cancer, I've been the beneficiary of Xtandi, a life-extending drug co-marketed in the US by Astellas, a Japanese-owned pharmaceutical company in partnership with Pfizer. The average U.S. wholesale price of Xtandi is greater than $150,000/year, four times what the same drug is sold for in Canada and more than five times the price Xtandi is available for in Japan. According to the Redbook survey, the U.S. average wholesale price (AWP) was $109 for a single 40 mg capsule of Xtandi in 2018. In 15 high-income countries surveyed, the AWP for Xtandi was less than half the U.S. price. In 11 of the 15 it was less than one-third and in six it was less than one-fourth.

. . .

Upon learning that cancer patients in other developed countries can purchase Xtandi for a fraction of the cost it's sold in the U.S. I was shocked to find out that its preclinical development was funded by US taxpayers with grants made by NIH and DoD to researchers at UCLA. UCLA subsequently licensed a company named Medivation which in turn sold global rights to Astellas for $765 million in 2009, retaining a 50% ownership interest. Then, in 2014 after FDA approvals were obtained, Medivation was acquired by Pfizer for $14 billion. In announcing the acquisition, Ian Read, Chairman and Chief Executive Officer, Pfizer, declared, "The proposed acquisition of Medivation is expected to immediately accelerate revenue growth and drive overall earnings growth potential for Pfizer." Not mentioned was that the $14 Billion acquisition cost would be borne by cancer patients, and disproportionately so in the United States.

When Astellas and Pfizer are pricing Xtandi in the U.S. at almost $450/day for a standard dose of the drug, the time is long past due for the Government to exercise its march-in rights.

. . .

March-in provisions were initially included in the 1980 Bayh-Dole Act, P.L. 96-517, which President Biden supported when he served on the Senate Judiciary Committee, and a

bi-partisan Congress enacted to address concerns about the commercialization of technology developed with U.S. funding. As a U.S. Senator, Vice President Harris, and as Attorney General of California, HHS Secretary Becerra both championed the federal exercise of march-in rights to bring down the cost of high-priced drugs.

In 2017, the Republican-led Senate Armed Services Committee directed DoD "to exercise its rights…to authorize third-parties to use inventions that benefited from DoD funding whenever the price of a drug, vaccine or other medical technology is higher in the U.S. than the median price charged in the seven largest economies that have a per capita income at least half the per capita income of the U.S." And during the 2020 campaign both Presidential candidates proposed tying U.S. drug prices to those paid by consumers in other countries.

. . .

For over two years a request filed by prostate cancer patients has been pending before the Secretary of the Army asking DoD to find terms under which Xtandi (originally known as "enzalutamide") are made available to the American public are "unreasonable," and invoke DoD's march-in rights. Doing so would send a clear message that excessive drug pricing will not be tolerated any longer.

. . .

February 4, 2019

Dr. Mark T. Esper
Secretary of the Army
101 Army Pentagon
Washington, DC 20310-0101

RE: U.S. Army rights in the patents for the prostate cancer drug enzalutamide

Dear Dr. Esper,

My name is Clare Melvin Love. I live in Hoquiam, Washington, near the Pacific Ocean. From 1967 through 1969, I served in the U.S. Army, including a tour in Vietnam in 1968, in the signal corps, Specialist 5th Class. In 2016, I was diagnosed with prostate cancer. This is my second bout with cancer.

My name is David P Reed, PhD. I am a resident of Needham, Massachusetts. I have worked as a computer scientist and an adjunct professor at MIT. I was recently diagnosed with prostate cancer.

We are writing to ask that the U.S. Army use its rights in patents on the prostate cancer drug sold by the Japanese firm Astellas under the brand name Xtandi (generic name enzalutamide) in order to ensure that U.S. residents have access to the invention on reasonable terms, a legal obligation under 35 USC § 200, 201(f) and 202(c) of the Bayh-Dole Act.

The price of Xtandi in the United States is more than four times the median price in the seven high income countries identified by the U.S. Senate Armed Services Committee in 2017 to be used to determine if the U.S price on a Department of Defense (DoD)-funded drug is reasonable. The price in the U.S. is five times the reimbursed price in Japan, where Astellas is headquartered.

The failure by Astellas to make the drug available to the public on reasonable terms can and should be remedied by the U.S. government through exercising the federal government’s royalty-free or march-in rights in the patents.

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Introduction

We are specifically requesting that the Army make a determination that the terms under which the the invention is made available to the public are “unreasonable,” because the price of the drug in the United States is far higher than in any other high income country, and five times higher than the reimbursed price in Japan, where Astellas has its headquarters.

