UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

IPSEN BIOPHARMACEUTICALS, INC., *Plaintiff*, v. XAVIER BECERRA, Secretary, United States Department of Health and Human Services, *et al.*, *Defendants.*	No. 22-cv-860 (DLF)

MEMORANDUM OPINION

Ipsen Biopharmaceuticals, Inc. brings this case against the Secretary of Health and Human Services and the Commissioner of the Food and Drug Administration (FDA) under the Administrative Procedure Act (APA), arguing that the FDA's decision to regulate its product as a drug, rather than a biological product, was arbitrary, capricious, an abuse of discretion, and contrary to law. Compl. ¶¶ 1–7, Dkt. 1. InvaGen Pharmaceuticals, Inc. intervened as a defendant. Minute Order of May 12, 2022. Before the Court are Ipsen's Motion for Summary Judgment, Dkt. 26, and the FDA's and InvaGen's Cross Motions for Summary Judgment, Dkts. 27, 28. For the reasons that follow, the Court will grant FDA's and InvaGen's motions and deny Ipsen's motion.

I. BACKGROUND

A. Legal Background

i. Regulation of drug products

The Food, Drug, and Cosmetic Act (for ease of reference, Drug Act) prohibits the introduction of "any new drug" into interstate commerce without prior approval by the FDA. 21 U.S.C. § 355(a). For this purpose, the Act defines "drug" to include "articles intended for use in

the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" and "articles (other than food) intended to affect the structure or any function of the body of man or other animals." *Id.* § 321(g)(1)(B)–(C).

As relevant here, there are three pathways through which new drugs may obtain FDA approval. First, a company may submit a new drug application (NDA) under § 505(b) of the Drug Act. 21 U.S.C. § 355(b). A new drug application is approved only if the company demonstrates, usually through clinical trials, that its drug is safe and effective for its proposed use. *See id.* § 355(b)(1)(A), (d) (specifying other requirements for NDAs). Second and alternatively, once the exclusivity and patent rights of a drug's sponsor have expired, *see, e.g.*, *id.* § 355(j)(2)(A)(vii), (5)(B)(iv), other companies seeking to market generic versions of that drug may submit an abbreviated new drug application (ANDA). *Id.* § 355(j). The FDA may approve an ANDA only upon finding that the generic drug is "bioequivalent" to a listed drug in several respects, including active ingredient, conditions of use, route of administration, dosage, and strength. *Id.* § 355(j)(4)(F) (requiring a generic's sponsor to show their product is "bioequivalent" to the listed drug); *id.* § 355(j)(8)(B) (defining "bioequivalent").

The third option, a § 505(b)(2) application, is "a sort of hybrid of the other two pathways." *Veloxis Pharms., Inc. v. FDA*, 109 F. Supp. 3d 104, 108–09 (D.D.C. 2015) (citation omitted). The § 505(b)(2) pathway allows a company to submit an NDA that relies, in whole or in part, on clinical studies that another entity conducted for an already-approved listed drug. *Id.*; *see* 21 U.S.C. § 355(b)(2). This middle-ground pathway is often used if a company's product is similar to—but not the bioequivalent of—a listed drug, for example due to a difference in strength or route of administration. *Veloxis*, 109 F. Supp. 3d at 109.

ii. Regulation of biological products

Different rules apply to products that qualify as "biological products." The Public Health Service Act (for ease of reference, Biologics Act) defines "biological product" to mean "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings." 42 U.S.C. § 262(i)(1). This definition has changed over time. Although it previously excluded proteins that were "chemically synthesized," Congress revised it in 2019 to include all proteins, regardless of their origin. *Compare id.* § 262(i)(1) (2012) (defining "biological product" to include "protein (except any chemically synthesized polypeptide)"), *with id.* § 262(i)(1) (2020) (defining the term to include "protein" without exception); Further Consolidated Appropriations Act of 2020, Pub. L. No 116-94, § 605, 133 Stat. 2534, 3127 (Dec. 20, 2019). The FDA since promulgated a rule to define a "protein" as "any alpha amino acid polymer with a specific, defined sequence that is greater than 40 amino acids in size" where the "amino acid chains . . . are associated with each other in a manner that occurs in nature." 21 C.F.R. § 600.3(h)(6).

