UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

DEPOMED, INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	Civil Action No. 12-cv-1592 (KBJ)
	)	
UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES, *et al.*,	)	
	)	
Defendants.	)	

MEMORANDUM OPINION

Plaintiff Depomed, Inc. ("Depomed") is a pharmaceutical company that, as relevant here, has developed a drug to treat a rare condition known as post-herpetic neuralgia ("PHN").[1] Depomed contends that its drug, which is called Gralise, was automatically entitled to a seven-year period of marketing exclusivity under the Orphan Drug Act (the "Act"), 21 U.S.C. §§ 360aa–360ee, once the drug satisfied two statutory requirements: (1) designation by the Food and Drug Administration ("FDA") as a so-called "orphan drug" for use in treating a rare disease or condition, and (2) receipt of FDA approval to be marketed to the public. Depomed brought the instant action against the FDA, the United States Department of Health and Human Services, and both agencies' respective directors (collectively "Defendants") after the FDA refused to recognize the exclusivity period for Gralise despite its having met the statutory criteria; the one-count complaint alleges that such refusal violated the Administrative Procedure Act ("APA"), 5 U.S.C. §§ 701–706. Defendants do not dispute that the FDA has

[1] PHN is nerve pain that sometimes arises as a complication of the shingles virus.

designated Gralise an orphan drug and has approved it to be marketed for treatment of PHN. Nevertheless, Defendants maintain that the FDA was not required to grant Gralise orphan drug exclusivity in the instant case because the FDA has already granted marketing approval to a drug called Neurontin for treatment of PHN, and according to the FDA, Depomed has not proven that Gralise is "clinically superior" to Neurontin—a requirement that the FDA has imposed because Gralise and Neurontin have the same active ingredient (gabapentin).[2] Through the instant action, Depomed requests declaratory and injunctive relief that, in essence, would force the FDA to recognize that Gralise is entitled to the statutory exclusivity period.

Before this Court at present are two dispositive motions: Plaintiff's motion for summary judgment, and Defendants' motion to dismiss or, in the alternative, for summary judgment regarding the complaint's allegation of a violation of the APA. Because this Court finds that the plain language of the Orphan Drug Act unambiguously requires the FDA to recognize that any drug that has been both designated as an orphan drug for treatment of a qualifying disease or condition and also approved for marketing is entitled to an exclusivity period, the Court will **GRANT** Plaintiff Depomed's motion for summary judgment and will **DENY** Defendants' motion to dismiss or, in the alternative, for summary judgment. Accordingly, judgment will be entered in Depomed's favor in this action, and the Court will order the FDA to recognize orphan-drug marketing exclusivity for Gralise for a period of seven years from the date the FDA approved Gralise for marketing. A separate order consistent with this opinion will follow.

[2] As explained in more detail below, Neurontin was never designated as an orphan drug, nor has the FDA recognized orphan-drug exclusivity for Neurontin.

I. BACKGROUND

A. Statutory And Regulatory Framework

1. The Orphan Drug Act

This case turns on the parties' competing interpretations of the statutory text and implementing regulations of the Orphan Drug Act. Congress enacted the Orphan Drug Act in 1983 as an amendment to the Food, Drug, and Cosmetic Act ("FDCA"). *See* Orphan Drug Act, Pub. L. No. 97-414, 96 Stat. 2049 (1983) (codified at 21 U.S.C. §§ 360aa–360ee (2012)). The Act's fundamental purpose is to provide drug manufacturers with incentives to research and develop so-called "orphan drugs[,]" *see id.* §§ 1(b)(1)–(3), which are drugs that treat certain "rare disease[s] or condition[s][,]" 21 U.S.C. § 360bb(a)(1).[3] As explained in the relevant congressional findings, prior to the Act's passage, it was considered generally financially impractical for pharmaceutical companies to develop such drugs. *See* § 1(b)(4), 96 Stat. at 2049 (noting that "so few individuals are affected by any one rare disease or condition" that "a pharmaceutical company which develops an orphan drug may reasonably expect the drug to generate relatively small sales in comparison to the cost of developing the drug and consequently to incur a financial loss"). Because Congress believed that it was "in the public interest" that orphan drugs be developed, it enacted the Act "to reduce the costs of developing such drugs and to provide financial incentives to develop such drugs[.]" *Id.* at §§ 1(b)(5)–(6).

By all accounts, the Act's chief "financial incentive[ ][,]" *id.*, is a seven-year period of marketing exclusivity granted to certain drugs pursuant to section 360cc of

[3] Under the Act, a "rare disease or condition" is one that either "affects less than 200,000 persons in the United States" or "for which there is no reasonable expectation" that drug developers will recoup the considerable costs associated with developing a new drug based on sales of that drug in the United States. 21 U.S.C. § 360bb(a)(2).

the Act. *See* 21 U.S.C. § 360cc(a).[4] The central issue in this case is the parties' disagreement over what conditions a drug must satisfy to qualify for this exclusivity. The statute's exclusivity provision provides in relevant part that

> if the [FDA] approves an application filed pursuant to section 355 of this title . . . for a drug designated under section 360bb of this title for a rare disease or condition, the [FDA] may not approve another application under section 355 . . . for such drug for such disease or condition for a person who is not the holder of such approved application . . . until the expiration of seven years from the date of the approval of the approved application[.]

Id. In other words, the plain language of the statute sets forth two procedural prerequisites for marketing exclusivity: first, the FDA must have "designated" the drug as an orphan drug, upon request from the drug's sponsor, pursuant to 21 U.S.C. § 360bb and its accompanying regulations[5]; and second, the FDA must have "approved" the designated orphan drug for marketing to the public pursuant to 21 U.S.C. § 355, which is the section of the FDCA that provides the general procedure for marketing approval of all the pharmaceutical products that the FDA regulates. If both conditions are met, then the Act provides that the FDA "may not approve another" such drug for marketing to the public for "seven years from the date" of the designated drug's approval. 21 U.S.C. § 360cc(a).

Congress also provided two exceptions to the statutorily-mandated exclusivity period. Under the statute, the FDA may approve the marketing of subsequent drugs without regard to an existing exclusivity period if:

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[4] Section 360cc also applies to "biological products" that are licensed pursuant to 42 U.S.C. § 262. No such products are at issue in this case.

[5] The implementing regulations for 21 U.S.C. § 360bb are codified in Subpart C of Part 316 of Title 21 of the Code of Federal Regulations. *See* 21 C.F.R. §§ 316.20–316.30 (entitled "Designation of an Orphan Drug"). It is undisputed in the instant case that the FDA has designated Gralise as an orphan drug within the meaning of Section 360bb and the applicable regulatory framework.

> (1) the [FDA] finds, after providing the [exclusivity] holder notice and opportunity for the submission of views, that in such period the holder of the approved application . . . cannot assure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated; or
>
> (2) such holder provides the [FDA] in writing the consent of such holder for the approval of other applications . . . before the expiration of such seven-year period.

