UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

AMGEN INC.,

Plaintiff,

v.

ALEX AZAR II, Secretary, U.S. Department of Health and Human Services, *et al.*,

Defendants,

and

AMNEAL PHARMACEUTICALS, LLC,

Intervenor-Defendant.

Civil Action No. 17-1006 (RDM)

MEMORANDUM OPINION

Amgen brought this action to challenge the decision of the Food and Drug Administration ("FDA") denying Amgen pediatric exclusivity for its drug, Sensipar (cinacalcet hydrochloride). In an earlier opinion and order, the Court granted the FDA summary judgment on all but one of Amgen's claims: its claim that the agency's denial of pediatric exclusivity for Sensipar was inconsistent with its decision to grant pediatric exclusivity for Johnson & Johnson's drug Ortho Tri-Cyclen. *Amgen Inc. v. Hargan*, --- F. Supp. 3d ---, 2018 WL 581006 (D.D.C. Jan. 26, 2018). As to that claim, the Court concluded that the FDA had failed to offer a "reasoned explanation" for why it reached a "disparate outcome[]" with respect to Ortho Tri-Cyclen. *Id.* at *15–18. On remand, the FDA reaffirmed its Sensipar decision and explained why, in its view, this result was consistent with its decision on Ortho Tri-Cyclen. *See* AR2d 1–5 [hereinafter Remand Decision]. After a last-minute discovery of an additional document relating

to the FDA's Ortho Tri-Cyclen decision, Dkt. 78, the Court remanded the case to the FDA "to address [Amgen]'s claim of inconsistent treatment in light of [the] newly discovered information," Minute Order (Feb. 7, 2018). The FDA issued an addendum to its Remand Decision, again concluding that its Sensipar and Ortho Tri-Cyclen decisions were not inconsistent. *See* AR3d 1–4 [hereinafter Remand Addendum]. Amgen has now renewed its motion for summary judgment on the grounds that the FDA's latest explanation is inadequate and that its denial of pediatric exclusivity for Sensipar thus remains arbitrary and capricious. Dkt. 83. The FDA, in turn, has renewed its cross-motion for summary judgment. Dkt. 84. For the reasons that follow, the Court will **DENY** Amgen's motion and will **GRANT** the FDA's cross-motion.[1]

I. BACKGROUND

Because the Court has already recounted the factual and legal background at length, *see Amgen*, 2018 WL 581006, at *1–6, only a brief summary of the background relevant to the pending motions is necessary. Subject to other requirements not relevant here, the sponsor of a new drug application will qualify for six months of pediatric exclusivity if (1) the FDA determines that "information relating to the use of [the] new drug in the pediatric population may produce health benefits in that population," 21 U.S.C. § 355a(b)(1); (2) it "issue[s] to the sponsor [of the drug] a written request for the conduct of pediatric studies for such drug," 21 U.S.C. § 355a(d)(1)(A); and (3) the sponsor's reports on its pediatric studies are "submitted [to] and

[1] Amgen's submission is captioned "Supplemental Brief in Support of Amgen's Motion for Summary Judgment," Dkt. 83 at 1, and the FDA's filing is captioned "Response to Plaintiff's Supplemental Brief in Support of Summary Judgment," Dkt. 84 at 1. Both parties request that the Court grant their motions for summary judgment. *See* Dkt. 83 at 11; Dkt. 84 at 11. The Court will, accordingly, construe Amgen's supplemental brief and the FDA's response as renewed motions for summary judgment.

accepted" by the FDA, 21 U.S.C. § 355a(b)(1). The pediatric exclusivity statute further provides, in relevant part, that the FDA's "only responsibility in accepting or rejecting the reports shall be to determine . . . whether the studies *fairly respond* to the written request." 21 U.S.C. § 355a(d)(4) (emphasis added). Under the FDA's interpretation of this provision, the "fairly respond" requirement is satisfied if a sponsor "meets the terms" of the written request or if the sponsor's studies yield information that is "clinically meaningful across all age groups and uses cited" in the request, thus satisfying the objectives of the request. AR 1637.

The FDA denied Amgen's request for pediatric exclusivity for Sensipar because Amgen's studies did not, in the agency's view, "fairly respond" to the written request, AR 1389, and it reaffirmed that decision in subsequent administrative proceedings, AR 1484; AR 1632. According to the FDA, Amgen's studies did not fully comply with the requirements of the written request: for one of the studies, the written request required a minimum of fifteen patients ages 28 days to < 6 years, but only four patients completed the study, AR 1645, and, in the FDA's view, Amgen's data did not yield "clinically meaningful" information on cinacalcet's safety in that age group—a key objective of the written request, AR 1647–48. Amgen brought this action under the Administrative Procedure Act, 5 U.S.C. § 701 *et seq.*, to challenge the FDA's denial of pediatric exclusivity for Sensipar. Dkt. 1 at 2 (Compl. ¶ 1). Both parties moved for summary judgment.

