Statement of Chairman Timothy J. Muris

in the matter of

Genzyme Corporation / Novazyme Pharmaceuticals, Inc.

After an extensive inquiry, the Commission has voted to close its investigation of Genzyme Corporation's September 2001 acquisition of Novazyme Pharmaceuticals Inc.[1] The Commission's investigation properly focused on how the transaction would affect the pace and scope of research into pharmaceutical products for a life-threatening medical condition affecting infants and young children for which no treatment presently exists. The facts of this matter do not support a finding of any possible anticompetitive harm. Moreover, on balance, rather than put patients at risk through diminished competition, the merger more likely created benefits that will save patients' lives.

This statement first discusses the principal evidence and reasoning for my vote to close the Commission's investigation of this merger.[2] The second section addresses some of my disagreements with the Dissenting Statement of Commissioner Thompson ("Dissent" or "Dissenting Statement").

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[1] The Commission's investigation of this matter was initiated shortly after the merger was consummated in the fall of 2001. Commission staff reviewed hundreds of documents, interviewed numerous witnesses, and compiled an exhaustive file upon which the Commission's decision to close is based.

[2] Consistent with confidentiality restrictions on nonpublic submissions, this statement cites publicly available sources. The evidence collected during this investigation is consistent with the cited public information, and, I believe, would only reinforce the facts and positions taken in this statement.

I. The Issues

A. Effects of Mergers on Innovation

The Commission uses the general principles and methodologies in the *Horizontal Merger Guidelines* when investigating mergers. Because the characteristics of companies, products, and markets vary considerably, the assessment of a merger typically depends heavily on specific facts learned in the investigation. Assessing the effects of a merger on the pace of innovation is especially fact-dependent. Under some circumstances, the Commission has used an "innovation market" to evaluate whether a merger was likely to reduce the incentives of the remaining firms to innovate. In particular, in several pharmaceutical cases in which the merging parties had developed products that were in clinical trials but had not yet obtained FDA approval, the Commission employed an innovation market analysis.[3]

At the same time, the Commission properly has been cautious in using innovation market analysis. In 1995, the Commission held extensive public hearings at which prominent economists testified regarding the teachings of economic theory and empirical research concerning the effect of increased concentration on the likely pace of innovation. In summarizing this testimony, the lengthy 1996 report *Anticipating the 21st Century: Competition Policy in the New High-Tech, Global Marketplace* (hereafter "Global Marketplace Report"), acknowledged that "economic theory and empirical investigations have not established a general

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[3] *See, e.g., Amgen Inc. and Immunex Corp.*, Docket No. C-4053 (consent order issued Sept. 3, 2002) (R&D for cytokines that promote the inflammation of human tissues); *Cytyc Corp.*, FTC Press Release (June 24, 2002) (development of DNA-based test for the human papillomavirus used to screen women for cervical cancer); *Pfizer Inc. and Warner-Lambert Company,* Docket No. C-3957 (consent order issued July 27, 2000) (R&D for solid cancerous tumor treatments). *See infra,* n.11.

causal relationship between innovation and competition."[4] Indeed, the most that could be said was that "no witness maintained that a merger of the only two firms developing a totally new product could *never* have any anticompetitive effects on innovation."[5]

In light of the lack of any clear theoretical or empirical link between increased concentration and reduced innovation, the Global Marketplace Report concluded by "advocat[ing] a conservative approach to the use of innovation market analysis."[6] In doing so, the Report made two recommendations, both of which I support, which characterize subsequent Commission decisions. First, the Report stated that it "seem[s] appropriate to limit the situations that the agencies examine to ones that involve very small numbers of innovation competitors."[7] Accordingly, except under "extraordinary circumstances," innovation market analysis should not even be considered unless the number of competitors is very small.[8]

Second, assuming that an innovation market analysis is appropriate, the Global Marketplace Report concluded that a "careful, intense factual investigation is necessary" to "distinguish between procompetitive and anticompetitive combinations of innovation efforts."[9]

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4 FTC Staff Report, *Anticipating the 21st Century: Competition Policy in the New High-Tech, Global Marketplace*, Vol. I, ch. 7, at 16 (May 1996) (hereafter "Global Marketplace Report").

5 *Id.* at 16 n.51 (emphasis in original).

6 *Id.* at 33.

7 *Id.*

8 *Id.*

9 *Id.* at 18, 20. *See also* Council of Economic Advisers, *Economic Report of the President*, Ch. 5, at 176 (1999).

To the extent there is consensus, it is that neither the presence of many

In particular, the Report noted that "there are a number of theoretical models that suggest when a monopolist may have a disincentive to invest in research and development." Antitrust enforcers "can examine whether the facts of a specific matter are generally consistent with a particular theoretical description."[10] Because "any application of this approach should proceed very carefully," the Report endorsed only the "judicious, careful use"[11] of innovation market analysis

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> competitors nor pure monopoly correlates systematically with optimal levels of innovation. But even in such polar cases, predictions about R&D activity are hard to make. The determination requires looking at the facts in each case, because market factors other than concentration, as well as a firm's regulatory status and the nature of its products and technologies, also affect innovation.

[10] *Id.* at 19.

[11] *Id.* at 5. For example, the Global Marketplace Report noted that "in almost all of the settings where the Commission has applied an innovation market analysis, it has been clear that entry would not constrain anticompetitive conduct." *Id.* at 38. In these cases, the FDA approval process has been particularly important "because it typically eliminates the probability of entry by substitutable R&D. In general, any new innovation effort would have to start at the beginning of the FDA process and thus would usually be required to conduct several years of testing before it could catch up with any current R&D efforts." *Id.* at 6. The FDA process accordingly has "permitted identification of the potential entrants and relatively secure conclusions that they would be unable to constrain anticompetitive conduct." *Id.* at 38.