The Biologics Act contains two pathways for approving products that qualify as biological products. First, a company that seeks to market a new biological product may submit to the FDA a biological license application (BLA). 42 U.S.C. § 262(a)(1). The agency may approve that application upon finding that the product is "safe, pure, and potent," usually shown through clinical trials, and that its production facility is "designed to assure" that quality. *Id.* § 262(a)(1)(C). Second, like the Drug Act, the Biologics Act also offers an abbreviated application process: when a company seeks to market a product that is "biosimilar" to or "interchangeable" with a product that has already been approved, it may submit an abbreviated biological license application

(ABLA). *Id.* § 262(k). For this purpose, one product is "biosimilar" to another if it is "highly similar" to that product and if "there are no clinically meaningful differences" between the products "in terms of the safety, purity, and potency." *Id.* § 262(i)(2). Likewise, one product is "interchangeable" with another if it is "biosimilar" to that product and if it "can be expected to produce the same clinical result . . . in any given patient." *Id.* § 262(k)(4)(A). The FDA may approve an ABLA upon finding sufficient evidence of either biosimilarity or interchangeability. *Id.* § 262(k)(3). But, unlike for other drugs, biological products that do not qualify as biosimilar or interchangeable have no intermediate pathway that would enable an applicant to rely on another listed biological product's clinical studies. *See* Hr'g Tr. at 25, 27.

iii. Biologics Price Competition and Innovation Act of 2009

Whether a new drug qualifies as a biological product has several implications. First, as suggested above, that classification determines whether the drug is subject to the general approval regime in § 505 of the Drug Act or the more specific regime in the Biologics Act. *See* 42 U.S.C. § 262(j) (providing that biological products approved under the Biologics Act do not also require approval under § 505). The question also determines whether licensing a generic version of the drug requires filing an ANDA or an ABLA, and thus the legal standard the generic must satisfy. *Compare* 21 U.S.C. § 355(j)(4) (requiring equivalence with the reference drug for an ANDA), *with* 42 U.S.C. § 262(k)(3) (requiring biosimilarity or interchangeability for an ABLA). And, as noted, the Biologics Act does not provide a pathway akin to the Drug Act's § 505(b)(2) that allows an applicant to rely on a listed product's clinical studies even if it is not considered a generic that qualifies for an abbreviated application. *Compare* 21 U.S.C. § 355(b)(2) (providing this pathway in the Drug Act), *with* 42 U.S.C. § 262(a)(2)(C) (providing no such pathway in the Biologics Act).

Recognizing that the FDA's classification decisions have substantial effects on the drug market, Congress has required the FDA to reconsider them over time. As relevant here, the Biologics Price Competition and Innovation Act of 2009 provided that, beginning on March 23, 2020, any "approved application for a biological product under section 505 of the [Drug Act] shall be deemed to be a license for the biological product" under the Biologics Act. Pub. L. No. 111-148, tit. VII, § 7002(e)(4), 124 Stat. 804, 817 (Mar. 23, 2010). In other words, the Act required the FDA to, on March 23, 2020, transition substances that were approved as drugs, but now meet the current definition of "biological products," to the Biologics Act. Consistent with that mandate, on that date the FDA published a list of biological products that it deemed to be licensed under the Biologics Act, although they were initially approved under the Drug Act. *See* FDA, *List of Approved NDAs for Biological Products That Were Deemed to be BLAs on March 23, 2020*, A.R. 2168–76.

B. Factual Background

Ipsen manufactures, markets, and sells a drug called Somatuline Depot. Compl. ¶ 8. The drug effects an "extended-release dosing of its active ingredient lanreotide acetate, a molecule that mimics the naturally occurring hormone somatostatin." *Id.* ¶ 44. The FDA approved the drug in 2007 pursuant to § 505 of the Drug Act. *Id.* ¶ 45; A.R. 342–71. Somatuline Depot is licensed "for the treatment of patients suffering from a rare hormonal disorder called acromegaly," which "results from a production of excess growth hormone [] by the pituitary gland." Compl. ¶ 45.

Although the FDA initially approved Somatuline Depot as a drug, Ipsen argues that the substance meets the amended definition of "biological product." *Id.* ¶¶ 49–52. More precisely, it contends that Somatuline Depot qualifies as a "protein," and thus a biological product, under the Biologics Act—*i.e.*, it is an "alpha amino acid polymer with a specific, defined sequence that is

greater than 40 amino acids in size." 21 C.F.R. § 600.3(h)(6); Compl. ¶ 50 ("Somatuline Depot is[] an amino acid polymer with a specific defined sequence composed of multiple amino acid chains where the total number of amino acids exceeds 40 amino acids."). Ipsen reasons that Somatuline Depot contains multiple copies of its active ingredient, lanreotide acetate, linked together "in a manner that occurs in nature" to form a "nanotube" greater than 40 amino acids long. Compl. ¶¶ 47, 51. Alternatively, Ipsen says, Somatuline Depot is at least "analogous" to a protein under the statute. *Id.* ¶ 52. Thus, Ipsen argues, the FDA is required to regulate Somatuline Depot as a "biological product" under the Biologics Act. *Id.* ¶¶ 49–52.

