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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

CHARLES SEIFE,

Plaintiff,

v.

FOOD AND DRUG ADMINISTRATION and DEPARTMENT OF HEALTH AND HUMAN SERVICES,

Defendants,

and

SAREPTA THERAPEUTICS, INC.,

Defendant-Intervenor.

1:17-cv-3960 (JMF)

NOTICE OF MOTION

PLEASE TAKE NOTICE that upon the accompanying declarations of Sarah Kotler and Nancy B. Sager, the memorandum of law dated April 6, 2018, and the declaration of Ian Estepan, which is being submitted by Defendant-Intervenor Sarepta Therapeutics, Inc. in support of its motion for summary judgment, ECF No. 72, defendants the United States Food and Drug Administration and the Department of Health and Human Services, by their attorney Geoffrey Berman, United States Attorney for the Southern District of New York, hereby move this Court,

before the Honorable Jesse M. Furman, United States District Judge, in the United States Courthouse, 40 Foley Square, New York, New York for summary judgment pursuant to Rule 56 of the Federal Rules of Civil Procedure.

Date: New York, New York
April 6, 2018

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UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

Charles Seife ***Plaintiff,*** **v.** **Food and Drug Administration and Department of Health and Human Services** ***Defendants*** **and** **Sarepta Therapeutics, Inc.** ***Defendant-Intervenor.***	)	**Case No. 1:17-cv-3960 (JMF)**

MEMORANDUM OF SAREPTA THERAPEUTICS, INC.
IN SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT

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Defendant-Intervenor Sarepta Therapeutics, Inc. ("Sarepta") submits this memorandum of law in support of its and the Food and Drug Administration's ("FDA") Motion for Summary Judgment on the ground that the information redacted in response to Plaintiff's Freedom of Information Act ("FOIA") request has been properly withheld pursuant to 5 U.S.C. § 552(b)(4) ("Exemption 4").

I. INTRODUCTION AND PROCEDURAL BACKGROUND

In June 2015, Sarepta completed the submission of a New Drug Application ("NDA") for its drug eteplirsen (trade name EXONDYS 51®) for the treatment of Duchenne muscular dystrophy ("DMD"), a rare disease afflicting young males. Sarepta's NDA was the culmination of more than a decade of work and an investment of millions of dollars. The NDA included two Clinical Study Reports, with supporting documentation (collectively "CSRs"), along with other statutorily-required data regarding the testing and development of eteplirsen. Much of the NDA reflects Sarepta's proprietary information.

This litigation relates to the request of Plaintiff Charles Seife ("Plaintiff" or "Seife") that FDA release the two CSRs. FDA released the CSRs after, in consultation with Sarepta, properly redacting certain confidential commercial information that is exempt from release pursuant to FOIA Exemption 4, which protects trade secrets and confidential commercial information from public release. As detailed in its *Vaughn* index justifying each withholding, FDA redacted those portions of the CSRs that have not previously been made public and that, under the governing regulatory regime, are not designated for publication because they are proprietary and their release would result in competitive harm to Sarepta ("Redactions"). (*Vaughn* index annotated by Plaintiff, Kristen E. Ittig Declaration ("Ittig Decl.") Ex. A ("Ex. A").) Plaintiff has identified a subset of the redactions to which it still objects ("Challenged Redactions"). (*Id.*)

As explained below, the Challenged Redactions are proper under FOIA Exemption 4. The testing, protocols, testing data, study design, study results, and other information that comprise the Challenged Redactions are the product of years of investment and work by Sarepta. If publicly released, this information could be exploited by a competitor to gain an unfair competitive advantage over Sarepta. The prospect of such competitive harm justifies withholding information pursuant to FOIA Exemption 4. Accordingly, summary judgment should be granted in favor of FDA and Sarepta.[1]

II. STATEMENT OF FACTS

A. Sarepta's Research

Sarepta began researching possible treatments for DMD patients in the 2000s. (Declaration of Ian Estepan ("Decl.") ¶¶ 10-12.) DMD is a progressively debilitating and ultimately fatal neuromuscular disease affecting approximately 9,000 to 12,000 young males in the United States. (*Id.* ¶ 4-5.) DMD is caused by mutations in the dystrophin gene that result in a lack of dystrophin in a patient's body. (*Id.* ¶ 6.) Dystrophin is a protein that plays a vital role in the structure of muscle cells, and the lack of dystrophin causes a progressive loss of muscle tissue and function. (*Id.*)

While the mutations in the dystrophin gene causing DMD vary, for more than half of patients, DMD is caused by the deletion of one or more exons (a sequence within the gene that will be expressed once transcribed by RNA). (*Id.* ¶ 8.) "Exon skipping" is a molecular biological process used to treat genetic diseases such as DMD; in simplest terms, exon skipping instructs the body's cellular machinery to "skip over" a segment of the gene sequence during the translation process. (*Id.* ¶ 9.) In the context of DMD, exon skipping can cause the body to skip

[1] The parties have agreed to limit the scope of the instant motion to the competitive harm, as defined by Exemption 4, relating to the Challenged Redactions. (*See* Dkt. 66, endorsed letter to Court from all parties.)

over the mutation on the dystrophin gene, resulting in the production of functional, albeit shortened, muscle strands. (*Id.*)

Scientists at Sarepta, in collaboration with others, created a modified version of DNA suitable for exon skipping in a therapeutic setting. (*Id.* ¶¶ 10-12.) The result of this multi-year collaboration was eteplirsen, a type of compound designed to cause exon 51 to be skipped during processing in patients with mutations amenable to such skipping. (*Id.* at ¶ 12.) DMD mutations amenable to skipping exon 51 comprise approximately 13% of DMD patients. (*Id.* ¶ 13.) Sarepta submitted an Investigational New Drug ("IND") Application to FDA for the use of eteplirsen to treat DMD in 2007. (*Id.* ¶ 14.) IND approval is necessary to conduct clinical trials, but is by no means a guarantee that the investigational drug will ever reach the market. The percentage of drugs subject to Phase 1 clinical testing that eventually complete the approval process is only 9.6%.[2] Having achieved preliminary success in proof-of-concept (known as "Phase 1") clinical studies, Sarepta initiated a 28-week double-blind, placebo-controlled "Phase 2" study in 2011 ("Study 201"). (*Id.* ¶ 15.) Twelve patients, each with DMD mutations amenable to exon 51 skipping, participated in this study. (*Id.* ¶ 17.) Sarepta transitioned Study 201 into a longer-term "Phase 2b" study in 2012 ("Study 202"). (*Id.* ¶ 16.)

Clinical trials compare a historical control group of untreated DMD subjects[3] to the study participants, whose progress is compared to "endpoints" to measure drug efficacy. "Clinical" endpoints consider direct effects on patients, and "surrogate" endpoints use lab measurements to track a marker affiliated with a disease. (*Id.* ¶ 35.) During the course of these studies, Sarepta measured and analyzed multiple endpoints, some of which—such as certain lymphocyte counts,

[2] *See* "Clinical Development Success Rates 2006-2015," Biotechnology Innovation Organization, *available at* www.bio.org/sites/default/files/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf

[3] Data regarding untreated DMD subjects is obtained via contract with third parties. (Decl. ¶ 33.)

the "timed 4-step test," and the North Star Ambulatory Assessment—have been publicly released, while other similar endpoints have not, and remain part of Sarepta's proprietary research and methodological knowledge. (CSR Excerpts, Ittig Decl. Ex. B ("Ex. B") at FDACDER00028 ("Bates 28"); Bates 6474.) After much research and expense, Sarepta chose an increase in dystrophin (measured via muscle biopsies taken at designated points during the study) as a surrogate endpoint and patients' ability to complete a six-minute walk test as a clinical endpoint. (*Id.* at Bates 28-29; Decl. ¶ 36.) The surrogate endpoint was the ultimate basis for FDA approval. (Decl. ¶ 26.) The FDA recently publicly confirmed that dystrophin is an acceptable surrogate endpoint to achieve accelerated approval, rendering Sarepta's research into correct measurement of dystrophin extremely valuable. (*Id.*)

The results of Studies 201 and 202 were documented in the CSRs. Each CSR consists of an approximately 100-page narrative document, accompanied by thousands of pages of attachments containing supporting data and background information. Dissemination of CSRs, and study results in general, is carefully controlled, even within Sarepta. Disclosure is limited to certain members of Sarepta's clinical development, regulatory, biostatistics, and data-management functions along with certain members of the executive committee. (*Id.* ¶ 19.) Clinical trials and the research that supports them are a costly undertaking, requiring the investment of hundreds of millions of dollars. The clinical trials themselves are conducted under strict confidentiality terms, including nondisclosure agreements executed with any third-party providers. (*Id.*) Confidentiality is of utmost importance to Sarepta not only to preserve its competitive advantage but also to protect itself from allegations of prior disclosure that could weaken Sarepta's intellectual property protections. (*Id.*)

B. FDA's New Drug Approval Process

The ultimate goal of any commercial drug development is FDA approval to market the resulting drug. The primary stage of the approval process is the submission by the company, and review by FDA, of the NDA. 21 U.S.C. § 355; 21 C.F.R. Part 314. NDAs are comprehensive reports of what the submitting company knows about its drug, including "full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use." 21 U.S.C. § 355(b)(1); *see also* 21 C.F.R. § 314.50. The documents to which Plaintiff requests access through this FOIA action were submitted to FDA as attachments to Sarepta's NDA for eteplirsen.

The FDA approval process can take years. But, the law allows for accelerated approval of drugs that treat a "serious or life threatening disease[]" and provide "meaningful therapeutic benefit to patients over existing treatments," if the manufacturer directly demonstrates the drug provides a "clinical benefit" or if the manufacturer indirectly does so by using a "surrogate endpoint." 21 U.S.C. § 356(c)(1)(A). Sarepta followed this established process to receive accelerated FDA approval for eteplirsen. After the success of Studies 201 and 202, Sarepta submitted an NDA on June 26, 2015; on September 19, 2016, FDA granted EXONDYS 51® accelerated approval to treat DMD patients.

C. Sarepta Faces Fierce Competition in the Market for DMD Treatments

Sarepta has achieved a hard-earned competitive advantage as the first company to achieve FDA approval of exon-skipping therapy for treatment of DMD. (*See* Decl. ¶¶ 44-60.) The principle of exon skipping is reproducible, and the public release of information regarding its application to DMD has led many other pharmaceutical companies to work to develop their own DMD treatments specifically utilizing exon skipping. (*Id.* ¶¶ 44-45.) All companies developing DMD treatments compete for the same small patient population, a population which

is made yet smaller in the case of each specific exon-skipping drug by the limited percentage of DMD patients that are potentially responsive to a drug that causes skipping of a particular exon (*i.e.* the exon where the DMD mutation is found in that patient). (*Id.* ¶ 50.) While Sarepta's eteplirsen studies were designed to induce exon 51 skipping, testing methods and study design are portable across exons. (*Id.*) At least three of Sarepta's direct competitors have already initiated clinical studies on the efficacy of exon skipping drugs on DMD in the United States:

- Daiichi Sankyo initiated a clinical trial of DS-5141b, an investigational exon 45 skipping therapy for DMD, in early 2016;
- Nippon Shinyaku initiated a clinical trial of NS-065/NCNP-01, an investigational exon 53 skipping therapy for DMD, in late 2016;
- Wave Life Sciences initiated clinical trials for WVE-210201, an investigational exon 51 skipping therapy for DMD, in late 2017, and has announced plans to initiate clinical trials for an exon 53 skipping candidate.[4]

(*Id.* ¶¶ 45, 47-49.) Furthermore, these three companies, along with PTC Therapeutics, Bamboo Therapeutics, and Solid Biosciences are specifically pursuing the development of drug therapies that cause DMD patients to produce dystrophin, the precise endpoint Sarepta pursued with eteplirsen. (*Id.* ¶ 46.) Sarepta's early advantage over these companies—its direct competitors—is due to its early innovation and significant investment of company resources. (*Id.*)

As one of the only companies to complete clinical trials of exon-skipping therapy for DMD, Sarepta has made critical advances in understanding DMD and its patient population, the usefulness of certain clinical endpoints in tracking improvements in the DMD patient population, and the mechanics of exon skipping. (*Id.* ¶ 52.) This invaluable knowledge is a direct result of Sarepta's early and extensive investments over the course of a decade into the study of DMD.

[4] *See* Don Seiffert, "Wave to begin trials next year on 'more efficient' drug for Duchenne, Boston Business Journal (May 9, 2016), *available at* https://www.bizjournals.com/boston/blog/bioflash/2016/05/wave-to-begin-trials-next-year-on-more-efficient.html.

(*Id.*) Sarepta's competitors are in more than one sense playing "catch up" to Sarepta. They are behind not only in developing their own treatments, but also in designing the testing and study regimens that will characterize and demonstrate the effectiveness of such treatments. While other companies' potential drugs may be directed at different exons than eteplirsen, Sarepta's study design, testing methods, and earned experience are directly applicable to any exon-skipping treatment. (*Id.* ¶¶ 50, 52.)

Sarepta's earned knowledge of DMD provides a continuing competitive advantage as Sarepta continues its DMD research. Sarepta utilizes its deep understanding of DMD to manage current studies and strategically plan and design future clinical trials, regulatory strategy, and competitive positioning for other treatments—including other exon-skipping drugs—in the company's pipeline. (*Id.* ¶ 53.) Sarepta is currently clinically developing potential treatments for DMD patients with genetic mutations amenable to exon 53 and exon 45 skipping; "Phase 3" trials for golodirsen (exon 53) and casimersen (exon 45) are underway. (*Id.* ¶ 54.) Sarepta also has preclinical drug candidates designed to skip exons 44, 52, 50, 43, 55, 8, and 35 in DMD patients. (*Id.*) Together, drugs causing exon skipping of all the exons Sarepta is developing could treat nearly 50% of DMD patients. (*Id.*)

Because DMD affects such a small patient population, in the future Sarepta will compete with other pharmaceutical companies for patients, both as eventual consumers of approved drugs and as participants in clinical trials. There is significant competition for participants in DMD clinical studies, and the dozens of planned trials for other exon-skipping DMD treatments will even further shrink the pool of possible participants. (*Id.* ¶ 51.) Moreover, clinical study competition does not end with patients. Pharmaceutical companies also compete to work with institutions that conduct clinical studies. (*Id.* ¶ 59.) Companies invest time and resources to

build relationships with institutions that conduct clinical trials. (*Id.*) With 27 DMD assets in clinical development with expected U.S. market approval between 2020 and 2027, this competition will only become more fierce and will favor those companies with established successes in developing DMD treatments. (*Id.*) Sarepta is currently unique in its demonstrated success with developing DMD treatments, but this advantage would erode if other companies gain access to Sarepta's proprietary information.

Sarepta is also ramping up to market DMD treatments globally. Because Sarepta is smaller than many of its competitors developing DMD treatments, Sarepta must build up its international infrastructure before it can fully benefit from its investments in the application of exon-skipping treatments to DMD. (*Id.* ¶ 55.) One of the reasons Sarepta carefully guards its proprietary information is to maintain its competitive advantage in the international marketplace. (*Id.*) Access to proprietary Sarepta analysis of DMD treatment results would aid a larger competitor with an established international infrastructure in efforts to leapfrog Sarepta and eliminate Sarepta's first mover advantage. (*Id.*)

Sarepta has taken concrete steps to enter the international marketplace. Eteplirsen is currently under review by the European Medicines Agency, and if it is approved would be able to be prescribed in the European Union. (*Id.* ¶ 56.) Sarepta also established a managed care access program ("MAP"), a mechanism through which physicians in 30 countries outside the U.S. can prescribe treatments not yet approved in the physician's home country for patients with unmet medical needs where there is no approved treatment available in the country or approved treatments are not suitable for the patient. (*Id.* ¶ 57.) If competitors with international infrastructure gained enhanced access to Sarepta's clinical study information, they could quickly

advance clinical development and approval programs internationally, thwarting MAP and effectively forcing Sarepta out of these markets. (*Id.*)

Despite its small size, Sarepta has made strategic investments and achieved early innovations in the utilization of exon skipping for DMD treatment. This has generated a significant competitive advantage for Sarepta with respect to both its existing drug and as Sarepta moves to expand its DMD treatment portfolio. Sarepta's competitive advantage would be severely jeopardized by publication of sensitive details of Sarepta's eteplirsen clinical trials, the very information Plaintiff seeks through this FOIA action.