See id. § 360cc(b).

2. Exclusivity Under The FDA's Implementing Regulations

While Congress did not direct the FDA to promulgate implementing regulations for the Act's exclusivity provision, *see* 21 U.S.C. § 360cc, the FDA did so nonetheless. The resulting regulations, which are entitled "Orphan-drug Exclusive Approval" and codified in Subpart D of Part 316 of Title 21 of the Code of Federal Regulations ("C.F.R."), largely parallel the statutory design of section 360cc, with at least one notable exception. The regulation entitled "Scope of orphan-drug exclusive approval" provides that

> [a]fter approval of a sponsor's marketing application for a designated orphan-drug product for treatment of the rare disease or condition concerning which orphan-drug designation was granted, FDA will not approve another sponsor's marketing application for the *same drug* before the expiration of 7 years from the date of such approval as stated in the approval letter from FDA[.]

21 C.F.R. § 316.31(a) (2012) (emphasis added). Elsewhere, the regulations define the term "same drug"—a term that the regulations use in place of the statutory term "such drug" that appears in 21 U.S.C. § 360cc—to mean, in relevant part, "a drug that contains the same active moiety as a previously approved drug and is intended for the same use as the previously approved drug," with the exception "that if the subsequent

drug can be shown to be clinically superior to the first drug, it will not be considered to be the same drug." 21 C.F.R. § 316.3(b)(13)(i).

The insertion of the "same drug" concept into the exclusivity regulations effectively limits the scope of exclusivity protection because under the regulations, only if a new drug uses the same active ingredient ("active moiety") to treat the same disease or condition as a drug that already has orphan-drug exclusivity *and* the new drug is also not found to be "clinically superior" to the existing orphan drug will the FDA consider the new drug to be the "same" as the drug with exclusivity and thereby forbid its marketing within the exclusivity period. *Id.*; *id.* § 316.31(a). Put another way, if the new drug *is* "clinically superior" to the drug with orphan-drug exclusivity—*i.e.*, the new drug has a "significant therapeutic advantage over and above" an "approved orphan drug[,]" 21 C.F.R. § 316.3(b)(3)—then the drugs are not considered to be the "same," and the FDA may approve the new drug notwithstanding the exclusivity period.

In short, the FDA's regulations permit the FDA to ignore a previously-approved drug's orphan-drug exclusivity in order to approve a new, clinically superior drug with the same active ingredient that will be marketed for treatment of the same disease or condition.[6]

3. Clinical Superiority Under The FDA's Implementing Regulations

Under the Act's implementing regulations, a finding of clinical superiority is also relevant at the designation stage of the orphan-drug exclusivity process. As explained above, in order to receive the seven-year period of orphan-drug exclusivity

[6] The FDA has amended several of the relevant implementing regulations recently, presumably in response to the filing of the complaint in the instant case. The new regulations went into effect on August 12, 2013, and while the amended language does shed light on the parties' arguments in this case, the FDA concedes that the new regulations do not apply to Depomed's claims. (*See* Notice of Promulgation of Final Rule, ECF No. 30; *see also infra* n.12.)

under the Act, the drug must first be "designated under section 360bb of this title for a rare disease or condition." 21 U.S.C. § 360cc(a). Congress authorized the FDA to promulgate regulations governing the section 360bb designation process, which the agency has done, *see* 21 C.F.R. §§ 316.20-316.30, and those regulations require, among other things, an analysis of the potential clinical superiority of a drug that is being considered for orphan-drug designation under certain specified circumstances.

For example, at all times relevant to the resolution of this case, section 316.20 of Title 21 of the C.F.R., which governs the "[c]ontent and format of a request for orphan-drug designation[,]" provided in relevant part that a sponsor may seek designation "of a drug that is otherwise the same drug as an already approved orphan drug . . . for the same rare disease or condition if [the sponsor] can present a plausible hypothesis that its drug may be clinically superior to the first drug." *Id.* § 316.20(a). Under that iteration of this regulatory requirement, when a sponsor seeks orphan-drug designation for the "same drug as an already-approved orphan drug . . . for the same rare disease or condition," the sponsor must include in its designation request "an explanation of why the proposed variation may be clinically superior to the first drug." *Id.* § 316.20(b)(5). Indeed, the regulation specifically states that the "FDA will refuse to grant a request for orphan-drug designation if" a sponsor seeking designation of a "same drug as one that already has orphan-drug exclusive approval for the same rare disease or condition . . . has not submitted a medically plausible hypothesis for the possible clinical superiority of the subsequent drug." *Id.* § 316.25(a)(3).

B. Factual And Procedural History

There are no material disputes regarding the facts of the instant case, which begin with the FDA's approval of Neurontin for treatment of seizures in 1993 and for

treatment of PHN in 2002, and continue through the procedural history of the instant case to the motions at issue in this Opinion.

1. The FDA's Approval Of Neurontin

The FDA first approved a drug with the active ingredient gabapentin in 1993, under the brand name Neurontin, for use in treating seizures. (Sealed Admin. R. ("SAR"), ECF No. 18-1, at 19.)[7] Neurontin was subsequently approved for the treatment of PHN on May 24, 2002. (Admin. R. ("AR"), ECF No. 17-6, at 27.) Although PHN qualifies as a "rare disease or condition" under the Act, 21 U.S.C. § 360bb(a)(2), Pfizer, the manufacturer of Neurontin, never sought or obtained orphan-drug designation for Neurontin for use in treating PHN and never received the benefit of the Act's exclusivity provision. (Defs.' Mem. in Supp. of Mot. to Dismiss or Mot. for Summ. J. & in Opp'n to Pl.'s Mot. for Summ. J. ("Defs.' Br."), ECF No. 21, at 19.) Since 2002, nearly 30 gabapentin products—that is, generic versions of Neurontin—have been approved and marketed for the treatment of PHN. (*Id.* (citation omitted).)

2. The FDA's Designation Of Gralise

a. Depomed's Initial Gralise Designation Request In 2006

On December 21, 2006, Depomed submitted a request to the FDA that the FDA designate Depomed's own gabapentin product, Gralise, as an orphan drug for the treatment of PHN pursuant to 21 U.S.C. § 360bb and 21 C.F.R. § 316.20. (SAR, ECF No. 18, at 4.) In its request, Depomed acknowledged that Neurontin (and other generic gabapentin products) had previously been approved for the treatment of PHN, but argued that no other gabapentin product had ever been designated as an orphan drug for

[7] Citations to the administrative record and to other documents the parties have filed refer to the page numbers assigned by the Court's electronic filing system.

treatment of PHN, and therefore Depomed did not need to provide a plausible hypothesis of clinical superiority in order to satisfy the submission criteria for orphan-drug designation applications under 21 C.F.R. § 316.20. (*Id.* at 19-21.) Depomed additionally argued that, if the FDA nevertheless required a demonstration of clinical superiority, Gralise satisfied that requirement based on studies showing that the extended-release formulation of Gralise—which required patients to take the drug only once per day, as opposed to Neurontin's three times per day—would result in increased patient compliance, and also that the extended-release formulation would lessen the side effects patients taking Neurontin and its generics typically experienced. (*Id.* at 20-21.)