The FDA disagrees. In 2020, the agency did not list Somatuline Depot among the drugs that would be transitioned to Biologics Act regulation. *Id.* ¶¶ 42–43, 57; *see also* FDA, *List of Approved NDAs for Biological Products That Were Deemed to be BLAs on March 23, 2020*, *supra*. When Ipsen contacted the agency to argue that Somatuline Depot should have been included, the agency rejected Ipsen's position. Compl. ¶¶ 58–61; *see also* A.R. 2130–35 (concluding in a memo that Somatuline Depot is not a biological product); *id.* at 2644–58 (reaching the same conclusion in a letter to Ipsen after a telephonic hearing and review of Ipsen's written responses to scientific questions). The FDA reasoned, in short, that the proper frame of reference for applying its definition of "protein" is a drug's "active ingredient," as opposed to the drug in its finished product form. A.R. 2133, 2648. Under that view, a drug qualifies as a "protein" only if its *active ingredient* is an amino acid polymer composed of at least 40 amino acids. *See* A.R. 2133. Because the active ingredient of Somatuline Depot—lanreotide acetate—contains only 8 amino acids, the FDA concluded that Somatuline Depot is not a protein. *Id.* It further concluded that Somatuline Depot is not "analogous" to a protein within the meaning of the Biologics Act because lanreotide acetate failed the size requirement, and "it would not be appropriate to interpret the statutory term . . . in

a way that would include amino acid polymers that are specifically excluded by the interpretation of the term 'protein' set forth in FDA's Biological Product Definition Final Rule." *Id.*; A.R. 2657.

Ipsen challenged the FDA's determination under the APA. Compl. ¶ 62; *see Ipsen Biopharmaceuticals, Inc. v. Becerra*, No. 20-cv-2437, 2021 WL 4399531, at *1 (D.D.C. Sept. 24, 2021). On September 24, 2021, the Court dismissed its complaint for lack of standing, concluding that Ipsen had failed to sufficiently allege an injury-in-fact stemming from the regulatory decision. *Ipsen*, 2021 WL 4399531, at *4. Ipsen argued that it suffered a competitive injury—namely, "that the FDA's failure to regulate Somatuline Depot as a biological product deprived it of the protections afforded by the approval pathway for biosimilars," under which it would allegedly be harder for future competitors to obtain approval for generic versions of Somatuline Depot. *Id.* (cleaned up). But the Court found that injury too attenuated, as it "rest[ed] on the 'highly speculative fear' that: (1) at least one company will submit an ANDA to market a generic version of Somatuline Depot; (2) the FDA will approve at least one ANDA for that purpose; and (3) at least one generic approved through this process will satisfy the requirements of ANDA equivalence *but not* the more demanding requirements of ABLA biosimilarity." *Id.* (quoting *Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 409–10 (2013)).[1]

Subsequently, in December 2021, the FDA approved an NDA submitted by InvaGen for a lanreotide acetate injection that treats acromegaly and gastroenteropancreatic neuroendocrine tumors. Compl. ¶ 64. InvaGen's product "has the same active ingredient, route of administration, dosage form and strengths as Somatuline Depot." Intervenor-Def.'s Mem. in Supp. of Cross-Mot.

[1] Ipsen also alleged an informational injury related to its patent protections, which the Court likewise rejected as insufficiently concrete. *See id.* at *9–10. Ipsen does not allege informational injury in the present case. *See generally* Compl.; Pl.'s Mem. in Supp. of Mot. for Summ. J. at 16–20, Dkt. 26-1; Pl.'s Reply at 19–23, Dkt. 33.

for Summ. J. (InvaGen Mem.) at 18, Dkt. 27-1; *see also* Compl. ¶ 67. InvaGen's drug was approved under the Drug Act's § 505(b)(2) pathway, which allowed InvaGen to use Ipsen's clinical data for Somatuline Depot. Compl. ¶ 65.

Ipsen brought this suit on March 30, 2022. It asserts that it now has standing to challenge the FDA's regulatory decision, because the § 505(b)(2) pathway that InvaGen used to obtain approval of a competing drug would not have been available had the FDA regulated Somatuline Depot under the Biologics Act. *Id.* ