IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

PAR STERILE PRODUCTS, LLC, *et al.*, Plaintiffs, v. ALEX M. AZAR II, Secretary of Health and Human Services, *et al.*, Defendants, and ATHENEX PHARMA SOLUTIONS, LLC, *et al.*, Intervenor-Defendants.	Case No. 1:17-cv-02221-APM REDACTED

PLAINTIFFS' MOTION FOR PRELIMINARY INJUNCTION

Plaintiffs Par Sterile Products, LLC and Endo Par Innovation Company, LLC (collectively, "Par") respectfully move the Court for a preliminary injunction (1) enjoining Defendant Food and Drug Administration's (FDA) unlawful *Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act* (Jan. 2017) (the *Bulk Compounding Decree*), *see* Ex. 3[1]; or alternatively, (2) enjoining the listing of vasopressin in Category 1 of the nominations list under the *Bulk Compounding Decree*, Ex. 8, and enjoining FDA from authorizing bulk drug compounding using vasopressin without compliance with the new-drug approval process, *see* 21 U.S.C. § 355, or the statutory exemption therefrom at 21 U.S.C. § 353b. In support of this motion, Par relies on the attached memorandum, which

[1] Attached to the Declaration of Andrew D. Prins, filed contemporaneously.

establishes that Par is likely to succeed on the merits and will suffer irreparable harm absent preliminary relief, that other interested parties will suffer little or no harm as a result of preliminary relief, and that preliminary relief is in the public interest. Should the Court conclude that Par has demonstrated a likelihood of success on the merits, but has not otherwise satisfied the requirements for preliminary relief, Par respectfully requests that the Court convert this motion to one for expedited summary judgment—the issues presented are purely legal and require no further factual development. *See, e.g.*, *March for Life v. Burwell*, 128 F. Supp. 3d 116, 120 (D.D.C. 2015); *Morris v. District of Columbia*, 38 F. Supp. 3d 57, 62-63 (D.D.C. 2014).

Counsel for Par conferred with counsel for Defendants and Intervenors regarding Par's request for preliminary relief; they oppose.

August 21, 2018

Respectfully submitted,

/s/ Philip J. Perry

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MEMORANDUM IN SUPPORT OF PLAINTIFFS' MOTION FOR PRELIMINARY INJUNCTION

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page(s)

CASES

STATUTES

REGULATIONS

OTHER AUTHORITIES

INTRODUCTION

Plaintiffs bring this motion for preliminary relief because Defendant Food and Drug Administration (FDA) has illegally authorized so-called "bulk compounders" to sidestep the drug approval process, enter the market, and compete with Plaintiffs' FDA-approved drug, in direct contravention of Congress's express statutory mandates to FDA. Intervenor Athenex is one such bulk compounder, and its intervention papers demonstrate exactly the irreparable harm Plaintiffs now face. And FDA's own statements over recent months recognize the need to remedy the statutory violations that have regrettably necessitated this motion.

Traditionally, the act of a pharmacy "compounding" a medication was a patient-specific process based on an individual patient's needs and a specific patient prescription from a physician. For example, a pharmacist might compound an ordinarily solid oral dosage into an oral liquid dosage for an elderly patient who could not swallow pills. By the early 1990s, however, the distinction between traditional pharmacy compounding and drug manufacturing began to blur, as nominal "pharmacies" opened factories to begin "manufacturing drugs" without FDA approval and without the attendant safety and efficacy protections required for federally approved drugs. *See generally Med. Ctr. Pharmacy v. Mukasey*, 536 F.3d 383, 389-90 (5th Cir. 2008). Such bulk compounders rationalize their practice as akin to traditional pharmacy compounding, but in practice they operate as large-scale drug manufacturers.

More than four years ago, Congress gave FDA very explicit instructions on how to address large-scale bulk compounding when it enacted the Drug Quality and Security Act (DQSA) amendments to the Federal Food, Drug, and Cosmetic Act (FDCA). Congress passed the DQSA in response to a national catastrophe: an unlicensed bulk drug compounder, the New England Compounding Center, had mass-produced purportedly sterile drugs outside of the FDA approval process. Dozens of people who took the compounded drug died and hundreds more were sickened.

See 159 Cong. Rec. 14,610, 14,650 (2013) (statement of Rep. Murphy). The "outbreak [wa]s one of the worst public health disasters in our country's history." *Id.*

The DQSA set forth clear ground rules for bulk compounding. Bulk compounders are not allowed to sidestep the lengthy scientific processes for FDA new drug approval unless several very specific criteria are met. *See generally* 21 U.S.C. § 353b. Congress instructed that bulk compounders could not compound any drug that would be "essentially a copy" of an FDA-approved drug. *Id.* § 353b(a)(5). And, as relevant here, FDA may allow bulk compounding of a specific drug substance only if FDA first determines, through a statutorily mandated multi-step process involving public notice and comment, that the compounded drug is genuinely necessary to meet an unaddressed "clinical need." *See id.* § 353b(a)(2)(A). Ignoring both of those explicit statutory requirements and the regime put in place by Congress, FDA instead implemented its own regime through its *Bulk Compounding Decree*, which is nominally labeled an "interim guidance" document. *See* Ex. 3, FDA, *Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act* (Jan. 2017) [hereinafter *Bulk Compounding Decree*].[2] Under the *Decree*, FDA accepts "nominations" from bulk compounders for a "Category 1" list of substances that can then be permissibly compounded, with no determination of whether the compounded drug would be "essentially a copy" of an FDA-approved drug and without the mandatory statutory process for assessing whether there is a "clinical need" for the compounded drug. *See id.* at 5.

Plaintiffs are the owner and manufacturer of an FDA-approved drug, Vasostrict®, which contains the active ingredient vasopressin. Plaintiffs initiated this suit in October of 2017,

[2] All exhibits referenced in this memorandum are attached to the Declaration of Andrew D. Prins, filed contemporaneously.

explaining in detail how FDA's *Decree* not only violates the DQSA but is also fundamentally at odds with core elements of the FDCA, including its new drug approval process (which specifically addresses "generic" and other follow-on drug products) and statutory protections for patent holders. *See* Compl. ¶¶ 43-51, 68-82, ECF No. 1. In response, FDA changed course. It initiated a new process to comply with the DQSA, and made several public statements recognizing the need to conform its bulk compounding regime to the requirements set by Congress in the statute:

- "A critical component of the FD&C Act is its restrictions on compounding drugs that are essentially copies of FDA-approved or commercially available products."[3]
- "Because they are subject to a lower regulatory standard, compounded drugs should only be distributed to meet the needs of patients whose medical needs cannot be met by an FDA-approved drug."[4]
- "The FDA's decisions will be guided by the conditions set forth in the statute, so that bulk drug substances are placed on the 503B bulks list only when there is clinical need to compound drugs using these substances."[5]
- "[C]ompounding drugs using bulk drug substances, when the use of an FDA-approved drug or a drug compounded using an FDA-approved drug would meet patients' medical needs, can undermine the drug approval process by reducing the incentive for drug manufacturers to seek approval of brand or generic drugs."[6]

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[3] Ex. 5, FDA, *2018 Compounding Policy Priorities Plan* (Jan. 2018) [hereinafter *2018 Priorities Plan*].

[4] *Id.*

[5] *Id.*

[6] Ex. 6, Press Release, FDA, *Statement from FDA Commissioner Scott Gottlieb, M.D., on a key step in advancing FDA's oversight of drug compounding and implementing new laws governing outsourcing facilities* (Mar. 23, 2018) [hereinafter *2018 Clinical Need Guidance Announcement*].

Despite recognizing that need to comply with the DQSA, FDA did not alter the *Bulk Compounding Decree*, and retained for the time being that purportedly "interim" regime even though the DQSA was now over four years old. But, as part of the process to bring its program into compliance, FDA stated that it would begin making the required clinical need determinations before the end of 2018, *see* Joint Mot. for Stay ¶ 7, ECF No. 17, and that, "as FDA evaluates bulk drug substances, it intends to publish a notice for public comment in the Federal Register that describes its proposed position on each substance along with the rationale for that position."[7]

In good faith, at FDA's request, Plaintiffs agreed to a temporary stay of this case to give FDA time to comply with the DQSA, but both parties recognized that it would be necessary to lift the stay so Plaintiffs could seek a preliminary injunction if any bulk compounder attempted to introduce a vasopressin product under the *Decree*. *See* Joint Mot. for Stay ¶ 8(b), ECF No. 17. Until very recently, the identity of only one potential vasopressin compounder was publicly known, and Plaintiffs Par Sterile sued that compounder—QuVa Pharma, Inc. ("QuVa")—in the United States District Court for the District of New Jersey and obtained a preliminary injunction before QuVa was able to come to market. *Par Pharm., Inc v. QuVa Pharma, Inc.*, No. 17-cv-6115-BRM-DEA, 2018 WL 1374023, at *10 (D.N.J. Mar. 16, 2018). Throughout this period, however, Intervenor Athenex actively concealed its intent to bulk compound vasopressin, purposefully disguising its identity by submitting documentation regarding vasopressin to FDA anonymously through its lawyers, BakerHostetler. Indeed, although Plaintiffs specifically

[7] Ex. 7, FDA, *Evaluation of Bulk Drug Substances Nominated for Use in Compounding Under Section 503B of the Federal Food, Drug, and Cosmetic Act* 7 (2018) [hereinafter *2018 Clinical Need Guidance*].

mentioned Athenex's lawyers' disguised submission in their Complaint,[8] Athenex declined to intervene in this suit when it was filed in 2017, or when Par and FDA in good faith negotiated multiple, publicly-announced stays of the litigation earlier this year. Athenex instead inequitably lay in wait until Monday of last week, when it launched a blitz campaign to bring its illegal vasopressin product to market and finally intervened here. And Athenex readily admits that it would not be entering the market at all if FDA, through the *Bulk Compounding Decree*, had not specifically authorized bulk compounding of vasopressin. *See* Athenex Mem. in Supp. of Mot. to Intervene at 6, ECF No. 19-1 [hereinafter Athenex Mem.] ("After FDA published its 2017 Guidance, Athenex fully committed to operating a 503B compounding business.").

A preliminary injunction is warranted here. First, FDA's violation of the law is obvious and unavoidably clear—indeed, FDA essentially admits that the *Bulk Compounding Decree* does not comply with the DQSA and undermines the FDCA's new drug approval process. Second, Plaintiffs face imminent irreparable harm; Judge Martinotti of the District of New Jersey already found in very similar factual circumstances that "Par has proffered substantial evidence it would suffer irreparable harm beyond that which money damages could remedy" from competition by a bulk compounder, *Par Pharm.*, 2018 WL 1374023, at *9, and Intevenor Athenex has already supplied the Court with direct evidence of that harm in this case. Third, the balance of equities tips heavily in Plaintiff's favor. FDA has no legitimate interest in violating the law and undermining the safety of the drug supply. And while Athenex will undoubtedly point to maintaining its own illegal product as a counterweight, Athenex's inequitable conduct is

[8] *See* Compl. ¶ 67 ("On information and belief, at least one other compounder is also working to prepare a bulk compounded vasopressin drug for launch. Through its counsel, that undisclosed compounder has also recently filed a 'nomination' for vasopressin under FDA's Bulk Compounding Decree." (citation omitted)).

abundantly clear: Athenex pursued its secret strategy with its eyes wide open to the risk, and cannot now legitimately claim that its interests in compounding vasopressin—which is only one of several compounded products it manufactures—are entitled to any weight in the balance of equities.