III. ARGUMENT

A. Standard of Review

Summary judgment is appropriate when the pleadings and evidence demonstrate that "there is no genuine issue as to any material fact and that the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(c). "In order to prevail on a motion for summary judgment in a FOIA case, the defending agency has the burden of showing that its search was adequate and that any withheld documents fall within an exemption to the FOIA." *Carney v. U.S. Dep't of Justice*, 19 F.3d 807, 812 (2d Cir. 1994). *See Gertskis v. U.S. E.E.O.C.*, 2013 WL 1148924 at *14 (S.D.N.Y. March 20, 2013) (Furman, J.) (in a FOIA summary judgment motion, an agency need only submit affidavits or declarations that demonstrate (1) the agency's thorough search and (2) a reasonably detailed explanation of why the material is exempt from release) (cites omitted); *Wilner v. Nat'l Sec. Agency*, 592 F.3d 60, 73 (2d Cir. 2009) (affidavit is sufficient to show applicability of claimed exemption). Summary judgment is warranted when the submitted "affidavits describe the justifications for nondisclosure with reasonably specific detail, demonstrate that the information withheld logically falls within the claimed exemption, and are not controverted by either contrary evidence in the record nor by evidence of agency bad faith."

Id. (citing *Larson v. Dep't of State*, 565 F.3d 857, 861-62 (D.C. Cir. 2009)). "Ultimately, an agency's justification for invoking a FOIA exemption is sufficient if it appears logical or plausible." *Id.*

B. The Challenged Redactions are Confidential Commercial Information under FOIA Exemption 4 and are Exempt from Disclosure

The Redactions, including those challenged by Plaintiff, were carefully and narrowly drawn to encompass only material covered by Exemption 4. Exemption 4 provides that FOIA's mandatory disclosure provisions do not apply to agency records that are or contain "trade secrets and commercial or financial information obtained from a person and are privileged or confidential." 5 U.S.C. § 552(b)(4). Exemption 4 thus protects information which is (i) commercial or financial, (ii) obtained from a person, and (ii) confidential or privileged.[5] Where, as here, documents fall within Exemption 4, they ***must*** be withheld.[6]

"To determine whether information is confidential for the purposes of Exemption 4, this Circuit has adopted a two-part test formulated by the District of Columbia Circuit." *Inner City Press/Community on the Move v. Bd. of Governors of Fed. Reserve Sys.*, 463 F.3d 239, 244 n.10 (2d Cir. 2006) (citing *National Parks & Conservation Ass'n v. Morton*, 498 F.2d 765, 770 (D.C. Cir. 1974)). Under this test, information is confidential for the purposes of Exemption 4 if its disclosure would either: "(1) impair[] the government's ability to obtain information—necessary information—in the future, or (2) caus[e] substantial harm to the competitive position of the

[5] The parties agree that the redacted information is commercial in nature and was obtained from a person. Briefing will accordingly cover only the last prong of the test for withholding under FOIA Exemption 4. (*See* Dkt. 65.)

[6] Because the Trade Secrets Act (18 U.S.C. § 1905) is at least as broad in coverage as FOIA Exemption 4, a "finding that requested material falls within [Exemption 4] will be tantamount to a determination that [the agency] cannot reveal it." *CNA Fin. Corp. v. Donovan*, 830 F.2d 1132, 1144 (D.C. Cir. 1987). A determination that information falls within Exemption 4 thus divests an agency of its discretion under the FOIA to disclose such information. *See McDonnell Douglas Corp. v. Nat'l. Aeronautics & Space Admin.*, 180 F.3d 303, 305 (D.C. Cir. 1999); *Pacific Architects & Eng'rs, Inc. v. Dep't of State*, 906 F.2d 1345, 1347 (9th Cir. 1990).

person from whom the information was obtained." *Cont'l Stock Transfer & Trust Co. v. SE*C, 566 F.2d 373, 375 (2d Cir. 1977) (per curiam) (adopting the *National Parks* test).

Notably, unlike other FOIA exemptions, the application of Exemption 4 does not require an analysis of the general public's interest in disclosure of information. *Cf. Associated Press v. U.S. Dep't of Defense*, 554 F.3d 274, 284 (2d Cir. 2009) (applying the public interest balancing test for protecting law enforcement materials under FOIA Exemption 7(c)). Instead, this Court looks only to the impact that disclosure would have on the government's ability to collect the proprietary information and on the company's competitive position. The public's curiosity about a company's business practices is not a proper consideration under FOIA. Indeed, the "philosophy of the [FOIA] statute" is to permit people "to know what their ***government*** is up to." *U.S. Dep't of Justice v. Reporters Com. For Freedom of Press*, 489 U.S. 749, 772-73 (1989) (quoting Justice Douglas dissent in *EPA v. Mink*, 410 U.S. 73, 80 (1973)) (emphasis added). FOIA's purpose is not advanced by publicly releasing a company's proprietary information upon request. The FDA regulations recognize this interest, and require decisions about all mandatory releases under its regulations and governing statutes to be made in accordance with FOIA standards. In this case, as with other applications, FDA has released an enormous amount of data and information about eteplirsen from its file, including volumes of information from Sarepta's NDA.[7]

Furthermore, there is no obligation to release piecemeal redactions where the unredacted portions of the document would be "of little informational value" to the requester. *Mead Data Center v. U.S. Dep't of the Air Force*, 566 F.2d 242, 261 n.55 (D.C. Cir. 1977); *accord Inner City*

[7] The detailed information FDA makes public after approving a drug can be accessed online. For example, all of the extensive publicly disclosed information regarding eteplirsen is available here: Drug Approval Package: Exondys 51 Injection (eteplirsen), *available at* https://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/206488_TOC.cfm.