On May 8, 2007, the FDA denied Depomed's designation request, on the grounds that Neurontin had already received marketing approval and thus

> there is no rationale for supporting, with taxpayer monies, the clinical development of an identical product for an identical indication as one which has been approved after the most thorough evaluation possible. This point remains valid even when the rare disease product initially approved to market was never designated as an Orphan product.

(AR, ECF No. 23-2, at 58.) The FDA further rejected Depomed's contentions regarding clinical superiority because "there is no data presented in th[e] current application to bolster the contention" that Gralise would have the potential beneficial effects Depomed had hypothesized. (*Id.*) The FDA gave Depomed 60 days to cure the purported defects in its request for designation, but Depomed declined to do so.

b. Abbott Labs's Renewed Designation Request For Gralise In 2010

On March 26, 2010, Abbott Labs ("Abbott"), a drug manufacturer that had acquired the rights to Gralise, renewed Depomed's previous request for orphan-drug designation of Gralise for the treatment of PHN. (SAR, ECF No. 18, at 76.) In its

request, Abbott argued that the FDA's reasons for denying designation to Gralise the first time around were incorrect under the Act and also under the FDA's own implementing regulations. (*Id.* at 79.) Abbott asserted that sections 316.23 and 316.25 of Title 21 of the C.F.R. "identify with specificity the circumstances under which a request for orphan drug designation must, or may, be denied[,]" and that none of the reasons identified therein applied to Gralise. (SAR, ECF No. 18, at 79-84.) In particular, Abbott contended that section 316.25(a)(3)—which provided at that time that an application for designation will be denied where the drug in question is "otherwise the same drug as one that already has orphan-drug exclusive approval . . . and the sponsor has not submitted a medically plausible hypothesis for the possible clinical superiority of the subsequent drug"—was inapplicable to Gralise because there was no other drug that "already has orphan-drug exclusive approval" for PHN. (SAR, ECF No. 18, at 83.) In support of its position, Abbott pointed not only to the language of section 316.25(a)(3), but also to the definition of "orphan drug exclusive approval" in section 316.2(b)(12), which, in Abbott's words, "means approval that carries with it the seven-year orphan drug exclusivity that bars approval of the 'same drug.'" (SAR, ECF No. 18, at 83.) Abbott conceded that Neurontin "arguably is the 'same drug'" as Gralise, but maintained that even if it was, Neurontin had never received exclusivity and accordingly could not be considered a drug that "already has orphan-drug exclusive approval." (*Id.*) For the same reasons, Abbott argued that it was not required to provide a plausible hypothesis of clinical superiority in its renewed designation request for Gralise. (*Id.* at 84.)[8]

[8] Abbott also noted in its designation request that it did not believe designating Gralise as an orphan drug would have any effect on the gabapentin products already on the market for treatment of PHN, nor

On June 17, 2010, the FDA sent Abbott a two-page letter rejecting its designation request. (AR, ECF No. 23-2, at 61-62.) The FDA's stated reason for the denial was the "lack of evidence for clinical superiority." (*Id.* at 61.) In responding to Abbott's arguments regarding section 316.25(a)(3), the FDA focused on the notion that Gralise was the "same drug" as Neurontin, and therefore, in the FDA's view, was subject to the clinical superiority hypothesis. To back up its position, the FDA pointed to the definition of "orphan drug" found in section 316.3(b)(10), arguing that under that definition "there is no regulatory requirement that a drug obtain orphan drug designation in order to be defined as an orphan drug[.]" (*Id.* at 61.) The FDA also invoked the regulatory definition of "same drug" to maintain that Abbott "must show clinical superiority in order for" the FDA to consider Gralise to be a different drug than Neurontin. (*Id.* at 61-62.) Finally, the FDA pointed to the language of section 316.20(b)(5), which it claimed requires "an explanation of why" Gralise "may be clinically superior to" Neurontin before Gralise could be designated as an orphan drug. (*Id.* at 62)

c. Abbott Labs's Amended Designation Request, Which Included A Hypothesis Of Clinical Superiority

On September 1, 2010, Abbott submitted an amended designation request. (AR, ECF No. 23-2, at 64-71.) In its amended request, Abbott reiterated its objections to the FDA's interpretation of the relevant regulations, but it also presented a clinical superiority hypothesis based on the same potential effects that Depomed had cited in its original request for designation (*i.e.*, that because Gralise required only one dose per day as opposed to Neurontin's three, it might help patients adhere to their medication

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would it have any effect on the approval of gabapentin products for treatment of conditions other than PHN. (SAR, ECF No. 18, at 84.)

regime, and would also lessen potential side effects). (*Id.* at 70-72.) Abbott supported this hypothesis with data from two studies—one showing that, as a general matter, patients were more compliant with once-daily medication regimes, and the second indicating that extended release gabapentin (such as Gralise) may have a lower incidence of side effects than Neurontin. (*Id.*)

On November 8, 2010, the FDA granted Abbott's request and designated Gralise as an orphan drug for the treatment of PHN, noting that "the comparison of the incidence of [side effects] of [Gralise] to the reported incidence of [side effects] of Neurontin . . . is adequate for supporting a plausible hypothesis that [Gralise] is clinically superior[.]" (AR, ECF No. 23-2, at 116.) Significantly for present purposes, the FDA also explicitly noted that "should [Abbott] obtain marketing approval for [Gralise], [Abbott] will have to *prove* clinical superiority based on improved safety, to the FDA, in order to obtain seven years of marketing exclusivity[.]" (*Id.* (emphasis added).)

3. FDA Approval Of Gralise And Refusal Of Exclusivity

On January 28, 2011, the FDA granted Abbott marketing approval for Gralise pursuant to 21 U.S.C. § 355(b)(2).[9] (AR, ECF No. 17-2, at 43.) The FDA maintained, however, that despite securing designation and approval, Gralise was not entitled to the seven-year period of orphan-drug exclusivity under the Act because Abbott had not proven that Gralise was clinically superior to Neurontin. (AR, ECF No. 19-1, at 4.) In a phone call with Abbott on February 9, 2011, the FDA explained, essentially, that it had considered Gralise's orphan-drug designation to be conditional because it was

[9] Marketing approval pursuant to 21 U.S.C. § 355 comes with a statutory three-year exclusivity period that is completely separate from the orphan-drug exclusivity period at issue in this case. *See* 21 U.S.C. § 355(c)(3)(E)(iii).

based on a "hypothesis of clinical superiority over" Neurontin and that "[i]n order for Abbott to receive exclusivity they would have to prove this hypothesis[,]" which, the FDA asserted, Abbott had failed to do in its application for approval. (*Id.*)

4. Subsequent Proceedings

Depomed reacquired the rights to Gralise in March of 2011, and subsequently pressed the FDA on the agency's position regarding orphan-drug exclusivity for Gralise. On September 9, 2011, Depomed sent a letter to the FDA requesting a meeting and arguing (1) that the plain language of the exclusivity provision of the Act required the FDA to recognize exclusivity for any designated orphan drug that had been granted marketing approval; (2) that the FDA had erred in requiring proof of clinical superiority for orphan-drug designation in the first place; and (3) that the FDA had sufficient evidence of clinical superiority in any event. (AR, ECF No. 23-2, at 28-56.)

