ORAL ARGUMENT NOT YET SCHEDULED

No. 18-5046

IN THE

United States Court of Appeals for the District of Columbia Circuit

AMGEN INC.,

Plaintiff-Appellant,

v.

ALEX AZAR, in his official capacity as, SECRETARY, UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES, and SCOTT GOTTLIEB, M.D., in his official capacity as COMMISSIONER OF FOOD AND DRUGS, FOOD AND DRUG ADMINISTRATION,

Defendants-Appellees,

AMNEAL PHARMACEUTICALS, LLC,

Intervenor-Appellee.

On Appeal from the United States District Court
for the District of Columbia,
No. 17-cv-1006, District Judge Randolph Moss

EMERGENCY MOTION FOR INJUNCTION PENDING APPEAL AND TO EXPEDITE BRIEFING AND ARGUMENT

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February 23, 2018

CERTIFICATE AS TO PARTIES, RULINGS, AND RELATED CASES

Pursuant to Circuit Rule 28(a)(1), Amgen Inc. certifies the following:

A. PARTIES

1. The following are parties in this Court:

a. Plaintiff-Appellant: Amgen Inc.

b. Defendants-Appellees: Alex Azar, in his official capacity as Secretary, United States Department of Health and Human Services; and Scott Gottlieb, M.D., in his official capacity as Commissioner of Food and Drugs, Food and Drug Administration.

c. Intervenor-Appellee: Amneal Pharmaceuticals, LLC.

2. For purposes of Federal Rule of Appellate Procedure 26.1 and Circuit Rule 26.1, Amgen Inc. is a biopharmaceutical company. Amgen Inc. is a publicly held corporation and has no parent corporation, and no publicly held corporation owns 10% or more of the stock in Amgen Inc.

B. RULINGS UNDER REVIEW

Amgen Inc. is appealing two rulings of Judge Randolph Moss. First, Amgen is appealing Judge Moss's memorandum opinion and order denying Amgen's motion for summary judgment, entered on January 26, 2018. *See Amgen Inc. v. Hargan*, No. CV 17-1006 (RDM), 2018 WL 581006 (D.D.C. Jan. 26, 2018).

Amgen also is appealing Judge Moss's order denying Amgen's renewed motion for summary judgment following remand on February 17, 2018. Dkt. Nos. 88, 89.

C. RELATED CASES

Amgen is not aware of any related cases as that term is defined in Circuit Rule 28(a)(1)(C).

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Appellant Amgen Inc. moves for an injunction pending appeal and to expedite briefing and consideration of its appeal. Amgen seeks an injunction requiring FDA to maintain the status quo and temporarily refrain from approving generic versions of Amgen's prescription drug product Sensipar® pending resolution of Amgen's appeal. This relief is necessary to preserve Amgen's right to seek appellate review of FDA's denial of an additional period of marketing exclusivity (called "pediatric" exclusivity) for Sensipar. A patent covering Sensipar is set to expire on March 8, 2018 and FDA is currently barred from approving generic versions of Sensipar until that date. The additional exclusivity sought by Amgen would normally take effect on that date, barring FDA from approving generic versions of Sensipar for an additional six months. If a generic drug enters the market before resolution of Amgen's appeal, it will flood the market in days, wiping away Amgen's exclusivity and effectively eliminating Amgen's ability to seek appellate review.

Amgen requests a ruling on this motion by March 5, 2018. Amgen also requests expedited briefing and argument. Amgen proposes that it file its opening brief on March 6; that responsive briefs be filed on March 23; and that Amgen file its reply on April 6. Amgen further requests that argument be scheduled on the earliest available date after briefing.

Amgen contacted the parties to seek their positions. The federal defendants oppose the requested injunction and proposed briefing schedule. Amneal has not yet, as of the filing of this motion, responded with its position.

INTRODUCTION

In this appeal, Amgen challenges FDA's denial of pediatric exclusivity for Sensipar, a drug used to regulate excess calcium in the blood of certain dialysis patients. The governing statute requires FDA to confer a short additional period of marketing exclusivity on a drug sponsor that conducts pediatric studies at the agency's request, as long as the sponsor's study reports "fairly respond" to the request and satisfy standard scientific protocols and filing requirements. 21 U.S.C. § 355a(d)(4). Amgen conducted seven years' worth of pediatric studies on Sensipar at FDA's request, gathering thousands of pages of data on a vanishingly small pediatric population and satisfying the agency's detailed written request in every respect save one. But FDA denied pediatric exclusivity on the ground that Amgen had failed to "fairly respond" to the written request, because the agency concluded it had neither met all of the written request's terms nor achieved all its "objectives," which the agency defined as "meaningful" labeling "across all age groups and uses cited" in the written request. A191.

That results-based, full-compliance standard is flatly inconsistent with the controlling statute, which requires that sponsors "fairly respond"—not that they

satisfy all of the request's terms or "objectives." It is also flatly inconsistent with at least one past exclusivity grant, where the agency awarded exclusivity despite the sponsor's studies neither producing "meaningful labeling" nor fulfilling the request's terms.

FDA also violated basic principles of fair notice and retroactive rulemaking by applying its never-before-announced "fairly respond" standard to Amgen without any prior notice. The agency's public pronouncements on the issue signaled something much different. A statement remains on FDA's website that pediatric exclusivity decisions are not tied to labeling decisions ("meaningful" or otherwise). Ex. A, Resp. to Q. 9. A diligent entity searching publicly available FDA memoranda also would have found records describing the product that *received* exclusivity despite markedly failing the agency's "perfect compliance or meaningful labeling" standard. For FDA to apply an unannounced, "fairly respond" standard to Amgen is not fair notice, and constitutes impermissible retroactive rulemaking.

An injunction pending appeal is warranted. Amgen is likely to prevail on the merits of its appeal and it will suffer irreparable injury without an injunction. The public interest and balance of equities also weigh in favor of injunctive relief. In order to ensure that the injunction maintaining the status quo lasts no longer than necessary, Amgen is also seeking expedited briefing, which will allow Amgen

meaningful judicial review while pausing any regulatory action that could effectively extinguish Amgen's appeal.

BACKGROUND

The Statutory Framework. The Food, Drug, and Cosmetic Act (FDCA) mandates that all new prescription drugs obtain FDA approval before they can be marketed. 21 U.S.C. § 355(a). Manufacturers of brand name (pioneer) drugs must demonstrate the safety and effectiveness of their products in order to gain approval. Once approved, a pioneer drug may be entitled to certain periods of marketing exclusivity and patent-related protections. After those periods expire, FDA may approve competing manufacturers' generic drugs, which are essentially copies of the innovator product that can rely on FDA's finding of safety and efficacy for the pioneer drug. *Id.* § 355(j)(1)–(2).

Due to a longstanding lack of information about the use of drugs in pediatric populations, most drugs are prescribed to children "off label," without dosing instructions, posing potentially serious risks to pediatric patients. To remedy these deficiencies, Congress in 1997 passed the Best Pharmaceuticals for Children Act (BPCA), which created an incentive in the form of a short additional period of market exclusivity for sponsors to undertake vital testing in pediatric populations. S. Rep. No. 105-43, at 51 (1997). The statute is straightforward: FDA issues a written request for pediatric studies if it "determines that information relating to

the use of a … drug in the pediatric population may produce health benefits in that population." 21 U.S.C. § 355a(b)(1), (c)(1). But the statute limits FDA's role in determining whether to accept the resulting reports:

> The Secretary's only responsibility in accepting or rejecting the reports shall be to determine, within the 180-day period, whether the studies [(i)] fairly respond to the written request, [(ii)] have been conducted in accordance with commonly accepted scientific principles and protocols, and [(iii)] have been reported in accordance with the requirements of the Secretary for filing.

Id. § 355a(d)(4). If each of these criteria is met, FDA must accept the reports, and the six-month extension of exclusivity applies. *Id.* §§ 355a(b)(1), (c)(1).