The relevant patents granted by the U.S. Patent and Trademark Office (USPTO) are patents 7709517, 8183274 and 9126941. The patents expire in 2026 and 2027. All three patents were assigned to the Regents Of The University Of California, have a disclosure of government rights as a consequence of Department of Defense (Army) grant number W81XWH0410129, and identify Charles L Sawyers as the lead inventor. At the time when the patents were filed, Sawyers was a researcher at UCLA, whose work was supported by the DoD Prostate Cancer Research Program (PCRP). The Department of Defense Prostate Cancer Clinical Trials Consortium also supported a critical early trial .

The July 2017 DoD NDAA Directive

We recognize that the Department of Defense and the National Institutes of Health both rejected a march-in request on Xtandi, filed in 2016 by the Union for Affordable Cancer Treatment (UACT) and Knowledge Ecology International (KEI). However, I also note that in July 2017, the Senate Armed Services Committee included a directive to the Department of Defense, in connection with the Appropriation, to “exercise its rights” including march-in rights under § 203 of title 35, “whenever the price of a drug . . . is higher in the United States than the median price charged in the seven largest economies that have a per capita income at least half the per capita income of the United States.” The full text of the directive is below:

> **Licensing of federally owned medical inventions**
> The committee directs the Department of Defense (DOD) to exercise its rights under sections 209(d)(1) or 203 of title 35, United States Code, to authorize third parties to use inventions that benefited from DOD funding whenever the price of a drug, vaccine, or other medical technology is higher in the United States than the median price charged in the seven largest economies that have a per capita income at least half the per capita income of the United States.
>
> 115TH Congress, 1st Session, 2017, Senate Report 115–125. National Defense Authorization Act for Fiscal Year 2018. Report to accompany S. 1519, on page 173. July 10, 2017.

The U.S. price of Xtandi

The recommended dose for Xtandi is four 40 milligram capsules per day, for as long as the drug is tolerated and effective.

According to the Redbook, the January 8, 2018 Average Wholesale Price (AWP) and Wholesale Acquisition Cost (WAC) for Xtandi were, respectively, $109.05192 and $90.87658 per 40 milligram capsule.

Data for Medicare Part D is only available for 2012 to 2016. During that period, the cost to Medicare increased from $63.72 to $76.69 per capsule of Xtandi.

Prices for Xtandi have gone up every year. From 2012 to 2016, the Medicare Part D prices increased by 20 percent. From June 28, 2016 to January 8, 2018, the AWP price increased by 16.4 percent.

At January 2018 prices, the cost of 4 capsules per day and per year are as follows in Table 1.

Table 1: U.S. costs of 4 capsules of Xtandi per day and per year

Price	Date	Daily	Annual
Average Wholesale Price (AWP)	Jan 8, 2018	$436.21	$159,215.80
Wholesale Acquisition Cost (WAC)	Jan 8, 2018	$363.51	$132,679.81
Medicare Part D	2016	$306.76	$111,967.40

How does this compare to some other household figures?

Table 2 provides some comparisons to average wages and prices of other expenses.

Table 2: Examples of price/wage comparisons

Item	**Cost**
Median value of home in 2018 (Zillow)	$222,800
Median annual mortgage payment (2018)	$12,360

Tuition for one year, Harvard University (2018)	$46,340
Tuition, room, board, and fees, Harvard University (2018)	$67,580
Average annual cost of renting residential housing (August 2018)	$16,860
Tesla 2019 Model S 75D electric car	$66,750
Average salary of high school teacher in 2017	$62,860
Basic pay for active duty soldiers, Staff Sergeant (E6), 6 years of experience	$39,049
Median household income (June 2018)	$62,175
Average cost of nursing home care for a shared room (2018)	$85,775
National Average Wage Index for 2017	$50,323
Median household savings (2018)	$11,700
Average annual outlays on food stamps, per person (2018)	$1,512
Average salary of Registered Nurse (2018)	$64,690
Cadillac 2019 Escalade	$75,195
58 grams of gold (same weight as annual dose of Xtandi)	$2,435[1]

Note that Xtandi is 65 times more expensive than gold, by weight.

One year of Xtandi was 3.4 times the annual cost of tuition at Harvard, 2.5 times the average wage of a high school teacher or registered nurse, 2.1 times the cost of a Cadillac Escalade, 2.4 times the cost of a new Model S 75D Tesla electric car, and 1.86 times the cost of one year of nursing home care.

Table 3 has data on the average amount of money saved in US 401(k) retirement accounts, by age, as calculated by Fidelity for CNBC.

Table 3: Average 401(k) balance by age

401(k) balances as of the second quarter of 2018

Age 20 to 29: $11,500

[1] Gold was trading at $41.69 per gram, January 10, 2018.

