Congress of the United States
Washington, DC 20510

July 7, 2016

The Honorable Robert M. Califf, MD
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Califf:

We understand that the Food and Drug Administration (FDA) is evaluating whether to grant approval to several pharmaceutical companies who have applied to make a generic equivalent of Crestor (rosuvastatin calcium), marketed by AstraZeneca Pharmaceuticals LP and its affiliate iPR Pharmaceuticals, Inc. We urge FDA to approve all eligible applications to produce a generic version of Crestor.

Crestor is one of the world's most widely prescribed medicines for high cholesterol, with global sales of more than $5 billion last year, including $2.8 billion in the United States.[1] It was prescribed more than 20 million times in the United States last year and has a retail price of $260 per month.[2] FDA approval of generic versions of this drug has the potential to drastically reduce health care costs, both to individual patients and to our health care system. Historically, generic drug prices have fallen by half, on average, in the 12 months following generic entry.[3]

Americans pay, by far, the highest prices in the world for prescription drugs. We now spend nearly $400 billion a year on prescription drugs, and high prices put life-saving medicines out of reach for too many Americans.[4] Nearly one in five Americans do not fill their prescriptions because they cannot afford them.[5] At the same time that Americans are skipping or cutting the medicine they need, pharmaceutical companies are generating record profits.

On May 31, 2016, AstraZeneca filed a Citizen Petition with FDA to block all generic Crestor approvals. AstraZeneca argues that because it recently secured a seven-year exclusivity extension under the Orphan Drug Act to sell Crestor to treat children with a rare genetic disease, the company should also be able to extend its monopoly for all uses of Crestor. Before FDA

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[1] Andrew Pollack, *AstraZeneca Pushes to Protect Crestor From Generic Competition,* New York Times (June 27, 2016).
[2] *Id.*
[3] Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation, *Understanding Recent Trends in Generic Drug Prices* (Jan. 27, 2016).
[4] *Medicines Use and Spending Shifts: A Review of the Use of Medicines in the U.S. in 2014,* IMS Institute for Healthcare Informatics (Apr. 14, 2015).
[5] *Trends in Coverage, Medical Debt, and Access to Care: Findings from the Commonwealth Fund Biennial Health Insurance Survey*, Commonwealth Fund (Jan. 15, 2015).

made a decision on the petition, AstraZeneca sued FDA in a further effort to block upcoming generic Crestor approvals.[6]

AstraZeneca argues that because orphan drug exclusivity was not explicitly addressed in the statute Congress passed in 2001 to close the pediatric labeling loophole, then there is no statutory basis for the pending carve-out.[7] This argument is wrong, and it was rejected by the United States District Court for the District of Maryland, which recently considered the same argument in a case regarding the drug Abilify (aripiprazole).[8] AstraZeneca is attempting to exploit an old loophole that has been closed by Congress and disavowed by the courts.

AstraZeneca has also tried to justify extending its monopoly on safety grounds. However, the district court in the Abilify case rejected a safety argument similar to AstraZeneca's. The court found that the relevant pediatric patient population in that case (less than 120,000) was far smaller than the overall U.S. patient population and must be weighed accordingly. Here, the relevant pediatric population for Crestor is approximately 300 patients, a tiny subset of the 20 million patients who could benefit from a lower cost generic equivalent.[9]

AstraZeneca has already enjoyed 12 years of market exclusivity for Crestor with revenues over $16 billion from Crestor in the last three years alone.[10] Those exclusivity periods have now come to an end. Any additional regulatory exclusivity AstraZeneca has obtained under the Orphan Drug Act does not cover all uses, especially those no longer protected by patents or exclusivities.

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[6] *AstraZeneca Pharm. LP v. Burwell*, No. 1:16-cv-01336 (D. D.C.) (June 27, 2016).

[7] Petition at p. 20. AstraZeneca surrendered its three-year data exclusivity period under 21 C.F.R. § 314.108(b)(5), claiming only the seven-year orphan drug exclusivity, in a blatant attempt to circumvent § 355A(o). *See* June 24, 2016 letter from Joseph A. Cash, Jr. to FDA, which was submitted to the Petition docket.

[8] *Otsuka Pharm. Co. v. Burwell*, No. GJH-15-852, 2015 WL 3442013, at *7 (D. Md. May 27, 2015) (endorsing FDA's "precedent addressing the specific question of whether to approve ANDAs that carve out pediatric information protected by orphan drug exclusivity"). FDA's authority to carve out such information from the label of the generic drug is clear. *See, e.g., Spectrum Pharms., Inc. v. Burwell*, No. 15-5166, 2016 WL 3126834, at *3 (D.C. Cir. June 3, 2016) (noting that "FDA allows labeling carve-outs under the Orphan Drug Act just as it does for generics generally under the Food, Drug, and Cosmetic Act"); AstraZeneca also filed a temporary restraining order against FDA on June 30, 2016.

[9] *See* Petition at p. 7, fn. 11 *citing* George Yuan, Jian Wang, & Robert A. Hegele, "Heterozygous Familial Hypercholesterolemia: an Underrecognized Cause of Early Cardiovascular Disease," *Canadian Med. Ass'n J.* (Apr. 11, 2006) available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1421462/ (last visited June 30, 2016) (noting that homozygous familial hypercholesterolemia is extremely rare, affecting about 1 in 1 million people against a total U.S. population of about 330 million).

[10] AstraZeneca Annual Report 2015, available at http://www.astrazeneca-annualreports.com/2015/assets/pdf/AZ_Annual_Report_2015.pdf (last visited July 5, 2016).

Pharmaceutical companies should not be permitted to block millions of patients from accessing lower cost generic equivalents at the last minute just so they can maximize their profits. This would be a disastrous anticompetitive, anti-consumer result.

Sincerely,

BERNARD SANDERS
United States Senator

ELIJAH E. CUMMINGS
United States Representative

JAN SCHAKOWSKY
United States Representative

LLOYD DOGGETT
United States Representative

JOHN SARBANES
United States Representative

STEVE COHEN
United States Representative

PETER WELCH
United States Representative

MARCY KAPTUR
United States Representative

cc: The Honorable Sylvia Mathews Burwell