Amgen's Sensipar. FDA approved Sensipar in March 2004. A133. In May 2010, FDA issued a written request to Amgen, seeking pediatric studies of Sensipar in populations ranging from four weeks to seventeen years old. A59–69. After several subsequent amendments, FDA's request sought four studies. A74.

Amgen ultimately performed nine studies over the span of roughly eleven years, covering 103 pediatric patients who received at least one dose of Sensipar in interventional clinical trials, plus 113 patients who received Sensipar in less formal studies. A94, tbl. 2. As to the four studies in FDA's written request, Amgen completed Studies 1, 2, and 4 precisely according to the terms of the request. A98–110, 117, 192. Amgen could not, however, satisfy the agency's request for 18 completers for Study 3—the youngest patient group (28 days to 6 years)—because of a perfect storm of circumstances: to name a few, that most vulnerable

pediatric population is first in line for transplants and correspondingly less inclined to participate in studies; a patient's death in another Sensipar pediatric study halted *all* Sensipar pediatric studies; and it was exceedingly difficult even to attract potential study candidates given the infinitesimal size of the affected pediatric population. Amgen nevertheless was able to glean data on 17 patients in Study 3, 11 of whom exceeded 12 weeks of treatment and 4 of whom met all the request's terms. A158.

Amgen submitted its study reports as directed on the deadline. A85. Its submission met every requirement of the written request except one: the number of completers in Study 3. A98–110.

FDA denied pediatric exclusivity. A122. The agency agreed that "Amgen has met the literal terms of the [written request] for Studies 1, 2, and 4." A125. It also agreed that Study 3 fell short by a single criterion. A131. FDA nevertheless concluded that because "this criterion was not met," Amgen "failed to fairly respond" to the written request. *Id.* FDA interpreted the phrase "fairly respond" to require either full compliance with the terms of the written request or full achievement of "meaningful pediatric labeling" across "all of the age groups and indications requested based on the studies conducted." A124. According to FDA, Amgen's "failure to provide sufficient safety data" in the youngest pediatric group "prevent[ed] FDA from drawing any conclusions about the safety of the product"

in that population. A131. Ultimately, because the agency found insufficient "safety information" pertaining to the group of patients in Study 3, Amgen "failed to fairly respond" to the written request. *Id.*

Procedural History. Amgen filed this lawsuit within 72 hours of FDA's decision. Because a statutory deadline directs FDA to make its exclusivity determinations nine months before the expiration of an affected patent, which for Amgen is on March 8, Amgen sought a TRO. 21 U.S.C. §§ 355a(b)(1), (c)(1). Following the TRO hearing, the parties stipulated that "any future decision requiring FDA to accept Amgen's study reports for Sensipar . . . shall be deemed to relate back, *nunc pro tunc*, to . . . the date of FDA's initial determination." Dkt. No. 15 at 2. After a remand for further agency proceedings, the parties briefed cross-motions for summary judgment by mid-December, culminating in a hearing on January 11.

On January 26, the District Court granted and denied each party's motion in part. The District Court found the statutory phrase "fairly respond" to be ambiguous, and found FDA's interpretation reasonable. A24–29. The court also rejected Amgen's fair-notice argument, asserting that an agency need not provide fair notice unless it imposes "a criminal or civil penalty or sanction" or rejects "a filing as untimely or for failing to comply with some other filing requirement." A39. However, the District Court noted that FDA had granted pediatric

exclusivity to another drug product, Ortho Tri-Cyclen (OTC), even though its studies had not met the terms of the written request, and had produced labeling similar to Sensipar's. The District Court remanded for an explanation of this seemingly disparate treatment of two similarly situated entities. A37.

On February 5, FDA issued a decision on remand, admitting that the OTC studies did not meet the terms of its written request but taking the position that FDA must have *thought* they did at the time it granted exclusivity, only to discover later that they did not. Dkt. No. 77. But the next day, FDA filed a "notice of correction," because a newly discovered document contradicted that assertion. Dkt. No. 78. The District Court remanded again for another explanation, leading FDA to issue another remand decision on February 8. Following expedited briefing, the District Court accepted FDA's explanation on remand and granted summary judgment in FDA's favor on February 17. Amgen then moved for a stay pending appeal in the District Court. That motion was denied on February 22 at 6:59 pm. Dkt. No. 96.