FDA's *Bulk Compounding Decree* is flatly violative of the law. This Court would be justified in preliminarily enjoining the full operation of that regime. *See* Ex. 3, *Bulk Compounding Decree*. Alternatively, on this preliminary injunction motion, the Court could narrowly tailor a remedy to address the specific harm to Plaintiffs by enjoining only FDA's actions under the *Decree* authorizing compounding of vasopressin. Ex. 8, FDA, *Bulk Drug Substances Nominated for Use in Compounding Under Section 530B of FDCA* (July 30, 2018).

BACKGROUND

A. Statutory Framework For New Drug Approvals

The FDCA regulates drug manufacturing, marketing, and distribution in interstate commerce. The Act prohibits the introduction of any "new drug" into interstate commerce absent premarket approval by FDA. 21 U.S.C. § 355(a). With certain exceptions not relevant here, the term "new drug" encompasses "any drug." *Id.* § 321(p); 21 C.F.R. § 314.200(e)(1).

The principal pathway for premarket approval is a New Drug Application (NDA) pursuant to FDCA Section 505(b)(1). A full NDA must contain fulsome reports of investigations of the safety and effectiveness of the product candidate gathered through expansive clinical trials. 21 U.S.C. § 355(b)(1). This pathway is typically used for truly new drugs. In 1984, Congress amended the FDCA through the Hatch-Waxman amendments to create additional, streamlined statutory approval pathways for certain follow-on drug products (*e.g.*, generics), Pub. L. No. 98-417, 98 Stat. 1585 (1984), but again conditioned approval on submission of extensive scientific

information and required FDA's approval prior to marketing in order to assure safety and efficacy. *See, e.g.*, 21 U.S.C. § 355(j)(2)(A); *Fulgenzi v. PLIVA, Inc.*, 711 F.3d 578, 585-86 (6th Cir. 2013).

When enacting the Hatch-Waxman amendments, Congress recognized that it must "balance between two competing policy interests: (1) inducing pioneering research and development of new drugs and (2) enabling competitors to bring low-cost, generic copies of those drugs to market." *Andrx Pharm., Inc. v. Biovail Corp.*, 276 F.3d 1368, 1371 (Fed. Cir. 2002). Imitator drugs can quickly flood the market and devastate a previously approved drug's economic viability, so the Hatch-Waxman amendments instituted a framework that prohibits FDA from approving follow-on drugs where patent disputes may arise. If an unexpired patent exists potentially covering the drug product at issue, an applicant for a follow-on drug product must certify that it will not seek approval prior to the expiration of that patent (if it is listed in the so-called Orange Book[9]) or that the patent is invalid or will not be infringed. *See* 21 U.S.C. § 355(b)(2)(A)(i)-(iv), (j)(2)(A)(vii)(I)-(IV). In the case of a certification that the subject patent is invalid or will not be infringed, the applicant must provide notice to each relevant patent owner to explain its invalidity or non-infringement rationale. *Id.* § 355(b)(3), (j)(2)(B). If the patent owner then sues within 45 days, FDA must refrain from approving the follow-on application for up to 30 months to allow that litigation to proceed. *See id.* § 355(c)(3)(C), (j)(5)(B)(iii).

B. FDA's Historical Regulation Of Compounding And Congress's Intervention

Traditionally, compounding refers to the process by which a pharmacist combines or alters drug ingredients pursuant to a physician's prescription to create a medication that meets the unique

[9] The "Orange Book" is the colloquial reference to the list of "Approved Drug Products with Therapeutic Equivalence Evaluations" maintained by FDA pursuant to 21 U.S.C. § 355(j)(7)(A).

needs of an individual patient. *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 360-61 (2002). A patient may, for example, be "allergic to an ingredient in a mass-produced product," and his physician may accordingly prescribe a compounded drug that does not contain the offending ingredient, which the pharmacist may then provide. *Thompson*, 535 U.S. at 360.

In the early 1990s, however, concerns emerged that certain pharmacists were creating large-scale outsourcing operations by "purchasing bulk quantities of drug products, 'compounding' them into specific drug products before receiving individual prescriptions, and marketing those drugs to doctors and patients." *Med. Ctr. Pharmacy*, 536 F.3d at 389. In other words, those pharmacists were "manufacturing drugs under the guise of compounding them." *Id.* And profound health issues emerged as a result. For example, some compounders altered approved drugs and caused people literally to lose their eyes. *See* Ex. 9, Associated Press, *Eye Drop Injuries Prompt an F.D.A. Warning*, N.Y. Times, Dec. 9, 1990. FDA responded by announcing broad regulatory authority over compounding and threatening enforcement actions based on an *ad hoc* list of factors FDA would consider when evaluating a given pharmacy. *See* 57 Fed. Reg. 10,801, 10,906 (Mar. 30, 1992).

In 1997, Congress determined that a statutory solution was needed and replaced FDA's policy through the Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296 (FDAMA). As relevant here, it made plain that "compounded drugs *are* 'new drugs'" regulated by the FDCA. *Med. Ctr. Pharmacy*, 536 F.3d at 394. And it added a statutory framework—at Section 503A (21 U.S.C. § 353a)—for determining whether a compounded drug would be exempt from the FDCA's drug-approval process, which generally requires, *inter alia*, that compounding occur "in response to a valid prescription for an identified individual patient" or in "limited quantities." *Thompson*, 535 U.S. at 364.

After the Supreme Court invalidated advertising-related provisions of the FDAMA on First Amendment grounds in 2002, FDA took the position that the FDAMA's other provisions were not severable and issued a new policy, substantially similar to the one it employed *before* the FDAMA. *See* Ex. 10, FDA, *Compliance Policy Guide* § 460.200 (May 29, 2002) [hereinafter *CPG 460.200*]. This policy "strongly suggested" FDA would not enforce the statute against certain bulk compounders. Anna B. Laakmann, *Customized Medicine and the Limits of Federal Regulatory Power*, 19 Vand. J. Ent. & Tech. L. 285, 305-06 (2016); *see* Ex. 10, *CPG 460.200* at 4.

As a result of FDA's new policy, the bulk-compounding industry quickly reemerged, with "outsourcing facilities" manufacturing large quantities of drugs for wholesale distribution under the guise of compounding. *See* 159 Cong. Rec. at 14,649 (statement of Rep. DeGette); *id*. at 14,650 (statement of Rep. Green) ("Large operators were able to sell products interstate in an unregulated gray area."). In 2012, that issue came to a head after a tragedy in which the New England Compounding Center manufactured and shipped throughout the country a drug contaminated with infectious agents including black mold that led to an outbreak of fungal meningitis. *See* Ex. 11, Kurt Eichenwald, *Killer Pharmacy: Inside a Medical Mass Murder Case*, Newsweek, Apr. 16, 2015. Dozens of individuals died and hundreds were infected. *Id.* Unlike a traditional compounder, the facility was "selling large shipments of drugs without prescriptions." *Id.* In other words, it was "conducting business like a manufacturer." *Id.* As FDA has admitted, this tragedy was not "an isolated event." *See* Ex. 12, FDA, *FDA's Human Drug Compounding Progress Report* 4-5 (2017). Instead, because "FDA does not verify the[] safety, effectiveness, or quality" of compounded drugs before they are marketed, these products have generated "a long

history of serious adverse events associated with contaminated, super-potent, mislabeled, or otherwise poor quality compounded drugs." *Id.*

Following this incident, the bulk-compounding industry attracted intense media and legislative scrutiny. Congress and the public quickly realized that what happened at the New England Compounding Center was very likely to happen again—numerous other unsafe facilities were already in operation throughout the country. *See* 159 Cong. Rec. 16,825, 17,223 (2013) (statement of Sen. Feinstein) ("You might think that a story like this is rare. What we have learned is that it is not. . . . [Forty-eight] other compounding companies were found to be producing drugs that were either unsafe or were made in unsafe environments.").

Congress responded by enacting the DQSA, imposing further restrictions on bulk compounding. The DQSA reenacted Section 503A without the advertising-related provisions the Supreme Court had held unconstitutional. And it also added a new section, 503B, that specifically targeted the "outsourcing facilities" that constitute the bulk-compounding industry. DQSA, Pub. L. No. 113-54, 127 Stat. 588, Title I § 102(a)(2) (2013) (codified as amended 21 U.S.C. 353b).

C. Congress's Statutory Regime Governing Bulk Drug Compounding

Section 503B makes plain that "[i]f a compounded drug does not qualify for an exemption under the [DQSA], it would be subject to all of the requirements of the [FDCA] . . ., including the new drug approval . . . requirements." *See* Ex. 13, Letter from Margaret Hamburg, FDA, to Colleague at 2 (Jan. 8, 2014) [hereinafter Dear Colleague Letter]; 21 U.S.C. § 353b(a). It also establishes a narrow exception for bulk compounders that register as "outsourcing facilities." 21 U.S.C. § 353b(a). Such a facility may distribute drug products that are not patient specific and which are compounded from bulk drug substances, but it may do so only if multiple statutory requirements are satisfied. *See id.* Two requirements are especially relevant here:

First, an outsourcing facility may compound using bulk drug substances in only two situations. The first is if the substance appears on a list of substances for which FDA has determined, through notice and comment, that there is a clinical need (the "Clinical Need List"):

> (i) the bulk drug substance appears on a list established by the Secretary identifying bulk drug substances for which there is a clinical need, by—
>
> > (I) publishing a notice in the Federal Register proposing bulk drug substances to be included on the list, including the rationale for such proposal;
> >
> > (II) providing a period of not less than 60 calendar days for comment on the notice; and
> >
> > (III) publishing a notice in the Federal Register designating bulk drug substances for inclusion on the list[.]

Id. § 353b(a)(2)(A)(i). The second is if the compounded drug product appears on a list of drugs that FDA has determined are in shortage in the United States (the "Shortage List"):

> (ii) the drug compounded from such bulk drug substance appears on the drug shortage list in effect under section 506e at the time of compounding, distribution, and dispensing[.]

Id. § 353b(a)(2)(A)(ii).

Second, the compounded drug product must not be "essentially a copy of one or more approved drugs." *Id.* § 353b(a)(5). A compounded drug product generally is considered essentially a copy of an approved drug if the two products are "identical or nearly identical," or if the compounded drug product uses a component of an approved drug but is not clinically different from the approved drug:

> (2) The term "essentially a copy of an approved drug" means—
>
> > (A) a drug that is identical or nearly identical to an approved drug . . . unless . . . the drug appears on the drug shortage list in effect under section 506e at the time of compounding, distribution, and dispensing; or
> >
> > (B) a drug, a component of which is a bulk drug substance that is a component of an approved drug . . . unless there is a change that produces for an individual patient a clinical difference, as determined by the prescribing practitioner, between the compounded drug and the comparable approved drug.

Id. § 353b(d)(2).