Age 30 to 39:	$42,700
Age 40 to 49:	$103,500
Age 50 to 59:	$174,200
Age 60 to 69:	$192,800

Source: Fidelity, and CNBC

Note that the cost of one year of Xtandi treatment is approximately 82 percent of the average balance for a 401(k) retirement savings account at typical retirement age. This is an astonishing claim on the resources of cancer patients.

Comparison of Xtandi price to high income countries

The U.S. average wholesale price of $109 per 40 milligram capsule is far higher than the price that Astellas charges in other high income countries.

In no other high income country is the price even up to half the U.S. price. In 11 of the 15 high income countries surveyed, the price is less than one-third the U.S. AWP. In six high income countries, the price is less than one-fourth the U.S. AWP.

In Japan (the country where Astellas has its headquarters), the government reimbursement rate is JPY2,354 per 40 milligram tablet,[2] or just $21.72 (at current exchange rates[3]), less than one-fifth the U.S. price.

The following price data is from Drugdatabase.info:

Table 4: 2018 prices for Xtandi in 15 high income countries and the United States

Country	Date	Price per one 40 mg capsule in USD	GDP per capita US$ (2017, World Bank)
United States, AWP	Jan 1, 2018	$109.05	$59,532
United States, WAC	Jan 1, 2018	$90.88	$59,532
Denmark	May 17, 2018	$44.58	$56,308
Iceland	May 21, 2018	$40.45	$70,057
Germany*	May 21, 2018	$37.07	$44,470

[2] Japan Pharma Outlook 2027, Pharma Intelligence Informa UK, July 2018. https://pharmaintelligence.informa.com/~/media/informa-shop-window/pharma/files/reports/japan-pharma-outlook-2027-report-extract-v2.pdf. JPY2,354 per tablet.

[3] 1.00 JPY = 0.009227 USD

Finland	May 17, 2018	$36.96	$45,703
Switzerland	May 22, 2018	$36.09	$80,190
Netherlands	May 17, 2018	$34.39	$48,223
UK*	May 17, 2018	$33.00	$39,720
France*	May 21, 2018	$31.19	$38,477
Norway	May 17, 2018	$28.64	$75,505
Sweden	May 17, 2018	$26.09	$53,442
South Korea*	Jan 9, 2019	$25.19	$29,743
Australia	May 17, 2018	$24.84	$53,800
Italy*, SSN facilities	Jan 13, 2019	$22.33	$31,953
Canada*	May 17, 2018	$22.77	$45,032
Japan*	Jul 1, 2018	$21.70	$38,428

*Countries referenced in 2017 DoD NDAA SAS Directive

The Senate Armed Services Committee set as a standard the median price for the seven countries with the highest GDP and at least 50 percent U.S. per capita income. This would include Japan, Germany, the UK, France, Italy, Canada and South Korea, in 2017. For those seven countries, the median price is $25.19. The U.S. AWP is 4.3 times higher. The U.S. WAC price is 3.6 times higher.

Costs of manufacturing enzalutamide

In 2016, a Canadian firm, Biolyse, offered to sell a generic version of enzalutamide to the U.S. government for $3 per 40 milligram capsule,[4] an amount that would have allowed Biolyse to recover its costs of developing, registering, manufacturing and distributing the drug while also earning a profit.

One expert subsequently reported sales of the active pharmaceutical ingredient for enzalutamide at $6,000 per kilogram, a number that would likely come down over time.

Both figures are high, relative to the per kilo costs of some other drugs, no doubt due to the limited size of the market for generic APIs. At the $6,000 per kilo figure, the cost of the API for one 40 milligram capsule of enzalutamide would be $0.24.

Manufacturing costs include more than the API. One rule of thumb is to double the API costs.

[4] https://www.keionline.org/wp-content/uploads/BiolysePharma-letter-CMS-22April2016.pdf

Glenmark, a company that is U.S. FDA approved for manufacturing several other drugs[5], offers a generic version of enzalutamide in India, where the UCLA patents are not in effect, marketed as Glenza. The prices for Glenza vary considerably depending upon the distributor and the quantity.

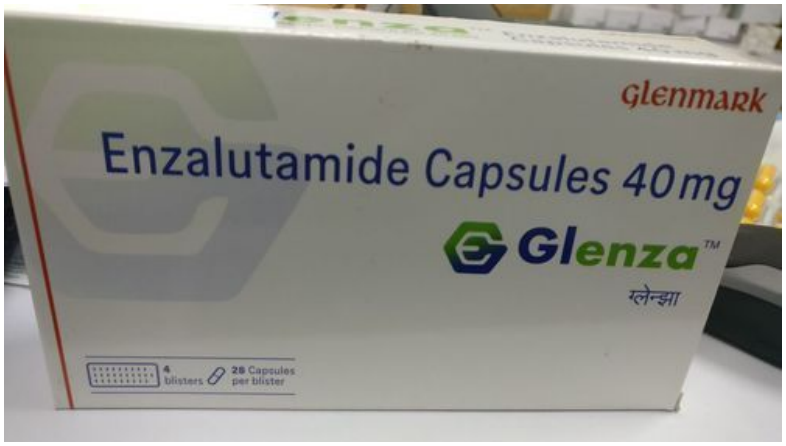

Figure 1: Glenza, 40mg x 112 capsules

Sales of Xtandi

Xtandi was approved by the FDA in August 2012. Sales have increased every year, and have exceeded $2 billion per year beginning in 2016.

Medicare Part D spending

In the calendar year 2016, U.S. Medicare Part D spending for Xtandi was $907,585,915.

The increase in the Medicare price from 2012 to 2016 was 20.4 percent, compared to an increase in the Consumer Price Increase[6] of 4.5 percent over the same period.

Medicare Part D utilization increased by 232 percent from 2013 to 2016.

[5] Glenmark currently has 246 FDA approvals listed in the FDA Orange Book.
[6] CPI-U was 240.0 in 2016, and 229.6 in 2012.

Table 5: Medicare Part D spending on Xtandi

Year	Unit Price	Dosage units	Total Spending	Change in spending
2012	$63.72	547,731	$34,898,756	
2013	$64.85	3,569,568	$231,503,731	562 %
2014	$69.41	6,444,098	$447,311,084	92 %
2015	$73.94	10,693.617	$790,655,731	77 %
2016	$76.69	11,834,328	$907,585,915	15 %

In the Astellas fiscal year 2017, roughly half of global sales for Xtandi were in the United States.

Global sales

Astellas forecasts its fiscal year 2018 global sales at 310.3 billion yen, or $2.86 billion USD.

Since introduction, Xtandi has generated more than $11 billion in global sales.

Conclusion

In 2016, the Union for Affordable Cancer Treatment (UACT) and KEI petitioned the DoD and the NIH, asking that the government use royalty-free or march-in rights to address unreasonable price discrimination against U.S. residents by Astellas for the prostate cancer drug Xtandi/ enzalutamide. The DoD and the NIH rejected the request. In July 2017, the U.S. Senate Armed Services Committee included a directive in the National Defense Authorization Act which set a standard for determining if the pricing of a DoD-funded drug was reasonable, and directed the DoD to use its Bayh-Dole rights if it was not.

The petitioners are two prostate cancer patients, and are hereby asking the U.S. Army to use the federal government’s royalty-free or march-in rights on the three patents listed in the FDA Orange Book for Xtandi, on the grounds that the price is not reasonable.

We have provided evidence that the price of Xtandi in the United States is more than four times the median price in the seven high income countries identified by the U.S. Senate Armed Services Committee in 2017 to be used to determine if the U.S price on a DoD-funded drug is

reasonable. We also note that the price in the U.S. is five times the reimbursed price in Japan (where Astellas is headquartered).

Thank you for your attention to this critical issue. We look forward to receiving your response.

Sincerely,

Clare M Love
clare.love@workingagenda.com
621 M Street
Hoquiam, Washington 98550

David P. Reed, PhD.
Needham, Massachusetts

ANNEX - US Redbook Prices for Xtandi

RED BOOK Product Details

Product Information

Product Name:	XTANDI	**Code:**	NDC
Active Ingredient(s):	enzalutamide	**Identifier:**	00469-0125-99
Manufacturer/Distributor:	ASTELLAS PHARMA US, INC.	**Unit Dose:**	N
Form:	CAPSULE, LIQUID FILLED	**Single Source:**	Y
Strength:	40 mg	**Repackager:**	N
Size:	120s ea	**Generic:**	N
Route of Admin:	ORAL	**Add'l Description:**	(LIQUID CAPSULE)
Orange Book Code:	--		
DEA Class:	RX		

Current Pricing Information:

	Package	Unit	Effective Date
AWP	13086.23	109.05192	01/08/2018
WAC	10905.19	90.87658	01/08/2018
DIR	--	--	--
FUL	--	--	--

AWP Unit Pricing History:

Effective Date	Unit	% Change
01/08/2018	109.05192	5.9
06/21/2017	102.97633	3.8
01/04/2017	99.22842	5.9
06/28/2016	93.70008	5.9

J-Codes:

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