The pediatric exclusivity statute extends existing patent protections by six months. 21 U.S.C. 355a(b)(1)(B), (c)(1)(B). A patent covering Sensipar expires on March 8, 2018. Barring injunctive relief, FDA will be free to start approving generic versions of Sensipar on that date. If a generic drug is approved before resolution of the appeal, Amgen anticipates it will flood the market within days,

virtually eliminating Amgen's pediatric exclusivity rights before this Court is able to consider the issues raised on appeal. Amgen therefore requests an injunction to maintain the status quo, pause any impending generic approvals, and preserve its rights pending appeal.

ARGUMENT

A motion for injunctive relief pending appeal is governed by the usual factors: (1) the movant's likelihood of success on the merits, (2) whether the movant will suffer irreparable harm, (3) whether granting the requested relief would substantially harm other parties, and (4) the public interest. *Washington Metro. Area Transit Comm'n v. Holiday Tours, Inc.*, 559 F.2d 841, 843 (D.C. Cir. 1977); *Greater New Orleans Fair Hous. Action Ctr. v. HUD*, Nos. 10-5257, 10-5269, 2010 WL 9941065 (D.C. Cir. Sep. 22, 2010).

Amgen is also seeking expedited briefing and argument. A movant for expedited consideration must show that the decision under review "is subject to substantial challenge," and that the delay will cause irreparable injury. *D.C. Circuit Handbook of Practice and Internal Procedures* 33 (Jan. 26, 2017). The Court may also expedite cases "in which the public generally" has "an unusual interest in prompt disposition" and the reasons are "strongly compelling." *Id.* Each of these tests is met here.

I. AMGEN PRESENTS A SUBSTANTIAL CHALLENGE TO THE DISTRICT COURT'S DECISION AND HAS A STRONG LIKELIHOOD OF SUCCESS ON THE MERITS.

A. FDA Applied An Unlawful Interpretation of "Fairly Respond."

FDA relied on—and the District Court accepted—an unsupportable interpretation of "fairly respond," as that term is used in 21 U.S.C. § 355a(d)(4).[1] In denying pediatric exclusivity to Sensipar, FDA asserted that a sponsor must do one of two things to merit exclusivity: it must *either* fully meet all the terms of the written request *or* produce "clinically meaningful [information] across all age groups and uses cited in the WR" such that "the objectives of the WR have nevertheless been met." A191. Thus, "a sponsor that fails to meet the terms of a WR *and* fails to generate meaningful data to inform practitioners on how to use the drug in pediatric populations cannot be considered to have 'fairly responded' to that WR." *Id.*; *see also* A173, 124.

FDA's requirement of perfect success—either through full compliance with each term of a written request or full achievement of the request's objectives—cannot be reconciled with the statute's plain language. The statute permits FDA to consider "only" whether the studies "*fairly* respond" to the request. "Fairly" means "moderately," "passably," or "reasonably well." *See* Webster's II New

[1] On August 18, 2017, Congress amended 21 U.S.C. § 355a to add a few new provisions, not relevant here, which resulted in the renumbering of some of the provisions that *are* relevant here. For the convenience of the Court, we will cite to the current version of the statute in this brief.

College Dictionary (1995) (moderately); Oxford English Dictionary (2017) (reasonably well; tolerably; passably); *Black's Law Dictionary* (6th ed. 1981) (reasonably). "Respond" means "reply" or "answer." *See* Oxford English Dictionary (2017); Webster's II New College Dictionary (1995). Taken together, the words "fairly respond" mean to "answer reasonably well." While there might be some debate around the margins about what that phrase means in the abstract, there can be no reasonable debate about what it does *not* mean in this context. The statutory language does not permit FDA to require applicants to fully satisfy its request—whether it be by complying with all its terms or achieving all its objectives.