In essence, these provisions require the following process to authorize a substance for bulk compounding. First, FDA must make a record-based determination that bulk compounding using a particular drug substance is necessary to satisfy a "clinical need" unmet by approved drug products. *See id.* § 353b(a)(2)(A)(i). Second, FDA can make such a determination ***only after*** publishing a proposal in the Federal Register that includes "the rationale for such proposal" and provides "a period of not less than 60 calendar days for comment." *Id.* § 353b(a)(2)(A)(i)(I)-(II). Third, FDA must publish its ultimate decision in the Federal Register. *See id.* § 353b(a)(2)(A)(i)(III). And finally, FDA cannot authorize bulk compounders to produce a drug simply to compete with or replace an FDA-approved drug. *See* 21 U.S.C. § 353b(a)(5).

D. FDA's Extra-Statutory Regime For Bulk Drug Compounding

Rather than implement the regime that Congress instructed it to implement, FDA created its own extra-statutory framework for regulating bulk compounding. In July 2014, FDA opened a docket to accept "nominations" of bulk drug substances for inclusion on the Clinical Need List. *See* Bulk Drug Substances That May Be Used To Compound Drug, 79 Fed. Reg. 37,750, 37,751 (July 2, 2014). Although many substances have been *nominated*, FDA has never taken the statutorily mandated notice and comment and record-based evaluation to add any substances to the Clinical Need List. Instead, in October 2015, FDA proposed to establish an "Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act." 80 Fed. Reg. 65,770 (Oct. 27, 2015). The extra-statutory regime this document established—as finalized in June 2016 and amended in January 2017—allows bulk compounding using the nominated substances notwithstanding the statutory requirements. *See generally* Ex. 3, *Bulk Compounding Decree*.

Under its unlawful regime, FDA has grouped the nominated substances into three categories: Category 1 comprises substances "Currently Under Evaluation," which "may be eligible for inclusion on the [Clinical Need List], were nominated with sufficient supporting information for FDA to evaluate them, and do not appear on any other [Category] list." *Id.* at 5. Category 2 comprises substances that were nominated with sufficient supporting information but for which "FDA has identified significant safety risks relating to the use of these substances in compounding pending further evaluation." *Id.* at 5-6. Category 3 comprises substances that were nominated without sufficient supporting information. *Id.* at 6.

Under this regime, a substance may be included in Category 1 if it may be eligible for inclusion on the Clinical Need List. *See id.* at 5-6. But FDA conducts *no* record-based review before placing substances in Category 1—by its plain terms, the *Bulk Compounding Decree* places substances in Category 1 if they have merely been nominated "with adequate supporting information for FDA to evaluate [them]," ostensibly at some indeterminate, hypothetical future date. *Id* at 8. And FDA conducts *no* clinical need analysis before placing bulk drug substances on the list. *See* FDA Answer ¶ 7, ECF No. 11 ("Defendants . . . admit that FDA has not yet developed the final list of substances that may be used for compounding based on clinical need by '503B Outsourcing Facilities,' described in 21 U.S.C. § 353b . . . ."). Nor does it determine whether the resulting compounded drugs would be essentially copies of already approved products.

The *Bulk Compounding Decree* explicitly provides a binding regulatory safe harbor from the requirements of the FDCA, stating that FDA "does not intend to take action against an outsourcing facility for compounding a drug using a bulk drug substance that does not appear on the [Clinical Need List] and that is not used to compound a drug that appears on the [Shortage List] at the time of compounding, distribution, and dispensing, provided that" the substance is in

Category 1 and certain other conditions are satisfied. Ex. 3, *Bulk Compounding Decree* at 8. In other words, even though Section 503B authorizes bulk compounding only if the bulk substance appears on the Clinical Need List or the drug compounded from the substance appears on the Shortage List, FDA has failed to implement that requirement since 2013. Instead, FDA treats a substance's inclusion in Category 1 of its nominations list as sufficient to authorize bulk compounding using that substance. FDA has confirmed this interpretation of the *Bulk Compounding Decree* in warning letters to outsourcing facilities, stating that "you should only compound drug products using bulk drug substances that may be used in compounding under section 503B, or that are eligible for the interim regulatory policy described in [the *Bulk Compounding Decree*]."[10] And in others it has explained that, in contrast to Category 1 substances, only those "in Category 2 or Category 3 . . . cannot be used for compounding."[11] Indeed, before Par filed its Complaint, Defendant FDA Commissioner Gottlieb apparently admitted in an interview with Reuters on September 15, 2017, that many compounders are operating in a manner inconsistent with the FDCA and that FDA's *Bulk Compounding Decree* should be revisited.[12] And, of course, as a result of this suit FDA has now acknowledged that it must now comply with the express provisions of the DQSA.

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[10] *See* Ex. 14, Letter from Karlton Watson, FDA, to Mary Moyer, INCELL Corp. (Oct. 28, 2016) [hereinafter INCELL Enforcement Letter].

[11] *See* Ex. 15, Letter from Monica Maxwell, FDA, to Eddie W. Glover, US Compounding, Inc. (Oct. 10, 2017) [hereinafter US Compounding Enforcement Letter]; *see also* Ex. 16, Letter from Steven Porter, FDA, to Navid Vahedi, Fusion IV Pharm., Inc. (Feb. 21, 2018) [hereinafter Fusion IV Enforcement Letter] (expressing that "FDA does not intend to take action against an outsourcing facility" in compliance with the *Decree*).

[12] *See* Ex. 17, Nate Raymond, *Exclusive: FDA Plans New Compounding Pharmacy Policy, Agency Head Says*, Reuters (Sept. 15, 2017, 5:29 PM).

E. Par's Drug, Vasostrict®, The Only FDA-Approved Vasopressin Product

Par is the manufacturer of Vasostrict®, a lifesaving injection that raises blood pressure to ensure adequate blood delivery to patients' vital organs. Pera Decl. ¶¶ 3, 6. In 2012, Par submitted an NDA under Section 505(b)(2) of the FDCA seeking marketing approval for Vasostrict®. Pera Decl. ¶ 6. Because it is administered intravenously to patients in emergency rooms, intensive care units, and other sensitive hospital settings, Vasostrict® must be manufactured and maintained in sterile conditions. Pera Decl. ¶ 8. The active ingredient in Vasostrict® is vasopressin, and Vasostrict® is the *only* FDA-approved drug product containing vasopressin. Pera Decl. ¶¶ 3, 6. FDA approved Vasostrict® as a treatment for septic shock and post-cardiotomy shock in April 2014. Pera Decl. ¶ 6. According to FDA, approval of the NDA was "critical to ensuring the safety and efficacy" of vasopressin. *See* Ex. 18, Mary Ross Southworth & Anna M. Fine, *FDA Information on Vasostrict Storage*, FDA News for Health Prof'ls (May 2015). Compounded products, in contrast, lack any of the assurances of safety and efficacy that are part of FDA's review of an NDA. Par continues to hold the NDA for Vasostrict® today, and there are six unexpired patents associated with Vasostrict® listed in the Orange Book. Pera Decl. ¶ 7.

F. FDA's Authorization To Bulk Compound Vasopressin

On April 19, 2017, QuVa, which is not a party to this suit, submitted a two-page nomination for vasopressin pursuant to the *Bulk Compounding Decree*. *See* Ex. 4, Letter from Travis Leeah, QuVa, to FDA at 2-3 (Apr. 19, 2017) [hereinafter QuVa Vasopressin Nomination]. QuVa's nomination identified *no clinical need* for vasopressin not served by Vasostrict®. QuVa instead contended—without any factual support—that by compounding vasopressin as a pre-diluted mixture that is essentially a copy of the dilution of Vasostrict® used currently by hospitals, healthcare providers would receive a vasopressin product that is more convenient to administer

and less susceptible to dosing error. *See* QuVa Vasopressin Nomination at 2-3. FDA never solicited public comment on QuVa's nomination (or indeed, any other nomination). FDA nonetheless, over Par's objections (Prins Decl. ¶ 2) added vasopressin to Category 1, authorizing bulk compounding using vasopressin. Prins Decl. ¶ 4.[13]

G. History Of This Case And Subsequent Developments

Par filed its Complaint on October 26, 2017. Par was preparing to file a motion for preliminary relief in this case, *see* Compl. ¶¶ 65-67, ECF No. 1 (discussing the threat of irreparable harm to Par), but successfully obtained a preliminary injunction in another case prohibiting QuVa from coming to market, *Par Pharm.*, 2018 WL 1374023, at *10. At FDA's request, Par agreed to stay this case pending implementation of a new plan to come into compliance with the FDCA. *See* Joint Mot. for Stay ¶ 4, ECF No. 13. On January 18, 2018, FDA released its *2018 Compounding Policy Priorities Plan* and updated and finalized a guidance document interpreting the "essentially a copy" provision of Section 503B. *See* Ex. 5, *2018 Priorities Plan*; Ex. 20, FDA, *Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act* (2018) [hereinafter *Copies Guidance*].

In those documents, FDA repeatedly emphasized the importance of precluding compounders from copying FDA-approved drugs. Ex. 5, *2018 Priorities Plan* ("A critical component of the FD&C Act is its restrictions on compounding drugs that are essentially copies of FDA-approved or commercially available products."); *id.* ("We also intend to prioritize review

[13] Intervenor Athenex submitted another nomination of vasopressin, but disguised its identity by making that submission through its counsel, Baker Hostetler; however, this nomination came after FDA added vasopressin to Category 1, and thus could not have been part of the basis for the agency's decision. *See* Ex. 19, Letter from Baker Hostetler LLP, to FDA at 2-3 (July 27, 2017) [hereinafter Athenex Vasopressin Nomination]. Moreover, this five-page nomination suffered from many of the same deficiencies as QuVa's nomination.

of situations that could adversely impact the public health and premarket approval process, such as compounding using a bulk drug substance to produce a product that can otherwise be made by diluting an FDA-approved drug according to its labeled instructions."). In addition, FDA committed to issue a guidance document interpreting the "clinical need" provision of Section 503B by March 2018. *See id*. In making this announcement, Defendant Gottlieb recognized that FDA should "be guided by the conditions set forth in the statute, so that bulk drug substances are placed on the 503B bulks list only when there is clinical need to compound drugs using these substances." *Id.* Although Par maintained that the *Bulk Compounding Decree* must be withdrawn, it ultimately agreed to a short stay of the case in light of these developments and because no competitors were yet compounding bulk vasopressin (or, to Par's knowledge, were close to doing so). *See* Joint Mot. for Stay ¶ 4(b)(iii), ECF No. 13. However, Par and FDA agreed that Par could lift the stay and seek preliminary injunctive relief if any entity began compounding bulk vasopressin. *Id*.

On March 23, 2018, FDA issued the contemplated guidance document interpreting the "clinical need" provision of Section 503B. *See* Ex. 7, *2018 Clinical Need Guidance*. That document set forth the agency's tentative procedure for assessing whether and how to add a nominated bulk drug substance to the statutory Clinical Need List. Among other things, FDA recognized that "compounded drug products are subject to a lower regulatory standard than FDA-approved drugs" and should accordingly "only be used by patients whose medical needs cannot be met by an FDA-approved drug." *Id.* at 4. FDA then established a stringent test it said it would use to determine whether the statutory clinical need is present for a "bulk drug substance" that "is a component of an FDA-approved drug." *Id.* at 10. Specifically, the FDA will determine whether (1) "an attribute of the FDA-approved drug product makes it medically unsuitable to treat patients" and "the drug product proposed to be compounded is intended to address that attribute," and (2)

whether there is "a basis to conclude that the drug product proposed to be compounded must be produced from a bulk drug substance rather than from an FDA-approved product. *Id.* If—and only if—both of those criteria are satisfied, FDA will then proceed to conduct a multi-factor "balancing test" to determine whether to include the substance on the Clinical Need List. *Id.* As required by the statute, FDA would then publish its proposed position on each substance in the Federal Register for public comment. *Id.* at 7.