Commission cases brought subsequent to the Global Marketplace Report have remained in accord with this analysis. See *Amgen Inc. and Immunex Corp*. Docket No. C-4053 , (complaint Sept. 3, 2002) (Amgen cytokine product on the market, Immunex product in early FDA clinical trials) (Complaint ¶ 21); *Cytyc Corp.*, FTC Press Release (June 24, 2002) (Cytyc cervical cancer testing product on the market, Digene already applied for FDA approval, with final approval expected in 2002); *Glaxo Wellcome plc and SmithKline Beecham plc,* Docket No. C-3990 (complaint December 15, 2000) (SmithKline "has the most advanced development effort towards a herpes vaccine. Glaxo has been developing a vaccine for HSV infection" and "had planned . . . to design Phase III clinical trials this year . . ." Other firms "that have undertaken efforts to develop a prophylactic herpes vaccine either have failed in their efforts or are far behind . . . with vaccines that are only in pre-clinical stages of testing.") (Complaint ¶ 22); Pfizer Inc. and Warner-Lambert Company, Docket No. C-3957 (complaint July 27, 2000) (Pfizer and Warner have EGFr-tk inhibitors in human clinical testing) (Complaint ¶ 24); *Ciba-Geigy Limited, et al.,* 123 F.T.C. 842 (1997) (Ciba [through its 46.5% interest in Chiron] and Sandoz, are "the two leading commercial developers of gene therapy products," they "control the substantial proprietary rights necessary to commercialize gene therapy products" and "control

to uncover those fact-specific instances in which a monopolist faces reduced incentives to innovate.[12]

An analysis based on the specific facts of this case is necessary for assessing the likely effects of the Genzyme/Novazyme merger on the pace of innovation for therapies for Pompe disease and therefore on patient welfare. As I have noted, neither economic theory nor empirical

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critical gene therapy proprietary portfolios, including patents, patent applications, and know-how" (Complaint ¶ ¶ 14, 15); "GTI's [Sandoz wholly owned subsidiary] U.S. clinical development is being closely coordinated with trials that Sandoz is conducting in Europe" (Separate Statement of Chairman Pitofsky, et al.); "Viagene continues to maintain a leadership position in the development of gene transfer technology products for human therapy, having initiated eight phase I clinical trials, and, in late 1994, begun the first phase II clinical study in the field of gene therapy." (Viagene December 1994 10-K, at p. 3.) Viagene was subsequently acquired by Chiron.); *Baxter Int'l and Immuno Int'l* Docket No. C-3726 (Complaint, Mar. 24, 1997) (Baxter and Immuno are two of only a few firms "seeking FDA approval" for fibrin sealants) (Complaint ¶ 10).

[12] The Dissent states that there has been "more recent thinking" since the 1996 Global Marketplace Report on the proper approach to innovation markets, citing, inter alia, the 2000 Antitrust Guidelines for Collaborations Among Competitors ("Joint Venture Guidelines"). However, I am not aware of – nor does the Dissent identify – any change in economic thinking on this subject between 1996 and 2000, either as reflected in the hearings that preceded the Joint Venture Guidelines, or more generally in the economics literature. Indeed, the Global Marketplace Report accurately reflects the relevant economic learning on this subject.

Rather than identify particular changes in economic learning, the Dissent's claim appears to be that "more recent thinking" can be inferred from Section 1.3 of the Joint Venture Guidelines, which states that competitor collaborations will be analyzed under the Horizontal Merger Guidelines if their competitive effects are the same as those produced by a merger, and Section 4.3, which provides a safety zone for certain R&D joint ventures. Neither provision supports the inference that the Dissent would draw. Section 1.3 simply makes plain that sufficiently permanent collaborations will be analyzed under the fact-specific approach followed in the Horizontal Guidelines. As for Section 4.3, to the extent it reflects any further learning, that learning is in the direction of exercising even *more* caution in the application of innovation market analysis. *Compare* Global Marketplace Report at 33 (citing "safety zone" in IP Guidelines as illustrative of need for "conservative approach" to innovation market analysis) *with* Joint Venture Guidelines at Section 4.3 (creating even broader safety zone than that prescribed by IP Guidelines).

research supports an inference regarding the merger's likely effect on innovation (and hence patient welfare) based simply on observing how the merger changed the number of independent R&D programs. Rather, one must examine whether the merged firm was likely to have a reduced incentive to invest in R&D,[13] and also whether it was likely to have the ability to conduct R&D more successfully.

B. Background on Pompe Therapy Research Programs

Several thousand individuals, mostly infants and children, suffer from Pompe disease, a genetic disorder that is often fatal, particularly for the young.[14] Because there is not yet an effective treatment for Pompe disease, any measure that accelerates the introduction of the first effective therapy, even by a matter of months, would save lives and reduce suffering. For Pompe patients, the paramount goal is the earliest possible introduction of an effective treatment, in quantities sufficient to treat them.

Over the past several years, four research programs for enzyme replacement therapies for Pompe disease have obtained at least preliminary positive results in some animal experiments. Two programs, initiated by Pharming and Synpac, were abandoned after the commencement of

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[13] Mere reductions in dollar outlays on R&D following a merger should not be presumptively considered a reduction in competition or in innovation efforts. Such reductions may reflect efficiencies in consolidation of R&D functions. In addition, although not a consideration in this case, analyzing the welfare effects of shifts in R&D expenditures among potential pharmaceutical products for life-threatening diseases raises very difficult issues.

