UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

AMGEN, INC. Plaintiff, v. THOMAS E. PRICE, MD in his official capacity as Secretary of Health and Human Services, and SCOTT GOTTLIEB, M.D., in his official capacity as Commissioner of Food and Drugs; Defendants.	)	Case No. 1:17-cv-01006-RDM

FEDERAL DEFENDANTS' MEMORANDUM IN SUPPORT OF MOTION TO DISMISS AND IN OPPOSITION TO PLAINTIFF'S MOTION FOR TEMPORARY RESTRAINING ORDER AND/OR PRELIMINARY INJUNCTION

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Federal Cases

Federal Statutes

Federal Regulations

Other Authorities

*Authorities upon which we chiefly rely are marked with asterisks

With this suit, Amgen challenges a decision of the Food and Drug Administration ("FDA") denying Amgen a six-month period of pediatric exclusivity for its drug Sensipar after it failed to "fairly respond" to FDA's request that it conduct four pediatric studies of the drug. Amgen complains that FDA's rejection is based on the failure of one of the studies, when it successfully completed the other three. But Amgen glosses over the fact that the study it failed to complete was a critical safety study in the youngest, most vulnerable patients who will likely continue to be exposed to the drug without adequate information regarding its safe use. Amgen agreed to FDA's written request describing the four studies needed for pediatric exclusivity, never complaining that they were "near impossible" to complete until the moment it filed this complaint. Yet, despite FDA working with Amgen and accommodating it at every turn– amending the written request no fewer than five times to make the requirements of the studies less stringent or reduce their scope—Amgen nevertheless failed to "fairly respond" to FDA's request, by, among other things, terminating the key safety study after only four of the requested fifteen subjects had completed it.

Notwithstanding its own clear failure to produce the study results FDA requested (and which Amgen agreed to submit), Amgen has launched a two-pronged attack on FDA's pediatric exclusivity determination – challenging it both in this Court and via a request for administrative reconsideration in a bid to preserve its lucrative marketing monopoly for Sensipar and stave off generic competition for an additional six months. With its immediate motion, Amgen seeks a temporary restraining order to secure a court-ordered favorable pediatric exclusivity determination within the nine-month window prior to the expiration of Amgen's key patent— a prerequisite for pediatric exclusivity under the statute. Amgen thus asks this Court—prior to any decision on the merits—to reverse FDA's considered scientific judgment and force FDA to

accept Amgen's studies as satisfying the requirements for pediatric exclusivity. Not only has Amgen failed to establish any entitlement to relief, however, such a drastic measure is unnecessary because this Court could, in the unlikely event it decides to reverse FDA's determination, make that determination retroactive to the date of the original decision. The Court should therefore decline Amgen's unprecedented TRO request and dismiss its unripe complaint.

I. INTRODUCTION

Amgen's motion for injunctive relief fails for a number of reasons. First, as a threshold matter, Amgen's request is not ripe. Amgen has chosen to proceed simultaneously before this Court and the Agency, and has raised novel arguments and facts in both proceedings that FDA was not given the opportunity to consider when making its initial decision. As a result, the Agency is now in the untenable position of having to both reconsider the merits of its decision while simultaneously defending that decision before this Court, without the benefit of having considered Amgen's new arguments in the first instance. But parties may not seek judicial review of agency decisions while simultaneously asking for administrative reconsideration, and this Court should dismiss or stay this action to allow the Agency to first fully consider Amgen's new contentions.

Nor has Amgen met its burden to prove any of the four prongs necessary for the extraordinary injunctive relief it seeks. Amgen is not likely to succeed on the merits because its claim is not ripe; it must exhaust its administrative remedies now that it has chosen to initiate FDA's internal formal dispute resolution process over the Agency's decision. And even if Amgen could proceed before the Court and this Agency simultaneously, Amgen is unlikely to succeed on the merits of its challenge to the Agency's initial decision that it did not fairly

respond to the Agency's written request for pediatric studies. FDA's interpretation and implementation of the pediatric exclusivity provision, including its interpretation of an inherently ambiguous term, "fairly respond," as well as FDA's scientific determination, is entitled to the utmost deference. The Agency has the scientific expertise to weigh the results of the clinical studies and other evidence and draw conclusions about whether the standard for pediatric exclusivity has been met, which this Court is required to give deference. And the Agency's application of that expertise was entirely reasonable. Here, Amgen agreed that fifteen pediatric patients were to complete a pivotal safety study, yet only four patients actually did so, and only one of those four was exposed to the drug for the full duration of the study. Amgen then failed to provide meaningful, corroborative information that would have otherwise enabled it to meet the applicable standard. The Agency's conclusion that Amgen's studies do not "fairly respond" in these circumstances easily meets the deferential standard of review under the Administrative Procedure Act.

Amgen has also failed to demonstrate that it will suffer irreparable harm in the absence of extraordinary injunctive relief or that the balance of equities weighs in its favor. But the harm that Amgen asserts rests only on the ***possibility*** that a future FDA or court decision that is favorable to Amgen would not relate back to a date earlier than June 8, 2017, a circumstance which would be necessary to preserve the nine-month window prior to expiration of the patent to be extended required by the statute. *See* 21 U.S.C. § 355a(c)(2). But FDA is prepared to stipulate, or otherwise not oppose an order from this Court, that any decision in Amgen's favor would relate back to May 22, 2017, which is the date on which FDA initially determined Amgen's eligibility for pediatric exclusivity. Further, this Court has clear authority to relate a decision back in time. *See Ethyl Corp. v. Browner*, 67 F.3d 941, 945 (D.C. Cir. 1995). In these

circumstances, the possibility of harm absent the injunction that Amgen seeks is exceedingly small, if it exists at all, and clearly fails to meet the standard that irreparable harm be "likely" in *Winter v. NRDC, Inc.*, 555 U.S. 7, 22 (2008). Even if Amgen does not obtain pediatric exclusivity for this drug, such failure would not rise to the level of "irreparable harm" under the stringent standard in this Circuit, which requires a showing that the loss would threaten the existence of Amgen's broader, multi-billion dollar business.

Amgen also fails to show that the remaining factors warrant relief. The balance of the hardships weigh in the favor of the federal defendants. FDA and the integrity of its decisions and processes will be harmed should the temporary restraining order (TRO) be issued. Further, the public interest would not be served by the relief that Amgen seeks. To the contrary, the public has an interest in ensuring that FDA administers the pediatric exclusivity program such that it ensures applicants provide information of sufficient value in order to earn the six-month pediatric exclusivity (and thus delay possible market competition).

For all of these reasons, Amgen's complaint should be dismissed, and its motion for a temporary restraining order and/or a preliminary injunction should be denied.

II. STATUTORY AND REGULATORY BACKGROUND

A. New Drug Applications

Under the Federal Food, Drug, and Cosmetic Act ("FDCA"), pharmaceutical companies seeking to market the initial version of a drug (also known as the "innovator" or "pioneer" drug) must first obtain FDA approval by filing a new drug application ("NDA") containing extensive scientific data demonstrating the safety and effectiveness of the drug. 21 U.S.C. § 355(a), (b). An NDA applicant must also submit information on any patent that claims the drug, or a method of using the drug, for which a claim of patent infringement could reasonably be asserted against an unauthorized party. 21 U.S.C. § 355(b)(1), (c)(2). FDA publishes the patent information it receives in "Approved Drug Products with Therapeutic Equivalence Evaluations" (the "Orange Book", *available at* http://www.fda.gov/cder/ob/).

B. Abbreviated New Drug Applications

The Drug Price Competition and Patent Term Restoration Act of 1984 (known as the "Hatch-Waxman Amendments"), codified at 21 U.S.C. § 355 and 35 U.S.C. §§ 156, 271, and 282, permits, among other things, the submission of abbreviated new drug applications ("ANDAs") for approval of generic versions of approved drug products. 21 U.S.C. § 355(j). ANDA applicants need not submit clinical data (*i.e.*, from human clinical trials) to demonstrate the safety and efficacy of their product, as in an NDA. Rather, an ANDA relies on FDA's previous findings that the product approved under the NDA is safe and effective. Specifically, under 21 U.S.C. § 355(j), the Agency approves duplicates of "listed" drugs on the basis of chemistry and other data (including a demonstration of bioequivalence[1]) without evidence from literature or clinical data to establish effectiveness and safety.

[1] Two drugs are considered bioequivalent if, in general, the rate and extent of absorption of the generic drug do not show a significant difference from the rate and extent of absorption of the listed drug. 21 U.S.C. § 355(j)(8)(B).

C. Pediatric Exclusivity

Congress has provided for various periods of exclusivity— periods during which FDA may be prohibited from either accepting or approving certain drug applications. Often running concurrently with the protection traditionally offered by the patent system, exclusivity is an additional means by which pharmaceutical companies can delay competition. Though the several types of exclusivity vary by criteria for eligibility, length, scope, and type of application involved, they all share a common purpose: to provide incentives for certain types of research and/or drug development. *Compare*, *e.g.*, 21 U.S.C. § 355(c)(3)(E)(ii) (5-year new chemical entity exclusivity), to *id.* § 355(c)(3)(E)(iii)-(iv) (3-year exclusivity), to *id.* § 360cc (7-year orphan-drug exclusivity) to 42 U.S.C. § 262(k)(7) (12-year biological product exclusivity). At issue in this case is a unique exclusivity provision that extends all other existing exclusivity periods and every patent term that applies to all of the sponsor's drug products containing a particular active moiety[2], by six months. *See generally* 21 U.S.C. § 355a. Notably, the six month exclusivity period, if earned, is remarkably broad: it applies to all such patents and/or exclusivity periods for all of the sponsor's products containing the active moiety studied, regardless of whether they have any relationship to the pediatric disease or condition that the sponsor studied in order to qualify.