Like FDA's other statements earlier this year, the guidance document showed that compounding bulk vasopressin is particularly inappropriate because patient needs can be adequately served by diluting Vasostrict® according to its instructions. *See* Pera Decl. ¶ 13. FDA explained that, in many situations, "compounding using the FDA-approved drug product instead of a bulk drug substance would meet patients' medical needs and present less risk. For example, outsourcing facilities often dilute FDA-approved products to produce intravenous bags for hospitals." Ex. 7, *2018 Clinical Need Guidance* at 4. Later in the document, FDA summarized the relevant policy considerations as follows:

> [C]ompounding a drug product from a bulk drug substance that is a component of an FDA-approved drug when there is no clinical need to do so, perhaps because of economic incentives, undermines the drug approval process. For example, use of bulk drug substances to compound a formulation of a needed concentration, route of administration or dosage form rather than simply diluting or otherwise manipulating the approved drug reduces the incentive for sponsors to invest in and seek FDA-approval of such drugs. The drug approval process is critical to ensure patient access to pharmaceuticals whose quality, safety and effectiveness have been established.

Id. at 6.

However, notwithstanding this recognition that clinical need under the statute turns on whether the FDA-approved drug is medically unsuitable for certain patients *and* that the product proposed to be compounded cannot use the FDA-approved drug product, FDA left its *Bulk Compounding Decree* in place. And under that *Decree*, FDA has authorized drug production using

bulk drug substances that satisfy *neither* of those criteria. Par agreed to stay this litigation once more on March 30, 2018, again with the critical stipulation that the stay should be lifted if an entity began bulk compounding vasopressin. Joint Mot. for Stay ¶ 7, ECF No. 17.

Athenex moved to intervene in this suit on August 13, 2018, explaining it had begun selling bulk compounded vasopressin that same day. *See* Athenex Mem. at 1.

ARGUMENT

The Court considers four factors in assessing entitlement to preliminary relief: "(1) the movant's showing of a substantial likelihood of success on the merits, (2) irreparable harm to the movant, (3) substantial harm to the nonmovant, and (4) public interest." *Davis v. Pension Ben. Guar. Corp.*, 571 F.3d 1288, 1291 (D.C. Cir. 2009). "Courts in this Circuit traditionally have analyzed these four factors on a 'sliding scale,' whereby 'a strong showing on one factor could make up for a weaker showing on another,'" *Cigar Ass'n of Am. v. FDA*, 2018 WL 3304627, at *3 (D.D.C. July 5, 2018) (Mehta, J.) (quoting *Sherley v. Sebelius*, 644 F.3d 388, 392 (D.C. Cir. 2011)), and judges in this District have recently used that approach in a number of cases, *see, e.g.*, *Cigar Ass'n*, 2018 WL 3304627, at *3; *Beacon Assocs., Inc. v. Apprio, Inc.*, 308 F. Supp. 3d 277, 284, 287 n.9 (D.D.C. 2018), *appeal docketed*, No. 18-7073 (D.C. Cir. May 15, 2018); *Davis v. Billington*, 76 F. Supp. 3d 59, 69 n.5 (D.D.C. 2014). Here, Par is highly likely to succeed on the merits and all the remaining factors for equitable relief weigh heavily in Par's favor.

I. PAR IS HIGHLY LIKELY TO SUCCEED ON THE MERITS

FDA's *Bulk Compounding Decree* and specific authorization to bulk compound vasopressin are unlawful because they conflict with the plain language and structure of the FDCA. In Section 503B, Congress specified the circumstances in which bulk compounded drugs may legally be marketed, but here FDA is authorizing marketing where those criteria are not satisfied. Likewise, the FDCA provides that, unless an exception applies, drugs may be marketed only upon

compliance with the lengthy FDA-approval process, and it *requires* FDA to deny applications that do not satisfy the statutory requirements. Multiple cases hold that FDA may not authorize the marketing of drugs where those requirements are not met, but that is exactly what FDA has done here. FDA's regime and authorization to bulk compound vasopressin are *ultra vires* and must therefore be set aside, and nothing shields the agency's unlawful actions from judicial review.

A. FDA's *Bulk Compounding Decree* And Authorization To Bulk Compound Vasopressin Conflict With The Plain Language And Structure Of The FDCA

1. The *Decree* And Authorization Violate Section 503B

The *Decree* explicitly purports to determine the circumstances in which bulk compounded drugs may be legally brought to market. Specifically, it establishes a "nomination" process that authorizes bulk compounding so long as (1) the bulk drug substance used to compound appears in Category 1 of FDA's nominations list, and (2) the finished drug product is compounded in compliance with the provisions of Section 503B *other than* the requirements for the drug substance or drug product to be included on the Clinical Need List or Shortage List. *See* Ex. 3, *Bulk Compounding Decree* at 8. It then expressly authorizes the marketing of drugs that satisfy these extra-statutory requirements, stating that "FDA does not intend to take action against an outsourcing facility for compounding a drug using a bulk drug substance that does not appear on the [Clinical Need List] and that is not used to compound a drug that appears on the FDA drug shortage list at the time of compounding, distribution, and dispensing, provided that the following conditions are met[.]" *Id.*

But Congress has already directly spoken to this issue in Section 503B, delineating the specific circumstances in which bulk compounding may occur. And FDA "ha[s] no authority to change Congress's clear command." *Cf. Sw. Bell Corp. v. FCC*, 43 F.3d 1515, 1517 (D.C. Cir. 1995). In Section 503B, Congress determined that bulk compounding may occur only when there

is a "clinical need"—determined on a record produced pursuant to statutory notice-and-comment procedures, and memorialized on a published Clinical Need List—or when there is a drug shortage and the drug appears on FDA's Shortage List. 21 U.S.C. § 353b(a)(2)(A). Thus, the *Bulk Compounding Decree* directly conflicts with Section 503B, in multiple respects:

- Contrary to the plain language of Section 503B, FDA conducts *no* record-based review for clinical need before authorizing bulk compounding under the *Bulk Compounding Decree*. By its plain terms, the *Decree* places a substance in Category 1 (thereby authorizing bulk compounding using that substance) if it has merely been nominated "with adequate supporting information for FDA to evaluate," ostensibly at some indeterminate, hypothetical future date, whether there is such a clinical need. *Compare* Ex. 3, *Bulk Compounding Decree* at 8 (authorizing bulk compounding with a substance "nominated" with "adequate supporting information for FDA to evaluate it"), *with* 21 U.S.C. § 353b(a)(2)(A)(i) (requiring that the "bulk drug substance appear[] on a list established by the Secretary identifying bulk drug substances for which there is a clinical need").

- Rather than utilizing the prescribed notice-and-comment procedures in Section 503B(a)(2)(A)(i)(I)-(II) for proposing a clinical need determination, the *Bulk Compounding Decree* accepts a nomination without subjecting it to notice and comment. *Compare* Ex. 3, *Bulk Compounding Decree* at 6-7 (accepting nominated "substances [that] ***may be*** eligible for inclusion on the 503B bulks list" (emphasis added)), *with* 21 U.S.C. § 353b(a)(2)(A)(i) (requiring "notice in the Federal Register," "including the rationale" for the proposed determination, and "a period of not less than 60 calendar days for comment").

- Instead of authorizing bulk compounding of authorized substances identified in a Federal Register notice and Clinical Need List, the *Decree* authorizes compounding of substances

added to a file on FDA's website. *Compare Bulk Compounding Decree* at 8 (authorizing bulk compounding for a "substance appear[ing] on 503B Category 1 on FDA's website"), *with* 21 U.S.C. § 353b(a)(2)(A)(i)(III).

In other words, rather than authorizing bulk compounding for which FDA has found, based on record evidence developed during notice and comment, that there is a clinical need, FDA's *Bulk Compounding Decree* authorizes compounding based on a determination that the nominations submitted are sufficiently complete to enable FDA's substantive review regarding clinical need *at some later, unspecified date.* Worse still, FDA conducts no record-based analysis to determine whether any compounded drug authorized under the *Decree* would be essentially a copy of an FDA-approved drug. *See* 21 U.S.C. § 353b(a)(5) (prohibiting such compounded drugs). For these reasons, FDA's *Bulk Compounding Decree* conflicts with Section 503B and is invalid. *See, e.g.*, *Colo. River Indian Tribes v. Nat'l Indian Gaming Comm'n*, 466 F.3d 134, 139 (D.C. Cir. 2006) ("Agencies are . . . 'bound, not only by the ultimate purposes Congress has selected, but by the means it has deemed appropriate . . . .'" (quoting *MCI Telcomm. Corp. v. AT&T Co.*, 512 U.S. 218, 231 n.4 (1994))).

For the same reasons, FDA's specific authorization to bulk compound vasopressin violates Section 503B. FDA authorized such bulk compounding based on QuVa's nomination, rather than a determination through notice and comment that there is a clinical need. QuVa's nomination did not even attempt to identify such a clinical need, and neither QuVa's nomination nor Athenex's nomination (which was submitted after FDA made its decision) included supporting evidence. *See* QuVa Vasopressin Nomination; Athenex Vasopressin Nomination. FDA admits that it did not evaluate whether there is a clinical need to bulk compound vasopressin. FDA Answer ¶ 10 ("FDA has not yet made a final determination of whether there is a clinical need to compound using bulk

vasopressin."). Moreover, Athenex's vasopressin products, like QuVa's contemplated vasopressin products—vasopressin diluted in a saline or dextrose solution—mimic how Vasostrict® is prepared for use. *See* Pera Decl. ¶ 9; Ex. 4, QuVa Vasopressin Nomination; Ex. 19, Athenex Vasopressin Nomination. Thus, not only has FDA authorized bulk compounding vasopressin without the required showing of clinical need, but bulk compounders have used that authorization to release drugs that are essentially copies of Par's FDA-approved drug despite the explicit statutory prohibition against such copies.[14]

2. The *Decree* And Authorization Are Inconsistent With The Structure Of The FDCA

The broader statutory structure confirms that the *Bulk Compounding Decree* and FDA's authorization to bulk compound vasopressin are unlawful. The FDCA provides that a drug generally may be marketed only upon satisfaction of statutory criteria and FDA's approval: "No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug." 21 U.S.C. § 355(a). The statute sets forth the prerequisites for approval, requiring the sponsor to submit an application with detailed scientific information to enable FDA to evaluate

[14] FDA may argue that its *Bulk Compounding Decree* does not conflict with Section 503B because it is merely an "interim" measure while FDA complies with the statute. That argument would fail because Congress did not authorize FDA to proceed with any "interim" measure that is inconsistent with 503B or provide any grace period for compliance. Notably, in another part of 503B, Congress *did* authorize an interim approach. Congress told FDA to develop a list of drugs that "present demonstrable difficulties for compounding," 21 U.S.C. § 353b(a)(6), (c)(3)—another criterion for lawful compounding under the 503B exemption. And although that list must, like the Clinical Need List, be promulgated via notice and comment, *id.* § 353b(c)(1), Congress expressly allowed FDA to use an "interim list" while the permanent one is created, *id.* § 353b(c)(3)(A). Congress's absence of any similar grant of authority regarding the Clinical Need List confirms that FDA lacks that power. *See Russello v. United States*, 464 U.S. 16, 23 (1983) ("[W]here Congress includes particular language in one section of a statute but omits it in another section of the same Act, it is generally presumed that Congress acts intentionally and purposely in the disparate inclusion or exclusion." (citation omitted)).

the safety and effectiveness of the drug. *See*, *e.g.*, *Id.* § 355(b)(1), (j)(2). The FDCA also circumscribes FDA's review, *requiring* the agency to deny applications that do not satisfy the statutory standards. *See id.* § 355(d) (requiring denial if there is "insufficient information to determine whether such drug is safe" or "there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have"); *see also id.* (providing additional mandatory grounds for denial). Section 503B functions as a limited exemption from that general framework for authorized bulk compounding. *See* 21 U.S.C. § 353b(a) ("Sections 502(f)(1), 505, and 360eee-1 . . . shall not apply to a drug compounded by or under the direct supervision of a licensed pharmacist in a facility that elects to register as an outsourcing facility *if each of the following conditions is met* . . . ." (emphasis added)).