All of the parties (and the court) agreed that FDA's first requirement—perfect compliance with the request's terms—is a nonstarter. As the District Court correctly held in an earlier pediatric exclusivity case: "[S]ection 355a(d)(3) . . . plainly does not require compliance with every single provision of a written request, but requires only that a pediatric study 'fairly respond' to a written request." *Merck & Co. v. FDA*, 148 F. Supp. 2d 27, 30 (D.D.C. 2001).

The District Court concluded, however, that the second requirement, requiring satisfaction of all the study's objectives (so as to result in "meaningful labeling" across "all" populations and uses studied), was a reasonable interpretation of an "ambiguous" directive. A22.

That cannot be. First, the "objectives" of the written request were in fact spelled out as "objectives" in the written request. And Study 3's "objective" was *not* to achieve "meaningful labeling" across all ages and uses studied. The study's two objectives were "[t]o evaluate the safety and tolerability of cinacalcet in pediatric patients ages 28 days to < 6 years" and "[t]o characterize the PK profile in pediatric patients." A75. Amgen did both. FDA's reformulation of Study 3's "objectives" is impermissibly post hoc and completely self-serving.

In any event, interpreting "fairly respond" to mean "full achievement of the WR's objectives" is just as outcome-driven as requiring "full compliance with the WR's terms." Congress expressly chose *not* to tie pediatric exclusivity to achieving the "objective" of obtaining labeling or dosing information across all studied populations. Nothing in subsection (d)(4)—which defines FDA's "only" obligation when deciding whether to accept the reports—instructs the agency to answer whether the requested studies demonstrate safety and efficacy of the drug across all study groups. The study results are relevant only to informing the agency's labeling decision—a decision completely separate from whether to accept the reports. 21 U.S.C. § 355a(j).

Built into the concept of "fairly respond" is some amount of tolerance for failure. By definition, requiring sponsors to achieve the study's objectives by

supplying "meaningful labeling" across "all" age groups and uses is inconsistent with—indeed, it is unambiguously foreclosed by—the term "fairly."

B. FDA's "Fairly Respond" Standard Violates Basic Principles of Fair Notice and Retroactive Rulemaking.

FDA also violated fundamental APA principles by applying a previously unannounced "fairly respond" standard that had been formulated and applied completely out of public view (until now). An agency may not apply an interpretation of a statute or regulation to a regulated entity unless it provides "fair notice," meaning that a regulated party must "be able to identify, with 'ascertainable certainty,' the standards with which the agency expects parties to conform." *See General Elec. v. EPA*, 53 F.3d 1324, 1328-29 (D.C. Cir. 1995).

FDA's "meaningful labeling" standard was *never* publicly announced before now. Not as a regulation. Not through public adjudication. Not as informal public guidance. In fact, the agency's website tells regulated entities the opposite: "Pediatric exclusivity is not tied to approval of labeling containing information on pediatric use based on the studies conducted." Ex. A, Resp. to Q. 9.[2] It simply cannot be that an agency may clearly state on its website that something is *not* required, and then lawfully require that very thing in a subsequent adjudication, without notice.

[2] This FAQ document is collected along with the BPCA and other key documents in a historical documents file on FDA's website. *See* www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm315263.htm.

Nor is this a situation where the agency's undisclosed interpretation merely espouses the natural reading of the statute. The natural reading of "fairly" suggests a reasonableness standard—the natural outgrowth of the District Court's decision a few years earlier in *Merck*, 148 F. Supp. 2d 27 (D.D.C. 2001). That is a far cry from requiring achievement of all the study's objectives, let alone "meaningful" labeling across all ages and uses.

FDA generally publishes only four pieces of information about each of its pediatric exclusivity decisions: (i) the product's sponsor; (ii) the date on which exclusivity was granted; (iii) the written request; and (iv) certain review division memoranda.[3] Until this lawsuit, a regulated entity trying to discern FDA's "fairly respond" standard would have been forced to comb through the agency's public review division memoranda for clues. Among those public documents is a memorandum demonstrating that FDA granted exclusivity to another drug, OTC, even though its studies failed to meet a term of the written request, and resulted in labeling similar to Sensipar's. A265; *see also* A210 (publicly available memorandum noting, with original emphasis, that "the majority of the 123 subjects treated . . . did not meet either the DSM-IV diagnostic criteria for anorexia nervosa

[3] 21 U.S.C. § 355a(e) and (k); www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/UCM514985.pdf; www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm049997.htm.

or the DSM-IV diagnostic criteria modified by the sponsor for anorexia nervosa").[4] FDA argued below that it *thought* the OTC studies met the terms of the written request at the time it granted exclusivity. A265. But it relied on *nonpublic* documents to support that conclusion. A267–289; A293–298.