Press, 463 F.3d at 249 n.10 ("information that is inextricably intertwined with exempt information cannot be disclosed" (internal quotation and citation omitted)). Here, Sarepta undertook the difficult task of reviewing the voluminous information requested and redacting only the information that has not previously been publicly disclosed and that Sarepta believes would cause competitive harm if released. The redactions asserted do not encompass information that was reasonably segregable from unprotected material; where block redactions are asserted, no finer parsing is required under law. (*Id.*)

1. Release of the Redacted Information Would Impair the Government's Ability to Obtain Such Material in the Future

Withholding of the redacted information is appropriate because its release would "impair the Government's ability to obtain necessary information in the future." *National Parks*, 498 F.2d at 770. Congress and FDA have devised a disclosure system that both protects the public and protects companies investing in complex experimental research. The drug approval process is fruitful for FDA and profitable for companies precisely because the government is given access to more information than is the public. The FDA gains detailed access to a company's study information in order to review drug safety, and companies do not risk exposing proprietary details by fully engaging with the government regulators. If the rule were that FDA published every document companies provided as part of drug approval applications, then such applications would be far less detailed and would adhere only to the bare minimum requirements. In other words, these applications are fulsome and exceed requirements precisely because they are protected. As explained by the D.C. Circuit in a FOIA case involving the releasability of drug application information in response to a FOIA request, "[a]pplicants spend a great deal of resources to obtain data for an IND or NDA, and FDA could not expect full and frank disclosure if it later released such proprietary information into the public domain."

Judicial Watch, Inc. v. Food & Drug Admin., 449 F.3d 141, 148-49 (D.C. Cir. 2006). Because of FDA's interest in complete and fulsome documentation supporting companies' NDAs, this Court should not mandate disclosure of the redacted elements of Sarepta's CSRs.

2. Disclosure of the Redacted Information Would Likely Cause Substantial Competitive Harm to Sarepta

The redactions also satisfy the second prong of the *National Parks* test, because disclosure "is likely . . . to cause substantial harm to the competitive position of" Sarepta. *National Parks*, 498 F.2d at 770. Federal courts have long recognized that confidential documents companies submit as part of NDAs may be properly withheld from disclosure under FOIA Exemption 4 because of competitive harm that could result from their release. *See, e.g.*, *Webb v. HHS*, 696 F.2d 101, 103 (D.C. Cir. 1982) (finding competitive harm would result from release of detailed data in submitting company's NDA). *See also Citizens Commission on Human Rights v. Food and Drug Admin.*, 1993 WL 1610471 (C.D. Cal. May 10, 1993), *affirmed in relevant part* 45 F.3d 1325 (9th Cir. 1995) ("The Court finds that an NDA by definition contains trade secret information because it contains significant information about how a pioneer drug product is formulated, chemically composed, manufactured, and quality controlled."); *Pub. Citizen Health Research Group v. NIH*, 209 F. Supp. 2d 37, 47 (D.D.C. 2002) (recognizing that the "pharmaceutical industry is a highly competitive market where companies routinely attempt to discover a possible advantage over their competitors"). As explained by the D.C. Circuit:

> The FDA requires applying companies to submit volumes of information related to a drug's development, composition, safety, and manufacture. 21 U.S.C. § 355(b)(1). A company must submit this information in an Investigational New Drug application ("IND") even prior to conducting clinical trials of a drug. 21 C.F.R. pt. 312. All the information from the IND also goes into the company's New Drug Application ("NDA"), the formal application for sale and marketing approval from the FDA. 21 C.F.R. pt. 314. Each stage of the FDA's administrative processes therefore depends directly on submissions from outside the agency.

> The submission-dependent nature of the approval process means Exemption 4 extends to at least some information contained in INDs and NDAs…. Exemption 4 does not categorically exempt all information in INDs and NDAs, however, and the FOIA requester must have adequate descriptions in order to distinguish between protected and unprotected information.

Judicial Watch, Inc., 449 F.3d at 148-49. Such competitive harm is straightforward, falling into two broad categories.

First, other companies researching similar drugs could use specific technical information about Sarepta's testing activities described within the materials to bypass steps in or simplify their own clinical studies of similar drugs. For example, in *Public Citizen Health Research Group v. Food and Drug Administration*, the D.C. Circuit found the test for competitive harm was met when the submitting company explained that release of certain information from a drug application "could direct a competitor … to pursue the same avenues of research and development" as did the submitting company. 185 F.3d 898, 905 (D.C. Cir. 1999). The D.C. Circuit also found that when "[t]he development and marketing of new antifungal products is ... being actively engaged in by a number of other drug companies," competitive harm would result from the release of proprietary details from the company's drug application because those other companies "could make use of the information in the INDs in order to eliminate much of the time and effort that would otherwise be required to bring to market a product competitive with the [submitting company's product]." *Id.* at 906. Indeed, other companies could use the information to create their own NDAs with much less effort than required of the original submitting company. *See Webb*, 696 F.2d at 103 ("If a manufacturer's competitor could obtain all the data in the manufacturer's NDA, it could utilize them in its own NDA without incurring the time, labor, risk, and expense involved in developing them independently."); *Citizens Commission on Human Rights*, 1993 WL 1610471 ("[I]f all research data and results were

released to the public, a competitor would not only be privy to confidential trade secrets and business information of Lilly, but could also use the information to submit its own NDA to FDA for the same or similar drug product"); *Campaign for Responsible Transplantation v. FDA*, No. 00-2849, slip op. at 10 (D.D.C. Sept. 24,2004) (protecting information contained in IND because "sponsors would have much less incentive to make the enormous investments required . . . if other companies could [get a] free ride on their research developments and investments").