Congress provided this significant incentive to "address a longstanding concern that only 20 percent of prescription medications on the market have been tested and approved for use in children." S. Rep. 107-79 at 1 (2007); *see id.* at 2 ("Drug companies have studied several drugs in children and those drugs now carry appropriate pediatric labeling because of the FDAMA pediatric exclusivity provision."); *see also id.* at 4 ("FDA had granted 37 drugs pediatric

[2] An active moiety is "the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt . . . or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance. 21 C.F.R. 314.3(b).

exclusivity as of September 7, 2001. The results of the pediatric studies have provided new and useful information for use of these medicines in children, 19 of which have been relabeled to include pediatric information."). Congress put FDA in charge of determining the type and extent of the studies that would be needed to obtain pediatric exclusivity. The Agency generally asks for a full range of studies designed to provide meaningful information regarding use of the drug in all of the pediatric populations in which the drug is likely to be used. 21 U.S.C. § 355a(a) (defining "pediatric studies" as at least one clinical investigation "in pediatric age groups (including neonates in appropriate cases) in which it is anticipated to be used"); *id.* § 355a(c) (noting that, to be eligible for exclusivity, the studies must be "completed using appropriate formulations for each age group for which the study is requested").

Under this statutory regime, FDA first determines whether "information relating to the *use of an approved drug* in the pediatric population may *produce health benefits* in that population." *Id.* § 355a(c)(1) (emphasis supplied);[3] and then asks the sponsor in writing to "conduct pediatric studies" in order to elicit the information that would lead to health benefits for pediatric patients. *Id.* § 355a(d)(1). The written request (including any amendments) serves as an agreement against which the sponsor's eligibility for pediatric exclusivity is later measured. As such, a written request is required to be reviewed by FDA's internal pediatric review committee before issuance, *see id.* § 355a(f), and generally includes specific details regarding study design and endpoints, number of patients to be studied and study duration, among others. In order to qualify for pediatric exclusivity, the sponsor must agree to the Agency's request, *id.* §

[3] This provision embodies Congress's goal of encouraging research leading to health benefits in pediatric patients, rather than a generalized inquiry into the use of drugs in children that would not potentially provide any benefit for pediatric patients, even if a drug's sponsor may be willing and able to conduct such studies in return for a six month extension to exclusivity.

355a(d)(2)(A), conduct and submit the agreed-upon studies memorialized in the written request, and submit certain adverse event information relating to the use of the drug. *Id.* § 355a(d)(2)(B).

Finally, before a sponsor can qualify for pediatric exclusivity, FDA must review, and accept or reject the results of the pediatric studies. FDA will reject a sponsor's reports of its studies if they do not "fairly respond" to the Agency's written request, have not been conducted in accordance with scientific principles and protocols, or have not been reported in accordance with FDA's requirements for filing. *Id.* § 355a(d)(3).

D. Exception to Pediatric Exclusivity

The FDCA also provides that FDA "shall not extend" the applicable patent or exclusivity period with pediatric exclusivity "if the determination made under subsection (d)(3) is made later than nine months prior to the expiration of such period." 21 U.S.C. § 355a(c)(2).[4]

III. FACTUAL BACKGROUND

A. Amgen's Sensipar (cinacalcet hydrochloride injection)

FDA approved Sensipar in March 2004 for the treatment of secondary hyperparathyroidism in adult patients with chronic kidney disease (CKD) on dialysis, and for the treatment of hypercalcemia in adult patients with parathyroid carcinoma. Amgen has listed several patents for Sensipar, including one that will expire on March 8, 2018. FDA has publicly

[4] This temporal provision was introduced with other amendments with the Best Pharmaceuticals for Children Act of 2007. Its intent was to discourage sponsors from submitting studies close to the expiration of exclusivity or patent protection and obtaining *de facto* exclusivity during the period FDA spent making its pediatric exclusivity determination. Prior to amendment, the statute provided for up to a 90-day delay of approval of follow-on products if a sponsor submitted its pediatric study reports, but FDA had not determined eligibility for pediatric exclusivity at the time of patent or exclusivity expiry. Under the previous statutory language, generic approvals, and those of other follow-on competitors otherwise eligible for approval, were required to be delayed while the pediatric exclusivity determination was made. *See* 21 U.S.C. § 355a(e) (1997).

disclosed that four generic versions of cinacalcet have been "tentatively approved" and are awaiting the expiry of applicable patent(s) or exclusivity period(s).[5]

Sensipar appears to be a profitable drug: In the first quarter of 2017, its sales in the U.S. totaled $337 million, comprising roughly 6.4% of Amgen's total world-wide sales of $5,199 billion for that quarter. Amgen, Form 10Q at 26 (Q1 2017).[6] Since at least August 2008, Amgen has been challenging generic applicants who wish to market generic versions of cinacalcet.[7] *See, e.g.*, FDAnews, *Teva, Barr Challenge Sensipar Patents, Face Lawsuit*, August 6, 2008.[8]

B. FDA's written request for pediatric studies of cinacalcet

As required by the statute, FDA determined the type and extent of pediatric studies that would demonstrate that the use of cinacalcet would lead to health benefits for certain pediatric patients. FDA then issued a written request, dated May 5, 2010, that Amgen conduct such studies. FDA specified that the goal was to "investigate the potential use of cinacalcet hydrochloride in the treatment of secondary hyperparathyroidism (HPT) in pediatric patients with chronic kidney disease (CKD) receiving dialysis." Compl. Ex. 3 at 1 (ECF No. 1-4). The request specified that studies would be conducted to "obtain needed pediatric information on cinacalcet" and that, to do so, a placebo-controlled study was appropriate because "the benefit of cinacalcet hydrochloride has not been demonstrated for children." *Id.* at 2. To demonstrate such benefit, FDA requested, among other things, that Amgen conduct a 30-week randomized,

---

[5] *See* Drugs@FDA: FDA Approved Drug Products, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm (search and follow the link for "cinacalcet hydrochloride").
[6] Available at https://www.sec.gov/Archives/edgar/data/318154/000031815417000009/amgn-2017331x10q.htm.
[7] Indeed, Amgen has already developed and obtained approval for Parsabiv, a next-generation product which Amgen touts as being superior to Sensipar. *See* PR Newswire, *Study Results Published in the Journal of the American Medical Association Show Amgen's Parsabiv™ (Etelcalcetide) Significantly Reduced Serum Parathyroid Hormone in Adults With Secondary Hyperparathyroidism on Hemodialysis* (Jan. 10, 2017), *available at* http://www.prnewswire.com/news-releases/study-results-published-in-the-journal-of-the-american-medical-association-show-amgens-parsabiv-etelcalcetide-significantly-reduced-serum-parathyroid-hormone-in-adults-with-secondary-hyperparathyroidism-on-hemodialysis-300388962.html. Amgen has also not asserted that it will be unable to sustain the loss of six months of additional Sensipar monopoly pricing.
[8] Available at http://www.fdanews.com/articles/109195-teva-barr-challenge-sensipar-patents-face-lawsuit.

double-blind, placebo-controlled, safety and efficacy study followed by a 26-week open-label (i.e., not containing a placebo arm), safety extension in pediatric patients ages 28 days to < 17 years with chronic kidney disease and secondary hyperparathyroidism receiving dialysis. *Id.* This study was to enroll 100 patients, which the Agency made clear "describe[d] the minimum size of the trial." *Id.* at 7. FDA believed this was a reasonable, attainable enrollment goal given Amgen's estimate of 2,200 potentially eligible pediatric patients with chronic kidney disease requiring dialysis in the United States in 2007 alone. *Id.* at 1. Finally, the Agency stated that the goal of the written request was to, among other things, "demonstrate the efficacy of cinacalcet" and to "evaluate [its] long-term safety in pediatric patients." *Id.* at 3.

Amgen agreed to these terms and accepted the Written Request, which issued on May 5, 2010.

C. Amgen's conduct of studies and multiple requests to amend the written request

As Amgen later struggled to meet both the terms and the goals of the written request, FDA worked diligently with the company to revise it while still expecting sufficient enrollment to provide meaningful data. Among other things, FDA amended its written request five times. Each amendment accommodated Amgen's request for less stringent parameters or a reduced scope for its studies, and introduced more flexibility in the manner in which the requisite information could be obtained. The detailed history of FDA's interactions with Amgen is fully recounted in the Agency's decision letter. Compl. Ex. 2, at 3-5 (FDA, Correspondence rejecting Amgen's study reports). By the time Amgen submitted its data, FDA had, among other things, removed the younger patient population (28 days old to less than six years old) from the scope of the safety and efficacy study, and allowed extrapolation of efficacy for this group based on data from older patients (between six and eighteen years old). *Id.* at 6.

To characterize the risk of cinacalcet in that younger population, Amgen was asked to conduct a modest, open-label study that would last 26 weeks. (This study is referred to as Study 3.) FDA asked that a minimum of fifteen patients complete Study 3 in order to achieve the study's goal. *Id.* at 6. Amgen accepted this modification on December 14, 2010. *Id.* at 4. Amgen did not inform the Agency that it wanted to decrease the number of patients completing Study 3 down to four patients—approximately 27 percent of the number specified in the original request—until it asked for a sixth amendment to the written request on December 3, 2015, five years after it had agreed to fifteen patients. Indeed, the first time Amgen argued that fifteen patients completing this study would be "impossible," "practical[ly] impossib[le]," or "almost impossible" was in this litigation. *See* Pl.'s Mem. (ECF No. 3) at 8-9, 31-32. By contrast, between 2010 and 2015, Amgen asked for (and obtained FDA's approval of) several amendments to the written request, all of which resulted in a decrease in, among other things, the length or enrollment sizes of other studies, and in general made it easier for Amgen to meet the terms of the written request, *see* Compl. Ex. 2, at 6-7 (FDA, Correspondence rejecting Amgen's study reports).

On December 27, 2012, a 14-year old patient in one of the trials died. Amgen waited over a month to report this death to FDA, at which time FDA imposed a partial clinical hold. Amgen then waited another five months, until July 2013, to contact the Agency about pediatric exclusivity, but only to inquire whether it would qualify for pediatric exclusivity without any further pediatric studies. *Id.* at 4. FDA informed Amgen that the information it had thus far gathered would not suffice to qualify Amgen for pediatric exclusivity. *See* Compl. Ex. 1, at 6 (Type A Meeting Minutes from September 4 2013) ("FDA does not agree to make any labeling revisions [for cinacalcet] with the current data."); *see also id.* at 7 ("FDA stated that they did not

believe that the sponsor's current program was sufficient to inform the public on the safe use of cinacalcet in the pediatric renal dialysis population and as such would not be adequate to support a Written Request.") The minutes of the September 4, 2013, meeting also show that, after FDA informed Amgen that the data available at that time would not qualify for pediatric exclusivity, "Amgen agreed to proceed in a collaborative manner." *Id.* at 6.

In 2015, five years after starting Study 3, Amgen realized that it had failed to recruit a sufficient number of patients and that it would fall far short of the modified goal it agreed to in 2010. Facing an approaching deadline in the form of the expiry date of its key patent on March 8, 2018, rather than completing the study so that it could generate meaningful data that would lead to health benefits for pediatric patients, Amgen instead asked FDA to agree to reduce the required number of patients that would compete the study by 73% (four instead of fifteen). *See* Compl. Ex. 2, at 8 (FDA, Correspondence rejecting Amgen's study reports) (five out of the nine subjects who failed to complete the study did so due to study closure in June 2016). FDA was skeptical that it could both accommodate Amgen's sixth request and fulfill the goal of pediatric exclusivity—to obtain studies that provide useful information about the use of the drug in all relevant pediatric subpopulations. Specifically, when presented with a request that it agree that data from four patients (rather than fifteen) would be sufficient to meet the goals of the study, the Agency disagreed, and denied Amgen's request on December 24, 2015. FDA also denied Amgen's December 3, 2015, request to meet regarding their Amgen's submission of its study reports (which was planned for November 2016) as premature, and asked Amgen to "resubmit the meeting request once [Amgen is] closer to submitting the [reports]." Compl. Ex. 13 (FDA, Type C Meeting Denial, December 24, 2015). That meeting took place on September 21, 2016. Compl. Ex. 2, at 5 (FDA, Correspondence rejecting Amgen's study).

D. Amgen's untimely request for formal dispute resolution

Amgen submitted its reports in a supplemental NDA on November 23, 2016. On May 5, 2017, before the expiry of the statutory 180-day period, *see* 21 U.S.C. § 355a(d)(3), and before FDA had completed its analysis of Amgen's clinical study data and determined whether such data "fairly responded" to the written request, Amgen submitted a request for formal dispute resolution, ostensibly to "preserve [its] ability to lodge an appeal of a pending [pediatric exclusivity] decision." Compl. Ex. 10, at 1 (Formal Dispute Resolution Request). Despite frequent communication with the Agency, and FDA's refusal to amend the written request on December 24, 2015, Amgen claimed that it had only recently become aware that FDA may not "view Amgen's studies favorably" on May 1, 2017, *id.* at 8. Citing "extraordinary circumstances," it initiated a formal dispute under FDA's procedures and asked the Agency to "independently assess" whether Amgen would qualify for pediatric exclusivity, even though the scientific reviewers who evaluated the application and the Agency experts who decide pediatric exclusivity issues (the Pediatric Exclusivity Board) had not yet rendered a decision. *Id.* at 9. Because FDA cannot reconsider or otherwise conduct formal dispute resolution for a decision that has not yet been made, FDA rejected Amgen's request on May 19, 2017, and advised the company that it could submit a request for reconsideration after it had received a decision on pediatric exclusivity if it decided to contest that decision. Compl. Ex. 16 (FDA, Dispute Not Accepted Letter).

E. FDA's decision to reject Amgen's studies

Consistent with 21 U.S.C. § 355a(d)(3), FDA evaluated Amgen's study reports to determine whether they were sufficient under the statute, and responded within the 180-day statutory timeframe. On May 22, 2017, FDA sent Amgen a letter decision, explaining its

interpretation of the applicable statutory standard, and its reasoning and rationale underlying its decision to deny exclusivity. FDA described the scientific bases for the Agency's conclusion, made after considering the entirety of Amgen's submissions and the written request as a whole, that Amgen had failed to "fairly respond" to the written request. FDA reiterated that the goals of Study 3 had been to "evaluate the safety and tolerability of cinacalcet in pediatric patients ages 28 days to < 6 years of age when used chronically as intended in patients undergoing dialysis, and to characterize the cinacalcet PK profile in these pediatric patients," and that it "was designed to provide safety information during both cinacalcet titration and at stable effective doses" because "safety data for a minimum of 15 patients completing 26 weeks was considered by FDA to be a critical amount of information required to determine whether the product is safe in young pediatric patients for chronic use." Compl. Ex. 2, at 7-8 (FDA, Correspondence rejecting Amgen's study reports). The Agency noted that, even after it had agreed to modify the written request to remove the younger pediatric population from the larger safety and efficacy trial, and accepted that Amgen could extrapolate efficacy to the younger population, Amgen still was unable to meet the smaller number of patients that had been specified in the written request for Study 3. Moreover, the data Amgen generated were also insufficient both qualitatively and quantitatively, even when considered along with Amgen's submission as a whole, including information Amgen had provided in an *ad hoc* manner to address the acknowledged deficiencies with the data from Study 3. *See id.* at 8-10. ("Amgen's failure to provide sufficient safety data in the 28 day to < 6 year old age group prevents FDA from drawing any conclusions about the safety of the product in patients < 6 years of age when used as intended.").

FDA explained that its conclusion was not based solely on Study 3's shortcomings. Specifically, the Agency noted that "[i]f the totality of safety information Amgen submitted had

provided an appropriate safety assessment in younger children and supported a label description—even if the exact minimum number of patients had not been met in Study 3—this element of the [written request] could have been adequately satisfied and Amgen's response could be considered a fair response to the [written request] as a whole." *Id.* at 10. Because Amgen had failed to provide "sufficient safety data for pediatric patients < 6 years of age . . . to clearly establish the safety profile of the drug for pediatric patients in accordance with the objectives of the amended written request," FDA concluded that Amgen had failed to fairly respond to the written request. Simply put, both the numbers of enrollees who completed the study and the nature and quantity of additional scientific data provided by Amgen were insufficient to formulate an adequate safety profile for the intended chronic use of cinacalcet in the youngest pediatric patients.

F. Current Litigation and Request for Formal Dispute Resolution

Amgen sued FDA on May 25, 2017, seeking a temporary restraining order and/or a preliminary injunction to compel FDA to accept its study reports and extend pediatric exclusivity to cinacalcet. Pl.'s Mot, ECF No. 3. Amgen argues that this extraordinary relief is necessary to preserve the status quo, so that, in the event that FDA decides in its favor on reconsideration or it obtains a favorable decision from this Court, that exclusivity will not be barred by operation of the nine-month exception in 21 U.S.C. § 355a(c)(2). That is, because FDA has insufficient time remaining to resolve the internal dispute resolution process by June 8, 2017, Amgen feared that it would lose its pediatric exclusivity.

Also on May 25, 2017, Amgen submitted an administrative request for formal dispute resolution that raised new arguments about other pediatric exclusivity decisions that FDA has made for different drugs. FDA has issued draft guidance regarding its formal dispute resolution

process and sets a 30-day timeframe to complete that process.[9] However, sponsors should generally first submit a request for reconsideration by the original decisionmaker before seeking a request for formal dispute resolution at the supervisory level. *Id.* at 5. On May 30, 2017, Amgen declined the agency's request to convert its request for formal dispute resolution to the one for reconsideration. FDA is currently considering whether it will accept Amgen's request for formal dispute resolution in view of Amgen's disregard for the Agency's process and simultaneous request for judicial review, and expects to reach a decision in the very near future.

IV. ARGUMENT

A. Plaintiff's Case Should Be Dismissed for Lack of Finality, Ripeness, and Failure to Exhaust

1. The Agency's Decision Is Not Final

It is well-established that a party may not seek judicial review of an agency decision while simultaneously asking the agency to reconsider its decision because a "request for administrative reconsideration renders an agency's otherwise final action non-final with respect to the requesting party." *Clifton Power Corp. v. FERC*, 294 F.3d 108, 110 (D.C. Cir. 2002); *City of New Orleans v. SEC*, 137 F.3d 638, 639 (D.C. Cir. 1998); *TeleSTAR, Inc. v. FCC*, 888 F.2d 132, 134 (D.C. Cir. 1989) ("filing of a challenge to agency action before the agency has issued its decision on reconsideration is incurably premature" so that "when a petition for review is filed before the challenged action is final and thus ripe for review, subsequent action by the agency on a motion for reconsideration does not ripen the petition for review or secure appellate jurisdiction"); *see also In ICC v. Brotherhood of Locomotive Engineers*, 482 U.S. 270, 284-85 (1987) (noting that, while 5 U.S.C. § 704 might "relieve parties from the requirement of

[9] *See* https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM343101.pdf, at 3-4.

petitioning for rehearing before seeking judicial review," it does not "prevent petitions for reconsideration that are actually filed from rendering the orders under reconsideration non-final"); *Stone v. INS*, 514 U.S. 386, 392 (1995) (holding that under the APA, the "timely filing of a motion to reconsider renders the underlying order non-final for purposes of judicial review"); *King v. Leavitt*, 475 F. Supp. 2d 67, 71 (D.D.C. 2007) (dismissing complaint against FDA, and denying motion for a preliminary injunction, because plaintiffs had effectively filed a petition for reconsideration while simultaneously filing court action).

Here, Amgen filed a motion for a temporary restraining order challenging the agency's decision on the same day that it filed a request for formal dispute resolution of that very decision. If FDA accepts this request for administrative review, FDA's initial decision will be rendered nonfinal and not reviewable under the APA. *Stone*, 514 U.S. at 392; *King*, 475 F. Supp. 2d at 71.

2. Amgen's Claims Are Not Ripe

In addition, Amgen's claims on the merits are not ripe. "[I]injunctive and declaratory judgment remedies are discretionary, and courts traditionally have been reluctant to apply them to administrative determinations unless these arise in the context of a controversy 'ripe' for judicial resolution." *Abbott Laboratories v. Gardner*, 387 U.S. 136, 148 (1967). The purpose of this doctrine is "to prevent the courts, through avoidance of premature adjudication, from entangling themselves in abstract disagreements over administrative policies, and also to protect the agencies from judicial interference until an administrative decision has been formalized and its effects felt in a concrete way by the challenging parties." *Id.* at 148-49. The ripeness doctrine is rooted in both Article III limitations on judicial power and prudential reasons for declining to exercise jurisdiction. *Reno v. Catholic Soc. Servs., Inc.*, 509 U.S. 43, 58 n.18 (1993).

To determine whether an agency decision is ripe for review, courts examine "both the fitness of the issues for judicial decision and the hardship to the parties of withholding court

consideration." *Abbott Labs.*, 387 U.S. at 149. In evaluating the fitness of an issue for judicial review, courts should consider whether the issue is "purely legal" and whether the agency action is final, *id.*, or, on the other hand, whether "the courts would benefit from further factual development of the issues presented." *Ohio Forestry Ass'n v. Sierra Club*, 523 U.S. 726, 733 (1998). With respect to the hardship factor, there must be a "sufficiently direct and immediate" impact on the plaintiff's "day-to-day business," such that the plaintiff faces the dilemma of either complying with the challenged agency action or risking prosecution for failure to do so. *Abbott Labs.*, 387 U.S. at 152. A court must also consider "whether judicial intervention would inappropriately interfere with further administrative action." *Ohio Forestry Ass'n*, 523 U.S. at 733. Finally, "[a] claim is not ripe for adjudication if it rests upon contingent future events that may not occur as anticipated, or indeed may not occur at all." *Texas v. United States*, 523 U.S. 296, 300 (1998) (internal quotation and citation omitted).

Here, Amgen's claims fail both factors. First, they are not "fit" for review because Amgen's claim that FDA should have found that Amgen's studies "fairly respond" to the written request is necessarily fact-specific, and depends on the nature of the written request and the studies. Although Amgen claims that this is a legal determination, Pl.'s Mem. at 21, FDA must evaluate the factual information in those studies to determine if they fairly respond. *See* Section IV.B.1.g, *infra*. Moreover, Amgen has raised new arguments based on new facts about other drugs in both the dispute resolution and this lawsuit. Pl.'s Mem. at 26-30; Compl. Ex. B[10], at 14-15. FDA should have the opportunity to consider these arguments in the first instance before being required to defend its initial decision in this Court. Thus, FDA's decision is factual, not "purely legal," and is not fit for review.

[10] FDA intends to file the May 25, 2017 request for dispute resolution (Ex. B) with this Court after it has heard from Amgen about whether it has confidentiality concerns about that document.

With respect to the second prong of the ripeness test, the only immediate hardship that Amgen asserts is the mere possibility that the date of any favorable decision would not relate back to the date of FDA's May 22, 2017, decision, and that the nine-month exception to pediatric exclusivity would thereby bar Amgen from receiving such exclusivity. Pl.'s Mem. at 34. But this Court has clear authority to order the date of any favorable decision to relate back to May 22, 2017, and FDA would not oppose such an order. *See* Section IV.B.2, *infra*. Thus, Amgen's hardship claim evaporates and it becomes clear that its claim is not ripe.

3. Amgen Has Failed to Exhaust its Administrative Remedies

Amgen's claims can similarly be dismissed for failure to exhaust its administrative remedies. *See Bowen v. New York*, 476 U.S. 467, 484 (1986); *Ass'n of Flight Attendants-CWA v. Chao*, 493 F.3d 155, 160 (D.C. Cir. 2007). Although Amgen was not required to file a request for formal dispute resolution, because it did so, it must now await completion of FDA's process (assuming FDA accepts this request). *See ICC v. Brotherhood of Locomotive Engineers*, 482 U.S. at 284-85. Amgen argues that it has already exhausted its administrative remedies because it would be futile to get the agency decision it thinks it needs before June 8, 2017. Pl.'s Mem. at 39. But that futility argument lacks merit because this Court has the authority to relate back a favorable decision to the date of FDA's original decision. *See* section IV.B.2, *infra*.

Amgen has made new arguments about different drugs in its request for dispute resolution. *See* Pl.'s Mem. at 26-30; Compl. Ex. B, at 14-15. The agency should have the opportunity to address those arguments in the first instance. *See Parisi v. Davidson*, 405 U.S. 34, 37 (1972) ("The basic purpose of the exhaustion doctrine is to allow an administrative agency to perform functions within its special competence – to make a factual record, to apply its expertise, and to correct its own errors so as to moot judicial controversies."). Amgen even appears to agree and understands that its administrative appeal should proceed; it has asked for a TRO ordering the

agency to accept the study reports pending either a favorable decision in that administrative appeal, or further order from this Court. Pl.'s Mem. at 41.

In these circumstances, Amgen's claims are subject to dismissal for failure to exhaust.

B. Amgen Fails to Establish Any of the Factors Necessary for a TRO

Preliminary injunctive relief is an "extraordinary and drastic" remedy that "may only be awarded upon a clear showing that the plaintiff is entitled to such relief." *Munaf v. Geren*, 553 U.S. 674, 689-90 (2008); *see also Winter*, 555 U.S. at 22; *Mpoy v. Fenty*, 674 F. Supp. 2d 163, 165 (D.D.C. 2009) ("Injunctive relief is an extraordinary remedy, and plaintiff bears a substantial burden to obtain it."). To obtain a preliminary injunction, a party must establish that: (1) it is likely to succeed on the merits; (2) it is likely to suffer irreparable harm in the absence of preliminary relief; (3) the balance of equities tips in its favor; and (4) an injunction would serve the public interest. *Winter*, 555 U.S. at 20.

It is "particularly important" for a movant to demonstrate likely success on the merits. *Astellas Pharma U.S., Inc. v. FDA*, 642 F. Supp. 2d, 10, 16 (D.D.C. 2009) ("[A]bsent a 'substantial indication' of likely success on the merits, 'there would be no justification for the court's intrusion into the ordinary processes of administration and judicial review.'"). Moreover, a party seeking preliminary injunctive relief must demonstrate an actual "likelihood" of success on the merits, not merely the existence of "questions 'so serious, substantial, difficult and doubtful, as to make them fair ground for litigation . . . .'" *Munaf*, 553 U.S. at 690 (citations omitted). Nor is a mere "possibility" of irreparable harm sufficient to justify such relief:

> Our frequently reiterated standard requires plaintiffs seeking preliminary relief to demonstrate that irreparable injury is *likely* in the absence of an injunction. . . . Issuing a preliminary injunction based only on a possibility of irreparable harm is inconsistent with our characterization of injunctive relief as an extraordinary remedy that may only be awarded upon a clear showing that the plaintiff is entitled to such relief.

Winter, 555 U.S. at 22 (citations omitted, emphasis in original).

1. Amgen Has No Likelihood of Success on the Merits

a. Amgen Cannot Succeed Challenging The Merits Of An Unripe Claim

For all of the reasons described above, if FDA undertakes administrative review of Amgen's request for dispute resolution, Amgen's claims should be dismissed for lack of final agency action and ripeness, as well as failure to exhaust administrative remedies. . *See AstraZeneca Pharm. v. FDA*, 850 F. Supp. 2d 230, 249-50 (D.D.C. 2012) (denying motion for preliminary injunction and dismissing plaintiff's claims as unripe without prejudice). Alternatively, FDA would not object to this Court retaining jurisdiction and staying this case so that, if FDA were to decide in Amgen's favor upon administrative review, this Court could order the date of that decision to relate back to a date earlier than June 8, 2017. *Cf. Hi-Tech Pharmacal Co. v. FDA*, 587 F. Supp. 2d 1, 13 (D.D.C. 2008) (denying plaintiff's motion for preliminary injunction for lack of final agency action, but retaining jurisdiction when agency exclusivity decision was forthcoming).

b. FDA's Scientific Decisions Are Entitled to Substantial Deference

FDA's administrative decisions are subject to review under the Administrative Procedure Act ("APA"), and may be disturbed only if "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). This standard is highly deferential to the agency. *Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402, 416 (1971). The agency's administrative decision is entitled to a presumption of validity. *Fla. Power & Light Co. v. Lorion*, 470 U.S. 729, 743 (1985); *Camp v. Pitts*, 411 U.S. 138, 142 (1973). The reviewing court must consider whether the agency's decision was based upon consideration of the relevant factors and whether there has been a clear error of judgment.

Overton Park, 401 U.S. at 416. However, a reviewing court is "not empowered to substitute its judgment for that of the agency," *id.,* and must uphold the agency's action so long as it is "rational, based on consideration of the relevant factors, and within the scope of the authority delegated to the agency by statute." *Motor Vehicle Mfrs. Ass'n of the United States, Inc., v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 42 (1983). In applying the arbitrary and capricious standard, the court reviews the administrative record assembled by the agency and does not undertake its own fact finding. *See, e.g., Camp,* 411 U.S. at 142.

When, as here, an agency's decision is based on evaluation of scientific information within the agency's area of technical expertise, its decisions are traditionally accorded great deference. *See Weinberger v. Bentex Pharms., Inc.*, 412 U.S. 645, 653-54 (1973) (The FDA is "peculiarly suited" to evaluate conflicting scientific reports, a matter "not . . . well left to a court without chemical or medical background," because it "necessarily implicates complex chemical and pharmacological considerations."). Courts "review scientific judgments of the agency 'not as the chemist, biologist, or statistician that [they] are qualified neither by training nor experience to be, but as a reviewing court exercising [its] narrowly defined duty of holding agencies to certain minimal standards of rationality.'" *Troy Corp. v. Browner*, 120 F.3d 277, 283 (D.C. Cir. 1997) (*quoting Ethyl Corp. v. EPA*, 541 F.2d 1, 36 (D.C. Cir. 1976)); *see also Int'l Fabricare Inst. v. EPA*, 972 F.2d 384, 389 (D.C. Cir. 1992) ("The rationale for deference is particularly strong when [the agency] is evaluating scientific data within its technical expertise."); *Sw. Pa. Growth Alliance v. Browner,* 121 F.3d 106, 117 (3d Cir. 1997); *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp. 212, 216 (D.D.C., 1996) (*citing Federal Power Comm'n v. Fla. Power & Light Co.*, 404 U.S. 453, 463 (1972)).