[14] Pompe Disease is a rare and fatal genetic disorder caused by a deficiency of the enzyme acid alpha glucoside. Without this enzyme, glycogen accumulates in the lysosome of cells and rapidly destroys muscle fibers. Patients with Pompe disease experience severe muscle weakness, difficulty breathing and cardic insufficieny. Ulimately, patients require wheel chair assistance and mechanical ventilation and succumb to cardiopulmonary failure.

human trials, because the enzymes could not be produced on a commercial scale.[15] The two programs that currently survive are one initiated by Genzyme in 1999 but developed principally beginning in 2001 ("Genzyme's internal program")[16] and one initiated by Novazyme in 1999 that builds on basic research by its founder and Chief Scientific Officer, Dr. William Canfield ("the Novazyme program").[17]

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[15] Genzyme 2001 10-K, p. 7, states that both the Pharming and Synpac products were in phase II trials as of March 1, 2002. Nevertheless, Genzyme's Paul Kaufman stated on Aug. 22, 2001, that Genzyme had previously announced that it planned to switch from developing the Pharming product to developing a CHO [Chinese Hamster Ovary] enzyme product "based on manufacturing considerations." www.worldpompe.org/newspatient.html; see also Genzyme 2001 10-K, p. 11. The Synpac program involved a CHO enzyme. In an April 17, 2002, press release, Genzyme announced that it would not proceed with development of the Synpac product because that product could not be produced on a commercial scale. Genzyme stated that "Genzyme's internally developed CHO product, when compared with the Synpac enzyme, provided a similarly robust response profile in terms of glycogen clearance. Due to the significantly greater production yields of the Genzyme CHO enzyme, it offers the clearest and most efficient pathway to commercialization based on both clinical and manufacturing considerations." www.amda-pompe.org/Genzyme.htm. Moreover, in an April 17, 2002, joint statement with the International Pompe Association, Genzyme stated that "Genzyme's decision to shift further development from the Synpac CHO product to its own internally produced CHO derived enzyme . . . will allow Genzyme not only to gain better control of production but is also expected to yield more mature enzyme in a shorter period of time. Shifting to the Genzyme produced CHO should ultimately lead to an increased supply of the drug." "IPA/Genzyme Meeting April 16-17 [2002]-Joint Statement," www.worldpompe.org/ipagen.html.

[16] Genzyme 10-Q for quarter ending March 31, 2002, p. 55 ("During the first quarter of 2002, to accelerate the progression to regulatory approval, we concluded a comparison of all of our enzyme programs for the treatment of Pompe disease. The enzyme programs included: [i] the internally produced CHO enzyme program that began in 1999; [ii] the CHO enzyme licensed from Synpac (North Carolina), Inc. in 2000; and [iii] the enzyme obtained in the Novazyme acquisition in 2001.") Genzyme Press Release, April 17, 2002, refers to "the internally produced CHO enzyme that it [Genzyme] began developing last year." See generally Genzyme: Pompe Patient Program, Development History, www.genzyme.com/pompe/pompe_history.asp.

[17] Company information available at www.bioscorpio.com/novazyme_pharmaceuticals_inc.htm.

Genzyme is a large biotech company with substantial experience in developing therapies for lysosomal storage disorders, a group of 41 diseases that includes Pompe. In 2001, Genzyme had 5,200 employees[18] and sales of $982 million, including $570 million in sales of its enzyme replacement therapies for Gauche disease, a lysosomal storage disorder.[19] Novazyme was a small research company founded in 1999. It had approximately 80 employees, including approximately 70 scientists working under the supervision of Dr. Canfield.[20] It had no sales revenue because it had no products or services to sell.

When Genzyme and Novazyme merged over two years ago, in September 2001, Novazyme's Pompe program was at an early, preclinical research stage. Novazyme had some promising early results in mice,[21] but at the time of the merger it faced major research obstacles that had to be resolved before it would be ready for clinical trials.[22] Indeed, soon after the

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[18] Genzyme 2001 10-K, p. 33, data for Dec. 31, 2001.

[19] Genzyme Press Release, March 5, 2003. Genzyme was the first company to offer a safe and effective treatment for a lysosomal storage disorder, and it and Transkaryotic Therapies Inc. remain the only two companies that have brought to market an effective therapy for a lysosomal storage disorder. Genzyme now markets therapies for two lysosomal storage diseases, Gauche and Fabry.

[20] Novazyme Interview, May 21, 2001, www.worldpompe.org; Genzyme Press Release, Aug. 7, 2001.

[21] Novazyme Press Release, April 2, 2001.

[22] Genzyme's 2002 Form 10-K, p. GG-24, states with respect to Novazyme's technology: "As of the acquisition date, the technology platform had not achieved technological feasibility and would require significant further development to complete."

merger it became apparent that the obstacles were greater than was understood at the time of the merger, with the result that the program remains in the preclinical stage even today.[23]

Genzyme, meanwhile, previously had entered into joint ventures with Pharming (1998) and Synpac (2000) to develop treatments for Pompe disease.[24] These joint ventures preceded any significant internal development effort at Genzyme.[25] By the time of the Novazyme merger, commercialization of the Pharming product had been abandoned; the Synpac enzyme had shown more promise and was in clinical trials, but manufacturing problems were preventing production on a scale sufficient for commercialization. (Early in 2002, Genzyme announced the suspension of the Synpac program for this reason.[26]) As a result of these scalability problems, Genzyme had begun to ramp up its own internal research program shortly before the Novazyme merger.[27] At the time of the merger, this Genzyme internal effort was still in early preclinical testing. Indeed,

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[23] Genzyme's 2001 Form 10-K, p. GG-24, states with respect to Novazyme's technology: "We currently estimate that it will take approximately three years and an investment of approximately $75 million to $100 million to complete the development of, obtain approval for and commercialize the first product based on this technology platform." A year later, Genzyme's 2002 Form 10-K, p. GG-28, revised this estimate: "As of December 31, 2002, we estimate that it will take approximately six to eight years and an investment of approximately $100 million to $125 million to complete the development of, obtain approval for and commercialize the first product based on this technology platform." From these two statements, one can infer that during 2002 Genzyme learned that an unexpected additional three to five years of preclinical research and $25 million would be required for the Novazyme technology.

[24] Genyme 10-Q, March 31, 2002, pp.55, 59. As the 1996 Global Marketplace Report notes, in biotechnology, "most of the R&D is performed by very small firms that market their output to larger companies with the capabilities to commercialize it." 1996 Global Marketplace Report at 18.

[25] *Supra* nn.15, 16.

[26] *Id*.

[27] *Id*.

Genzyme did not commence clinical trials based on this research until 2003, more than a year after the merger with Novazyme.[28]

A high percentage of research programs that have reached animal testing fail to result in safe and effective human therapies.[29] Genzyme's experience with the Pharming and Synpac enzymes for Pompe illustrates the uncertainties that surround early-stage development of such therapies by biotechnology companies. Based on this experience with these other programs - which no evidence uncovered during the investigation contradicted - Novazyme's program may have had about a 20 percent chance of success at the time of the merger.

Moreover, unfortunately there was and still is a significant chance that Genzyme's internally-developed enzyme will fail. Although the odds facing Genzyme's internal program have improved materially since the time of the merger – the product is no longer at the preclinical stage, but has advanced to pivotal (Phase II/III) clinical trials[30] – a significant number

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[28] Genzyme Press Release, Mar. 5, 2003, stated that Genzyme had begun screening patients for inclusion in the first of two clinical studies for its internal product.

[29] Even drugs that have entered Phase I human trials have failure rates around 75 percent. J. A. DiMasi, "Risks in New Drug Development: Approval Success Rates for Investigational Drugs," *Clinical Pharmacology & Therapeutics* 297 (May 2001) (75.8 -77.4 percent); R. M. Abrantes-Metz, C. P. Adams, and A. D. Metz, "Pharmaceutical Development Phases: A Duration Analysis," Bureau of Economics, Federal Trade Commission, draft, Mar.28, 2003 (73.6 percent); C. P. Adams and V. V. Brantner, "New Drug Development: Estimating Entry from Human Clinical Trials," Bureau of Economics, Federal Trade Commission, at 20 (July 7, 2003) (88 percent for all drugs, 75 percent for biologicals).

[30] *Supra* n.28; Genzyme Press Release, May 29, 2003; Genzyme Pompe Patient Program Clinical Trials (www.genzyme.com/pompe/pompe_clinical.asp) and Genzyme Corporate Pipeline (http://www.genzyme.com/research/pipeline/pipe_home.asp); National Institutes of Health Clinical Trials (http://www.clinicaltrials.gov).

of drugs that reach this stage still do not obtain FDA approval. Relevant studies indicate that failure rates are at least 25 percent.[31]

C. Anticompetitive Theories and Evidence of Likelihood of Anticompetitive Harm

In analyzing the potential anticompetitive effects of the Genzyme/Novazyme merger, one must consider the nature and extent of the competition between Genzyme and Novazyme that would have existed absent the merger. Because of the relatively limited number of Pompe patients, therapies for Pompe disease fall under the Orphan Drug Act (ODA). The first Pompe therapy to gain FDA approval will obtain seven years of market exclusivity under the ODA. A second therapy may break that exclusivity only by establishing superiority over the first therapy.

One potential anticompetitive harm arising from the merger relates to whether Genzyme and Novazyme would have engaged in a "race to market" absent the merger.[32] In order for Genzyme and Novazyme to have been in a race to market absent the merger, at least one of them would have had to believe that altering its expenditures on R&D would significantly change its probability of beating the other company to the market with a therapy for Pompe.

The investigation did not reveal evidence that either company believed that it was in such circumstances. The evidence points to the anticipated superiority of Novazyme's

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[31] A number of studies report failure rates of 25 percent or higher for Phase III drugs, e.g., 21.5-27.1 percent (DiMasi, *supra* n.29, at 303); 43.3 percent (R. M. Abrantes-Metz et al., *supra* n.29 at 32); 62 percent for all drugs and 47 percent for biologicals (Adams and Brantner, *supra* n.29).

