

Congress of the United States

Washington, DC 20510

March 15, 2017

Dr. Stephen Ostroff
Acting Commissioner
U.S. Food and Drug Administration
10901 New Hampshire Avenue
Silver Spring, MD 20993

Dear Acting Commissioner Ostroff:

We write to express our concern and request information regarding the unusual circumstances surrounding the recent approval by the Food and Drug Administration (FDA) of a brand name version of the more than 20-year-old drug, deflazacort.

On February 9, 2017, FDA approved Emflaza (deflazacort) to treat patients age 5 years and older with Duchenne muscular dystrophy (DMD) – a rare genetic disorder that causes progressive muscle deterioration and weakness. This painful and debilitating condition cuts short the lives of most patients in their twenties.¹

FDA's recent approval of Emflaza appears to have relied largely on research conducted decades ago, including 21-year-old clinical trial data on efficacy from a 1995 study measuring muscle strength.²

Within a day of approval, Marathon Pharmaceuticals, the company that will market Emflaza, announced it would sell the drug for the obscenely high price of \$89,000 a year.³ Generic deflazacort, sold by Sanofi under its trade name Calcort, is a corticosteroid that has long been available for sale around the world (but not in the United States) for about \$1,000 year to treat many conditions, including DMD.⁴

According to FDA's website, deflazacort first received an orphan drug designation in 2010 under the trademark name Calcort.⁵ In recent years, FDA has allowed DMD patients to import the drug. As FDA acknowledged in its press release announcing Emflaza's approval,

¹ U.S. Food and Drug Administration, *FDA Approves Drug to Treat Duchenne Muscular Dystrophy* (Feb. 9, 2017) (online at <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm540945.htm>).

² John Carroll, *Marathon's Cheap, Old Steroid Breezes Through the FDA for Duchenne MD, and Gets Priced at \$89K*, Endpoints News (Feb. 9, 2017) (online at <https://endpts.com/an-old-steroid-breezes-through-the-fda-for-duchenne-md-a-disease-that-has-confounded-developers/>).

³ Joseph Walker, *Marathon Pharmaceuticals to Charge \$89,000 for Muscular Dystrophy Drug After 70-Fold Increase*, Wall Street Journal (Feb. 10, 2017) (online at www.wsj.com/articles/marathon-pharmaceuticals-to-charge-89-000-for-muscular-dystrophy-drug-1486738267).

⁴ Ed Silverman, *Marathon CEO, Who Was Praised by Martin Shkreli, Causes a New Stink Over Drug Pricing*, STAT (Feb. 10, 2017) (online at <https://www.statnews.com/pharmalot/2017/02/10/marathon-dmd-martin-shkreli-drug-pricing/>).

⁵ U.S. Food and Drug Administration, *Search Orphan Drug Designations and Approvals* (online at www.accessdata.fda.gov/scripts/opdlisting/oopd/detailedIndex.cfm?cfgridkey=315110) (accessed Mar. 11, 2017).

“Corticosteroids are commonly used to treat DMD across the world.”⁶

Parents of children with DMD were heartened by FDA’s approval of a treatment for DMD. Many, however, were outraged by the price that Marathon announced. The high price was especially troubling in light of the incredibly lucrative benefits FDA has granted to Marathon and the limited amount of innovative research the company appears to have conducted to develop Emflaza.⁷

Among those lucrative benefits is the agency’s designation of Emflaza as an orphan drug, thereby granting Marathon sales exclusivity – a monopoly on the market – for seven years. Furthermore, even though the drug is a very old steroid, because Marathon sought approval to treat a rare pediatric disease, the company also received a valuable pediatric Priority Review Voucher (PRV), worth potentially hundreds of millions of dollars, to use or sell to another pharmaceutical company.⁸

FDA’s mission includes advancing public health by making medical products “more effective, safer, and more affordable.”⁹ It is also the agency’s responsibility to ensure corporations are not gaming the system.

A review of a number of the documents related to the original University of Rochester application for orphan drug status and earlier clinical trials has raised serious questions about FDA’s decision regarding Emflaza. Therefore, we ask for responses to the following questions:

1. The agency reportedly decided to approve Emflaza largely based on efficacy data from 1995.¹⁰ According to the FDA press release issued on February 9, 2017, “The effectiveness of deflazacort was shown in a clinical study of 196 male patients who were 5 to 15 years old at the beginning of the trial with documented mutation of the dystrophin gene and onset of weakness before age 5.”¹¹ Is it standard practice for FDA to rely on 20-year-old efficacy data and, if so, how many times has this happened in the last 15 years? If this is not a standard practice, is Emflaza’s approval an exception?
2. FDA approved the brand name Emflaza for deflazacort, assigning a brand name to a compound that no longer had patent protection or market exclusivity in the U.S. How many

⁶ U.S. Food and Drug Administration, *FDA Approves Drug to Treat Duchenne Muscular Dystrophy* (Feb. 9, 2017) (<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm540945.htm>).

⁷ John Carroll, *The scoop: Marathon's R&D program for Duchenne MD drug likely came in at a bargain basement price*, Endpoints News (Mar. 7, 2017) (online at <https://endpts.com/the-scoop-marathons-rd-program-for-duchenne-md-drug-likely-came-in-at-a-bargain-basement-price>).

⁸ Sarah Karlin-Smith, *Double Whammy? New Drug Approval Raises Concerns About Pricing, Abuse of Rare Disease Incentives*, Politico (Feb. 10, 2017) (online at www.politicopro.com/health-care/story/2017/02/double-whammy-new-drug-approval-raises-concerns-about-pricing-abuse-of-rare-disease-incentives-147936).