Amgen thus first learned of the "perfect compliance or meaningful labeling" standard upon receiving FDA's letter denying its request for pediatric exclusivity, long after Amgen accepted the agency's written request and performed seven years' worth of studies. A113. That is not fair notice. *See Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 158–159 (2012) ("It is one thing to expect regulated parties to conform their conduct to an agency's interpretations once the agency announces them; it is quite another to require regulated parties to divine the agency's interpretations in advance.").

The District Court concluded that agencies need only comply with the fair notice requirement when they impose "a criminal or civil penalty or sanction" or reject "a filing as untimely or for failing to comply with some other filing requirement." A39. But the doctrine covers far more than that meager subset. The Supreme Court found one broadcaster lacked fair notice of a rules change even though the broadcaster was not monetarily penalized *at all*. *FCC v. Fox Television Stations, Inc.*, 567 U.S. 239, 253 (2012). And this Court regularly applies the fair-

[4] *See* www.accessdata.fda.gov/drugsatfda_docs/nda/2005/021690s000_MedR.pdf.

notice rule in cases involving neither penalties nor mere filing requirements. *U.S. v. Chrysler Corp.*, 158 F.3d 1350, 1354-55 (D.C. Cir. 1998) (applying fair-notice doctrine to recall order); *SNR Wireless License Co., LLC v. FCC*, 868 F.3d 1021, 1045–46 (D.C. Cir. 2017) (applying fair-notice doctrine to FCC's denial of an opportunity to re-negotiate agreements found not to qualify for wireless spectrum auction bidding credits); *see also Univ. Med. Ctr. v. Sebelius*, 856 F. Supp. 2d 66, 86 (D.D.C. 2012) (rejecting HHS's argument that fair notice requirement did not apply to regulation regarding computation of resident time for reporting purposes).

Nor is there any merit to the District Court's suggestion that Amgen was not harmed by the agency's surprise reveal because the "meaningful labeling" standard is somehow more "generous" than the prior "meet all terms of the written request" standard. A41. That standard was not just ungenerous; it was rejected as *unlawful* in *Merck*, 148 F. Supp. 2d. at 30.

FDA's use of its new interpretation against Amgen also violated key principles of retroactive rulemaking. *See Retail, Wholesale & Dep't Store Union, AFL-CIO v. NLRB*, 466 F.2d 380, 390 (D.C. Cir. 1972). All of the *Retail Union* factors counsel against application of FDA's surprise "fairly respond" standard here. The standard was announced for the first time to Amgen in the course of its adjudication and represents an abrupt departure from the reasonably ascertainable meaning of the statute. Amgen relied upon that plain meaning in deciding to (and

continuing to) pursue pediatric exclusivity, and in negotiating its labeling with FDA. Application of the "new" standard to Amgen imposes a significant burden—the denial of several months' exclusivity to which Amgen otherwise should have been statutorily entitled. And there is no statutory interest in having Amgen surprised by application of the new rule. *See id*.

C. FDA's Disparate Treatment of Similarly Situated Entities Is Arbitrary and Capricious.

Finally, the District Court further erred by accepting FDA's deficient explanation for its disparate treatment of OTC and Sensipar. A56. Despite two remands, FDA failed to reconcile its grant of exclusivity to OTC with its denial of exclusivity to Sensipar. FDA provided several different explanations for FDA's treatment of OTC, without committing to any of them: the agency could have thought the terms of the written request were met despite the contradictory evidence; maybe the agency made a mistake in granting exclusivity; or perhaps it applied a different standard altogether. A265.