Given that the statute expressly bans unapproved drugs and specifies in great detail how FDA may approve drugs, it has long been recognized that FDA may not create extra-statutory mechanisms to authorize the marketing of drugs. Indeed, this District has addressed this precise issue before, repeatedly. In "1962, the FDCA was amended to require NDAs to show that a drug is not only safe, but also effective for its intended uses." *United States v. Sage Pharm., Inc.*, 210 F.3d 475, 478 (5th Cir. 2000). This created an "enormous" administrative hassle for FDA, requiring that many previously approved drugs be subject to agency clearance again to ensure effectiveness. *United States v. Alcon Labs.*, 636 F.2d 876, 887 (1st Cir. 1981). Rather than deal with this burden, FDA twice attempted to authorize the marketing of drugs that had not been approved pursuant to the amended FDCA. But this District correctly rejected both attempts. In *Hoffmann-LaRoche, Inc. v. Weinberger*, this District enjoined FDA's policy authorizing the marketing of certain drugs for which an approval application had been submitted but not yet approved, holding that "FDA's policy . . . contravene[d] the clear statutory requirement of

preclearance mandated by" Congress's amendments. 425 F. Supp. 890, 892, 894-95 (D.D.C. 1975). Next, FDA issued regulations authorizing the marketing of unapproved over-the-counter drugs. *See Cutler v. Kennedy*, 475 F. Supp. 838, 844 (D.D.C. 1979). This District again enjoined FDA's circumvention of the new-drug approval framework because the "regulations formally authorize[d] the continued marketing of . . . drug products in the absence of an administrative determination that those products [were] generally recognized by experts as safe and effective," which "flies in the face of the statutory scheme." *Id.* at 854-57.[15]

These results are not at all surprising, given that both Congress and FDA have repeatedly emphasized that "FDA has no legal authority to permit the marketing of any unapproved 'new drug.'" H.R. Rep. No. 98-1168, at 21 (1984); *see also* Br. of United States as Amicus Curiae at 8-9, *Fla. Breckenridge, Inc. v. Solvay Pharm., Inc.*, No. 98-4606 (11th Cir. July 20, 1998) ("The [FDCA's] comprehensive scheme of regulation prohibits the sale of *any* drug that has not obtained FDA approval of an NDA (or ANDA) unless [a statutory exemption applies]."). Congress's addition of multiple detailed statutory exemptions to the framework confirms this settled law: FDA is not empowered to craft its own extra-statutory solutions, *see, e.g.*, *Andrus v. Glover Constr. Co.*, 446 U.S. 608, 616-17 (1980) ("Where Congress explicitly enumerates certain exceptions to a general prohibition, additional exceptions are not to be implied."); *NRDC v. EPA*, 489 F.3d 1250,

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[15] The D.C. Circuit later upheld an amended version of FDA's regulations because, unlike the initial version, it did not include "an implied promise of immunity," *Cutler v. Hayes*, 818 F.2d 879, 886 (D.C. Cir. 1987), to the sponsors of unapproved over-the-counter drugs. *See id.* at 892-94. By contrast, the *Bulk Compounding Decree* offers precisely such a promise. *See* Ex. 3, *Bulk Compounding Decree* at 7 (stating that FDA "does not intend to take action against" such compounders); *see also* Ex. 14, INCELL Enforcement Letter (directing a company to "only compound drug products using bulk drug substances that may be used in compounding under section 503B, *or* that are eligible for the interim regulatory policy described in [the *Bulk Compounding Decree*]" (emphasis added)); Ex. 15, US Compounding Enforcement Letter; Ex. 16, Fusion IV Enforcement Letter.

1259-60 (D.C. Cir. 2007) (similar), and FDA *knows it*. *See* Ex. 13, Dear Colleague Letter ("If a compounded drug does not qualify for an exemption under [the DQSA], it would be subject to all of the requirements of the [FDCA] . . . including the new drug approval . . . requirements.").

In other contexts, too, courts have repeatedly recognized that federal agencies are forbidden from crafting extra-statutory alternatives to detailed statutory compliance frameworks. The Supreme Court recently did so in *Utility Air Regulatory Group v. EPA*, 134 S. Ct. 2427 (2014) ("*UARG*"). *UARG* involved EPA's decision to regulate greenhouse gas emissions as air pollutants. This had enormous consequences for industry because the Clean Air Act "requires permits for sources with the potential to emit more than 100 or 250 tons per year of a relevant pollutant," and counting greenhouse gasses as pollutants triggered this requirement for thousands of new entities. *Id.* at 2436, 2444. To mitigate this problem, EPA announced it would "tailor" its regulatory scheme so that, contrary to the statute, only sources that emit over 100,000 tons of greenhouse gases would be subject to the relevant regulatory burdens. *Id.* at 2437-38. But because this scheme "purport[ed]" to "establish with the force of law that otherwise-prohibited conduct will not violate the" relevant statute, the Court struck it down. *Id.* at 2445. FDA's *Bulk Compounding Decree* and authorization to bulk compound vasopressin are invalid for the same reason. *See also, e.g.*, *NRDC*, 489 F.3d at 1259 ("Had the Congress intended to exempt [other substances], it could likewise have expressly provided for their exemption *in the statute*." (emphasis added)); *Fin. Planning Ass'n v. SEC*, 482 F.3d 481, 488 (D.C. Cir. 2007) (similar); *Sierra Club v. EPA*, 294 F.3d 155, 160 (D.C. Cir. 2002) (similar).

Because the *Bulk Compounding Decree* authorizes compounding in circumstances that do not comply with the new-drug approval process or any statutory exemptions to that process (such as Section 503B), the *Decree* does an impermissible end-run around Congress's comprehensive

regime for bringing drugs to market. Worse still, it does affirmative violence to Congress's regime. Congress, through the Hatch-Waxman amendments, has already established an elaborate scheme specifically to address the issue of follow-on drugs—*i.e*, those drugs that are identical or nearly identical to an already approved drug, as Anthenex's drug is to Par's. *See* 21 U.S.C. § 355(b)(2), (j). But to protect the viability of the drug-development market, Congress incorporated robust patent-protection features into that scheme. For example, under the Hatch-Waxman amendments, a follow-on drug applicant must provide a certification regarding the patents listed in the Orange Book and provide notice to the patent holder, *id.* § 355(b)(2)(A), (3)(C); (j)(2)(A), (j)(2)(B)(iii), the patent holder is entitled to confidential access to the follow-on drug application, *id.* § 355(c)(3)(D)(i)(I)(cc), (j)(5)(C)(i)(I)(cc), and most importantly, approval of the drug application is automatically stayed for up to 30 months in the event the patent holder initiates litigation, *id.* § 355(c)(3)(C), (j)(5)(B)(iii). And, to prevent circumvention of this process through bulk compounding, Section 503B expressly prohibits bulk compounding of drugs "identical or nearly identical" to an already approved drug in the absence of a drug shortage. 21 U.S.C. § 353b(a)(5), (d)(2). The *Bulk Compounding Decree* respects none of these Congressional limits, and instead allows outsourcing facilities to manufacture follow-on drug products under the guise of "bulk compounding." FDA has repeatedly admitted that the *Decree* undermines this Congressional scheme. *See, e.g.*, Ex. 5, *2018 Priorities Plan* ("Sponsors would be less likely to invest in and seek approval of innovative, life-saving medications if compounders could, after a drug is approved, compound 'substitutes' that may be less expensive because they have not gone through the premarket approval process."); *id.* ("We . . . intend to prioritize review of situations that could adversely impact the public health and premarket approval process, such as compounding using a bulk drug substance to produce a product that can otherwise be made by

diluting an FDA-approved drug according to its labeled instructions."); Ex. 21, *Examining Implementation of the Compounding Quality Act: Hearing Before the H. Comm. on Energy & Commerce*, 115th Cong. (Jan. 30, 2018) (testimony of Scott Gottlieb, M.D., FDA) ("Receiving a compounded drug when a commercially available or approved drug meets the patient's medical needs puts that patient at unnecessary and unacceptable risk from receiving a drug that has not been proven safe and effective and that may have been produced under substandard manufacturing conditions. The DQSA reflects the recognition that this practice can also undermine the new drug and abbreviated new drug approval processes in the United States. Why would sponsors seek approval of applications for life-saving treatments if compounders could simply produce copies of those drugs?"); Ex. 6, *2018 Clinical Need Guidance Announcement* ("[C]ompounding drugs using bulk drug substances, when the use of an FDA-approved drug or a drug compounded using an FDA-approved drug would meet patients' medical needs, can undermine the drug approval process by reducing the incentive for drug manufacturers to seek approval of brand or generic drugs.").

FDA's authorization to bulk compound vasopressin is a particularly egregious example of the harm to the Hatch-Waxman process. In the absence of the *Bulk Compounding Decree*, Athenex, QuVa, and others would have had to file a follow-on drug application with FDA before marketing their vasopressin products. That would have involved extensive scientific and medical review by FDA. And because certain uses of vasopressin are covered by Par's up to six unexpired patents listed in the Orange Book, these companies would have also had to certify that Par's patents are invalid or would not be infringed by their vasopressin products, *see* 21 U.S.C. § 355(b)(2)(A), (j)(2)(A)(vii). This would have resulted in up to a 30-month stay of FDA approval while any patent litigation was resolved. But under the *Decree* and vasopressin authorization, a company like Athenex may simply register as an outsourcing facility and then go directly to market. Indeed,

Athenex has *admitted* in judicial filings that it used the *Decree* to bypass Hatch-Waxman's protections. *See* Compl. ¶¶ 27-28, *Athenex Pharma Sols., LLC v. Par Pharm., Inc.*, No. 1:18-cv-00896 (W.D.N.Y. Aug. 13, 2018), ECF No. 1 ("Athenex's compounded vasopressin products are exempted from certain FDA drug approval requirements including the scheme established by the Hatch-Waxman Amendments for resolving patent disputes. Thus, Athenex does not need to provide a Paragraph IV certification to Par prior to marketing its compounded vasopressin products and Par would not be able to bring a patent infringement suit under the Hatch-Waxman Amendments and be entitled to an automatic 30-month stay to keep Athenex's compounded vasopressin products off the market."). And Athenex is even behaving exactly like a traditional pharmaceutical manufacturer, yet without the regulatory rigor attendant to that privilege. For example, manufacturers who do not enjoy the advantages of FDA's unlawful regime would not be able to launch new promotional materials without at minimum submitting them to FDA via Form 2253. *See* 21 C.F.R. § 314.81(b)(3)(i); *see also* Ex. 22, Athenex advertisement (attaching pop-up advertisement from Athenex website stating "Ready to save on vasopressin?" and providing ordering information).