Such deference has repeatedly been applied in cases under the FDCA. *See, e.g., Serono Labs v. Shalala*, 158 F.3d 1313, 1320 (D.C. Cir 1998) (FDA's determination of "sameness" rests on agency's evaluation of scientific data within its area of expertise and is entitled to high level of deference from court); *Henley v. FDA*, 77 F.3d 616, 621 (2d Cir. 1996) ("FDA possesses the requisite know-how to conduct such [scientific] analyses, by sifting through the scientific evidence to determine the most accurate and up-to-date information regarding a particular drug . . . . We therefore defer to its reasonable findings."); *Schering Corp. v. FDA*, 51 F.3d 390, 399 (3d Cir. 1995) (FDA's "judgments as to what is required to ascertain the safety and efficacy of drugs fall squarely within the ambit of the FDA's expertise and merit deference from us."); *Tri-Bio Laboratories, Inc. v. United States*, 836 F.2d 135, 142 (3d Cir. 1987) ("in evaluating scientific evidence in the drug field, the FDA possesses an expertise entitled to respectful consideration by this court"); *Astellas*, 642 F. Supp. 2d at 19-20 ("high level of deference" must be afforded to FDA in choosing methodologies to test bioequivalence of a drug).

c. FDA's Statutory and Regulatory Interpretations Receive Deference

In reviewing FDA's construction of the FDCA, the Court is governed by the two-step analysis of *Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837 (1984). *See, e.g., Novartis Pharms. Corp. v. Leavitt*, 435 F.3d 344, 349 (D.C. Cir. 2006) ("We have held on a number of occasions that FDA interpretations of the FDCA receive deference . . ."); *Mylan Laboratories, Inc. v. Thompson*, 389 F.3d 1272, 1280 (D.C. Cir. 2004). The first question under *Chevron* is "whether Congress has directly spoken to the precise question at issue." *Id.* at 842. If, after this Court "exhaust[s] the 'traditional tools of statutory construction,'" *Natural Res. Def. Council, Inc. v. Browner*, 57 F.3d 1122, 1125 (D.C. Cir. 1995) (quoting *Chevron*, 467 U.S. 837, 843 n. 9), the intent of Congress is clear, "that is the end of the matter." *Chevron*, 467 U.S. 837,

842. Put another way, the Court must initially decide "whether the statute unambiguously forbids the Agency's interpretation." *Barnhart v. Walton*, 535 U.S. 212, 218 (2002).

If, however, the statute "is silent or ambiguous with respect to the specific issue," the Court proceeds to the second prong of *Chevron*, under which "the question for the court is whether the agency's answer is based on a permissible construction of the statute." *Chevron*, 467 U.S. at 843. *See generally County of Los Angeles v. Shalala*, 192 F.3d 1005, 1012-13 (D.C. Cir. 1999). The D.C. Circuit has held that deference to FDA's application of the FDCA is particularly appropriate because of "the complexity of the statutory regime" and "FDA's expertise." *Mylan v. Thompson*, 389 F.3d at 1280.

d. FDA has properly interpreted an ambiguous statutory provision

Amgen's contention that the Agency's interpretation must fail at *Chevron* step one lacks any merit. The applicable statutory provision, 21 U.S.C. § 355a(d)(3), provides:

> (3) Meeting the studies requirement. Not later than 180 days after the submission of the reports of the studies, the Secretary shall accept or reject such reports and so notify the sponsor or holder. The Secretary's only responsibility in accepting or rejecting the reports shall be to determine, within the 180-day period, whether the studies ***fairly respond*** to the written request, have been conducted in accordance with commonly accepted scientific principles and protocols, and have been reported in accordance with the requirements of the Secretary for filing (emphasis added).

The term "fairly" is inherently ambiguous. *See, e.g.*, *Grand Canyon Air Tour Coal. v. F.A.A.*, 154 F.3d 455, 467 (D.C. Cir. 1998) (the term "substantial" is inherently ambiguous), *Cablevision Sys. Corp. v. F.C.C.*, 649 F.3d 695, 722–23 (D.C. Cir. 2011) (the term "unfair" is inherently ambiguous). Rather than provide definite criteria for FDA to assess whether to accept or reject studies, Congress did not speak directly to the precise issue, and left considerable discretion to FDA to determine whether studies are "fairly" responsive. Thus, the intent of Congress is clear only to the extent that Congress left this evaluation to FDA. Nor does Amgen

even seriously propose a plain meaning for "fairly respond," other than its apparent belief that any amount of "quid" should result in the same substantive "quo" of exclusivity.

Amgen's plain meaning argument boils down to the assertion that "fairly respond" concerns a purely legal, not scientific judgment. *See* Pl.'s Mem. at 21 (asserting that "'fairly respond' reflect[s] a purely legal judgment as to which FDA has no expertise"). If Amgen's argument were to be accepted, the standard for obtaining pediatric exclusivity becomes: 1) sponsor attempts to conduct pediatric studies according to the written request, 2) sponsor fails, 3) sponsor submits whatever data is available to FDA, resulting in 4) automatic delay in generic competition for an additional six months. Under this view, the written request is merely a formality and any quantity of information that the sponsor submits will suffice to qualify the sponsor to maintain a monopoly by delaying generic competition for an additional six months. Thus, Congress's requirement that the information be submitted to FDA in the first place would be rendered meaningless, as would the requirement that FDA's internal review committee review the written request before it is issued. Thus, in addition to rendering FDA's role to a clerical one, merely accepting whatever data a sponsor chose to submit, no matter how erroneous or insubstantive, Amgen's "plain meaning" interpretation also violates the maxim that "a statute must, if possible, be construed in such fashion that every word has operative effect." *See, e.g., Landgraf v. USI Film Prod.*, 511 U.S. 244, 295 (1994).

Because the phrase "fairly respond" is ambiguous, FDA has the delegated authority to interpret and apply that standard. That interpretation is entitled to judicial deference under *Chevron* step two. When Congress has not directly addressed the issue or has done so ambiguously, the Court may not "simply impose its own construction on the statute," but rather must determine whether the agency's construction is based on a permissible interpretation of the

statute. *See Chevron*, 467 U.S. 843; *id.* at 843-44 & n.11 (in case of ambiguity, the court must uphold the agency's interpretation if construction is permissible under the statute; a court need not conclude that agency construction was the only one it permissibly could have adopted or even the reading the court would have reached); *see also Barnhart*, 535 U.S. 212, 218 (reviewing court must decide: (1) whether the statute unambiguously forbids agency interpretation, and (2) whether the agency interpretation exceeds the bounds of the permissible).

As its May 22, 2017 letter decision explains, FDA interprets the phrase "fairly respond" in the context of the pediatric exclusivity provision as a whole and in light of the objectives of the statute and its legislative history. *See* Compl. Ex. 2, at 1-3 (FDA's Correspondence Rejecting Amgen's Study Reports). The statute makes clear that its purpose is to generate clinical information on the use of drug products in children that will result in a health benefit to pediatric populations. *See* 21 U.S.C. § 355a(c)(1) ("If the Secretary determines that information relating to the *use of an approved drug* in the pediatric population *may produce health benefits* in that population," the Agency initiates the process that can potentially result in pediatric exclusivity by sending a written request to the sponsor of the drug) (emphasis supplied). In light of the breadth and value of the benefit at stake (and the potential costs to third party payors and the public due to delayed access to generic alternatives) FDA's interpretation aims to ensure that the carrot of "exclusivity" results in studies that will meaningfully benefit the public health. Accordingly, FDA carefully crafts its written requests to elicit the information that is most likely to lead to health benefits for all relevant pediatric populations. As FDA has explained:

> In determining the scope of a [written request], FDA asks: (1) Is there a health benefit to studying this drug for the proposed indication in the pediatric population; (2) In what age groups in the pediatric population does this indication occur; (3) What information does the Agency currently have regarding use of this drug for this condition in relevant pediatric age groups; and (4) What studies are necessary to fill in the gaps in pediatric information in the Agency's possession

> and to fully label drug products containing the active moiety for relevant pediatric populations?
>
> Compl. Ex. 2, at 1 (FDA's Correspondence Rejecting Amgen's Study Reports)

The Agency's expertise and its experience with pediatric studies indicate that health benefits are most likely accrue "when the information that a physician needs to properly prescribe a medication is described in the product's labeling." *Id.* at 2. The legislative history confirms the validity of this approach. Congress has explained that one of its goals for the pediatric exclusivity provision is to incorporate pediatric use information into drug labeling. For example, the report accompanying subsequent legislative amendments to the pediatric exclusivity provision explains that before Congress enacted that provision, "regulatory efforts to address the lack of pediatric studies and *insufficient labeling information* had been largely unsuccessful. . . . Neither of [FDA's] 1994 initiatives increased substantially the number of drugs with *adequate pediatric labeling*." S. REP. 107-79, 3 (2001) (emphasis supplied). Congress noted that pediatric exclusivity had "provided new and useful information for use of these medicines in children, 19 of which have been *relabeled to include pediatric information*." *Id.* at 4. The same report also cited FDA's 2001 Status Report to Congress for the proposition that "[a]s a result of the pediatric exclusivity provision . . . critical drugs used to treat a variety of conditions (e.g., gastro intestinal reflux disease, diabetes mellitus, pain, asthma, hypertension) have or soon will have pediatric use information in their labeling." *Id.* Accordingly, when FDA evaluates the information that the sponsor submits in response to the written request to determine whether the sponsor has "fairly respond[ed]" to the written request, the Agency engages in a multifactorial analysis that aims to determine whether the sponsor met the terms and/or met the objectives of the written request. *See id.* at 2-3. ("Ultimately, the Board considers a "fair response" to the [written request] to be one that responds to the specific elements in the [written

request] in light of the objective stated in the [written request] and the overall purpose of the [pediatric exclusivity provisions of the FDCA].").

Amgen contends that the Agency applies a "perfect compliance" standard because it interprets "fairly respond" to mean "comply to the letter." Pl.'s Mem. at 16, 18. But that is an exceptionally narrow representation of the Agency's standard, intended to prop up its "plain meaning" argument. It is true that, had Amgen complied with all the terms of the Agency's written request, it may well have been eligible for pediatric exclusivity. This makes sense: Since FDA determines the type, nature and extent of the studies that a sponsor should conduct, and formally makes a request specifying those parameters in writing, a sponsor meeting the terms of the written request exactly can be said to have "fairly responded" to it. But the Agency's interpretation of what it means to "fairly respond" to the written request is more expansive than just compliance with the terms of the written request; under the Agency's interpretation, a sponsor who has not complied with the exact terms of a written request may still be considered to have "fairly responded" to it if the information the sponsor has provided is "likely to generate information that will provide a health benefit (including meaningful pediatric labeling) in the relevant populations that the [written request] asked the sponsor to study." Compl. Ex. 2, at 3 (FDA's Correspondence Rejecting Amgen's Study Reports).

Amgen also asserts that "fairly respond" also does not mean "fully respond," or "completely respond," or "substantially respond." *Id.* These contentions are not consistent with the dictionary meaning of "fairly," which is "to a full degree or extent."[11] More importantly, however, they are also not availing in light of the actual standard that the Agency has spelled out. Compl. Ex. 2, at 1-3 (FDA's Correspondence Rejecting Amgen's Study Reports). FDA has

[11] The Merriam-Webster Dictionary, *available at* https://www.merriam-webster.com/dictionary/fairly.

explained that, in the absence of compliance with the terms of the written request (to which the sponsor has previously agreed), a sponsor will nevertheless be considered to have "fairly responded" (and be eligible for pediatric exclusivity), if the studies' results are "interpretable," or "will provide information that otherwise yields a health benefit for pediatric populations." Compl. Ex. 2, at 2 (FDA's Correspondence Rejecting Amgen's Study Reports)

Although it professes surprise throughout its pleadings, Amgen appears to have been aware of the Agency's interpretation. For example, the basis for Amgen's untimely dispute resolution request on May 9, 2017, was apparently "unanticipated statements by [FDA] regarding pediatric labeling." Compl. Ex. 10, at 2 (Formal Dispute Resolution Request). Simply put, Amgen surmised, during labeling negotiations which generally precede an FDA action on a pending application, that the Division would determine that Amgen's studies would not lead to pediatric labeling describing how to safely and effectively use the drug in relevant pediatric populations. Since it knew it had also not met the terms of the written request, in the absence of such useful labeling, Amgen understood that it was likely that Amgen would not receive pediatric exclusivity.

Amgen is not happy with the result because it undermines its efforts to delay competition from generic versions of Sensipar. That does not mean that this Court should accept Amgen's invitation to second guess FDA's scientific determination regarding the sufficiency of Amgen's studies with respect to a health benefit for pediatric patients.

e. FDA may evaluate the sufficiency of safety data to determine eligibility for pediatric exclusivity

Amgen latches onto an unrelated provision requiring certain labeling changes when pediatric studies are conducted to buttress its assertion that FDA may not evaluate the scientific

sufficiency of studies a sponsor conducts in response to a written request. See Pl.'s Mem. at 23-25. As with Amgen's "plain meaning" argument, this, too, lacks merit.

The FDCA provides that, if FDA determines that a pediatric study demonstrates, or fails to demonstrate, the safety or efficacy of a drug in pediatric populations, such determination shall be included in that drug's labeling, even if the study results are "inconclusive." *See* 21 U.S.C. § 355a(j). This provision cannot be interpreted to limit the ability of FDA to evaluate whether clinical studies conducted pursuant to a written request "fairly respond" to such request. This provision was added to the statute in 2007, ten years after the Agency started applying the "fairly respond" standard. If Congress meant to limit the scope of the "fairly respond" standard, not only would it do so directly, but it would have made such clarification when it amended this section before 2007.[12] *See United States v. Rutherford*, 442 U.S. 544, 554 n.10 (1979) ("[O]nce an agency's statutory construction has been fully brought to the attention of the public and the Congress, and the latter has not sought to alter that interpretation although it has amended the statute in other respects, then presumably the legislative intent has been correctly discerned."). Given that background, Amgen's assertion that the new provision was meant to "categorically" prevent the Agency from assessing the substance of the pediatric studies is meritless.

Section 355a(j) is best understood as addressing a separate concern: that results of certain studies, particularly those that had failed, were not being disseminated. With this provision, Congress established a very low bar for determining when information from pediatric studies would be added to product labeling, to facilitate the incorporation of information from all studies

[12] Moreover, at the time of the 2007 Amendments, Congress recognized that pediatric exclusivity had led to multiple important labeling changes. As one of the co-sponsors of the original legislation noted, pediatric exclusivity had caused the incorporation of "[u]seful new pediatric information [into] product labeling for more than 119 drugs." 153 Cong Rec S11837 (2007) (Remarks of Senator Dodd). In praising the legislation's success over the last ten years, Senator Dodd emphasized that it had "[led] to approximately 120 pediatric label changes." *Id.* at S11838. Senator Alexander echoed the same sentiment: "By extending drug patents in exchange for additional research on how these drugs affect children, this program has prompted studies on 144 products and led to 122 label changes on some of the most frequently prescribed medicines for children." 153 Cong. Rec. S12050 (2007).

in children, even the failed or inconclusive ones. This would enable patients, doctors, and sponsors to have access to all the information regarding the use of a particular drug in children. In so doing, Congress could not have intended that the same low bar would also apply to the determination of whether pediatric studies "fairly respond" to a written request, a determination which potentially results in a very significant financial benefit (at a potentially large cost to taxpayers) to the sponsor that conducts such studies.

f. FDA properly determined that Amgen's studies did not fairly respond to the Agency's written request

As explained above, Amgen was aware that the goal of FDA's written request for pediatric studies was to obtain the information needed to understand the safety and effectiveness of the long term use of cinacalcet in the pediatric population. Accordingly, Amgen was also aware that its studies had to yield at least some useful information on the safety and efficacy of cinacalcet in the relevant pediatric populations, or, failing that, at the very least comply with the terms of the Agency's written request. Amgen failed to accomplish either objective.

Amgen now contends that FDA held it to an impossible standard. That assertion is belied by the record of the interactions between the Agency and Amgen, indicating that they engaged in regular back and forth regarding the conduct of Amgen's studies; FDA accommodated all but one of Amgen's requests for amendments. More importantly, Amgen's argument is undermined by the fact that it accepted the design parameters for Study 3 in 2010. Those parameters were, as with all such studies, developed and finalized after negotiations between the parties. Amgen never took the position that the parameters were impossible (or almost impossible); indeed, it did not ask the Agency to amend the number of completing patients, until 2015. Amgen also tries to blame the clinical hold (which was imposed because of the death of a patient receiving cinacalcet), general nephrologists's alleged reluctance to treat children, and alleged FDA

intransigence for its failures. *See* Compl. at ¶¶ 38-40. In sum, Amgen blames everyone but itself. The facts demonstrate the fallacy of this argument.

The Agency's decision to reject Amgen's study reports was based on FDA's reasonable interpretation of what a sponsor needs to do in order to "fairly respond" to the written request. As the Agency's decision explained, FDA considered the information Amgen submitted in light of the objectives of that written request. The Agency evaluated whether Amgen's submission "responds to the specific elements in the [written request] in light of the objective stated in the [written request] and the overall purpose of the [FDCA]." Compl. Ex. 2, at 3 (FDA's Correspondence Rejecting Amgen's Study Reports). Ultimately, FDA considered the totality of Amgen's information and determined that it had failed to "fairly respond" to the written request, not simply because the agreed upon number of completers had not been met, but because Amgen's data were qualitatively and quantitatively inadequate. Many of the subjects in Study 3 had been exposed to inadequate doses, *see id.* at 8 ("[M]any of the non-completers who received cinacalcet in Study 3 were exposed to doses that were too low to adequately characterize the safety of the product"), and/or for an inadequate length of time. *Id.* at 9 ("[T]he median exposure for the 18 patients enrolled fell far short of [the] minimum level [of exposure]."). Information from another study was also inadequate to inform the Agency's analysis of Study 3, as was the retrospective chart review Amgen provided to address these acknowledged deficiencies. *See id.* As a result, FDA determined that Amgen had failed to provide "to provide sufficient safety data in the 28 day to < 6 year old age group prevents FDA from drawing any conclusions about the safety of the product in patients < 6 years of age when used as intended." *Id.* at 10. Because Amgen had failed to meet "an important element of the [written request]" and also failed to provide adequate data to meet the objectives of the written request, the Agency concluded that

Amgen had failed to fairly respond to the written request. That determination is a textbook example of an Agency applying its scientific expertise and technical experience to the underlying facts. FDA's determination is consistent with the statutory standard and bedrock principles of deference to agency interpretation of ambiguous statutory provisions. It fits comfortably with a long line of cases where courts have recognized that Congress has delegated to FDA the authority to make science-based, factual determinations, especially in situations that require the application of Agency's scientific expertise. *See, e.g.*, *Weinberger v. Bentex Pharms., Inc.*, 412 U.S. 645, 653-54 (1973); *Serono Labs v. Shalala*, 158 F.3d 1313, 1320 (D.C. Cir 1998); *Henley v. FDA*, 77 F.3d 616, 621 (2d Cir. 1996); *Schering Corp. v. FDA*, 51 F.3d 390, 399 (3d Cir. 1995); *Tri-Bio Laboratories, Inc. v. United States*, 836 F.2d 135, 142 (3d Cir. 1987). The Court should decline Amgen's request to disturb FDA's determination.

g. FDA's decision to deny Amgen pediatric exclusivity is not arbitrary

Amgen contends that FDA has treated it differently because the Agency recognized pediatric exclusivity in other cases where other sponsors also failed to meet the precise terms of a written request. This contention ignores the highly case- and fact-specific nature of the relevant inquiry. As already discussed, FDA must evaluate the sufficiency of clinical study results submitted in response to a written request. Each such evaluation involves a different drug and pediatric condition, as well as a written request that has been crafted to meet very specific needs. Therefore, each inquiry into the scientific sufficiency of a particular sponsor's studies will necessarily be an individualized determination.

FDA has not had the opportunity to fully consider Amgen's arguments about other drugs in the first instance; these arguments are being raised to FDA for the first time both in this Court and in the pending request for dispute resolution. Nevertheless, as an initial matter, certain facts are readily distinguishable. For example, Amgen claims that the sponsor of abatacept also failed

to meet the precise number of enrollees for a pediatric study. Amgen ignores the fact that the shortfall was only 8% as opposed to Amgen's 73% shortfall here. Moreover, the additional information supplied for abatacept was of sufficient quality to enable a conclusion that the product was safe for use in children (again, unlike the case here), leading to the appropriate labeling changes. And so it is with another example: The sponsor of zolmitripan was able to make up the deficiency in the number of patients in one study by providing usable safety data from another such that the total number of patients exceeded the number in the written request (a fact that Amgen conveniently ignores).

