April 21, 2016

The Honorable Sylvia Mary Mathews Burwell
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201
Via: Sylvia.Burwell@hhs.gov

Francis Collins, M.D., Ph.D.
Director
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892
Via: Francis.Collins@nih.hhs.gov

Dear Secretary Burwell and Director Collins:

We have recently become aware of academic research indicating that the price of Xtandi (enzalutamide) is a primary factor in determinations by payors that restrict access to the medicine. I submit this research as evidence to supplement our petition, particularly the discussion under the second subheading ("The high prices for Xtandi create hardships on U.S. patients") on pages five through nine, in which we detailed, *inter alia*, how insurers in the U.S. were restricting access to Xtandi due to the high price.[1]

Our petition suggested that one option to increase access to generic enzalutamide would be for the Department of Health and Human Services or the National Institutes of Health to use the royalty-free rights in patents under 35 USC § 202(c)(4), which offers the path of least resistance under the Bayh-Dole Act. With regard to exercising march-in rights, our argument primarily focused on 35 USC § 203(a)(1) and the requirement of "practical application," as defined under 35 USC § 201(f) to require public availability "on reasonable terms." But equally applicable, particularly in light of this new evidence, is 35 USC § 203(a)(2), which provides that "action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees."

[1] The KEI/UACT petition regarding Xtandi is available here: http://keionline.org/sites/default/files/Xtandi-March-In-Request-Letter-14Jan2016.pdf.

In 2014, a study published by Leslie Wilson *et al*. calculated the cost effectiveness of three metastatic castration-resistant prostate cancer (mCRPC) treatments -- Zytiga (abiraterone), Xtandi (enzalutamide), and Jevtana (cabazitaxel) -- and found that the price of Xtandi is the single limiting factor rendering Xtandi less cost-effective than Zytiga. This study was detailed in the Journal of Oncology Pharmacy Practice:

> L. Wilson et al. New therapeutic options in metastatic castration-resistant prostate cancer: Can cost-effectiveness analysis help in treatment decisions? *Journal of Oncology Pharmacy Practice* 2014, Vol. 20(6) 417–425

According to the authors' incremental cost-effective calculations based upon 2012 prices, Xtandi would be the preferred treatment, if prices were decreased:

> Results: Abiraterone was the most cost-effective of the treatments ($123.4 K/quality-adjusted life year) compared to placebo, enzalutamide was $437.6 K/quality-adjusted life year compared to abiraterone, and cabazitaxel was $351.9 K/quality-adjusted life year compared to enzalutamide. Enzalutamide and cabazitaxel were not cost-effective compared to placebo at $154.3 K/quality-adjusted life year and $163.2 K/quality-adjusted life year, respectively. Acceptability curves showed abiraterone was cost-effective 29.3% of the time with a willingness to pay threshold of $100 K. The model was sensitive to changes in cost of the drugs, life expectancy, and survival rate. **Sensitivity analysis shows that enzalutamide can become the most cost-effective option if the price of the medication decreased by 26% and other drug costs remained the same. [emphasis added]**

The Wilson paper concludes with this comment:

> The results of our study can be useful in setting funding priorities for programs that are competing for scarce resources by making comparisons across all available treatment options.

This research illustrates way that health care providers will respond to the the excessive and discriminatory pricing of Xtandi. When prices are high, access to enzalutamide is downgraded in formularies, even when it is otherwise a superior treatment for patients.

The restriction of access is a dangerous and unnecessary risk taken with the lives of mCRPC patients, and one that begs for action to alleviate the health needs directly caused by Astellas's pricing. As we pointed out in our petition, the ramifications of forcing patients to take other mCRPC drugs prior to Xtandi can include a decrease in the effectiveness of Xtandi, or complete resistance.[2] Patients in treatment for prostate cancer already face enough challenges without the added risks associated with the excessive and discriminatory pricing of Xtandi.

A copy of the article is enclosed.

[2] See p.4 of the KEI/UACT petition.

Sincerely,

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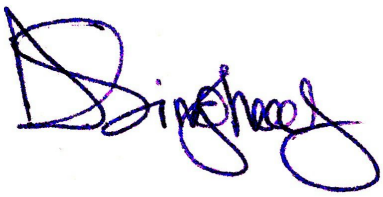

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