[32] *General Dynamics* teaches us that it is the competitive influence a firm will likely provide in the present and the future absent the merger that is the relevant yardstick, and not to rely merely on inferences based on past performance. *United States v. General Dynamics Corporation,* 415 U.S. 486 (1974).

program,[33] not to a likelihood that it could be brought to market first. Shortly after the merger, Genzyme stated that comparative testing showed that its internal Pompe enzyme could be developed and commercialized most quickly. Genzyme also stated that the promise of the Novazyme technology was to provide a basis for an improved second-generation therapy.[34]

Under these circumstances, the competition between Genzyme and Novazyme would not have had a substantial effect on the amount or timing of Genzyme's or Novazyme's R&D spending on Pompe, or on when the first Pompe therapy would reach the market. Regardless of Novazyme's program, Genzyme's incentive was to get a Pompe therapy to market sooner rather than later to earn profits on sales of its enzyme.[35] Changes in Novazyme's program would not likely have caused significant changes in Genzyme's program. Similarly, regardless of Genzyme's program, Novazyme's incentive was to get a superior Pompe therapy to market

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[33] A Novazyme Press Release, June 6, 2000, stated: "Dr. Kornfeld, a professor at Washington University School of Medicine in St. Louis, discoverer of the trafficking pathway for lysosomal enzymes and a board director at Novazyme, commented, 'I believe that the ability to target enzyme to the mannose 6-phosphate receptors has the potential to greatly enhance the clinical efficacy of replacement therapy. Novazyme is the only company at present with the technological ability to target these receptors, and I am excited to be involved as Novazyme works towards developing these novel biotherapies.'"

[34] Genzyme Press Release, Aug. 7, 2001, stated: "Novazyme has developed a series of novel protein engineering technologies that have been shown in preclinical studies to greatly enhance the targeting and uptake of replacement enzymes. Genzyme believes that these technologies could potentially lead to improved, second-generation versions of its marketed products and optimal first-generation products for the treatment of various lysosomal storage disorders."

[35] In principle, the pre-merger threat that Novazyme would soon follow with a superior product might have induced Genzyme to abandon its internal program. This did not happen, however, which is not surprising, given the relatively low probability that Novazyme would succeed.

sooner rather than later to earn profits on sales of its enzyme.[36] Changes in Genzyme's program would not likely have caused significant changes in Novazyme's program. Given the differences in the status of the Genzyme and Novazyme programs, and in the characteristics of the enzymes they hoped to produce, absent the merger there would not likely have been a "race to market" between Genzyme and Novazyme.[37]

A different potential anticompetitive harm focuses on how the merger might influence the "Novazyme program" if Genzyme's internal program succeeds. If Genzyme has one Pompe therapy on the market, it might then have less incentive to market a second therapy than would an independent company that does not already have a product on the market. Because the second therapy would cannibalize sales of Genzyme's internal product, a merger with Novazyme could have caused Genzyme to reduce its investment in the second therapy. Moreover, Genzyme might have an incentive to delay introduction of the second therapy until the end of its

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[36] In principle, the pre-merger risk that Novazyme would not develop a product sufficiently superior to Genzyme's to break market exclusivity could have induced Novazyme to abandon its program. Given Novazyme's optimistic expectations at the time of the merger for its enzyme, and the significant probability that the Genzyme program would fail, it is not surprising that Novazyme stuck with its program. Of course, one cannot now ascertain whether the setbacks that Novazyme's program later encountered would have substantially changed that assessment and caused Novazyme (absent the merger) to abandon its research effort.

[37] The Dissenting Statement suggests that the merger resulted in the loss of a second, different incentive – Genzyme's interest to get to the market "with as great a lead as possible in case Novazyme successfully developed an exclusivity-breaking product." This "first mover advantage" would leave Genzyme "more likely able to gain and retain Pompe patients". (Dissenting Statement at 5-6.) This postulated first mover advantage is unlikely: if a Novazyme product was sufficiently superior to break ODA exclusivity, it is not credible simply to suggest that Genzyme's first mover advantage would render doctors and patients unwilling to switch to Novazyme's product. This seems particularly unlikely here, where the condition is often fatal, and where there is a patient community and network, the International Pompe Association, that actively keeps abreast of developments in this area. See http://www.worldpompe.org.

initial seven years of market exclusivity in order to obtain a total of 14 years of exclusivity under the ODA.

In weighing the anticompetitive harm that might arise from concerns about the potential effects of cannibalization and acts to extend ODA exclusivity, I note at the outset that these harms are relevant only if the Genzyme internal program succeeds. The potential anticompetitive effect is a delay in the second Pompe therapy, not the first.

Moreover, given the regulatory structure of the ODA, Genzyme might not have an incentive to delay a second therapy because of fears of cannibalization or a desire to extend ODA exclusivity. Absent the merger, if Genzyme obtained ODA market exclusivity for its internal Pompe product, then Novazyme could not have brought a Pompe product to market unless that product was sufficiently superior to the Genzyme product to break Genzyme's ODA exclusivity. With the merger, however, that same superiority would give Genzyme incentives to bring the second Pompe product to market.

A different and superior Pompe therapy would increase total demand for Genzyme's products, by providing more effective treatment or by enabling the same treatment using lower dosages (and hence reduced side effects). A Novazyme treatment that required lower dosages might also reduce Genzyme's variable costs of production. If the supply of Genzyme's product were insufficient to satisfy demand, the lower dosage requirement of a product incorporating the Novazyme technology also might enable Genzyme to treat additional patients. Finally, there are 41 lysosomal storage disorders, most with no effective treatment. Genzyme wants to apply the

Novazyme technology to develop therapies for lysosomal storage disorders besides Pompe.[38] Development of a Pompe therapy that incorporates Novazyme's technology therefore might well have spillover benefits for Genzyme programs to develop therapies for other lysosomal storage disorders.