On September 25, 2012—more than one year after Depomed sent the letter to the FDA, but before the FDA had provided any formal response—Depomed filed its complaint in the instant lawsuit, alleging that the FDA's refusal to recognize exclusivity for Gralise violated the APA. (Complaint ("Compl."), ECF No. 1.) The FDA finally responded to Depomed's September 9, 2011, letter on November 13, 2012. (AR, ECF No. 17-2, at 1-26.) The FDA's response largely reiterated its prior positions regarding the regulations and also alluded to—but declined to detail because of "confidentiality constraints"—a number of instances in which the FDA had required a hypothesis of clinical superiority prior to granting designation. (*Id.* at 16 & n.38.)

Depomed filed its motion for summary judgment on January 1, 2013, essentially reiterating the arguments from its September 9, 2011 letter. (Pl.'s Mot. for Summ. J., ECF No. 20.) The FDA cross-moved for dismissal or, in the alternative, for summary

judgment on February 8, 2013. (Defs.' Mot. to Dismiss or Mot. for Summ. J., ECF No. 22.) This Court held a motions hearing on the parties' cross motions, and subsequently took the motions under advisement. (*See* Minute Entry of August 23, 2013.)

II. LEGAL STANDARDS

A. Standard For Dismissal Or Summary Judgment in Administrative Review Cases

"[W]hen a district court is reviewing agency action . . . the legal questions raised by a 12(b)(6) motion and a motion for summary judgment are the same." *Marshall Cnty. Health Care Auth. v. Shalala*, 988 F.2d 1221, 1222-1223 (D.C. Cir. 1993); *see also Nat'l Auto Dealers Ass'n v. FTC*, 864 F. Supp. 2d 65, 72 (D.D.C. 2012) (noting that motions to dismiss and motions for summary judgment "are normally judged under different legal standards," but "the inquiry in [APA] case[s] is the same" (citation omitted)). In most civil cases, summary judgment will be granted only "if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a); *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 247 (1986); *Moore v. Hartman*, 571 F.3d 62, 66 (D.C. Cir. 2009). "Summary judgment is [also] the proper mechanism for deciding, as a matter of law, whether an agency action is supported by the administrative record and consistent with the APA standard of review." *Loma Linda Univ. Med. Ctr. v. Sebelius*, 684 F. Supp. 2d 42, 52 (D.D.C. 2010) (citing *Stuttering Found. of Am. v. Springer*, 498 F. Supp. 2d 203, 207 (D.D.C. 2007)); *see also Richards v. INS*, 554 F.2d 1173, 1177 n.28 (D.C. Cir. 1977). However, due to the limited role a court plays in reviewing the administrative record to evaluate whether an agency has complied with the APA, the

typical summary judgment standards are not applicable. *Stuttering*, 498 F. Supp. 2d at 207. "Under the APA, it is the role of the agency to resolve factual issues to arrive at a decision that is supported by the administrative record," while "the function of the district court is to determine whether or not as a matter of law the evidence in the administrative record permitted the agency to make the decision it did." *Id.* (quoting *Occidental Eng'g Co. v. INS*, 753 F.2d 766, 769-770 (9th Cir. 1985)). In other words, "when a party seeks review of agency action under the APA, the district judge sits as an appellate tribunal," and "[t]he 'entire case' on review is a question of law." *Am. Bioscience, Inc. v. Thompson*, 269 F.3d 1077, 1083 (D.C. Cir. 2001) (footnote and citations omitted).

Notably, the APA provides a "default standard" of judicial review of agency actions on summary judgment when the governing statute does not otherwise provide one: "[a] court must set aside agency action it finds to be 'arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.'" *Tourus Records, Inc. v. DEA*, 259 F.3d 731, 736 (D.C. Cir. 2001) (quoting 5 U.S.C. § 706(2)(A)). "The 'arbitrary and capricious' standard of review as set forth in the APA is highly deferential," and the Court must therefore "presume the validity of agency action." *Am. Horse Prot. Ass'n v. Yeutter*, 917 F.2d 594, 596 (D.C. Cir. 1990) (citation omitted). Although the "court is not to substitute its judgment for that of the agency[,] . . . the agency nevertheless must examine the relevant data and articulate a satisfactory explanation for its action[,] including a rational connection between the facts found and the choice made." *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (citations and quotation marks omitted).

B. *Chevron* Framework

When assessing the validity of an agency's interpretation of a statute, the Court must apply the two-step framework under *Chevron, USA., Inc. v. NRDC*, 467 U.S. 837 (1984), to determine whether the agency has acted outside its authority. *See Ass'n of Private Sector Colls. & Univs. v. Duncan*, 681 F.3d 427, 441 (D.C. Cir. 2012).

The *Chevron* analysis first requires the reviewing court to determine "whether Congress has directly spoken to the precise question at issue." *Chevron,* 467 U.S. at 842. To resolve whether "the intent of Congress is clear" under this first step of *Chevron*, the court must exhaust the "traditional tools of statutory construction," including textual analysis, structural analysis, and (when appropriate) legislative history. *Id.* at 843 n.9; *see also Bell Atl. Tel. Cos. v. FCC*, 131 F.3d 1044, 1047 (D.C. Cir. 1997). "If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Chevron*, 467 U.S. at 842-843.

However, if the Court concludes that the statute is silent or ambiguous on the specific issue after employing these tools, the Court moves on to step two and defers to any agency interpretation that is based on a permissible construction of the statute. *Id.* at 843. An agency's construction is permissible "unless it is arbitrary or capricious in substance, or manifestly contrary to the statute." *Mayo Found. For Med. Educ. & Research v. United States*, 131 S. Ct. 704, 711 (2011) (citations and internal quotation marks omitted). In sum, "the whole point of *Chevron* is to leave the discretion provided by the ambiguities of a statute with the implementing agency." *Ass'n of Private Sector Colls.*, 681 F.3d at 441 (citations and internal quotation marks omitted).

III. ANALYSIS

In its motion for summary judgment, Depomed contends that the FDA's refusal to recognize that Gralise is entitled to orphan-drug exclusivity violates the unambiguous language of the Orphan Drug Act and thus that Depomed is entitled to judgment as a matter of law under *Chevron*'s step one. (Pl.'s Combined Mot. for Summ. J. & Mem. in Support ("Pl.'s Br."), ECF No. 20, at 24-34.) If the Court should find it necessary to proceed to step two of the *Chevron* analysis, Depomed argues that the FDA's construction of the Act as permitting the agency to insist on a showing of clinical superiority as a condition of granting exclusivity is unreasonable and therefore impermissible. (*Id.* 34-37.) Depomed also maintains that the FDA's decision to deny Gralise orphan-drug exclusivity unless and until Depomed proved that the drug was clinically superior to Neurontin was arbitrary and capricious in light of the agency's own regulations regarding the exclusivity issue. (*Id.* 38-45.)

In its own defense and in support of the agency's belief that Depomed's complaint must be dismissed, the FDA asserts that this Court must proceed to *Chevron*'s step two because nothing in the statute speaks to the precise question at issue here—which, in the agency's view, is whether exclusivity must be recognized when a drug is designated as an orphan drug and approved for marketing but is the same drug as one that has already been approved for the same disease or condition. (*See* Defs.' Br. at 37 ("Congress did not address the possibility that there may already be an approved same drug (with or without exclusivity) even before the newly approved drug at issue.").) The FDA maintains that, as a result of Congress's alleged silence on this issue, the Act is ambiguous, and thus the Court is required to defer to the agency's decision to deny exclusivity under these circumstances unless the new, approved orphan

drug can meet certain regulatory requirements (*i.e.*, the establishment of clinical superiority). (*Id.*) Furthermore, Defendants contend that accepting Depomed's interpretation of the statute could lead to outcomes that would be absurd insofar as they would clearly contravene the purpose of the Act.

As explained further below, this Court concludes that the plain language of the Orphan Drug Act requires the FDA to recognize exclusivity for Gralise. Consequently, the Court finds no need to proceed beyond *Chevron*'s step one, meaning that the Court's analysis need not, and does not, address Depomed's argument that the FDA's interpretation of the Act to permit regulations that require clinical superiority was unreasonable. The Court also finds it unnecessary to consider Depomed's alternative argument that the agency's decision to deny Gralise exclusivity was arbitrary and capricious within the meaning of the APA because that determination violated the agency's own exclusivity regulations.[10]

A. The Orphan Drug Act Unambiguously Requires Marketing Exclusivity When The FDA Has Designated An Orphan Drug And Has Approved That Drug For Marketing

An examination of any statute for indicia of ambiguity under *Chevron* must begin (and may end) with an analysis of the statutory text. *See, e.g.*, *Chevron*, 467 U.S. at 842-843; *Bell Atl. Tel. Cos.*, 131 F.3d at 1047. Section 360cc of Title 21 of the U.S. Code is entitled "Protection for drugs for rare diseases and conditions" and includes two subsections. Subsection (a), which is labeled "Exclusive approval, certification, or

[10] This Court also declines to address Depomed's related argument decrying the alleged arbitrariness of the FDA's initial requirement that Gralise present a plausible hypothesis of clinical superiority before it was designated as an orphan drug. (Pl.'s Br. at 38-45.) The question of whether the FDA violated its own designation regulations when it inserted a clinical superiority requirement into the designation process for Gralise need not be answered here because it is undisputed that Gralise *was* (belatedly) designated as an "orphan drug" and was subsequently approved for marketing. Therefore, the only pertinent legal question at issue on the instant facts is whether the FDA was authorized to refuse to recognize Gralise's marketing exclusivity under the Orphan Drug Act and its implementing regulations.

license[,]" establishes the statutory circumstances under which exclusivity attaches, while subsection (b), labeled "Exceptions" sets forth the two specific instances in which marketing exclusivity may nevertheless be denied. In its entirety, section 360cc reads as follows:

> **(a) Exclusive approval, certification, or license**
>
> Except as provided in subsection (b) of this section, if the Secretary—
>
> > **(1)** approves an application filed pursuant to section 355 of this title, or
> >
> > **(2)** issues a license under section 262 of title 42
>
> for a drug designated under section 360bb of this title for a rare disease or condition, the Secretary may not approve another application under section 355 of this title or issue another license under section 262 of title 42 for such drug for such disease or condition for a person who is not the holder of such approved application or of such license until the expiration of seven years from the date of the approval of the approved application or the issuance of the license. Section 355 (c)(2) of this title does not apply to the refusal to approve an application under the preceding sentence.
>
> **(b) Exceptions**
>
> If an application filed pursuant to section 355 of this title is approved for a drug designated under section 360bb of this title for a rare disease or condition or if a license is issued under section 262 of title 42 for such a drug, the Secretary may, during the seven-year period beginning on the date of the application approval or of the issuance of the license, approve another application under section 355 of this title or issue a license under section 262 of title 42, for such drug for such disease or condition for a person who is not the holder of such approved application or of such license if—
>
> > **(1)** the Secretary finds, after providing the holder notice and opportunity for the submission of views, that in such period the holder of the approved application or of the license cannot assure the availability of sufficient quantities of the drug to meet the

> needs of persons with the disease or condition for which the drug was designated; or
>
> **(2)** such holder provides the Secretary in writing the consent of such holder for the approval of other applications or the issuance of other licenses before the expiration of such seven-year period.

21 U.S.C § 360cc.

Examined closely, the text of the Act's exclusivity provision (§ 360cc(a)) employs the familiar and readily diagrammable formula, "if x and y, then z." Congress has crafted its command to the Secretary of the FDA in a manner that sets forth two circumstances—a drug that has been designated for a rare disease or condition, and the FDA's approval of a marketing application for that drug—that, if present, result in a particular consequence: a seven-year period of abstinence regarding marketing approval for other such drugs. When considered against the background fact that Congress has ordinarily authorized the FDA to approve an application for the marketing of any new drug, *see id.* § 355 et seq., section 360cc(a)'s language can only be interpreted as a *limitation* on the agency's authority in that regard. In other words, although it is convenient to characterize orphan-drug marketing exclusivity as something in the nature of a benefit that the FDA confers or withholds, (*see, e.g.*, Defs.' Br. at 10 ("The Orphan Drug Act confers a seven-year exclusivity period to certain drugs[.]"); Pl.'s Br. at 4 (discussing FDA's "decision to withhold exclusivity")), the text of section 360cc makes clear that the incentive Congress intended to create in the orphan drug context is not a thing to be "conveyed" to drug manufacturers at all; rather, it is a restriction of the FDA's ability to approve the marketing of other such drugs for the same rare disease or condition (referred to herein as "new such drugs") when a drug that has been designated as an orphan drug is approved for marketing.