Second, release of information regarding the company's general practices, beyond drug-specific information, can cause competitive harm. For example, pharmaceutical companies can be competitively harmed by the release of information regarding the third-party laboratories and contractors/consultants used in drug development. *See Appleton*, 451 F. Supp. 2d at 141 n.7; *see also Pub. Citizen Health Research Group v. Food and Drug Admin.*, 2000 WL 34262802 (D.D.C. Jan. 19, 2000) (protecting researcher names). Furthermore, courts have recognized that companies have a protectable interest in material that could reveal information about work on successor drugs the company has not yet publicly released. *Pub. Citizen Health Research Group*, 185 F.3d at 905 (finding competitive harm when the submitting company "has just commenced clinical testing on a successor [drug] which was designed based on information learned during development of [the drugs described in those IND's]").

Sarepta's declarations and accompanying exhibits demonstrate both of these categories of competitive harm. Plaintiff challenges the redaction of four distinct types of information, the competitive harm associated with the release of which is described in detail below. Due to the volume of materials (over 35,000 pages) at issue on this motion, Sarepta will not discuss here every redaction challenged by the Plaintiff. Rather, Sarepta directs the Court to certain representative examples within each of the four categories of Challenged Redactions.

a. Clinical Study Procedures

First, Plaintiff challenges the redaction of certain procedures that Sarepta followed in conducting its clinical studies. Plaintiff apparently recognizes that clinical study procedures are protectable under FOIA Exemption 4, as Plaintiff does not challenge the redaction of all procedure descriptions in the CSRs. (*See, e.g.*, Ex. B at Bates 2975-2985 (not challenged redactions of the schedule of study procedures, described at *Vaughn* index, Ex. A at 14).) Instead, Plaintiff challenges the withholding of study procedures only when they relate to what Plaintiff evidently finds to be particularly interesting aspects of Sarepta's studies. The limited nature of this challenge, however, does not impact the validity of the redactions, and the Plaintiff's curiosity does not render Sarepta's competitive interest in protecting the information less acute. As described, the procedures Sarepta employed to test eteplirsen are translatable to other programs, both inside and outside of Sarepta. (Decl. ¶ 22-28.) This means that Sarepta's competitors could use these procedures themselves, without having to invest the significant resources that Sarepta did to develop them, or could use knowledge of these procedures to anticipate Sarepta's future work. (*Id.*) Because of the small DMD patient population, information about the disease and its patients are scarce, and even the most elementary aspects of Sarepta's clinical trials required a significant investment of resources to develop. (*Id.* ¶ 24.) Given the limited amount of information generally available from studies, the disclosure of even small amounts of confidential information could be meaningful to competitors. Sarepta developed these procedures through years of research on how to dose, how much to dose, how often to dose, and whether dosages should remain fixed or change over the course of treatment. (*Id.* ¶ 25.) Sarepta's competitors have yet to determine a final dosing procedure for their DMD drug candidates, and access to Sarepta's successful procedures would allow them to bypass years of expensive trial and error Sarepta undertook to develop its procedures. (*Id.*)

For example, the redacted paragraph on Bates page 58, in CSR 201, provides the precise procedure Sarepta followed to determine the amount of dystrophin in individual patients. (*See* Ex. B.) As described, dystrophin was the clinical endpoint Sarepta used to demonstrate eteplirsen's efficacy, and Sarepta invested significant resources into researching accurate methods of measuring dystrophin. (Decl. ¶ 26.) This paragraph contains minute description of how Sarepta obtained this measurement, down to details of the slides on which the tissue biopsies were kept, what Sarepta did to those slides, and how Sarepta measured the contents of the slides. These methods are not publicly available, and so long as they remain confidential, Sarepta's competitors must develop their own validated procedures in order utilize dystrophin as a clinical endpoint. (*Id.*) Sarepta's research into dystrophin quantification has become even more valuable with recent FDA guidance confirming that dystrophin levels may be utilized as a surrogate endpoint to obtain accelerated FDA approval. (*Id.* ¶ 27.) Providing Sarepta's competitors access to the redacted information could, under this guidance, directly result in the approval of competing drugs under accelerated timelines. (*Id.*) This same competitive harm analysis applies to the next three paragraphs in CSR 201, which provide similar details regarding the procedures Sarepta used to measure overall dystrophin intensity levels, dystrophin protein levels, and lymphocyte infiltration. (Ex. B at Bates 58-59.)

Another example of the competitively sensitive information Plaintiff seeks is the paragraph titled "Dose Modification, Reduction, or Delay" on Bates 21640. (*Id.*) This paragraph details the steps Sarepta took during its clinical study should a particular situation arise. Again, details such as this could be copied or selectively adapted by Sarepta's competitors, all without the initial investment undertaken by Sarepta to develop its study procedures. While some

information regarding Sarepta's clinical study procedures have been publicly released, this paragraph's details have not. (*See* Decl. ¶¶ 22-24.)