In short, an analysis of Genzyme's incentives in this case does not clearly indicate whether Genzyme would have an incentive to delay the second Pompe product in the event that the first proved successful. Additional evidence is at hand, however, regarding the parties' own assessment of their incentives. In particular, the terms of the Genzyme/Novazyme merger agreement strongly suggest that Genzyme was *not* planning to delay the Novazyme program when it acquired Novazyme. Novazyme's President and CEO, John F. Crowley, two of whose children suffer from Pompe disease, was placed in charge of the merged company's Pompe

[38] Genzyme Press Release, Aug. 7, 2001, stated: "Novazyme has developed a series of novel protein engineering technologies that have been shown in preclinical studies to greatly enhance the targeting and uptake of replacement enzymes. Genzyme believes that these technologies could potentially lead to improved, second-generation versions of its marketed products and optimal first-generation products for the treatment of various lysosomal storage disorders." On Aug. 22, 2001, Genzyme spokesman Paul Kaufman stated: "As we develop therapies for Pompe disease and other lysosomal storage diseases, we will continue to invest in technologies that will improve on our existing products and products in development. Therefore, Genzyme is making continuous investments in enzyme replacement technology, and hence, our investment in Novazyme, with its specific technology." Following meetings with Genzyme on April 16-17, 2002, the International Pompe Association, a patient organization, stated: "Genzyme's development of the Novazyme NZ-1001 product, as a potential next-generation therapy for Pompe's disease, is proceeding and continues to be in pre-clinical development. It is intended that Novazyme's science, which focuses on targeting and uptake of enzyme, will continue to serve as a central component in the efforts to develop improved second-generation versions of the Pompe ERT, improve upon some of their current marketed products, as well as help to develop new therapies for the treatment of additional lysosomal storage disorders."

program.[39] It seems unlikely that Genzyme would have given this role to Mr. Crowley if it had wanted to delay the development and introduction of a promising second Pompe therapy.

Furthermore, the merger agreement provided for two milestone payments totaling $87.5 million to former Novazyme shareholders if two products employing certain of Novazyme's technologies were approved by the FDA within specified time limitations.[40] At the same time, Genzyme placed substantial Novazyme shareholders, including not only Mr. Crowley but also Dr. Canfield (the scientist on whose research the Novazyme program was based), in pivotal positions within the merged company's Pompe program.[41] If Genzyme wanted to delay development of a promising Novazyme product, it would have been irrational to create a large incentive for Novazyme shareholders inside and outside Genzyme to blow the whistle – and possibly litigate – if Genzyme failed to pursue the promise of the Novazyme technology. Nor would it have been prudent to place these Novazyme shareholders in a position within the company where they could not help but learn of any effort to underfund or otherwise delay the Novazyme program. Finally, because the Genzyme/Novazyme merger was consummated more than two years ago, the Commission looked for evidence that the merger has had anticompetitive

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[39] Genzyme Press Release, Mar. 5, 2003, reports that two of Crowley's children have Pompe disease. Conflict of interest concerns that may have led to Crowley's resignation from Genzyme in December 2002, are recounted by Geeta Anand, *Clinical Trials: For His Sick Kids, A Father Struggled to Develop a Cure*, The Wall Street Journal, August 26, 2003 at A1. The conflict, as discussed in the article, concerned his efforts to get his children access to treatment versus the knowledge that his children were not the best candidates for clinical trials.

[40] Genzyme Press Release, Aug. 7, 2001.

[41] Genzyme Press Release, Aug. 7, 2001, states that Crowley was made senior vice president of Genzyme Therapeutics and would assume overall responsibility for the company's Pompe programs. Canfield was made senior vice president for glycobiology and would continue to lead the team at Novazyme's Oklahoma City facilities.

effects. There is no evidence that the merger reduced R&D spending on either the Genzyme or the Novazyme program or slowed progress along either of the R&D paths. Although there have been schedule changes since the merger, there is no evidence that they resulted from anything other than the difficulties that attend challenging research efforts.

D. Merger Benefits

The Commission also investigated whether the merger has made it more likely that the Genzyme program or the Novazyme program will produce a successful therapy, or will do so sooner. The merger made possible comparative experiments[42] and provided information that enabled the Novazyme program to avoid drilling dry holes. By accelerating the Novazyme program, the merger may have increased its odds of success. Moreover, the merger made possible synergies that will help avoid a delay in the Novazyme program.[43]

In weighing merger benefits, the Commission considers whether they are merger-specific. In this case, important merger benefits that were offered have in fact been achieved. We are not dealing with vague claims about uncertain benefits some time in the future. The issue is how these benefits compare to the *expected value* of benefits that would have been

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[42] Genzyme Press Release, April 17, 2002, describes the "comprehensive, blinded pre-clinical analysis comparing all four Pompe enzymes" and the results of that analysis.

[43] In a statement issued following meetings on April 16-17, 2002, the International Pompe Association stated: "We . . . believe that Genzyme is doing everything in their power to develop ERT [enzyme replacement therapy] as quickly as possible....We recognize the importance of the comprehensive studies conducted by Genzyme in order to compare all forms of Pompe enzymes. Data shared with us, that was derived from this study, substantiates Genzyme's claim that they are pursuing the most efficient pathway to commercialization. This is based not only on manufacturing considerations, but on clinical analysis as well. This most important data will hopefully expedite both ERT and reimbursement approval." ("IPA/Genzyme Meeting," April 17, 2002.)

achieved absent the merger – for example, in the case at hand, if Novazyme had entered into a joint venture with a biotechnology company that did not already have a Pompe program. Unlike a proposed merger, which would involve uncertainty regarding both the proposed merger and an alternative joint venture, in this case only the results of a possible joint venture are uncertain. There is no reason to weigh equally the merger's actual benefits with the potential benefits of a joint venture that never occurred. Any number of factors – the possibility that the joint venture would not have occurred, that it would have failed before achieving any benefits, or that the benefits would have taken longer to achieve – render the benefits in the hypothesized "but for" world more conjectural. These speculative gains cannot offset concrete gains that will translate into immense benefits for patients if the Genzyme internal Pompe program fails and the Novazyme program succeeds. Many lives would be saved and much suffering prevented.

E. Weighing the Effects of the Merger

To reiterate, because there is currently no treatment for Pompe disease, the most important goal for patients is to get one effective treatment for Pompe disease on the market as soon as possible, in quantities sufficient to treat the patient population. Accelerating the first effective treatment by even a few months would greatly benefit patients. Patient welfare would also be increased by having a second effective Pompe treatment arrive on the market sooner, although the regulatory constraints of the ODA may hinder the ability to deliver a second product. Some patients who do not respond to the first therapy may respond to the second, while others may simply respond better to the second than to the first. Further, entry of a second therapy would likely cause a reduction in prices. These are significant considerations.

Nevertheless, for a fatal disease without any effective therapy, acceleration of the first effective treatment remains of paramount importance.

The evidence does not suggest that the merger has had a significant effect on the likelihood that Genzyme's internal program will succeed or, if it does succeed, on the date at which a therapy would be available. Consequently, an assessment of the merger must be based on comparing two alternative states of the world.

In the first, Genzyme's internal program fails. It is impossible to assign a precise probability to this event. In any case, the probability would depend on whether one looks at the issue when the parties merged or at present. Based on the rate of failure of such programs, it seems appropriate to estimate about a 25 percent chance that the Genzyme internal program will fail.[44] If the Genzyme internal program fails, then Genzyme will clearly want to pursue the Novazyme program. In this case, the merger is likely to have large patient benefits, because it appears that the merger has accelerated the Novazyme program.

In the alternative state of the world, Genzyme's internal program succeeds. For purposes of this analysis, this state appears to have a probability of around 75 percent. In this alternative state, as discussed previously, it would be anticompetitive for Genzyme to move forward with the Novazyme program more slowly than an independent company would have done, whether out of concerns over possible cannibalization or to extend its market exclusivity period. As also discussed previously, however, Genzyme had offsetting incentives not to delay the Novazyme program at all. There is no basis in the record for concluding that the circumstances that would give Genzyme an incentive to delay – concerns about cannibalization of sales of its internal

[44] *Supra* n.31.

product without sufficient offsetting expansion in demand, reduction in costs, or extension in product line – amount to anything more than a bare theoretical possibility. Indeed, the observable facts regarding Genzyme's behavior, such as the terms of its agreement with Novazyme and the structure of its Pompe program, strongly suggest Genzyme viewed the possibility of delay as so remote that it made no allowance for it in its plans.

In short, from the Commission's investigation, there are strong reasons to believe that the merger will benefit patients in the first state of the world, without a basis for concluding that the merger is likely to result in net harm to patients in the alternative state of the world. On balance, the merger is likely to be procompetitive, and thus patients' lives are more likely to be saved by this merger than to be put at risk.

One final consideration that warrants discussion is the effect of a complaint and eventual order in this case. Neither litigation nor a remedial order would likely benefit Pompe patients. To the contrary, litigation could adversely affect Genzyme's incentives to spend on R&D, and could disrupt the Novazyme research program. To an extent not typically seen in pharmaceutical cases, the Novazyme research effort appears to depend heavily on the efforts of one man – Dr. William Canfield, Novazyme's founder, chairman, and head of its research team. Dr. Canfield's testimony would be central to establishing numerous facts in the case, including, among others, any merger-specific efficiencies related to the Novazyme technology, as well as any claims of merger-related delays. Time that Dr. Canfield spends in the courtroom rather than the laboratory seems likely to delay the Novazyme research effort – precisely the harm that litigation in this matter would be brought to avoid.

A remedy in this case also appears problematic. Although we have issued and will continue to issue complaints against consummated mergers when appropriate, unwinding the merger of preclinical research efforts on the particular facts of this case raises numerous issues. For example, because this is an ODA market, a nonexclusive license to the Novazyme product, such as the Dissent suggests, appears likely to create a powerful disincentive to innovate further in this technology. The chief value of the technology lies in its potential ability to "break exclusivity" as a superior drug; licensing the technology on a non-exclusive basis, however, would eliminate this value. (By definition, at least one competitor would have a drug product that was just as good.) Other potential remedies also appear to raise significant concerns.

II. Commissioner Thompson's Dissenting Statement

Although I disagree with the Dissenting Statement on several points,[45] two in particular

[45] For example, on page 4, the Dissent states that "[B]etween 1998 and 2001, Genzyme acquired control over the three other Pompe ERT [enzyme replacement therapy] R&D efforts in the world through joint venture or acquisition." Genzyme did acquire three Pompe R&D programs (Pharming in 1998, Synpac in 2000, and Novazyme in 2001). Nevertheless, the wording of the Dissent might cause a reader to conclude that there was a time when Genzyme, Pharming, Synpac, and Novazyme were all doing independent R&D on Pompe. In fact, when Genzyme formed a joint venture with Pharming in 1998, Genzyme did not have a Pompe program of its own. See *supra* n.14. When Genzyme acquired the Novazyme program in September 2001, the Pharming and Synpac programs had encountered serious obstacles, and Genzyme had decided that the Pharming product could not be commercialized. In April 2002, Genzyme announced that it would not proceed with further development of the Synpac product because that product could not be produced on a commercial scale. Genzyme Press Release, Apr. 17, 2002, states that "Genzyme's internally developed CHO product, when compared with the Synpac enzyme, provided a similarly robust response profile in terms of glycogen clearance. Due to the significantly greater production yields of the Genzyme CHO enzyme, it offers the clearest and most efficient pathway to commercialization based on both clinical and manufacturing considerations." Also, "Genzyme's decision to shift further development from the Synpac CHO product to its own internally produced CHO derived enzyme . . . will allow Genzyme not only to gain better control of production but is also expected to yield more mature enzyme in a shorter period of time. Shifting to the Genzyme produced CHO should ultimately lead to an increased supply to the drug." *Id.* During 2003, Genzyme's ability to conduct Phase II trials even for its internal Pompe enzyme was constrained by the volume of the enzyme that

require further discussion. First, some of the statements, which I find to be without support in the record, may cause unwarranted anxiety in the Pompe patient community. Second, the Dissent's proposed approach to innovation analysis, although undertaken for the purpose of safeguarding innovation, in fact would often have the opposite effect.

