Via E-Mail: antitrust@ftc.gov

July 15, 2014

Also via Regular Mail

Office of Policy and Coordination
Room 7117
Bureau of Competition
Federal Trade Commission
601 New Jersey Ave, NW
Washington, D.C. 20580
Telephone: (202) 326-3300

Re: Request for investigation into decision by Shire to not compete in U.S. market for Fabry's disease treatments

Dear Sir or Madam:

Knowledge Ecology International (KEI) is a non-profit organization that includes as its mission to protect consumers from excessive prices for drugs, vaccines and other medical technologies.

We are writing to ask the United States Federal Trade Commission to undertake an investigation into a possible conspiracy between the Icahn School of Medicine at Mount Sinai, formerly, the **Mount Sinai School of Medicine** (**MSSM**), [1] Sanofi, and Shire to restrain competition for treatments for Fabry's disease. Specifically, we ask that the FTC investigate the circumstances surrounding the simultaneous resolution of compulsory licensing proceedings in the United States and Germany for patents for the treatment of Fabry's disease, and the decision by Shire to withdraw its proposed registration of a biologic product that would compete directly with the Sanofi product, which enjoys a monopoly in the United States, but faces competition from Shire in Germany and other European countries.

Background

[1] The Mount Sinai School of Medicine has undergone several changes in its name and University affiliation since 1994, including past academic affiliations with CUNY and NYU.

Two U.S. biotech firms, both based in Cambridge, Massachusetts, originally developed competing treatments for Fabry's disease, a rare and severe disease.

Genzyme developed Fabrazyme. Transkaryotic Therapies developed Replagal. The development of both products benefited from NIH grants.[2]

Both firms have since been acquired by larger European firms. Transkaryotic Therapies was acquired by Shire on June 28, 2005. Genzyme was acquired by Sanofi on February 26, 2011.

On August 3, 2001, Transkaryotic Therapies and Genzyme both received European Medicines Agency approval, and 10 years of Orphan Drug status for Europe, which expired on August 3, 2011.

In 2003 Genzyme obtained a regulatory monopoly in the United States under the U.S. Orphan Drug Act. The U.S. exclusivity expired on April 24, 2010. Both products are expensive. The Genzyme product was priced at around $700 per day in 2010, or more than $250,000 per year, according to bills to patients.

The two companies compete in other markets.

Beginning in 2009, Genzyme's considerable problems with manufacturing biologic drugs led to a significant shortage of Fabrazyme production, and Genzyme reduced patient doses in the United States to 30 percent of what was medically appropriate. The Fabrazyme shortages lasted until late 2012.

In Europe, there was an initial rationing of access, but after reports of adverse medical outcomes from patients on reduced doses, the European Medical Agency asked that full dosages be restored. As a consequence, Genzyme suffered significant losses of market share to Shire, which was able to scale up manufacturing of Replagal.

The Icahn School of Medicine at Mount Sinai is the owner of an important patent on Fabrazyme. In US litigation, Shire's Replagal was found to be non-infringing. However, in April 2010, the middle of the Fabrazyme supply crisis, Mount Sinai sued Shire in Sweden and Germany for infringement of its patent, seeking to block production and sale of Replagal in Europe, and litigation over the patent was later expanded to include the UK and other countries. Mount Sinai sought injunctions to prevent Shire sales, and the destruction of Shire's infringing inventory.

[2] For background on the development of both treatments, see: Raphael Schiffmann and Roscoe O Brady, Development of enzyme replacement therapy for Fabry's disease, in *Fabry Disease: Perspectives from 5 Years of FOS*, Mehta A, Beck M, Sunder-Plassmann G, editors. Oxford: Oxford PharmaGenesis; 2006. http://www.ncbi.nlm.nih.gov/books/NBK11611/

Note that in some EU countries, including Germany and Sweden, Mount Sinai had been issued Supplementary Protection Certificates, which extended the patent term until August 2016, nearly 26 years after the initial application for the patent in the United States.

In August of 2010, several U.S. Fabry's patients filed an NIH Bayh-Dole March-In in the United States, seeking a compulsory license to the Mount Sinai patent in the United States.

The NIH rejected the U.S. Fabry's patients march-in petition, but required Mount Sinai to make monthly reports on steps taken to address the U.S. shortage of Fabrazyme, and report on the patent litigation in Europe.

Governmentattic.org has published a FOIA request that details the "regular updates to the National Institutes of Health (NIH) required from the Mount Sinai School of Medicine" regarding the Fabrazyme issue. In these email exchanges, the word injunction is mentioned 31 times.

It is clear from these emails that the NIH was putting pressure on Mount Sinai to withdraw its request for an injunction against Shire in Europe, on the grounds that an injunction would make the supply shortage worse, which at that time was hurting U.S. patients more than patients outside of the United States, and create an even larger embarrassment for the NIH, which had just denied the U.S. compulsory license request.

The NIH was in a position to push Mount Sinai, because it had world-wide rights on the Mount Sinai patent, as a consequence of funding the inventors research, but the NIH's interest in the injunction appeared to be limited to the anticipated period of the U.S. supply shortage.

During the crisis over the shortage of Fabrazyme, beginning in 2009, the US FDA invited Shire to reactivate its earlier application for marketing approval in the United States, an action that had been blocked under the Orphan Drug Act exclusivity since 2003. Shire then began a series of steps designed to obtain US marketing approval for Replagal. Since by 2009 Replagal had been used in Europe, Australia, Canada and in many other countries, with good results, Shire was optimistic the FDA would provide an approval.

Mount Sinai had been successful in its European infringement suit against Shire in Germany. But on March 1, 2011, Mount Sinai informed the NIH that it has been served with a Shire motion for a compulsory license for the territory of Germany. The German compulsory licensing proceeding was scheduled for the spring of 2012.

On March 14, 2012, Shire withdrew its application to the US FDA to sell Replagal in the United States. Less than two months later, on May 9, 2012, Mount Sinai granted Shire a non-exclusive license to use its patent in connection with the sale of Replagal in the European Union.

Request for investigation

The decision of Shire to withdraw its US BLA application for Replagal may have been part of a larger agreement to divide markets for Fabry treatments, and possibly to facilitate collusion on pricing, as Shire is now required to provide financial information to Mount Sinai, as regards its Replagal sales. As a consequence, U.S. patients are depending upon a single supplier for treatments, and are disadvantaged because there is both a lack of potential competition among suppliers and a less secure supply chain.

We ask the FTC to investigate the near simultaneous withdrawal of the US BLA application for Replagal with the Mount Sinai granting of a patent license to Shire for the European market.

We are attaching a detailed timeline of relevant dates and events. Note that the relationship between Mount Sinai and Genzyme is and was complex. For example, at the time of the supply crisis and the two compulsory licensing requests, Carl Icahn held a reported 4.9 percent of the shares in Genzyme, Inc., and as a consequence of a proxy battle, on June 9, 2010 placed a Mount Sinai official on the Genzyme Board of Directors. The school has also subsequently been named the Icahn School of Medicine at Mount Sinai.

The sequence of events served the interest of several parties. Mount Sinai was able to protect its monopoly in the United States, avoid a compulsory license in Europe, and collect money from patent royalties in several countries outside of the United States. The shareholders of Genzyme avoided losing market share in the United States and also avoided a weakened bargaining power with reimbursement entities- both outcomes at risk from an expected Shire entry into the US market following the termination of US Orphan Drug exclusivity. In one year following his Proxy battle, Carl Icahn realized a 36 percent increase in Genzyme share prices, worth more than $260 million. Shire avoided being shut-out of the markets in Germany, Sweden and other high income countries through August 2016.

The NIH also achieved its objectives of preserving its perfect track record of rejecting all Bayh-Dole March-In requests for compulsory licenses, even while finding it necessary to insist that Mount Sinai did not seek injunctions for patent infringement in Europe, a practice that sometimes is referred to as a compulsory license, when sanctioned by a court and subject to court ordered royalty payments, and certainly here, induced by the NIH, an entity with a global royalty free right in the patent.

But not everyone benefited. In particular, U.S. Fabry patients, who had just suffered through nearly three years of severe rationing of medication including, in some, cases no access and in other cases doses restricted to 30 percent of appropriate treatments, lost the opportunity for a second firm to enter the market. A second firm would have provided U.S. Fabry patients three concrete benefits. First, there would be more security of future supplies, should there be another manufacturing failure. Second, Fabry patients would have the opportunity to use either Fabrazyme or Replagal, and there is evidence that some patients do better with one than the other. Third, the availability of two suppliers can and should lead to price competition, particularly when prices bear very little relationship to manufacturing costs.

U.S. taxpayers did not benefit. The NIH funded the early development of both Fabrazyme and Replagal. But what the U.S. has received from those investments are two products, one not available in the United States, both owned by foreign firms, and both sold at extraordinarily high prices. Some of the patients who receive Fabrazyme at prices of $700 per day and higher, have the treatments reimbursed by Medicare, Medicaid or other government programs. Other patients use private insurance or in some cases, employee funded health insurance. The high prices for Fabrazyme drives up insurance premiums for everyone.

KEI asks the FTC to investigate the decision by Shire to withdraw its application to sell Replagal in the United States, including by reviewing all communications with The Icahn School of Medicine at Mount Sinai, Genzyme and Sanofi, and activist shareholders in Genzyme, to determine if a conspiracy existed whereby Shire agreed to withdraw its application to compete in the U.S. Fabry disease market if Mount Sinai granted a license to use an NIH funded invention in European markets.

Sincerely

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Attachments

1. Sales of Fabrazyme and Replagal
2. Timeline for Fabrazyme, Replagal
3. Documents related to “the Fabrazyme matter” including periodic regular updates to the National Institutes of Health (NIH) required from the Mount Sinai School of Medicine and Correspondence, 2011

1. Global Sales of Replagal and Fabrazyme

	Replagal	Fabrazyme
2006	$ 117.7	$ 359
2007	$ 143.9	$ 424.3
2008	$ 176.1	$ 494.3
2009	$ 193.8	$ 429.7
2010	$ 351.3	$ 188.2
2011	$ 475.2	
2012	$ 497.5	€ 292
2013	$ 467.9	€ 383