On January 26, 2018, the Court issued a memorandum opinion and order resolving most of Amgen's claims in the FDA's favor. *Amgen*, 2018 WL 581006, at *21. But the Court granted summary judgment in favor of Amgen on the limited ground that the FDA had failed to offer a "reasoned explanation" for why it reached a "disparate outcome[]" in the case of Johnson & Johnson's Ortho Tri-Cyclen. *Id.* The written request for Ortho Tri-Cyclen required Johnson &

Johnson to complete a study involving at least 120 adolescent women with anorexia nervosa as defined by the Diagnostic and Statistical Manual of Mental Disorders, fourth edition ("DSM-IV"). AR 1872. Johnson & Johnson received pediatric exclusivity in December 2003. AR2d 4. More than a year later, however, a clinical reviewer for the FDA, Dr. Brenda Gierhart, concluded that "the majority of the 123 subjects treated . . . did *not* meet . . . the DSM-IV diagnostic criteria for anorexia nervosa." AR 1916. Relying on this observation, Amgen asserted that it was arbitrary and capricious for the FDA to deny pediatric exclusivity for Sensipar after granting that benefit to another sponsor that neither met the terms of the written request nor achieved its objectives. Dkt. 60-1 at 45.

The Court concluded that, because the FDA's administrative determination did not "explain [its] rationale and [did not] identify the relevant evidence," the Sensipar decision was "at least in this one respect . . . arbitrary and capricious." *Amgen*, 2018 WL 581006, at *17. But the Court also noted that "[t]here may be an answer to Amgen's contention," including, for instance, that "Johnson & Johnson's study did, in fact, comply with the requirement[s]" of the written request, or that the FDA granted Johnson & Johnson pediatric exclusivity "based on the mistaken belief that [the study] was conducted in full compliance with the terms of the written request" and "the failure to enroll patients meeting the DSM-IV criteria was discovered only after the fact." *Id.* The Court, accordingly, remanded the case to the FDA "for the limited purpose of addressing whether the agency's prior decision granting pediatric exclusivity for Ortho Tri-Cyclen is consistent with its decision denying pediatric exclusivity for Sensipar and, if not, whether there is a reasoned explanation for the disparate outcomes." *Id.* at *21.

The FDA issued its Remand Decision and supplemented the administrative record on February 5, 2018. *See* Remand Decision. The FDA explained in its Remand Decision that it

granted pediatric exclusivity to Ortho Tri-Cyclen based on the agency's understanding in December 2003, when it was statutorily required to make the exclusivity determination, that Johnson & Johnson's studies met the terms of the written request. *Id.* at 1, 3–4. The FDA cited several internal documents that, it asserted, show that it believed Johnson & Johnson had "fulfill[ed] the terms" of the written request when "eligibility for [pediatric exclusivity] was decided." *Id.* at 3. The FDA further explained that "the realization that a majority of enrolled study subjects had not, in fact, met DSM-IV criteria for [anorexia nervosa] came after [Johnson & Johnson's] final study reports had been submitted . . . and evaluated" and "postdates the [exclusivity] decision." *Id.* at 4. The agency therefore concluded that it applied the same standard to both Ortho Tri-Cyclen and Sensipar and that Amgen's failure to meet the terms of its written request distinguishes the agency's exclusivity denial for Sensipar from the agency's grant of exclusivity for Ortho Tri-Cyclen. *Id.* at 4.

The day after it issued its Remand Decision, the FDA notified the Court that it had discovered an additional document showing that, *before* the FDA granted pediatric exclusivity for Ortho Tri-Cyclen, it asked Johnson & Johnson whether its study "subjects met the enrollment criteria." Dkt. 78 at 3. The Court held a status conference the following day. In light of the parties' representations at the status conference, the Court again remanded the case to the FDA to address the relevance of the "newly discovered information" to its Remand Decision and set an expedited briefing schedule. Minute Order (Feb. 7, 2018).