A. Factual Assertions Regarding Competitive Effects

Several of the Dissent's statements suggest that the Commission has found evidence that the merger already has caused, or is likely to cause, anticompetitive effects. I strongly disagree. For example, the Dissenting Statement expresses the view (at 4-5) that absent the merger Genzyme and Novazyme would have been involved in a "race to market" for Pompe therapies, and that this would likely have accelerated their R&D programs. It later states (at 9): "The evidence collected in this investigation showed that pre-merger competition did in fact bring an additional incentive to race in this particular innovation market." These assertions lack evidentiary support; instead, the evidence indicates that absent the merger, Genzyme's and Novazyme's R&D would not have been influenced substantially by efforts to increase their probabilities of being the first to market.[46]

Genzyme was able to manufacture. Genzyme Press Release, Sept. 10, 2003.

[46] The Dissent also makes some generalizations (nn.9, 21) about competitive behavior relating to innovation in products that fall under the ODA. The Dissent states (at n.9) that "[i]nnovator rivals in other Orphan Drug Act markets race to market to gain exclusivity, thus confirming that innovation competition in Orphan Drug Act markets is just as important as in any other innovation market." The merger investigation identified only one case in which there was a race to market – between Genzyme and Transkaryotic Therapies Inc. to obtain FDA approval for a therapy for Fabry disease. Genzyme 2002 10-K, p. 22. The existence of that one race hardly implies that there is a race every time two companies conduct R&D to find a therapy covered by the ODA.

Similarly, on pp. 5 (note 10) and 6, the Dissent refers to delays in the Novazyme project schedule since the merger. There is no evidence, however, that the merger caused those delays. Rather, they appear attributable to overly optimistic early projections and subsequent unexpected problems.

B. Innovation Market Analysis

The Dissenting Statement proposes that the Commission reject its previous approach to innovation market analysis, which was based on economic theory and empirical research, in favor of a rebuttable presumption of anticompetitive effects from a merger between the only two companies that are attempting to innovate in a product market. The Dissent states (at 3) that "the Horizontal Merger Guidelines . . . establish a rebuttable presumption of competitive effects for mergers if the change in, and resulting level of, market concentration is significant. I see no compelling reason why innovation mergers should be exempt from the Horizontal Merger Guidelines or the presumption of anticompetitive effects for mergers to monopoly and other mergers as discussed therein."

The reason why no presumption attaches is clear. There is no reason to believe, a priori, that a particular merger is more likely to harm innovation than to help it – which is, of course, simply another way of saying that there is no empirical basis for a presumption. The Dissent's rule would have the effect of routinely blocking mergers likely to accelerate innovation. Far from serving to protect consumer interests, therefore, such a rule would routinely put the Commission in the position of impeding those interests.

The same flaw underlies the negative inference that the Dissenting Statement proposes to draw about the merger because of its effect on what Genzyme could do. It states (at 5) that Genzyme "has acquired the power to decide unilaterally and at any time whether to postpone or terminate its own research efforts or Novzyme's R&D project." The Dissent also claims (at 7) that "the Novazyme acquisition . . . extinguishes any chance for competition to push innovation that could possibly bring the first or second Pompe ERT product to the actual goods market sooner." Anticompetitive behavior, however, depends on incentives as well as ability. There is no evidence that the merger significantly changed Genzyme's incentive to bring its first product to market. As discussed above, one cannot make a prediction about the effect of the merger on the Novazyme program without considering Genzyme's incentives. When those incentives are evaluated, the specific facts of this case do not indicate any likely effect on Genzyme's effort to bring a second Pompe therapy to market.

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The Dissent argues (at 14) that closing this investigation could call into question the Commission's continuing commitment to its merger enforcement policies, particularly with respect to innovation markets and innovation competition. Given that Commissioner Thompson and I have agreed on all but two of the dozens of mergers cases on which we have both voted over the past 30 months, this assertion lacks credible support. On the direction the Commission should take in analyzing innovation competition, however, Commissioner Thompson and I clearly disagree. The Commission should not stray from the well-considered and appropriate path that it has followed in recent years.[47] Commissioner Thompson, on the other hand, has

[47] In addressing the application of antitrust to innovation issues, the 1999 Annual Report of the President's Council of Economic Advisors states:

proposed that the Commission reject its previous fact-specific approach in favor of legal presumptions, despite the lack of any economic consensus supporting that approach. The adoption of presumptions without economic foundation would constitute a major step backward in antitrust law. Because such a presumption, if adopted, would frequently make the Commission itself an impediment to consumer welfare, I have written this public statement.

> When the overall level and the future path of innovation are at issue, case-by-case analysis of the economic facts is likely to be even more vital than in conventional antitrust investigations.

Council of Economic Advisers, *Economic Report of the President*, Ch. 5, at 177 (1999).