Yet another example is the redaction on Bates page 22992, part of Sarepta's Statistical Interim Analysis Plan used to analyze the results of Study 202. (*See* Ex. B.) In a list of measurements that Sarepta considered, the precise time at which Sarepta measured the changes from baseline in CD3, CD4, and CD8 lymphocyte counts in muscle biopsy tissue is redacted. Armed with this knowledge, Sarepta's competitors could conduct their own studies in which these lymphocyte counts are measured consistent with Sarepta's study without performing the research and analysis that Sarepta undertook to define this schedule. (*See* Decl. ¶ 23.) The ability to "retrospectively" design clinical studies in this way, so as to maximize likelihood of success, would provide an enormous benefit to Sarepta's competitors that was never available to Sarepta, as the first to invest in the development of these procedures. These, and the other redactions detailed in the *Vaughn* index, present the very type of competitive harm that federal courts have found sufficient for the application of FOIA Exemption 4 to information contained within NDAs. *Pub. Citizen Health Research Group*, 185 F.3d at 905; *Webb*, 696 F.2d at 103.

b. Clinical Study Results

The results of Sarepta's clinical studies are the key proprietary information that permitted Sarepta to submit the first NDA for a drug approved to treat DMD. While release of Sarepta's clinical study procedure would allow Sarepta's competitors to copy its studies, release of Sarepta's clinical study results would radically shortcut the procedures needed for Sarepta's competitors to study and market their own drug. (Decl. ¶¶ 29-31, 33.) The purpose of conducting clinical studies is to obtain these results; release of the results would provide Sarepta's competitors the benefit of Sarepta's study without having incurred the years of expense Sarepta incurred to obtain this data. (*Id*. ¶ 29.) The fact that DMD is an "orphan disease," and

is difficult to study due to small patient populations and heterogeneous progression, increases the value of Sarepta's study data. (*Id.* ¶ 30.)

This category of redactions is mainly comprised of tables of study results, both excerpted within the CSRs and attached in full to the CSRs. For example, a table is redacted on Bates 85 that contains the mean, median, standard deviation, minimum, and maximum data points recorded for four different patient groupings across three different variables. (*See* Ex. B.) Similarly, a redacted table on Bates 88 gives the statistical measurements of a particular test that Sarepta conducted across three patient groupings, described as a change from a baseline measurement. (*Id.*) These study results are not only presented in tabular format; for example, paragraphs redacted on Bates 91 and 92 provide narrative descriptions of the changes Sarepta observed in patients over the course of its study as compared to two baseline measurements. (*Id.*) Armed with this information, pre-sorted with indicators of their statistical significance, Sarepta's competitors could simply use the results of Sarepta's clinical studies in their own research without needed to collect study results of their own. (Decl. ¶ 29.)

The bulk of the redactions in the requested documents consist of individual study results by individual patient. (Ex. B at Bates 4210-6438, Bates 23044-35444.) These tables form the core work product of a clinical study. Plaintiff recognizes the personal privacy implications of releasing patient-level data and therefore limits his challenge to the specific study results by individual patient, excluding demographic and other information that may reveal a patient's identity. (*See* Dkt. 65.) However, the release of de-identified patient-level data, while ameliorating privacy concerns, can still result in competitive harm to Sarepta. A scientist employed by one of Sarepta's competitors could make productive use of this data to study, for example, changes over time in clinical outcomes, for purposes of designing a similar clinical

trial. (Decl. ¶ 30.) Armed with how Sarepta's data changed over the course of Sarepta's studies, a competitor could design a new clinical trial to mimic or selectively alter Sarepta's approach. (*Id.*) De-identified patient level data could also be exploited by competitors in to claim in a marketing campaign that their DMD treatments are superior, to undermine Sarepta's patent positions, or to interfere with patient recruitment in subsequent studies. (*Id.* ¶ 32.)

Even when de-identified, the thousands of pages of DMD patient data could contribute to the development of a historical external control set. (*Id.* ¶ 31.) The FDA announced in February 2018 that while it prefers placebo-controlled trials, due to the small patient population, it will consider DMD trials using external controls – meaning trials that compare patient outcomes to a historical dataset. (*Id.* ¶ 33.) Sarepta incurred significant expense to define a historical control set for Studies 201 and 202 – including paying for historical data and conducting extensive quality control of such data. (*Id.*) Because the general parameters of Sarepta's studies are public, the dataset attached to CSRs 201 and 202, even if de-identified, could contribute to a historical control set for Sarepta's competitors' studies, without any need for those competitors to even pay Sarepta for the data. (*Id.*) The control dataset purchased, reviewed, and utilized by Sarepta in its own studies was anonymized data, reinforcing the value of such data. (*Id.* ¶ 31.)

The results of Sarepta's clinical studies are the direct work product yielded by Sarepta's investment of millions of dollars and over a decade of research. Giving away the fruits of Sarepta's labor to Sarepta's competitors, when FDA has determined this information need not be released through its mandatory drug safety disclosure process, would be devastating to the company and antithetical to the purpose of FOIA.

c. Exploratory Endpoints

The third category of redactions Plaintiff challenges are descriptions of the various endpoints that Sarepta pursued, considered, and measured when conducting its clinical studies.

DMD's characteristics are not well understood, even within the scientific community. A significant part of the millions of dollars Sarepta invested to develop eteplirsen went to researching the disease itself: what it means to be a DMD patient, how DMD patients' lives can improve, and the impact of various compounds on DMD patients. (Decl. ¶ 34.) Part of this process required the defining of "endpoints" for the clinical studies, *i.e.* standards by which the effect of the drug are measured. These can be "clinical," relating to appearance or disappearance of symptoms or performance on physical tests; or "surrogate," tracking increase or decline of particular markers in the blood or tissue affiliated with the studied condition. (*Id.* ¶ 35.)