On February 8, 2018, the FDA issued an addendum to its Remand Decision and further supplemented the administrative record with newly discovered documents relating to its Ortho Tri-Cyclen decision. *See* Remand Addendum. These documents fill in several holes in the timeline discussed above. First, and most significantly, the medical officer who reviewed the

interim Ortho Tri-Cyclen data, Dr. Eric Colman, contacted Johnson & Johnson *before* he recommended granting exclusivity to ask "whether all of the subjects had Body Mass Index (BMI) values below the 10th percentile for age." *Id.* at 1–2; *see* AR3d 7. This benchmark, the FDA explains, provides one way to "fulfill[] one of the DSM-IV criteria." Remand Addendum at 1 n.5. Second, Johnson & Johnson responded to the FDA's inquiry on December 5 and December 8, 2003—once again, *before* the FDA granted exclusivity on December 18. *Id.* at 2; *see* AR3d 10–12, 14–18. Johnson & Johnson indicated that 74 out of 123 patients had BMIs above the tenth percentile, and it "provided a rationale that purported to explain why, in [its] opinion, the terms of the [written request] had been met." Remand Addendum at 2. Third, Dr. Colman "contributed to the annotated Written Request for the Pediatric Exclusivity Board, which concluded . . . that '[a]ll patients had a diagnosis of [anorexia nervosa] by DSM-IV criteria.'" *Id.* (quoting AR2d 18); *see also* AR3d 13. Finally, as noted, Dr. Colman recommended granting exclusivity on the grounds that "the requested study was conducted in agreement with the [w]ritten [r]equest." AR 1885; *see* Remand Addendum at 2.

In light of these new records, the FDA's Remand Addendum "correct[s] a factual inaccuracy in the [original] Remand Decision," acknowledging that the "FDA questioned whether subjects met the enrollment criteria *before* the date of the [e]xclusivity [d]ecision, contrary to what the Remand Decision stated." Remand Addendum at 1–2. But the new records, in the FDA's view, do not alter its conclusion that it applied the same standard to Sensipar and Ortho Tri-Cyclen. According to the FDA, the Sensipar studies fell short of full compliance with the written request, whereas the "FDA determined that the DSM[-]IV criteria had been met" when it granted exclusivity for Ortho Tri-Cyclen. *Id.* at 4. Reflecting some uncertainty about what happened, the FDA's Remand Addendum also advances two alternative arguments: (1) that

the requirement that study subjects meet the DSM-IV criteria was not, in fact, a requirement at all but a mere recommendation or suggestion, *id.* at 3; and (2) that "it cannot be entirely ruled out that [the] FDA relied on some other rationale to determine Ortho Tri-Cyclen's eligibility for [exclusivity]" and "[e]ven if [the] FDA were mistaken about whether the enrollment criteria were met . . . , that mistake would not justify making a similar mistake when evaluating other sponsors' studies," *id.* at 4.

Amgen has now renewed its motion for summary judgment with respect to its claim of inconsistent treatment. *See* Dkt. 83. It asserts that "there is nothing in the record that explains the [Pediatric Exclusivity] Board's . . . analysis," *id.* at 3, and that the FDA's "current musings are completely implausible in light of the record," which shows that a majority of the Ortho Tri-Cyclen subjects "did not meet the specified enrollment criteria," *id.* at 5–6. Amgen further contends that, to the extent the FDA applied different "fairly respond" standards to Sensipar and Ortho Tri-Cyclen, its decision on Ortho Tri-Cyclen "reinvigorates" Amgen's fair notice and retroactive rulemaking arguments. *Id.* at 8; *see id.* at 6–8. The FDA has also renewed its motion for summary judgment. Dkt. 84. The agency contends that it applied the same standard to both applications and that the FDA decided that the Ortho Tri-Cyclen studies "met the enrollment criteria in the [written request] at the time of the [exclusivity] decision." *Id.* at 3.

II. ANALYSIS

Amgen, as the party challenging the FDA's exclusivity decision, "has the burden of showing that the agency action was 'arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.'" *Advocates for Highway & Auto Safety v. Fed. Motor Carrier Safety Admin.*, 429 F.3d 1136, 1144 (D.C. Cir. 2005) (quoting 5 U.S.C. § 706(2)(A)). "The scope of review under the 'arbitrary and capricious' standard is narrow and a court is not to

substitute its judgment for that of the agency." *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983). This rule "applies with particular force in a case, like this one, involving scientific analysis and 'technical expertise.'" *Nat. Res. Def. Council, Inc. v. Rauch*, 244 F. Supp. 3d 66, 86 (D.D.C. 2017) (quoting *Marsh v. Or. Nat. Res. Council*, 490 U.S. 360, 377 (1989)). "When specialists express conflicting views," for example, "an agency must have discretion to rely on the reasonable opinions of its own qualified experts even if, as an original matter, a court might find contrary views more persuasive." *Marsh*, 490 U.S. at 378. That said, the Court must satisfy itself that the agency "examine[d] the relevant data and articulate[d] a satisfactory explanation for its action including a rational connection between the facts found and the choice made." *State Farm*, 463 U.S. at 43 (internal quotation marks omitted); *see also Regents of the Univ. of California v. Burwell*, 155 F. Supp. 3d 31, 48 (D.D.C. 2016).