In sum, FDA's *Bulk Compounding Decree* and authorization to bulk compound vasopressin are inconsistent with the overall structure of the FDCA, including its provisions for bringing drugs to market, ensuring the safety and effectiveness of marketed drugs, and protecting intellectual property rights. This confirms that the *Bulk Compounding Decree* and authorization to compound vasopressin are unlawful. *See Palisades Gen. Hosp. Inc. v. Leavitt*, 426 F.3d 400, 404 (D.C. Cir. 2005) (rejecting interpretation that "is inconsistent with the statutory structure").

B. The *Decree* and Authorization Are Judicially Reviewable

FDA and Athenex have indicated that they might argue that FDA's unlawful regime and authorization to compound vasopressin are shielded from judicial review because they are

exercises of enforcement discretion or non-final agency actions. FDA Answer at 22; Athenex Answer at 21, ECF No. 28; Athenex Mem. at 18 n.16. Any such arguments would be without merit. The Administrative Procedure Act "make[s] agency action presumptively reviewable," *Match-E-Be-Nash-She-Wish Band of Pottawatomi Indians v. Patchak*, 567 U.S. 209, 225 (2012), and nothing overcomes that presumption here.

First, FDA's *Bulk Compounding Decree* and authorization to bulk compound vasopressin are not exempt from review as "agency action[s] . . . committed to agency discretion by law," 5 U.S.C. § 701(a)(2), on the basis that they are exercises of so-called "enforcement discretion." Indeed, it is "commonsense" that "an otherwise reviewable legal interpretation does not become presumptively unreviewable simply because the agency characterizes it as an exercise of enforcement discretion." *NAACP v. Trump*, 2018 WL 3702588, at *7 (D.D.C. Aug. 3, 2018) (citation omitted). FDA may nonetheless argue that its actions qualify for an exception to the presumption in favor of judicial review where it "refus[es] to take requested enforcement action." *Heckler v. Chaney*, 470 U.S. 821, 831 (1985). This exception, known colloquially as the *Chaney* exception, is "very narrow," *id.* at 830 (citation omitted), and applies only when "the statute is drawn so that a court would have no meaningful standard against which to judge the agency's" refusal. *Nat'l Treasury Emps. Union v. Horner*, 854 F.2d 490, 495 (D.C. Cir. 1988) (quoting *Chaney*, 470 U.S. at 830). *Chaney* does not apply where the agency takes action by issuing a prospective policy of non-enforcement, which is precisely what the *Decree* does. *See Crowley Caribbean Transp. v. Peña*, 37 F.3d 671, 676 (D.C. Cir. 1994) (distinguishing between an unreviewable "single-shot," backward-looking decision not to enforce and a reviewable "statement of a general enforcement policy"); *OSG Bulk Ships, Inc. v. United States*, 132 F.3d 808, 812 (D.C. Cir. 1998) ("[A]n agency's adoption of a general enforcement policy is subject to review");

Alliance for Bio-Integrity v. Shalala, 116 F. Supp. 2d 166, 171 (D.D.C. 2000) (*Chaney* does not apply "to agency decisions not to enforce against a whole *class*" of regulatees). *Chaney* likewise does not apply to FDA's authorization to bulk compound vasopressin, because it is an "affirmative act of approval." *Chaney*, 470 U.S. at 831. Indeed, Athenex highlights this approval in its advertising, prominently describing its compounded vasopressin products as "503B products" and including the official FDA logo with the notation "FDA inspected." *See* Exs. 22-24. Agencies cannot shield such approvals behind *Chaney*'s narrow reviewability bar. *See Transp. Intelligence, Inc. v. FCC*, 336 F.3d 1058, 1062 (D.C. Cir. 2003); *see also id*. at 1063 (distinguishing between "an affirmative act of approval" and a "mere[] . . . refusal to take action"); Ex. 15, US Compounding Enforcement Letter (warning only Category 1 substances may be used for bulk compounding).

Even if the Court found *Chaney*'s presumption against reviewability applicable here, the presumption would be overcome because there is sufficient "legislative direction in the statutory scheme" regarding whether FDA can turn a blind eye to bulk drug compounding. *Chaney*, 470 U.S. at 833. As in *Cook v. FDA*, 733 F.3d 1 (D.C. Cir. 2013), this is a case in which Congress has "set[] forth precisely when the agency must determine whether a drug" may be lawfully marketed. *Id.* at 7. *Cook* involved another section of the FDCA, 21 U.S.C. § 381(a), which provides that FDA must refuse admission to drug imports that violate the Act. *See Cook*, 733 F.3d at 3. Instead of complying with the statute, FDA issued a policy in which it purported to "exercise its 'enforcement discretion not to review [certain] shipments and allow processing through [Customs'] automated system for importation." *Id.* at 4 (alteration in original). The D.C. Circuit invalidated FDA's policy, holding that if the agency finds that an imported "drug apparently violates the Act, the FDA must refuse[] [it] admission.'" *Id.* at 9 (alterations in original). The

same situation is present here. FDCA Section 505 provides that "[n]o person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug," 21 U.S.C. § 355(a), and that, "[i]f the Secretary finds [that the criteria for the approval of a drug are not met] . . . he *shall* issue an order refusing to approve the application," *id.* § 355(d) (emphasis added). And Section 503B makes plain that Section 505's new drug approval framework applies to bulk compounded drugs unless all the requirements for Section 503B's exception are satisfied. *See id.* § 353b(a) ("Sections 352(f)(1), 355, and 360eee–1 of this title shall not apply to a drug compounded by or under the direct supervision of a licensed pharmacist in a facility that elects to register as an outsourcing facility *if each of the following conditions is met*: . . . ." (emphasis added)). Thus, Congress has specified the precise circumstances in which FDA may exempt compounded drugs from the FDCA's new drug approval process, providing sufficient legislative direction to overcome *Chaney*.

Second, FDA's *Bulk Compounding Decree* and authorization to bulk compound vasopressin are not exempt from review as agency actions that are not "final." *See* 5 U.S.C. § 704. Agency action is final if it (1) "marks the consummation of the agency's decisionmaking process and is not of a merely tentative or interlocutory nature" and (2) is one from "which rights or obligations have been determined or from which legal consequences will flow." *Philip Morris USA v. USDA*, 202 F. Supp. 3d 31, 45 (D.D.C. 2016) (Mehta, J.) (citation and alterations omitted). Both requirements are satisfied here, and any doubt about that should be resolved in favor of Plaintiffs given that FDA has blatantly exceeded its statutory authority. *See Dart v. United States*, 848 F.2d 217, 221 (D.C. Cir. 1988) ("Judicial review is favored when an agency is charged with acting beyond its authority.").

The *Decree* and vasopressin's Category 1 listing "mark[] the consummation" of FDA's decisionmaking. *Philip Morris*, 202 F. Supp. 3d at 45. The *Decree* is the final, official product of the agency—resulting from a process of notice and comment. *See Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act; Guidance for Industry*, 81 Fed. Reg. 37,500, 37,502 (June 10, 2016) (noting procedural history and receipt of comments from industry). To be sure, the *Decree* contains stock language attempting to suggest non-finality. But such "boilerplate" should be disregarded in favor of a practical examination of what the agency has done. *See Philip Morris*, 202 F. Supp. 3d at 46 ("[B]oilerplate language . . . cannot dictate whether [guidance] is a final agency action fit for review."); *Appalachian Power Co. v. EPA*, 208 F.3d 1015, 1023 (D.C. Cir. 2000) (cautioning against deferring to an agency's "boilerplate" characterizations of its own actions); *Scenic Am. v. U.S. Dep't of Transp.*, 836 F.3d 42, 56 (D.C. Cir. 2016) (same). And the fact that FDA might characterize the *Decree* as temporary is meaningless: "all laws are subject to change[,] [e]ven that most of enduring of documents, the Constitution of the United States, may be amended from time to time"; but that does not mean the action is "therefore not final action." *Appalachian Power*, 208 F.3d at 1022; *see Scenic Am.*, 836 F.3d at 56 ("The fact that a [legal framework] might be interpreted again at some point in the indeterminate future cannot, by itself, prevent the initial interpretation from being final" for purposes of judicial review). At bottom, notwithstanding its "interim" label, the *Decree* has been in effect for multiple years and currently *is* the law. *See* Ex. 14, INCELL Enforcement Letter (requiring compliance with *Bulk Compounding Decree*); *see also* Ex. 15, US Compounding Enforcement Letter; Ex. 16, Fusion IV Enforcement Letter. It is therefore subject to review. *See Nat'l Mining Ass'n v. Jackson*, 768 F. Supp. 2d 34, 45 (D.D.C. 2011) (notwithstanding agency "representation that [guidance under review] is an interim

document, it is nonetheless being applied in a binding manner" and is therefore final); *Durso v. Napolitano*, 795 F. Supp. 2d 63, 67 (D.D.C. 2011) (observing "no authority for the proposition that an otherwise-authoritative order is not final . . . simply because it is subject to revision").

Moreover, the *Decree* and the vasopressin listing unquestionably determine "rights and obligations." *Philip Morris*, 202 F. Supp. 3d at 45 (citation omitted). The *Decree* gives compounders the right to engage in conduct that would otherwise be illegal, as Athenex's intervention in this suit makes indisputable. *See City of Dania Beach v. FAA*, 485 F.3d 1181, 1187-88 (D.C. Cir. 2007) ("interpretation" of regulatory scheme that authorized previously forbidden conduct deemed "reviewable 'final order'"); *Gen. Elec. v. EPA*, 290 F.3d 377, 387 (D.C. Cir. 2002) ("A document will have practical binding effect . . . if the language of the document is such that private parties can rely on it as a norm or safe harbor by which to shape their actions."). And Athenex demonstrates legal consequences in spades—the company is aggressively fighting to *preserve* the *Decree* precisely because it has substantial immediate effects for its business. *See generally, e.g.*, Athenex Mem. As Athenex explained, it began compounding vasopressin "in reliance on FDA's" *Bulk Compounding Decree*. *Id.* at 6. Indeed, it claims it made "significant investments in—and built its long-term business plan around" the *Decree*. *Id.* Athenex deems the rights conferred by the *Decree* as "significant" and "protectable." *Id.* at 16. And, as it rightly acknowledges, it will "be forced to cease compounding" vasopressin if the *Decree* is vacated since it is otherwise *not complying with the FDCA*. *Id.* at 2. Similarly, FDA has explained that industry must "either comply with the FDA's" *Bulk Compounding Decree* or "risk a possible 'enforcement action,'" making clear that the *Decree* effectively has the force of law. *See Philip Morris*, 202 F. Supp. 3d at 48 (finding final agency action where regulated entities must comply with the agency guidance or risk enforcement action); *see also* Ex. 14, INCELL Enforcement Letter (requiring

compliance with *Bulk Compounding Decree*); Ex. 15, US Compounding Enforcement Letter; Ex. 16, Fusion IV Enforcement Letter. And if FDA were to attempt to enforce the pertinent provisions of the FDCA/DQSA against Athenex while the *Decree* and vasopressin authorization are in effect, Athenex would certainly try to assert its reliance on the *Decree* in that action. *See United States v. Pa. Indus. Chem. Corp.*, 411 U.S. 655, 674 (1973) (holding corporate defendant was entitled to assert "it was affirmatively misled by the responsible administrative agency into believing that the law did not apply in this situation"); *State of Alaska v. U.S. Dep't of Transp.*, 868 F.2d 441, 447 (D.C. Cir. 1989) (concluding that agency action "purport[ing] to set forth bright-line tests to shape and channel agency enforcement" would make agency "hard-pressed to justify the prosecution of [entities] who comply with [agency's] rules").