The District Court accepted these alternative explanations, concluding that the agency subjectively applied the same "fairly respond" test to both drug products. A56. But FDA's subjective intent at the time of decisionmaking—to the extent it can even be divined, and regardless of whether it is now deemed erroneous—does not make for an adequate explanation. "After-the-fact claims about agency intentions do not work when agency actions evince the opposite."

Am. Wild Horse Pres. Campaign v. Perdue, 873 F.3d 914, 924 (D.C. Cir. 2017). To the extent FDA is suggesting (without overtly admitting) that the agency made a mistake in granting OTC exclusivity, that argument too would fail. "[T]here is no 'oops' exception to the duty of federal agencies to engage in reasoned decisionmaking." *Id.* This is especially true here, where FDA refuses to take a firm position on the question of whether it even *made* a mistake.

II. AMGEN WILL SUFFER IRREPARABLE HARM ABSENT INJUNCTIVE RELIEF.

Amgen will suffer irreparable harm absent injunctive relief and expedited review. The pediatric exclusivity statute's *quo* for the *quid* of pediatric studies is to extend existing exclusivities and patent protections by six months. *See* 21 U.S.C. § 355a(b)(1)(B), (c)(1)(B). FDA currently is prohibited from approving generic versions of Sensipar until a patent (U.S. Patent No. 6,011,068) expires on March 8, 2018. FDA has already tentatively approved several generic versions of Sensipar. Those tentative approvals can be converted to final approvals on March 8, absent an injunction, and generic manufacturers could flood the market within days.[5] Once on the market, generics cannot effectively be taken *off* the market to meaningfully restore Amgen's exclusivity. Amgen thus would lose its statutory

[5] A number of companies have filed applications to market generic versions of Sensipar. Amgen has filed patent lawsuits involving a different patent against many of these companies, but no order or agreement in those lawsuits currently prohibits those generics from entering the market after March 8.

exclusivity before its appeal could even be heard. That in and of itself will irreparably harm Amgen. *See Apotex, Inc. v. FDA*, No. CIV.A. 06-0627 JDB, 2006 WL 1030151, at *17 (D.D.C. Apr. 19, 2006) (loss of "a statutory entitlement … is a harm that has been recognized as sufficiently irreparable").

The loss of exclusivity will also cause real-world harm, including drastic loss of market share and irrecoverable losses measuring hundreds of millions of dollars. Within the first month following launch, generic oral drugs typically capture approximately 70% of market share. Georghiou Declaration ¶ 3. The numbers are even steeper at three months (88%) and six months (93%). *Id.*; *see also CollaGenex Pharm., Inc. v. Thompson*, No. 03-1405, 2003 WL 21697344, at *10 (D.D.C. Aug. 26, 2003) (noting that within two weeks of availability of a generic version of Zestril, the generic manufacturer achieved 91% market share).

There are several reasons for this well-recognized phenomenon. First, some state laws mandate or permit the substitution of generic drugs for innovator products, regardless of what product is prescribed. Georghiou Declaration ¶ 4. In addition, the formularies—official lists of covered medicines that may be prescribed—developed by insurance companies, pharmacy benefit managers, and dialysis clinics disproportionately favor generic versions of drugs. *Id.* ¶ 6. Sensipar's status on those formularies—and therefore its ability to secure coverage by third party payers such as public and private insurers—will be impaired upon

entry of a generic drug. *Id.*; *see also Hoffmann-La Roche Inc. v. Cobalt Pharm. Inc.*, Civil Action No. 07-4539, 2010 WL 4687839, at *11–12 (D.N.J. Nov. 10, 2010) (finding irreparable harm based on threat to brand name drug's formulary status and relationships with third party payers).