Applying these principles here, the Court concludes that the FDA has offered a reasoned explanation for why it reached different outcomes in response to the Ortho Tri-Cyclen and Sensipar applications for pediatric exclusivity. According to the FDA's Remand Decision and Remand Addendum, the agency applied the same standard to Ortho Tri-Cyclen and Sensipar and granted exclusivity for Ortho Tri-Cyclen because the agency "decided" that the Ortho Tri-Cyclen studies, unlike the Sensipar studies, "met the enrollment criteria in the [written request] at the time of the [exclusivity] decision." Dkt. 84 at 3. Although the FDA's description of the basis for its Ortho Tri-Cyclen decision may lack "crystal clarity," *Rauch*, 244 F. Supp. 3d at 86, the Court can "reasonably . . . discern[]" the agency's reasoning, as well as its rationale for reaching a different outcome with respect to Sensipar, *Alaska Dep't of Envtl. Conservation v. EPA*, 540 U.S. 461, 497 (2004).

As explained in the Remand Addendum, the DSM-IV "does not specify a particular BMI" for an anorexia nervosa diagnosis. Remand Addendum at 3 n.16. Rather, it asks more generally whether the patient "[r]efus[es] to maintain body weight at or above a minimally normal weight for age and height (e.g., weight loss leading to maintenance of body weight less than 85% of that expected; or failure to make expected weight gain during the period of growth, leading to body weight less than 85% of that expected)." AR 1919. In its Remand Addendum, the FDA stresses that diagnosing anorexia nervosa according to the DSM-IV criteria "involves . . . professional judgment" and that the DSM-IV does not employ "precise language about a purely objective criterion." Remand Addendum at 3.

According to "documents contemporaneous with the Ortho Tri-Cyclen [exclusivity] decision," Dr. Colman apparently "considered the issue" of whether the study participants satisfied the DSM-IV criterion and "consulted with [the sponsor]."[2] *Id.* at 2. In response to Dr. Colman's inquiry, Johnson & Johnson explained (1) that the DSM-IV "provides four *guidelines*, not criteria, for . . . anorexia nervosa in adults[,] [one of which] is a statement about 'weight loss leading to maintenance of body weight less than 85% of that expected;'" (2) that its expert consultants "pointed out that the concept of ideal body weight is meaningless in a growing adolescent population and that no such normative data exist;" (3) that one expert opined that BMI "may be used as a surrogate for body weight, but cautioned that any value chosen would be arbitrary since there are no accepted levels in the literature;" and (4) that the same expert opined that the tenth-percentile BMI threshold "could be used, but . . . would exclude many individuals with anorexia nervosa." AR3d 11 (quoting DSM-IV). Johnson & Johnson further asserted that

[2] Dr. Colman is, unfortunately, deceased. Remand Addendum at 1 n.3. As a result, the FDA can rely only on the documentary record of what occurred.

"it was important to enroll all subjects with the diagnosis of anorexia nervosa, including those with a BMI [exceeding the tenth percentile], to be able to generalize results from [the] study to the adolescent female population with anorexia nervosa." *Id.*

The FDA posits that Dr. Colman found this response satisfactory in part because he "viewed the enrollment criteria as not requiring patients to have a specific BMI." Dkt. 84 at 6; *see* Remand Addendum at 4. Dr. Colman then, according to the FDA, "determined that [Johnson & Johnson's] study had met the DSM-IV criteria and the terms of the [written request]." Remand Addendum at 2. The FDA points to two documents to buttress this account of the agency's decisionmaking process. First, before the Pediatric Exclusivity Board convened to issue a decision on Ortho Tri-Cyclen, Dr. Colman e-mailed an attachment containing his "portion of the exclusivity table," that is, the annotated Written Request.[3] AR3d 13; *see* Remand Addendum at 2; Dkt. 84 at 5. The annotated Written Request "is a key document and is presented to the Board to assist in its decision[-]making." Dkt. 84 at 5. The resulting annotated Written Request for Ortho Tri-Cyclen asserts that "[a]ll patients had a diagnosis of [anorexia nervosa] by DSM-IV criteria." AR2d 18. The FDA further asserts that this document, although undated, was submitted to the Pediatric Exclusivity Board, which ultimately decided to grant exclusivity for Ortho Tri-Cyclen. *See* Remand Addendum at 2. Second, several months after the FDA's decision, Dr. Colman noted that he had "recommended that the sponsor receive pediatric