The *Decree* and attendant listing of vasopressin also impose significant legal consequences on Par. In addition to subjecting Par to illegal competition, the *Decree* has stripped Par of important statutory rights by permitting Athenex to come to market in circumvention of the FDCA's patent protection procedures. *See Philip Morris*, 202 F. Supp. 3d at 48 ("chill[ing]" of "First Amendment" rights supported finding of finality); *Cobell v. Babbitt*, 91 F. Supp. 2d 1, 36-37 (D.D.C. 1999) (abridgement of party's "specific statutory rights" constitutes "legal consequence" rendering agency action final), *aff'd sub nom. Cobell v. Norton*, 240 F.3d 1081 (D.C. Cir. 2001).

Accordingly, FDA's actions are judicially reviewable.[16]

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[16] The additional, discretionary factors outlined in *Ciba-Geigy v. EPA*, 801 F.2d 430 (D.C. Cir. 1986), are also satisfied here. *See Philip Morris*, 202 F. Supp. 3d at 46 (considering (1) whether agency "has taken a definitive legal position regarding its statutory authority; (2) whether the case presents a purely legal question of statutory interpretation; and (3) whether the action imposes an immediate and significant practical burden on the regulated entity"). As in *Philip Morris*, the "first two factors are easily met" here because FDA has plainly taken the position that it is authorized to issue a dispensation to bulk compounders, and whether it is correct is a purely legal question.

II. THE REMAINING EQUITABLE FACTORS WEIGH HEAVILY IN PAR'S FAVOR

A. Without Interim Relief, Par Is Likely To Suffer Irreparable Harm

As the New Jersey District Court has already found, "Par . . . would suffer irreparable harm beyond that which money damages could remedy" from competition by a bulk compounder. *Par Pharm.*, 2018 WL 1374023, at *9. That is equally true now. Par will suffer imminent, severe economic losses as a result of illegal competition from bulk drug compounders, including Athenex, and these losses will be irreparable because of FDA's sovereign immunity and the difficulty in calculating them with reasonable certainty. Par will also suffer numerous forms of other irreparable harm.[17]

1. Par Faces Substantial Irreparable Economic Harm

Par will likely suffer substantial and irreparable economic harm [redacted] These economic losses cannot be recovered or easily quantified, and thus are irreparable.

Vasostrict® is the only FDA-approved vasopressin product on the market. Pera Decl. ¶ 6. [redacted] And Par would likely enjoy market exclusivity at least until this point. *See* Pera Decl. ¶¶ 6, 12. The FDCA establishes a detailed and orderly process for bringing follow-on drug products to market that balances the need for price competition

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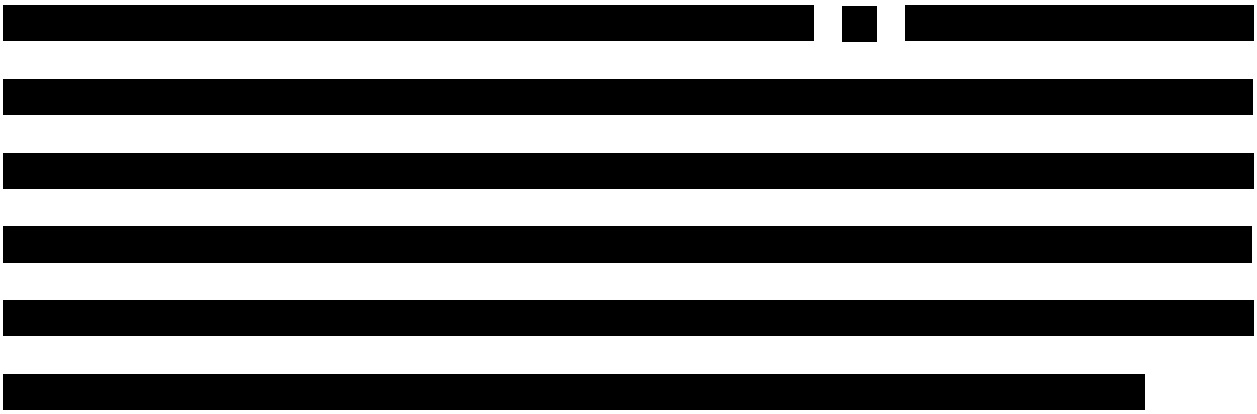
Immediate and significant practical burdens are also present because the *Decree* and vasopressin listing effectively authorize new competitors to Par. *See infra* pp. 36-40 (discussing harm to Par).

[17] For these reasons, there is no question that Plaintiffs have Article III standing. These harms are clearly traceable to FDA's *Decree* and authorization to compound vasopressin, and would be redressed by an order setting those actions aside.

with safety, efficacy, and protection for intellectual property. The *Decree* circumvents that process entirely, allowing both Athenex and potentially sixty other registered 503B facilities to launch their own vasopressin products with little or no warning. Meyer Decl. ¶ 12. [redacted] Indeed, Athenex has already touted its lower prices. *See* Ex. 22 (Athenex webpage advertisement); Athenex Mem. at 21 (emphasizing that Athenex's vasopressin products are "less expensive than Plaintiff's drug").

[redacted]



Even though some of these harms are economic in nature, they are clearly irreparable. The fact that the movant "has little hope of obtaining 'adequate compensatory or other corrective relief at a later date' if the injunction does not issue . . . weighs heavily in favor of granting the injunction." *O'Donnell Constr. Co. v. District of Columbia*, 963 F.2d 420, 428 (D.C. Cir. 1992) (citation omitted). Here, Par cannot be compensated for its losses because FDA has sovereign immunity. *See, e.g.*, *Nalco Co. v. EPA*, 786 F. Supp. 2d 177, 188 (D.D.C. 2011) ("Where a plaintiff 'cannot recover damages from the defendant due to the defendant's sovereign immunity . . . any loss of income suffered by plaintiff is irreparable *per se*.'" (omission in original) (quoting *Feinerman v. Bernardi*, 558 F. Supp. 2d 36, 51 (D.D.C. 2008))); *Smoking Everywhere, Inc. v. FDA*, 680 F. Supp. 2d 62, 77 n.19 (D.D.C. 2010) (same), *aff'd sub nom. Sottera, Inc. v. FDA*, 627 F.3d 891 (D.C. Cir. 2010).[18] Moreover, Athenex, and other vasopressin compounders acting in accordance with the *Bulk Compounding Decree*, may not be subject to suit. And even if there were a defendant from whom damages could be recovered, Par's losses will be difficult—if not impossible—to calculate with reasonable certainty, which also makes them irreparable. *See Lee*

[18] While some courts hold that such losses qualify as irreparable harm only if they are large in size, they do not require that the losses threaten the existence of the movant's business, as would often be required in the absence of sovereign immunity. *See, e.g.*, *N. Air Cargo v. U.S. Postal Serv.*, 756 F. Supp. 2d 116, 125 & n.6 (D.D.C. 2010). Par easily meets this standard. *See supra* pp. 36-38.

v. Christian Coal. of Am., Inc., 160 F. Supp. 2d 14, 31 (D.D.C. 2001) (concluding that monetary damages can constitute irreparable injury when "the nature of the plaintiffs' loss may make damages very difficult to calculate." (citation omitted)); *see also, e.g.*, *Bell Helicopter Textron, Inc. v. Airbus Helicopters*, 78 F. Supp. 3d 253, 274-75 (D.D.C. 2015) (Wilkins, J.) (damages that "defy attempts at valuation" are irreparable); *Gerard v. Almouli*, 746 F.2d 936, 939 (2d Cir. 1984); *Guidance Endodontics, LLC v. Dentsply Int'l, Inc.*, 633 F. Supp. 2d 1257, 1278 (D.N.M. 2008); *Mass. Mut. Life Ins. Co. v. Associated Dry Goods Corp.*, 786 F. Supp. 1403, 1417 (N.D. Ind. 1992); *N.Y. State Motor Truck Ass'n v. City of N.Y.*, 654 F. Supp. 1521, 1540-41 (S.D.N.Y.), *aff'd*, 833 F.2d 430 (2d Cir. 1987). [redacted]

2. Par Also Faces Irreparable Non-Economic Harms

Par is also likely to suffer multiple forms of non-economic injury for which it cannot be compensated. Such harms include Par's loss of the statutory protections afforded by the Hatch-Waxman amendments and the damage to its reputation by the sale of inferior and potentially dangerous products by compounders like Athenex.

First, because FDA authorized Athenex's vasopressin drugs through the extra-statutory *Decree*, Athenex was able to circumvent the patent-protection framework in the Hatch-Waxman amendments, and others are free to do so as well. *See* 21 U.S.C. § 355(b)(2)(A)(i)-(iv), (j)(2)(A)(vii)(I)-(IV). Par is entitled to that protection because it has unexpired patents listed in FDA's Orange Book. *See supra* pp. 7, 15. Par has therefore lost its statutory entitlement to initiate litigation and trigger a mandatory stay of the competing drug's approval for up to 30 months. *See* 21 U.S.C. § 355(c)(3)(C), (j)(5)(B)(iii). As this Court has repeatedly recognized in drug approval cases, "los[s] [of] a statutory entitlement . . . is a harm that has been recognized as sufficiently

irreparable" because "[o]nce the statutory entitlement has been lost, it cannot be recaptured." *Apotex, Inc. v. FDA*, 2006 WL 1030151, at *17 (D.D.C. Apr. 19, 2006), *aff'd*, 449 F.3d 1249 (D.C. Cir. 2006); *see also, e.g.*, *Wondie v. Mekuria*, 742 F. Supp. 2d 118, 123 (D.D.C. 2010) ("In copyright infringement cases, a copyright holder is '"presumed to suffer irreparable harm as a matter of law when his right to the exclusive use of the copyrighted material is invaded."' (citation omitted)). With the patent-protection framework removed, Par will suffer "irreparable harm . . . from not being allowed to sue [vasopressin manufacturers] until [they] hit[] the market with [their] generic product." *Eisai Co. v. Mut. Pharm. Co.*, 2007 WL 4556958, at *21 (D.N.J. Dec. 20, 2007).