As described above, to receive FDA approval, the submitting company must directly demonstrate the drug has a clinical benefit or indirectly demonstrate its clinical benefit through selection of endpoints. FDA must approve the endpoint selection, and discerning what endpoints will be acceptable to FDA entails a high level of uncertainty. FDA has an announced policy of encouraging companies to be creative in endpoint selection. (*Id.* ¶ 38.) Sarepta pursued multiple different endpoints in its study of eteplirsen and not all endpoints it explored were publicly released in connection with the drug. Deciding which endpoints to release requires the company to balance the need to demonstrate efficacy with a legitimate interest in protecting endpoints that might reveal future research directions or marketing prospects. (*Id.* ¶ 37.) For example, Sarepta's decision not to publicly release a particular endpoint in connection with its eteplirsen studies—a decision that would be revealed by the disclosure of the previously unreleased endpoints—could imply Sarepta is pursuing that endpoint in another study. (*Id.*) Given the FDA's readiness to consider multiple outcome measures if a record of improvement and accurate measurement is demonstrated, Sarepta's completed research into as-of-yet nonpublic endpoints gives Sarepta a distinct advantage over its competitors. (*Id.* ¶ 38.) While Sarepta individually

considered, tested, and analyzed multiple potential endpoints, if given the opportunity, Sarepta's competitors could simply pick up where Sarepta's research into nonpublic endpoints left off, potentially allowing their drugs to get to market faster. (*Id.* ¶¶ 36, 39.)

References to these non-public exploratory endpoints therefore have been redacted from the documents produced to Plaintiff. The redactions include narrative descriptions of these nonpublic endpoints (*see, e.g.*, Ex. B. at Bates 60-61), references to nonpublic exploratory endpoints in lists of measurements Sarepta took during its studies (*see, e.g., id.* at Bates 4170), descriptions of the endpoint measurements (*see, e.g., id.* Bates 6559-61), and instructions of how they were measured (*see, e.g., id.* at Bates 21643-45). Every reference to an unpublished exploratory endpoint must be redacted in order to maintain their confidentiality. Because endpoints are measured and considered throughout a clinical study, the endpoints Sarepta pursued in its eteplirsen research are referred to throughout the Study 201 and 202 CSRs, as noted on the *Vaughn* index entry for each such redaction. Due to the information these nonpublic endpoints reveal about the direction of Sarepta's present and future research, they are properly withheld under Exemption 4.

d. Adverse Events

Finally, Plaintiff seeks unredacted release of all information about adverse events that occurred to study participants during the course of the two studies, including the events themselves and the analysis Sarepta researchers performed regarding these events. Sarepta assiduously recorded the adverse events experienced during Studies 201 and 202 and pursued large amounts of additional data in the complex task of determining which of these adverse events, if any, were caused by the drug. (Decl. ¶ 40.) If this information were released, Sarepta's competitors could apply this analysis to their own studies without making similar investments. (*Id.*)

Releasing the redacted information describing adverse events would provide Sarepta's competitors a direct guide to interpreting the results of their own studies. Exon-skipping drugs share sufficiently similar chemistry and effect to produce many of the same chemical reactions in patients. (*Id.* ¶ 41.) As such, if the requested information about adverse events is released, competitors testing such similar drugs could leverage the eteplirsen adverse event data as being representative of the class of chemical compounds, without the corresponding investment of resources Sarepta made to determine which events arise from a chemical reaction. (*Id.*)

For example, in Study Report 201, the Agency proposes to redact a table in its entirety. This redaction covers a table setting forth an analysis funded by Sarepta of eighteen publicly available studies of chemically similar compounds to analyze the frequency at which particular negative effects have happened. (Ex. B at Bates 2964; Decl. ¶ 42.) The analysis served as a basis for Sarepta's effort to identify what effects arose strictly from the drug. (Decl. ¶¶ 42-43.) Some additional examples of detailed charts listing and analyzing adverse events, including patient-by-patient descriptions, are found at Bates 6570-72, 6574, and 6576. (*See id.*; Ex. B.)

Elsewhere, in the report for Study 202, Sarepta recorded several adverse effects experienced by study participants, and discusses what percentage of certain effects were determined to be "treatment related." (Ex. B at Bates 6477.) The same report contains patient-by-patient descriptions of adverse events, including 16 separate analyses of particular effects, including in each case a description of the analysis and additional testing done by Sarepta to confirm whether or not the effect was related to the drug. (*Id.* at Bates 6578-6582; *see also id.* at Bates 21650, 21652 (redacting description of procedure employed to report and identify adverse events for review).) Release of this sort of information spares any competitor the effort and

attention of zeroing in on the actual impacts of the drug, once the unrelated mishaps and health issues that occur in an ailing population are filtered out. (Decl. ¶ 40.)

Sarepta invested heavily in its research into and conclusions regarding adverse events. (*Id.* ¶ 43.) If this information were released, Sarepta's competitors would have a record of Sarepta's conclusions regarding adverse events and reactions to drugs like eteplirsen. They also would have access to Sarepta's methods for analyzing and distinguishing these effects— methods that are also the product of proprietary research and development. Granting its competitors access to such information will cause competitive harm to Sarepta. (*Id.*)[8] *See Pub. Citizen Health Research Group*, 185 F.3d at 906 (finding that release of proprietary details from an FDA drug application could allow a submitter's competitors to "make use of the information . . . in order to eliminate much of the time and effort that would otherwise be required to bring [a competitive drug] to market").

IV. CONCLUSION

Sarepta has made a considerable investment in the development of the proprietary scientific techniques and resulting data that were necessary to bring to market a revolutionary drug. Sarepta's submission of that proprietary data to FDA does not change its nature – it is confidential commercial information the release of which would harm both FDA's ability to gather similar information in the future and Sarepta's position in the competitive marketplace for this drug and similar therapies. As such, the Challenged Redactions are not releasable under FOIA. Sarepta therefore respectfully requests that the Court grant this Motion for Summary Judgment and affirm the Exemption 4 redactions asserted by FDA.

[8] Sarepta's competitors could also tailor marketing information to imply that since certain non-reaction effects did not occur in their own trials, their drug is somehow safer than eteplirsen. (Decl. ¶ 29.)

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Respectfully Submitted,

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