Amgen also faults the Agency for making "no effort to distinguish any of these precedents." Pl.'s Mem. at 30. As this Circuit noted in the very case Amgen cites: "It is important to note that we do not require agencies to address every conceivably relevant line of precedent in their archives." *Lone Mountain Processing, Inc. v. Sec'y of Labor*, 709 F.3d 1161, 1164 (D.C. Cir. 2013). FDA has made hundreds of pediatric exclusivity decisions. Moreover, FDA has a limited period of time to make each decision. *See* 21 U.S.C. § 355a(d)(3). If the Agency were required to evaluate and discuss every previous exclusivity decision, at the risk of being found to have acted arbitrarily, it would vastly impede the Agency's process.

h. Amgen has had all the process that it is due

Amgen argues that FDA violated procedural due process because Amgen allegedly relied on the "plain meaning" of the exclusivity statute, and did not have adequate notice of the standard that FDA would apply. Pl.'s Mem. at 32-33. But for all of the reasons previously stated, the statute does not have the "plain meaning" that Amgen suggests; that a mere sliver of evidence would satisfy its obligation. Nor did FDA fail to provide adequate notice of the substance of its approach. FDA routinely must decide whether product-specific evidence submitted by sponsors meets general standards. *See, e.g.*, 21 U.S.C. § 355(d)(4), (5). Whether a

sponsor's data "fairly responds" to a written request is similarly fact-specific, and the generality of the applicable standard does not render it fundamentally flawed. Rather, Congress entrusts expert agencies to make such decisions. *PDK Labs. v. U.S. Drug Enforcement Admin.*, 438 F.3d 1184, 1194–95 (D.C. Cir. 2006) (finding it appropriate for federal agencies to clarify a statutory term on a case by case basis).

Amgen also argues that FDA never indicated that it would not meet the pediatric exclusivity standard. Pl.'s Mem. at 33. But Amgen was on notice as of the date of the Written Request on May 5, 2010, of the number of study participants that were expected to complete each study, and had agreed to conduct its studies according to those expectations. Moreover, as of December 24, 2015, Amgen was aware that FDA would not amend the written request to further decrease the number of study completers to the four participants that Amgen now argues is sufficient. Thus, it should have been no surprise to Amgen that its data submission would not meet FDA's expectations.

In any event, Amgen does not meet the factors for showing a constitutional due process violation, which require a plaintiff to demonstrate that (1) it has a constitutionally protected property interest; and (2) that the procedures employed deprived the plaintiff of that interest without constitutionally adequate procedure. *See, e.g., Propert v. Dist. Of Columbia*, 948 F.2d 1327 (D.C. Cir. 1991). For the first factor, no promise of a constitutionally protected interest exists in a grant of exclusivity. There is simply no recognition that exclusivity rises to the level of a constitutionally-protected interest. *See* 59 Fed. Reg. 50,338, 50359 ("New drug exclusivity is not a property right, but is rather a statutory obligation on the agency."); FDA decision in Docket No. 86P-0452, at 2-3 (Mar. 6, 1987) ("The seven-year period of exclusive marketing is not a property right but is a prohibition against action by FDA. It does not affirmatively grant

any rights or privileges to the 'pioneer' sponsor."); *cf. Town of Castle Rock, Colo. v. Gonzales*, 545 U.S. 748, 767–68 (2005) (noting that "action that is directed against a third party and affects the citizen only indirectly or incidentally" is not the same as an entitlement that is eligible for protection under the Due Process Clause).

For the second factor, Amgen cannot demonstrate that FDA's procedures are deficient. The adequacy of an agency's procedures are evaluated using the three-factor test in *Mathews v. Eldridge*, 424 U.S. 319, 334-35 (1976): (1) the private interest that will be affected by the agency action; (2) the risk of erroneous deprivation and the probable value of any additional process; and (3) the government's interest (including the burdens) that any such additional process would entail. On the first factor, Amgen earns billions of dollars a year in revenue, and it already has approval of a next-generation product that it touts as superior to Sensipar.[13] For the second factor, FDA's existing process provides assurance against the risk of erroneous deprivation. Amgen and FDA engaged in extensive back-and-forth over the scientific and technical bases of the written request, and when FDA refused to further reduce the number of completers required for Study 3 as Amgen requested in December 2015, Amgen was on notice that the number of its study participants was not sufficient. Moreover, FDA affords Amgen a process for administrative review that Amgen has pursued, and Amgen must await the conclusion of that process before declaring it deficient. Finally, it would impose an undue burden on FDA to provide additional process; the Agency worked closely with Amgen, and revised the written request five times until it reached the point where it became clear that FDA's ability to obtain meaningful information about the pediatric use of cinacalcet could be in jeopardy.

[13] *See* First Quarter 2017 Amgen Earnings Call Transcript (Mar. 8, 2017), Ex. A.

Moreover, Amgen has a meaningful opportunity for administrative review, after which time it may challenge that decision in court if it is not to Amgen's liking. Due process requires no more. *See Biovail Corp. v. FDA*, 448 F. Supp. 2d 154, 163 (D.D.C. 2006).

2. Amgen Has Not Shown That It Will Suffer Irreparable Harm In The Absence Of A Temporary Restraining Order

Not only does Amgen have no likelihood of success on the merits, it also cannot demonstrate the harm required to receive the extraordinary remedy of a TRO. *Winter v. NRDC*, 555 U.S. 7, 20 (2008). "The *sine qua non* of granting any preliminary injunctive relief is a clear and convincing showing of irreparable injury to the plaintiff." *Experience Works, Inc. v. Chao*, 267 F. Supp. 2d 93, 96 (D.D.C. 2003). Further, "[t]o obtain injunctive relief, the petitioners must show that the threatened injury is not merely 'remote and speculative.'" *Almurbati v. Bush*, 366 F. Supp. 2d 72, 78 (D.D.C. 2005) (quoting *Milk Indus. Found. v. Glickman*, 949 F. Supp. 882, 897 (D.D.C. 1996)). Thus, proving "irreparable" injury is a considerable burden, requiring proof that the movant's injury is certain, great and actual—not theoretical—and imminent, creating a clear and present need for extraordinary equitable relief to prevent harm. *Wis. Gas Co. v. FERC*, 758 F.2d 669, 674 (D.C. Cir. 1985); *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp. 212, 220 (D.D.C. 1996) ("Irreparability of injury is a very high standard."); *Varicon Int'l v. OPM*, 934 F. Supp. 440, 447 (D.D.C. 1996).

In this circuit, "it is well-settled that economic loss alone will rarely constitute irreparable harm." *Astellas Pharma US, Inc. v. FDA*, 642 F. Supp. 2d 10, 22 (D.D.C. 2009); *see, e.g., Wis. Gas*, 758 F.2d at 674; *Mylan Pharm., Inc. v. Shalala*, 81 F. Supp. 2d 30, 42-43 ("Courts within the Circuit have generally been hesitant to award injunctive relief based on assertions about lost opportunities and market share"); *Bristol-Myers Squibb*, 923 F. Supp. at 220. Rather, economic loss may constitute irreparable harm "only where the loss threatens the *very existence* of the

movant's business." *Wis. Gas.*, 758 F.2d at 674 (emphasis added). Cases in this circuit have made clear that even irrecoverable financial loss does not rise to the level of irreparable harm unless the financial injury is "serious in terms of its effect on the plaintiff." *Gulf Oil Corp. v. Dep't of Energy*, 514 F. Supp. 1019, 1026 (D.D.C. 1981). *See also Apotex, Inc. v. Sebelius*, 700 F. Supp. 2d 138, 141 (D.D.C. 2010) (finding an irrecoverable multi-million dollar loss did not rise to the level of irreparable harm); *Hi-Tech Pharmacal Co. v. FDA*, 587 F. Supp. 2d 1, 11 (D.D.C. 2008) ("Irretrievable" monetary loss, may constitute irreparable harm only if it is "so severe as to cause extreme hardship to the business or threaten its very existence.") (internal quotation marks omitted); *Mylan Labs., Inc. v. Thompson*, 139 F. Supp. 2d 1, 27 (D.D.C. 2001) (To satisfy the standard of irreparable injury to justify a preliminary injunction, the movants' loss must be "more than simply irretrievable").[14]

"To demonstrate irreparable harm, 'the injury must be both certain and great; it must be actual and not theoretical,' and the movant carries the burden of showing that 'the injury complained of is of such imminence that there is a clear and present need for equitable relief to prevent irreparable harm.'" *Achagzai v. Broadcasting Board of Governors*, Civ. No. 14-768, 2016 WL 471274, at *4 (D.D.C. Feb. 8, 2016) (citations omitted).

Plaintiff's harm argument centers on the potential of losing six months of patent exclusivity. Pl's Br. at 34. However, it is far from certain that Plaintiff will suffer any harm at all. First, it is well settled that this Court can order any decision be retroactive to preserve the

[14] *See also, e.g., Astellas Pharma US, Inc. v. FDA*, 642 F. Supp. 2d 10, 22 (D.D.C. 2009); *Coal. for Common Sense in Gov't Procurement v. United States*, 576 F. Supp. 2d 162, 168- 69 (D.D.C. 2008); *Mylan Labs., Inc. v. Leavitt*, 484 F. Supp. 2d 109, 123 (D.D.C. 2007); *Apotex, Inc. v. FDA*, No. 06-0627 (JDB), 2006 WL 1030151 at * 17 (D.D.C. Apr. 19, 2006); *Biovail Corp. v. FDA*, 448 F. Supp. 2d 154, 164 (D.D.C. 2006); *Sandoz, Inc. v. FDA*, 439 F. Supp. 2d 26, 32 (D.D.C. 2006); *Sociedad Anonima Viña Santa Rita v. Dep't of Treasury*, 193 F. Supp. 2d 6, 14 (D.D.C. 2001); *Bristol-Myers*, 923 F. Supp. at 221; *Experience Works, Inc.*, 267 F. Supp. 2d at 96.

statutorily required nine-month window. In addition, any harm to the Plaintiff will be economic only and too small to warrant the extraordinary relief of a TRO or preliminary injunction.