Contrary to Defendants' *Chevron* step-one argument, there is nothing ambiguous about Congress's statutory statement that if the FDA designates a drug as an orphan drug and approves that drug for marketing, the agency cannot approve another application for the marketing of a new such drug for a period of seven years. As luck would have it for the FDA, the agency has the ability and the opportunity to control the circumstances under which marketing exclusivity attaches because the FDA is responsible for determining when to designate a drug as an orphan drug under section 360bb, and it is also the agency that has the duty of deciding when and under what circumstances a drug will be approved for marketing. But the language of the Act's exclusivity provision does not permit or invite any discretion on the part of the FDA regarding whether or not to continue authorizing new such drug marketing applications once an orphan drug has been so designated and approved. Indeed, Congress has specifically established the only two situations in which the FDA can carry on regardless. *See* 21 U.S.C. § 360cc(b) (permitting approval of new such drug applications if the agency "finds" within the seven-year exclusivity period that the manufacturer of a drug with marketing exclusivity "cannot assure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated" or if the manufacturer of the drug with marketing exclusivity provides its written consent to the approval of marketing applications for new such drugs within the exclusivity period).

As applicable here, it is undisputed that Gralise satisfies the exclusivity provision's unambiguously-worded circumstances (*i.e.*, designation and approval). Nevertheless, Defendants have offered several arguments to support their contention

that the Act's exclusivity provision is ambiguous under the circumstances presented and thus permits the FDA to impose additional criteria for exclusivity even after a drug has been designated an orphan drug and approved for marketing. First, Defendants point to the fact that *Chevron* requires the Court to determine "whether Congress has directly spoken to the precise question at issue[,]" 467 U.S. at 842, and they argue that the question at issue here is not what circumstances must exist for orphan-drug marketing exclusivity to attach but "which drugs are eligible for exclusivity in the first instance." (Defs.' Br. at 37.) Specifically, Defendants maintain that, where a drug for the same disease or condition has already been approved for marketing (*e.g.*, Neurontin), the statute fails to speak to whether a subsequent drug that has the same active ingredient and is for the same rare disease or condition should be entitled to marketing exclusivity, and it is this alleged "gap" in the statute that the FDA is entitled to fill with its clinical superiority criteria. (*See* Defs.' Br. at 37 ("Congress did not address the possibility that there may already be an approved same drug[.]").)

This Court is not persuaded. As an initial matter, "'the fact that a statute can be applied in situations not expressly anticipated by Congress does not demonstrate ambiguity. It demonstrates breadth.'" *PGA Tour, Inc. v. Martin*, 532 U.S. 661, 689 (2001) (quoting *Penn. Dep't of Corr. v. Yeskey*, 524 U.S. 206, 212 (1998)). Moreover, as the D.C. Circuit has noted repeatedly, the fact that Congress has "not mentioned" a particular agency concern in a governing statute does *not* mean that "Congress is 'silent or ambiguous' as to that issue[]" and thus the agency can do what it wishes. *Ethyl Corp. v. EPA*, 51 F.3d 1053, 1060 (D.C. Cir. 1995); *see also Grocery Mfrs. Ass'n v. EPA*, 693 F.3d 169, 191 (D.C. Cir. 2012) (the proposition that "*Chevron* step two is

implicated any time a statute does not expressly negate the existence of a claimed administrative power (*i.e.*, when the statute is not written in 'thou shalt not' terms), is both flatly unfaithful to the principles of administrative law, and refuted by precedent" (citing *API v. EPA*, 52 F.3d 1113, 1120 (D.C. Cir. 1995))). Rather, "'it is only legislative *intent to delegate* such authority that entitles an agency to advance its own statutory construction for review under the deferential second prong of *Chevron.*'" *NRDC v. Reilly*, 983 F.2d 259, 266 (D.C. Cir. 1993) (emphasis added) (quoting *Kansas City v. Dep't of Hous. & Urban Dev.*, 923 F.2d 188, 191-192 (D.C. Cir. 1991)). Indeed, "[w]ere courts to presume a delegation of power absent an express withholding of such power, agencies would enjoy virtually limitless hegemony, a result plainly out of keeping with *Chevron* and quite likely with the Constitution as well." *Ethyl Corp.*, 51 F.3d at 1060 (emphasis omitted).

In *Chevron*, the Supreme Court explained that Congress's "intent to delegate" rulemaking authority to the agency is manifest when the statute leaves the agency room "to fill any gap left, implicitly or explicitly, by Congress." 467 U.S. at 843. The D.C. Circuit has further clarified that "Congress leaves gaps in [a] program, either explicitly by authorizing the agency to adopt implementing regulations, or implicitly by enacting an ambiguously worded provision that the agency must interpret[.]" *Nat'l Fuel Gas Supply Corp. v. FERC*, 811 F.2d 1563, 1569 (D.C. Cir. 1987). Accordingly, in order to proceed to *Chevron* step two, an agency must affirmatively identify either an explicit or implicit gap in the statutory scheme that is indicative of congressional intent to provide that agency with the power to interpret the statute.

Here, Defendants rely on an alleged implicit grant of authority; specifically, the word "drug" as used in the Act's exclusivity provision, which, Defendants' argue, has been found to be ambiguous in one of the few cases to consider directly the provisions of the Orphan Drug Act. (*See* Defs.' Br. at 39 (citing *Baker Norton Pharms. v. FDA*, 132 F. Supp. 2d 30 (D.D.C. 2001) (holding that the FDA's promulgation of a regulation that defines "same drug" for the purpose of exclusivity was permissible because the term such "drug" as used in the Act was ambiguous).) Defendants are correct that the court in *Baker Norton* found "the word 'drug' in 21 U.S.C. § 360cc(a)" to be ambiguous; however, Defendants are wrong to suggest that the holding in that case has any bearing on the *Chevron* step-one analysis here. Properly understood, the term "such drug" in the exclusivity provision operates only to define the scope of the limit on the FDA's approval authority once a "designated drug" has been "approved" as required for exclusivity to attach. The court in *Baker Norton* was concerned only with the permissibility of the FDA's interpretation of what counted as "such drug" (and thus must not be approved within the seven-year preclusion period) under the FDA's regulatory framework. *See Baker Norton*, 132 F. Supp. 2d. at 34-38. But that question necessarily presumes the existence of a drug that has previously been designated and approved. *See* 21 U.S.C. § 360cc(a). Here, there has been no previously designated gabapentin product for treatment of PHN, so whether Gralise qualifies as a new "such drug" that is not entitled to marketing approval under the terms of the exclusivity period is not at issue. Thus, Defendants cannot rely on the "such drug" ambiguity identified in *Baker Norton* to justify the FDA's requirement of a showing of clinical superiority in the circumstances here.