[3] Initially, the FDA did not provide the Court with the attachment to Dr. Colman's email "due to concerns with waiving deliberative privilege." Dkt. 84 at 4. At the Court's request, however, and with Amgen's consent, the FDA submitted an unredacted version of the attachment to the Court for *in camera*, *ex parte* review. *See* Minute Order (Feb. 16, 2018); Dkt. 86; Dkt. 87. The Court has reviewed the attachment and concludes that the attachment does not alter its conclusion. The Court has also ordered the FDA to file a redacted version of the attachment on the docket. Minute Order (Feb. 16, 2018).

exclusivity" because "the requested study was conducted in agreement with the [w]ritten [r]equest." AR 1885.

Although the FDA candidly acknowledges some uncertainty about what occurred, this account makes sense of the documentary record and reasonably supports the FDA's conclusion that the agency believed that the Ortho Tri-Cyclen studies met the terms of the written request at the time it granted Johnson & Johnson pediatric exclusivity. With that premise in hand, the remainder of the FDA's reasoning is straightforward: For both Sensipar and Ortho Tri-Cyclen, the FDA applied a standard in which full compliance with the terms of the written request constitutes a "fair response." In the FDA's scientific judgment at the time of the relevant decisions, however, the Ortho Tri-Cyclen studies met the terms of the written request, and the Sensipar studies did not. Whether the FDA was, in fact, correct in determining that the Ortho Tri-Cyclen study subjects met the DSM-IV criteria is not the relevant question. All that matters for present purposes is whether the FDA applied an interpretation of "fairly respond" to Amgen that differed from the standard it applied to Johnson & Johnson, and the agency has reasonably explained that it did not do so.

Amgen pushes back on the FDA's characterization of the record, but the Court is unpersuaded. Most notably, Amgen argues that the Ortho Tri-Cyclen studies "failed to meet the terms of the written request," Dkt. 85 at 3, because Dr. Gierhart concluded in 2005 that a majority of the patients "did *not* meet . . . the DSM-IV diagnostic criteria for anorexia nervosa," AR 1916. But the FDA has offered a "satisfactory explanation" for that discrepancy. As the FDA has explained, "documents contemporaneous with the Ortho Tri-Cyclen . . . decision show that Dr. Colman considered the issue, consulted with [Johnson & Johnson], and determined that [the] study [subjects] had met the DSM-IV criteria and the terms of the [written request]."

Remand Addendum at 2. In addition, Dr. Colman "likely viewed the DSM[-]IV criteria more flexibly than [Dr. Gierhart]," and Dr. Colman's opinion controls because his findings—not Dr. Gierhart's—informed the FDA's decision on pediatric exclusivity. *Id.* at 4; *see id.* at 2 ("[Dr. Colman's] conclusion was presented to the [Pediatric Exclusivity Board], which in turn decided to recognize [exclusivity] for Ortho Tri-Cyclen."). Because Dr. Colman is deceased, Remand Addendum at 1 n.3, the FDA cannot be absolutely certain about all that occurred in 2003. But it doesn't need to be. It is enough that the FDA has considered the relevant material and has offered a reasoned explanation that supports the agency's conclusion that it applied the same "fairly respond" standard to the Ortho Tri-Cyclen and Sensipar study reports.[4] *See State Farm*, 463 U.S. at 43.

The question before the Court is whether the FDA applied an interpretation of "fairly respond" to Johnson & Johnson's request for exclusivity that is inconsistent with the one it applied to Amgen and that, if applied to Amgen, would require the FDA to grant exclusivity. Amgen has not met its burden of demonstrating that the FDA applied different standards. The Court, accordingly, is now satisfied that the FDA has offered a reasoned—and reasonable—basis for distinguishing the Ortho Tri-Cyclen precedent.

[4] In light of this holding, the Court need not reach Amgen's arguments on its fair notice and retroactive rulemaking claims, which rely on the premise that the agency applied a new or different standard to evaluate the Sensipar studies.

CONCLUSION

For the reasons stated above, the Court will **DENY** Amgen's renewed motion for summary judgment, Dkt. 83, and **GRANT** the FDA's renewed motion for summary judgment, Dkt. 84.

A separate Order will issue.

/s/ Randolph D. Moss
RANDOLPH D. MOSS
United States District Judge

Date: February 17, 2018