In the unlikely event this Court reverses FDA's determination, the Court has the power to make its decision retroactive to the original determination date to preserve the nine-month window. In *Ethyl Corp. v. Browner*, the D.C. Circuit discussed the equitable remedy *nunc pro tunc* (literally "now for then"), which is "traditionally used to apply a court's own order or judgment retroactively." 67 F.3d 941, 945 (D.C. Cir. 1995). This relief is "available in order to promote 'fairness to the parties,' and 'as justice may require.'" *Id.* (quoting *Weil v. Markowitz*, 898 F.2d 198, 200 (D.C. Cir. 1990); *Mitchell v. Overman*, 103 U.S. 62, 65, 26 L.Ed. 369 (1881)). The D.C. Circuit then explained that "[t]his circuit has extended the traditional doctrine to embrace agency conduct, where necessary to put the victim of agency error in the economic position it would have occupied but for the error." *Id.* (quoting *Delta Data Systems Corp. v. Webster*, 744 F.2d 197, 206–07 (D.C. Cir. 1984)) (internal quotations omitted). In the *Ethyl* case, the Environmental Protection Agency blocked Plaintiff Ethyl Corp.'s distribution of a fuel additive. *Id* at 941. The Court found EPA's actions inappropriate and ordered the EPA to recognize the plaintiff's registration *nunc pro tunc*, so that the additive would be considered to have been registered on a date prior to additional regulations that would have affected plaintiff's additive. *Id.* at 942. The D.C. Circuit held that "[b]ecause EPA should have granted the f(4) waiver on November 30, 1993, when it published its finding that Ethyl had met the only legal requirement for obtaining the waiver, we will treat the waiver as having been granted as of that date, *nunc pro tunc*." *Id.*

There are numerous other examples of courts in this circuit issuing orders to be retroactive to dates of agency decisions found to be erroneous. *See Salzer v. FCC*, 778 F.2d 869,

875–76 (D.C.Cir.1985) (vacating FCC order dismissing license applications and remanding agency to reinstate them *nunc pro tunc* when FCC demanded strict compliance with requirements for filing license applications under a deadline but failed to give adequate notice of what those requirements were); *McElroy Electronics Corp. v. FCC*, 990 F.2d 1351, 1353 (D.C. Cir. 1993) (same); *Maxcell Telecom Plus v. FCC*, 815 F.2d 1551, 1560 (D.C. Cir. 1987) (same); *Delta Data Systems Corp. v. Webster*, 744 F.2d 197, 206–07 (D.C. Cir. 1984) (holding bidder could require the agency to reselect a winning contractor *nunc pro tunc* where agency erred in treatment of bidder); *Office of Consumers' Counsel v. FERC*, 826 F.2d 1136, 1139 (D.C. Cir. 1987) (ordering Commission to provide the necessary remedy retroactive to the date of its finding of unlawfulness, when Commission had found rates unlawful but failed to order a remedy); *see also Depomed, Inc. v. United States Dep't of Health & Human Servs.*, No. 12-1592, ECF No. 33 (D.D.C. Sept. 5, 2014) ("FURTHER ORDERED that the FDA shall recognize orphan-drug marketing exclusivity for Gralise . . . for a period of seven years from the date the FDA approved Gralise for marketing.).

FDA has also made at least one exclusivity decision retroactive. *See* Citizen Petition Response (Re: Docket No. FDA-2011-P-0213) (Aug. 8, 2012) (stating, based on new information in the docket, "FDA rescinds Wilate's orphan-drug exclusivity, retroactive to December 4, 2009, the date of Wilate's approval.").

Plaintiff cites *Jacksonville Port Auth. v. Adams* to argue that relating back to the original decision date is such a legal "uncertainty" that it "establishe[s] a substantial risk of irreparable harm." Pl's Mem. at 34, n.13. Plaintiff claims that it is the uncertainty about FDA's ability to make a decision retroactive that is sufficient to establish a substantial risk of harm. *Id.* This argument, however, ignores the fact that the D.C. Circuit has fully explained that the judiciary—

to whom Plaintiff is actually petitioning—is authorized to provide this very relief. 556 F.2d at 56 ("In the interest of justice, the court may proceed as if action that should have been taken in the courthouse was timely taken.").

Should this Court overturn FDA's decision and make the decision retroactive to FDA's initial determination on May 22, 2017, FDA would not object to the retroactivity. The statutory requirement of an FDA determination more than nine months prior to patent expiration would be satisfied and Plaintiff would suffer no loss at all. With the equitable remedy of *nunc pro tunc* available, Plaintiff cannot demonstrate irreparable harm that is "both certain and great," and that is "actual and not theoretical," *Achagzai*, 2016 WL 471274, at *4. Finally, Amgen's potential economic loss is far below what is needed to support a TRO. Amgen is already in the process of replacing Sensipar with a new drug, Parsabiv. *See* First Quarter 2017 Amgen Earnings Call Transcript (Mar. 8, 2017), Ex. A ("[W]e have Parsabiv which is launching now in the US and is already launched in Europe which will be a replacement for Sensipar which faces patent expiry in 2018.") Further, based on first quarter of 2017 results, Sensipar only accounts for roughly 6.4% of Amgen's total world-wide sales. As such a small part of the total business, any damage to Amgen's hoped-for Sensipar profits for a six-month period is far from being a "loss [which] threatens the *very existence* of the movant's business." *Wis. Gas.*, 758 F.2d at 674 (emphasis added). Thus, Amgen cannot meet the second element needed to justify a TRO.

3. The Balance of the Hardships Weighs in Favor of the Federal Defendants

In contrast, the potential harm to FDA is real and immediate. Plaintiff wants this Court—prior to any ruling on the merits—to force FDA to accept pediatric studies that it, after careful consideration, had already rejected. Such a wholesale reversal of an FDA decision fundamentally undermines FDA's "interest in giving immediate force to [its] orders and an

interest in the authority and finality of [its] decision." *See Mylan v. Henney*, 94 F. Supp. 2d 36 (D.D.C. 2000), *rev'd on other grounds*, 276 F.3d 627 (D.C. Cir. 2002); *United States v. Commonwealth of Puerto Rico*, 764 F.Supp. 220, 224 (D.P.R.1991) (finding that government has an interest in giving immediate force to an agency's orders and an interest in the authority and finality of agency decisions in general).

Further, a TRO would also be disruptive to FDA's processes. It would inject uncertainty into FDA's process and will undermine FDA's decisions. *See Purepac Pharm. Co. v. Thompson*, 2002 WL 32934699 (D.D.C.) ("Finally, if Purepac's requested preliminary injunction is granted, there is a discernable risk of harm to FDA through the possible disruption of its processes.") *Mylan Pharms.*, 94 F. Supp. 2d at 59 (same); *see also V.N.A. of Greater Tift County, Inc. v. Heckler*, 711 F.2d 1020, 1035 (11th Cir. 1983) (same).

At the status conference, the Court raised the idea of FDA "provisionally" accepting Amgen's studies. This would not make the order acceptable. The end result is the same–FDA's considered decision would be discarded by the Court without a court decision on the merits. This would still undermine FDA's decision-making and violate FDA's interest in "giving immediate force to [its] orders and an interest in the authority and finality of [its] decision." *See United States v. Commonwealth of Puerto Rico*, 764 F. Supp. 220, 224 (D.P.R. 1991).

4. The Public Interest Is Not Served by Entry of a TRO

Amgen has failed to show that the entry of temporary injunctive relief would be in the public interest. The United States agrees, as Amgen argues, that "the public has an unmistakable interest in seeing that laws are faithfully executed by public officials." Pl.'s Mem. at 37. The public's and FDA's interests are aligned—the public needs predictability, availability of generic drugs, and information about pediatric use of drugs. Accordingly, the public has an interest in

FDA decision's staying in effect and not being overturned, even "provisionally," at the very least not before its merits are examined in light of the administrative record.

Amgen, however, is mistaken in arguing the public interest that FDA has "significantly diminish[ed] the incentives the pediatric exclusivity statute was to create." Pl.'s Mem. at 37. To the contrary, FDA's actions serve the public's interest in seeing that the pediatric exclusivity program is properly administered. *See Allina Health Services v. Sebelius*, 756 F. Supp. 2d 61, 71 (D.D.C. 2010) ("The public interest is served by the consistent and uniform application of regulations to similarly-situated parties, without carving out judicial exceptions for individual parties through the injunction mechanism.") This requires ensuring pediatric exclusivity attaches only when the applicant has provided an appropriate "quid" in order to receive the "quo"—particularly when both parts of the exchange are of critical importance to the public. But that "quid" comes with a "quo" that has a serious impact on the public—a delay of an additional six months before generic drugs are allowed onto the market. FDA's actions ensure a meaningful opportunity for the public to receive valuable information before a sponsor qualifies for six more months of patent monopoly.

Further, the TRO is not necessary to protect the public interest in FDA's administration of the pediatric exclusivity provisions. As explained above, should FDA decide exclusivity favorable to Amgen upon administrative review, or this Court overrule FDA's decision, the Court can relate back the reversal to May 22, 2017, the date of FDA's initial determination, preserving the nine-month window and rendering any TRO superfluous.

CONCLUSION

For the foregoing reasons, Amgen's complaint should be dismissed, and its motion for a temporary restraining order and/or preliminary injunction should be denied.

Of Counsel:

JEFFREY S. DAVIS
Acting General Counsel

ELIZABETH H. DICKINSON
Associate General Counsel,
Food and Drug Division

ANNAMARIE KEMPIC
Deputy Chief Counsel, Litigation

WENDY S. VICENTE
Senior Counsel

MUSTAFA ÜNLÜ
Counsel

U.S. Department of Health & Human Services
Office of the General Counsel
10903 New Hampshire Avenue
White Oak 31 Room 4562
Silver Spring, MD 20993-0002
(301) 796-3396

Respectfully submitted,

Assistant Attorney General

MICHAEL S. BLUME
Director

ANDREW E. CLARK
Assistant Director

_____/s/_____
Charles Biro
Trial Attorney, Consumer Protection Branch
U.S. Department of Justice
P.O. Box 386
Washington, DC 20044
Tel: (202) 307-0089
Fax: (202) 514-8742

Dated: May 31, 2017