⁹ U.S. Food and Drug Administration, *FDA Mission* (last updated Oct. 24, 2016) (online at www.fda.gov/AboutFDA/WhatWeDo) (emphasis added).

¹⁰ Robert Griggs, et al. *Efficacy and Safety of Deflazacort vs Prednisone and Placebo for Duchenne Muscular Dystrophy*, *Neurology* 87, no. 20 (2016): 2123-131 (online at www.ncbi.nlm.nih.gov/pmc/articles/PMC5109941/).

¹¹ U.S. Food and Drug Administration, *FDA Approves Drug to Treat Duchenne Muscular Dystrophy* (Feb. 9, 2017) (online at www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm540945.htm).

times has FDA taken such a step in the last 15 years?

3. The Priority Review Voucher and orphan drug programs are intended to incentivize companies to invest in innovative research for medicines that do not have large patient populations. The fact that FDA awarded Marathon a PRV and orphan drug status without the company conducting significant research of its own undermines the goals of these incentives. What processes does FDA have in place to ensure private companies are not manipulating a system meant to incentivize research for treatments of extremely vulnerable patient populations?
4. Did any FDA employees raise any concerns about granting Marathon the benefits of orphan drug status or a PRV for Emflaza? Please provide copies of memos, e-mails, or records of any such correspondence or documentation.
5. Several of the earlier efficacy studies involving deflazacort and DMD also involved prednisone – the two steroids were frequently tested against a placebo, but less frequently tested against each other.¹² Why did FDA agree to accept stability and dosage data from Marathon instead of asking for new efficacy testing?
6. It is our understanding that the 1995 study that formed the basis of the FDA's approval of Emflaza was conducted through the University of Rochester and was first funded by Marion Merrell Dow.¹³ Later, Marion Merrell Dow was acquired by Hoechst, which merged with Rhone-Poulenc and Schering to become Aventis, which merged with Sanofi-Synthelabo and eventually became Sanofi.¹⁴ Given this lengthy chain, what evidence did Marathon present to FDA regarding the integrity of the decades-old efficacy trial data? What information does FDA have regarding how Marathon came to obtain the 1995 data? Did FDA take any steps to verify the validity or integrity of the chain of custody of this information or verify the old data? Please explain.
7. Marathon's CEO has temporarily stopped the launch of Emflaza in the wake of adverse publicity. What has the company relayed to FDA about its intention to delay the launch?

¹² E. Matthews, et al., *Corticosteroids for the treatment of Duchenne muscular dystrophy (Review)*, Cochrane Library (2016) (online at www.cochrane.org/CD003725/NEUROMUSC_corticosteroid-therapy-duchenne-muscular-dystrophy).

¹³ Ellen Jean Hirst, *Duchenne muscular dystrophy drug could get OK for U.S. sales in 2016*, Chicago Tribune (Jan. 19, 2015) (online at www.chicagotribune.com/business/ct-marathon-muscular-dystrophy-drug-0119-biz-20150119-story.html).

¹⁴ *Hoechst AG to Buy Marion Merrell Dow / Acquisition worth over \$7 billion*, Reuters (May 5, 1995) (online at www.sfgate.com/business/article/Hoechst-AG-to-Buy-Marion-Merrell-Dow-3035234.php); David Morrow, *International Business; Rhone-Poulenc and Hoechst Agree on Start of Merger*, New York Times (Dec. 2, 1998) (online at www.nytimes.com/1998/12/02/business/international-business-rhone-poulenc-and-hoechst-agree-on-start-of-a-merger.html); *Hoechst, Rhone confirm deal*, CNNMoney (Dec. 1, 1998) (online at <http://money.cnn.com/1998/12/01/europe/hoechst>); Anita Raghavan, John Carreyrou, and Gautam Naik, *Sanofi to Swallow Aventis in a Deal Set at \$65 Billion*, Wall Street Journal (Apr. 26, 2004) (online at www.wsj.com/articles/SB108291923112092711); *Sanofi Changes Name, Pace of Acquisitions to Slow*, Reuters (May 6, 2011) (online at www.reuters.com/article/sanofi-idUSLDE74521Z20110506).

8. According to FDA's website, Marathon has already obtained an orphan drug designation for deflazacort for pediatric arthritis.¹⁵ It seems likely the company will pursue approval for this condition. Will this additional orphan drug designation extend deflazacort's exclusivity period? If so, by how many additional years?

We request responses to these questions no later than March 31, 2017. Your response should include documentation including written memos, notes, emails, correspondence, and records of agency telephone conversations pertaining to Marathon Pharmaceuticals and deflazacort.

Any queries about this request may be directed to Alicia Mundy of the Budget Committee staff at (202) 224-0642 or Will Cunningham of Ranking Member Cummings' staff at (202) 225-5051. Thank you for your attention to this matter.

Sincerely,



Bernard Sanders
United States Senator



Elijah E. Cummings
Ranking Member
House Committee on Oversight and
Government Reform
House of Representatives

cc: Janet Woodcock, Director, CDER, FDA

¹⁵ U.S. Food and Drug Administration, *Search Orphan Drug Designations and Approvals* (online at <http://www.accessdata.fda.gov/scripts/opdlisting/oopd/detailedIndex.cfm?cfgridkey=491715>) (accessed Mar. 14, 2017).