Defendants' general suggestion that the statute is not clear with respect to Congress's intentions regarding exclusivity when there is a prior, non-designated drug that treats the same rare disease or condition, or that Congress otherwise meant to delegate the exclusivity determination to the agency under those circumstances, is similarly baseless. Try as they might, Defendants cannot square their insistence that the FDA has the discretion to address this situation with the fact that, under the statute, Congress did not give the FDA any discretionary authority to grant or deny exclusivity at all—rather, as mentioned previously, Congress *forbade* the FDA from granting any further approvals when the statutory conditions were met. 21 U.S.C. § 360cc(a) (the FDA "may not approve another application" for seven years after a designated drug is granted approval). This structure suggests that the intent of Congress was to provide the FDA with a merely ministerial role in the exclusivity process, and certainly not to give it the authority to interpose additional requirements with respect to a drug that has received designation and approval. Indeed, based on the fact that the Act's exclusivity provision operates by *removing* FDA discretion to approve the marketing of certain other drugs, it is at least arguable that the Orphan Drug Act is exactly the kind of "thou shalt not" statute that the D.C. Circuit has found "expressly negate[s] the existence of a claimed administrative power" to interpret the circumstances in which the provision applies. *Ry. Labor Execs.' Ass'n v. Nat'l Mediation Bd.*, 29 F.3d 655, 671, *amended by* 38 F.3d 1224 (D.C. Cir. 1994).

Moreover, as noted, Congress not only unambiguously described the conditions necessary for exclusivity to attach, it also specifically enumerated the circumstances in which exclusivity would *not* result despite the fact that a drug had been designated and

approved. 21 U.S.C. § 360cc(b). The express statutory exceptions are significant because it is well-established that "[w]here Congress explicitly enumerates certain exceptions to a general prohibition, additional exceptions are not to be implied, in the absence of evidence of a contrary legislative intent." *Andrus v. Glover Const. Co.*, 446 U.S. 608, 616-617 (1980). Here, the statute generally prohibits the FDA from approving orphan drugs for the same indication as one that has previously been approved and designated, and also provides two specifically enumerated exceptions, neither of which includes the fact that a prior (non-designated) drug for the same disease or condition and with the same active ingredients might already be on the market. This Court will not impute to Congress an intention to authorize an exception that Congress itself did not think worth enacting. *See, e.g.*, *NRDC v. EPA*, 489 F.3d 1250, 1259-1260 (D.C. Cir. 2007) (holding that where Congress provides certain enumerated exceptions in a statute, an agency "may not, consistent with *Chevron,* create an additional exception on its own").

Thus, the Court concludes that the plain language of the exclusivity provision means precisely what it says, to wit, when a drug, like Gralise, has obtained both orphan-drug designation and marketing approval, the FDA is precluded from approving any other such drug for seven years from the date of approval.

B. Giving Effect To The Plain Language Of The Act Will Not Lead To An Absurd Result

Trying a different tack, Defendants offer two additional policy-oriented arguments regarding why this Court should not resolve this case in Depomed's favor at *Chevron* step one. (*See* Hr'g Tr., ECF No. 31, at 19:18-21 ("Your Honor, Depomed is accusing [the] FDA of mounting what they call a policy . . . defense . . . and in some

sense that's true because fundamentally this case really is about a policy choice[.]").) Generally speaking, Defendants maintain, first, that affirming exclusivity for Gralise could allow Depomed to cut off any new gabapentin entrants into the marketplace, which has been wide open for over a decade, without providing any benefit in the treatment of PHN; and second, that similarly-situated drug manufacturers could conceivably obtain successive periods of exclusivity for the same drug, provided that they obtained seriatim designations and approvals. (*See* Defs.' Br. at 47, 38.) Defendants contend that the FDA's requirement that Gralise prove its clinical superiority to Neurontin is reasonable precisely because it avoids such absurd results.

As a threshold matter, with respect to the propriety of addressing policy arguments in the context of a step-one *Chevron* analysis, this Court acknowledges that such arguments may be relevant to the first *Chevron* inquiry based on "the long-standing rule that a statute should not be construed to produce an absurd result." *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1068 (D.C. Cir. 1998). It is clear beyond cavil that in any exercise of statutory interpretation, whether under *Chevron* or otherwise, "[t]he plain meaning of legislation should be conclusive, *except* in the rare cases [in which] the literal application of a statute will produce a result demonstrably at odds with the intentions of its drafters." *United States v. Ron Pair Enters., Inc.*, 489 U.S. 235, 242 (1989) (emphasis added) (internal quotation marks and citation omitted). Thus, in the *Chevron* step-one context, "the rule that statutes are to be read to avoid absurd results allows an agency to establish that seemingly clear statutory language does not reflect the unambiguously expressed intent of Congress." *Mova*, 140 F.3d at 1068 (internal quotation marks and citations omitted).

Here, Defendants struggle valiantly to establish that the instant matter is one of those rare instances in which interpreting the Act literally would so defeat its purpose that Congress could not have meant the statute to be read in accordance with its plain language. As noted, Defendants' first policy-related argument is essentially that, because the purpose of the legislative scheme is to incentivize new and better drugs for the treatment of rare diseases, granting exclusivity to a drug like Gralise under the circumstances of this case—that is, where numerous functionally identical drugs for treatment of the same orphan indication are already on the market—is patently unnecessary and would also have the unfortunate result of essentially truncating the development of improved pharmaceuticals rather than encouraging them, as the legislature clearly intended. (*See* Defs.' Br. at 42 ("[R]eading the statute to require exclusivity . . . would undermine the very *raison d'etre* of the legislative scheme" by allowing "sponsors who have not shown their drugs to be any better than a previously approved drug" to get the benefits of exclusivity); Defs.' Reply in Supp. of Mot. to Dismiss or Mot. for Summ. J., ECF No. 27, at 26 (noting that, if Gralise receives exclusivity, "other products could no longer be approved by FDA to treat the orphan indication, post-herpetic neuralgia").)[11]

This policy argument misses the mark by a mile. To the extent that Defendants' contention is that Congress never would have intended for a "me too" drug like Gralise to get a benefit that the legislature devised to entice new entrants into the rare-disease

[11] In essence, Defendants' current position with regard to this scenario is no different than what the FDA stated in its original rejection of designation for Gralise in 2006: "[T]here is no rationale for supporting, with taxpayer monies, the clinical development of an identical product for an identical indication as one which has been approved after the most thorough evaluation possible." (AR, ECF No. 23-2, at 58.)

treatment market, Defendants' point is unfounded—nothing in the statute even remotely suggests that Congress intended to incentivize only one sponsor to produce a particular drug (although Congress certainly could have specified as much), and general market forces provide a plausible reason for a legislative scheme that deliberately incentivizes multiple manufacturers of the same pharmaceutical product. Nor can it be said that permitting Depomed to grasp the brass ring of exclusivity for Gralise is unfair to the manufacturers of the prior iterations of the drug, since each had every opportunity to seek exclusivity and failed to do so. If, on the other hand, Defendants are pointing to Gralise and are making the conceptually different argument that it would be "absurd" for the same drug as others already on the market to be permitted to cut off the development of new and improved versions, *that* result appears to be a function of granting a drug marketing exclusivity in any event—*i.e.*, the statute plainly incentivizes investment in drugs for rare diseases and conditions *precisely because* it prevents new (and potentially better) drugs from being adopted and marketed for that same condition—and thus is inherent in the exclusivity statute. Defendants may find it "absurd" that the legislature wished to encourage the production and marketing of certain drugs for rare diseases by prohibiting the marketing of others, but that is the incentive structure that Congress clearly intended and adopted.