Second, [redacted] As the only FDA approved seller of vasopressin, Par is subject to the FDA's full array of safety and quality standards, including pre-approval inspection, requirements for safety reporting, drug supply chain requirements, and having to determine the safety and effectiveness of the products to FDA's satisfaction before entering the market. But compounders are not subject to these same rigorous standards. As FDA admits, compounded drugs are less safe than FDA-approved drugs, and have repeatedly been found to be contaminated or sub- or super-potent, sometimes with tragic results. *See supra* pp. 9-10; Meyer Decl. ¶ 26. Given that healthcare providers are not always aware that their injectables come from compounders, a safety issue related to these compounded products may be wrongly attributed to Par. *Id.* [redacted] Such reputational damage clearly constitutes irreparable harm. *See Human Touch DC, Inc. v. Merriweather*, 2015 WL 12564162, at *2 (D.D.C. May 18, 2015) (Mehta, J.) (recognizing "irreparable harm" based on reputational damage to plaintiff's "relationships with its patients").

B. Other Interested Parties Would Suffer Little Or No Harm As A Result Of Interim Relief

Harm resulting from the prohibition of unlawful activities is not cognizable for purposes of the preliminary injunction analysis; accordingly, the Court should not consider any harm that would allegedly result from the fact that an injunction would prohibit FDA from authorizing bulk compounding of vasopressin. For one, "[t]he Government 'cannot suffer harm from an injunction that merely ends an unlawful practice.'" *R.I.L-R v. Johnson*, 80 F. Supp. 3d 164, 191 (D.D.C. 2015) (quoting *Rodriguez v. Robbins*, 715 F.3d 1127, 1145 (9th Cir. 2013)). Any manufacturers illegally compounding under the *Bulk Compounding Decree* likewise have no protectable interest. *See United States v. Diapulse Corp. of Am.*, 457 F.2d 25, 29 (2d Cir. 1972) (holding that there is no legally protected interest in distributing unapproved products in violation of the FDCA); *see also Fox Television Stations, Inc. v. FilmOn X LLC*, 966 F. Supp. 2d 30, 51 (D.D.C. 2013) (not giving weight to the defendant's allegation "that its business could be 'crippled' by an injunction," because the defendant "ha[d] no cognizable interest in continuing to infringe Plaintiffs' copyrights and thus [could not] complain of the harm it w[ould] suffer if ordered to cease doing so").

In any event, for FDA, the only potential "harm" is the administrative inconvenience of changing its policy, which is non-cognizable and FDA has already acknowledged it plans to do so. *see* Ex. 5, *2018 Priorities Plan*; *see, e.g.*, *League of Women Voters v. Newby*, 838 F.3d 1, 14 (D.C. Cir. 2016) (holding that the administrative burden on the defendants of restoring the status quo ante was outweighed by the potential harm to the plaintiffs); *Does v. District of Columbia*, 374 F. Supp. 2d 107, 117-18 (D.D.C. 2005) (holding that the administrative burden on the defendant of "establish[ing] new policies and practices," *id.* at 118, was outweighed by the potential harm to the plaintiffs).

So too, any alleged "harm" to Athenex constitutes non-cognizable self-inflicted injury because it was entirely foreseeable once Par filed its complaint. *See, e.g.*, *Lee*, 160 F. Supp. 2d at 33 ("The case law is well-settled that . . . irreparable harm [is absent] when the alleged harm is self-inflicted." (citation omitted)); *Safari Club Int'l v. Salazar*, 852 F. Supp. 2d 102, 122-23 (D.D.C. 2012) (no irreparable harm when party could avoid harm). Vasopressin was added to Category 1 of FDA's nominations list in July 2017, and Par filed suit to enjoin this action very shortly thereafter—in October 2017. Athenex was on constructive notice of that suit immediately, and substantial press regarding the suit likely conferred actual notice. *See, e.g.*, Ex. 25, Inside Health Policy, *Endo Sues FDA Over 503B Compounding Policy* (Oct. 27, 2017); Ex. 26, Nate Raymond, *Endo International Units Sue FDA Over Drug Compounding Policy*, Reuters (Oct. 26, 2017). It was only during a small window, between July and October 2017, that Athenex could have made expenditures in reliance on the *Decree* without recognizing the substantial probability that the *Decree* was invalid. Yet it does not appear Athenex made any substantial expenses in that window and, instead, it plowed ahead with its expenditures *after* Par filed suit. It made these expenditures with eyes wide-open to the probability they would not bear fruit.

Specifically, two of the expenditures Athenex highlights are construction of a new Dunkirk, New York, facility and renovations of its Clarence, New York, facility. Athenex Mem. at 6-7. Yet critical events regarding those items did not occur until *2018*. For example, Athenex did not even sign an agreement for design and construction of the Dunkirk facility until December 29, 2017. *See* Ex. 27, Athenex, Inc. Form 8-K (Jan. 5, 2018). Its Clarence expansion apparently began even later. A document regarding tax incentives for the expansion reflects that the expansion had not begun as of February 2018. *See* Ex. 28, Group V Real Estate, Inc. (Athenex

Pharma Solutions) Inducement Resolution; *see also* Ex. 30, Economic Development Corporation for Erie County, Project Name: Group V Real Estate (Athenex) (indicating 2/21/2018 approval).

And Athenex always had knowledge that its expenditures were being made in an arena with tremendous legal uncertainty because the *Decree* was not intended to be permanent. *See* Athenex Mem. at 3 (acknowledging the *Decree* is an interim measure). Its expenditures *during* that period of uncertainty should be disregarded or discounted. *See Kos Pharm., Inc. v. Andrx Corp.*, 369 F.3d 700, 728-29 (3d Cir. 2004) ("[T]he injury a defendant might suffer if an injunction were imposed may be discounted by the fact that the defendant brought that injury upon itself." (citation omitted)). Athenex could have easily avoided this dilemma by proceeding through the *actual* FDCA procedures for new drugs—just as Par was required to do. *See Second City Music, Inc. v. City of Chi., Ill.*, 333 F.3d 846, 850 (7th Cir. 2003) (litigant "contends that it does suffer irreparable injury because, without the aid of an injunction, it will go out of business. Yet two things could keep it in business; an injunction *or* a license" (emphasis added)). Moreover, even if Athenex cannot bulk compound vasopressin specifically, it could deploy its investments to manufacture one of the other five drugs it is compounding. *See* Ex. 29, Press Release, Athenex, *Athenex, Inc. Announces First Quarter 2018 Results* (May 14, 2018) ("[O]ur 503(b) outsourced facility[] currently markets 5 products . . . .").

The losses that Athenex or any prospective bulk compounder of vasopressin could potentially suffer are also outweighed by the losses Par incurs given its established position in the market. *See, e.g.*, *Bayer HealthCare, LLC v. FDA*, 942 F. Supp. 2d 17, 26-27 (D.D.C. 2013) (holding that the harm to a generic drug manufacturer that "ha[d] been anticipating and preparing to market" a drug but "ha[d] not proceeded far into the market since its very recent FDA approval," was outweighed by the potential harm to an established brand-name manufacturer of the drug).

Likewise, Par faces reputational harm that is not at issue for prospective bulk compounders of vasopressin. *See, e.g.*, *Russian Acad. of Scis. v. Am. Geophysical Union*, 1998 WL 34333239, at *9 (D.D.C. Dec. 17, 1998) (holding that the harm to the defendant in having to change the name of its publication was outweighed by the potential harm to the plaintiffs resulting from infringement of their trademark because the defendant's "new publication[] [was] not so associated with one name that it could not retain or recapture its goodwill"); *see also* Athenex Mem. at 21 (describing Athenex's vasopressin product as "part of Athenex's efforts to *build* its reputation for high quality and safe compounded products" (emphasis added)). Thus, neither FDA nor prospective bulk compounders of vasopressin would suffer any genuine harm as a result of interim relief, but even if they would, that harm is outweighed by the harm to Par.

C. The Public Interest Strongly Favors Interim Relief

"Forcing federal agencies to comply with the law is undoubtedly in the public interest." *Cent. United Life, Inc. v. Burwell*, 128 F. Supp. 3d 321, 330 (D.D.C. 2015), *aff'd*, 827 F.3d 70 (D.C. Cir. 2016). This is particularly true regarding FDA compliance with the DQSA. As noted, the DQSA was passed because the previous, unregulated state of bulk drug compounding led to dozens of deaths and hundreds of illnesses. Congress was apoplectic. *See, e.g.*, 159 Cong. Rec. at 14,650 (2013) (statement of Rep. Murphy) ("How we got here is a tragedy."). And in passing the DQSA it sought "to prevent against another tragedy like NECC's." *Id.* at 14,647 (statement of Rep. Pitts). Holding FDA to Congress's clear expectations and reducing the risk of another catastrophe is plainly in the public interest.

There is also a strong public interest in preserving incentives for development of drugs like Vasostrict® and ensuring that they proceed through the pre-market approval process. As FDA has recognized, drug "[s]ponsors would be less likely to invest in and seek approval of innovative, life-saving medications if [an outsourcing facility] could, after a drug is approved, compound

'substitutes' that may be less expensive because they have not gone through the premarket approval process." Ex. 5, *2018 Priorities Plan*. And finally, preservation of the new drug approval process is *itself* a strong factor favoring interim relief. *W. States*, 535 U.S. at 369 ("Preserving the effectiveness and integrity of the FDCA's new drug approval process is clearly an important governmental interest.").[19]

CONCLUSION

Par's motion for preliminary relief should be granted. This Court would be entirely justified in setting aside the entire *Bulk Compounding Decree*, *see* Ex. 3. At this preliminary stage, however, an injunction preliminarily (1) enjoining FDA's placement of vasopressin in Category 1 of FDA's nominations list, *see* Ex. 8, and (2) enjoining FDA from authorizing bulk drug compounding using vasopressin without compliance with the new-drug approval process, 21 U.S.C. § 355, or the statutory exemption therefrom at 21 U.S.C. § 353b, would be adequate to remedy Par's harm. *See U.S. Ass'n of Reptile Keepers, Inc. v. Jewell*, 106 F. Supp. 3d 125, 126 (D.D.C. 2015) (narrowly tailoring preliminary injunction in challenge to agency action to "preserve the parties' respective rights and interests" instead of "declar[ing] the challenged rule unlawful or vacat[ing] the rule"). Should the Court conclude that Par has demonstrated a likelihood of success on the merits, but has not otherwise satisfied the requirements for preliminary relief, Par respectfully requests that the Court convert this motion to one for expedited summary judgment—the issues presented are purely legal and require no further factual development. *See, e.g.*, *March for Life v. Burwell*, 128 F. Supp. 3d 116, 120 (D.D.C. 2015); *Morris v. District of Columbia*, 38 F. Supp. 3d 57, 62-63 (D.D.C. 2014).

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[19] Athenex may argue that the public interest favors the proliferation of "cheaper" drugs, like its illegally compounded vasopressin. But Congress already addressed that interest in the Hatch Waxman amendments.

August 21, 2018

Respectfully submitted,

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CERTIFICATE OF SERVICE

I certify that on August 21, 2018 I caused Plaintiffs' Motion for Preliminary Injunction; the supporting memorandum; the supporting declarations of Andrew D. Prins, Antonio Pera, and Christine S. Meyer; the exhibits to those declarations; and the notice of electronic filing to be delivered by email to the following:

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