As soon as a generic version of Sensipar is launched, Amgen expects a staggering loss of market share for Sensipar, to the tune of 73% within the first month, and 99% in the first six months. Georghiou Declaration ¶ 7. Amgen will be forced to drop prices to try to recapture some of that market share, which will lead to even further decreases in revenues. *Id.* ¶ 8. These losses will significantly impact the company's operations, including its R&D. *Id.* ¶ 11. These types of losses—which Amgen will never be able to recover from FDA—constitute irreparable harm. *See Philip Morris USA Inc. v. Scott*, 131 S. Ct. 1, 4 (2010) (Scalia, J., in chambers) ("If expenditures cannot be recouped, the resulting loss may be irreparable."); *see also Bayer HealthCare, LLC v. FDA*, 942 F. Supp. 2d 17, 26 (D.D.C. 2013) (finding irreparable harm where innovator drug company would "experience a decline in market share, price erosion, loss of customer good will, and loss of research and development funding as a result of [a generic's] entry into the market"); *Celsis In Vitro, Inc. v. CellzDirect, Inc.*, 664 F.3d 922 (Fed. Cir. 2012) (affirming finding of irreparable harm due to price erosion, damage to

ongoing consumer relationships, loss of customer goodwill, and loss of business opportunities).

Injunctive relief is needed to ensure that Amgen's statutory right is not lost forever. *See FTC v. Heinz, H.J. Co.*, No. 00-5362, 2000 WL 1741320, at *2 (D.C. Cir. Nov. 8, 2000) (granting injunction pending appeal when it would otherwise be "impossible to recreate" the status quo).

III. TEMPORARY INJUNCTIVE RELIEF SERVES THE PUBLIC INTEREST.

The public interest favors granting an injunction. "There is generally no public interest in the perpetuation of unlawful agency action. To the contrary, there is a substantial public interest in having governmental agencies abide by the federal laws that govern their existence and operations." *League of Women Voters of United States v. Newby*, 838 F.3d 1, 12 (D.C. Cir. 2016); *see also Bracco Diagnostics*, 963 F. Supp. at 30 ("Requiring [FDA] to act lawfully is also very much in the public interest."). This public interest overrides any countervailing public interest in the availability of a cheaper generic drug in the short term. *See Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998).

The public also has a strong interest in enforcing Congress's carefully crafted pediatric-exclusivity scheme, which encourages drug sponsors like Amgen to undertake costly and difficult pediatric testing that would otherwise not happen. *See Mylan Labs., Inc. v. Leavitt*, 484 F. Supp. 2d 109, 124 (D.D.C. 2007) (denying

generic manufacturers' motion for injunctive relief and noting that public interest favors not only generic competition, but also "promoting industry incentives to research and develop new drug treatments").

And of course, the public has an interest in meaningful judicial review. Effectively denying Amgen the benefit of the bargain struck by Congress—without permitting meaningful appellate review—would undermine the core purpose of pediatric exclusivity.

IV. NEITHER DEFENDANTS NOR INTERVENORS WILL BE SUBSTANTIALLY HARMED BY INJUNCTIVE RELIEF.

The balance of the equities also favors injunctive relief. On Amgen's side of the ledger, the risks it faces are grave, as explained above. FDA, for its part, can claim no legitimate interest in perpetuating an unlawful and impermissible interpretation of a critical exclusivity statute. As for the generic intervenors, entry of an injunction along with expedited briefing and argument will at worst *delay* a generic's entry into the market, but that temporary pause is necessary to enable appellate review of FDA's decision. *See* D.C. Cir. Practice & Internal Procedures R. VIII(B) (court may expedite case "to minimize possible harm to the parties or the public"). Any temporary harm to generic manufacturers is outweighed by the permanent loss of Amgen's meaningful appeal rights—and the statutory exclusivity to which it is entitled—if injunctive relief is denied.

CONCLUSION

For these reasons, the motion should be granted and FDA should be temporarily enjoined from approving any generic versions of Sensipar pending resolution of this appeal.

The Court should also order Amgen to file its opening brief on March 6; responsive briefs on March 23, Amgen's reply on April 6, and the Court should direct the Clerk to calendar the case for argument on the earliest available date following briefing.

Respectfully submitted,

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Dated: February 23, 2018

CERTIFICATE OF COMPLIANCE

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I certify that on February 23, 2018, the foregoing was electronically filed through this Court's CM/ECF system, which will send a notice of filing to all registered users.

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