The second potentially absurd result that Defendants identify is a variation on this same theme—and fails for the opposite reason. Defendants assert that, if the exclusivity statute is read in the manner that Depomed suggests, it could lead to orphan drug sponsors obtaining serial exclusivity or evergreen status for their drugs. (*See, e.g.*, Defs.' Br. at 38.) As far as this Court can tell, Defendants are worried that interpreting

the statute to mandate exclusivity whenever a drug has obtained designation and approval could lead to a situation in which sponsors that have exclusivity for a particular drug could simply tweak their formulation for that drug and resubmit applications for designation and approval after the initial exclusivity period has expired, thereby gaining successive exclusivity periods—a result that, according to Defendants, would contravene the most basic purpose of the statute. (*See id.*; *see also* AR, ECF No. 17-2, at 10.) However, under the statutory scheme as it currently exists, this result would only occur *if the FDA permitted it to happen.* While the prior policy concern (*i.e.*, that new and better drugs will be prevented from coming to market) would happen under the statute merely by virtue of the exclusivity requirement, the "serial exclusivity" problem would not arise at all if the FDA fashioned regulations to prevent such abuse in the context of the designation phase of the exclusivity process. *See* 21 U.S.C. § 360bb(d) (directing that the FDA "shall by regulation promulgate procedures for the implementation of" the designation requirement). For example, the FDA could require designation applicants to show clinical superiority before granting their product orphan-drug designation, a change in the regulations that would allow the FDA to maintain the benefits of its clinical superiority requirement and also forestall the hypothetical "serial exclusivity" problem while at the same time avoiding any conflict with the plain language of the statute's exclusivity provision. And, indeed, the FDA has already shown that it is willing to alter its designation regulations in response to unforeseen factual circumstances.[12] The Court sees no reason why a change to the

[12] As noted *supra*, n.6, after the complaint in this case was filed, the FDA amended the language of its regulations to comport more easily with the FDA's litigation position in this case. *See* 78 Fed. Reg. 35,117 (Jun. 12, 2013). Specifically, the FDA changed 21 C.F.R. § 316.25 to provide that a clinical superiority hypothesis is required for designation where "the drug is the same drug as an already

designation regulations, if implemented properly, could not remedy the supposedly "absurd" results that Defendants say may result from the plain language of the exclusivity provision, which casts doubt on Defendants' argument that the statute was not intended to be read in accordance with its plain meaning.

Finally, it is worth noting that, on the record before this Court, Defendants' policy concerns appear to be somewhat overblown. First of all, because the Orphan Drug Act simply directs the FDA to refrain from approving any other new such drug for a seven-year period, it is clear that the fate of Gralise will have no effect on the marketability of Neurontin or the many generics that were already on the market at the time Gralise was designated and approved.[13] Moreover, the record reflects that the particular circumstances of this litigation—that is, where the FDA has declined to recognize exclusivity for a drug that has been both designated and approved on the grounds that a prior un-designated same drug is already on the market—appear to be *sui generis*. Although the FDA has purported to identify fourteen prior instances that it claims provide precedent for its decision regarding Gralise (*see* Defs.' Br. at 51-53), none of the cited examples are in fact on all fours with the instant case. In five of those examples, the FDA denied *designation* to an applicant on the grounds that it had failed to provide an adequate hypothesis of clinical superiority, (*see* AR, ECF No. 17-8, at 41-44), and in the other nine examples, the FDA denied *marketing approval* for a drug

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approved drug," where before that regulation read "a drug that is otherwise the same drug as one that already has orphan-drug exclusive approval." The FDA also changed 21 C.F.R. § 316.24 by removing the language indicating that the FDA "will grant" a request for orphan-drug designation absent one of the problems identified in section 316.25. The new section 316.24 also explicitly ties designation to receipt of the materials that 21 C.F.R. § 316.20 requires. Finally, the rulemaking changes the term "already approved orphan drug" to "already approved drug" in section 316.20(b)(5).

[13] At the motions hearing in this case, counsel for Depomed acknowledged as much. (*See* Hr'g Tr. at 8:23-25 (Depomed's Counsel acknowledging that exclusivity for Gralise "would have no effect on any of" the gabapentin products already on the market).)

where another drug already had exclusivity and the applicant sponsor had not proven clinical superiority, (s*ee id.* at 44-46). In fact, in the only example reflected in the record that is substantially similar to the instant case, the FDA *recognized* exclusivity for a drug, Kogenate, even though another drug with the same active ingredient had previously been approved for marketing for the same rare disease or condition but had never been designated an orphan drug (just like Neurontin). (*See* Pl.'s Br. at 41-44; *see also* AR, ECF No. 17-8, at 51.)[14] It appears, then, that the purportedly "absurd" result that Defendants fear may arise out of the facts of this case rarely, if ever, actually occurs.

Lastly, it is clear on this record that the circumstances of this case do not raise the specter of the "serial exclusivity" scenario. No gabapentin product has ever enjoyed exclusivity for the treatment of PHN, and thus there is nothing "serial" about the relief Depomed seeks. What is more, the serial exclusivity issue is not unique to the Orphan Drug Act. In *Mova Pharmaceutical Corp. v. Shalala*, the D.C. Circuit recognized that a similar problem could potentially arise in the context of the exclusivity period provided for generic drugs under 21 U.S.C. § 355(j)(5)(B)(iv), yet that court still rejected an FDA rationale that would have addressed this potential issue. *See* 140 F.3d at 1065 n.4 ("[T]he statute might conceivably be read to confer this 180-day [exclusivity] period on a second or third applicant in some situations."). This Court, too, is not moved to alter its reading of the plain language of the Orphan Drug Act based on the potential that,

[14] The FDA has attempted to distance itself from its decision regarding Kogenate by characterizing the decision as an "outlier decision" that is "inconsistent" with the FDA's other precedents. (*See* Defs.' Br. at 51; AR, ECF No. 17-8 at 51.) But Defendants fail to provide any support for this assertion, particularly because, as explained above, the ordinary course examples it cites are not, in fact, on all fours with the instant case.

under other unspecified circumstances that the agency might easily remedy, the exclusivity provision could be subject to abuse.

IV. CONCLUSION

The plain language of the exclusivity provision of the Orphan Drug Act requires the FDA to recognize exclusivity for any drug that the FDA has designated and granted marketing approval, and there is no dispute that Gralise has satisfied both of those criteria. Consequently, the Court concludes that Gralise is entitled to exclusivity and that the FDA must recognize as much without requiring proof of clinical superiority or imposing any additional conditions on Depomed. As set forth in the separate order accompanying this opinion, summary judgment will be entered in favor of Depomed.

DATE: September 5, 2014

Ketanji Brown Jackson

KETANJI BROWN JACKSON
United States District Judge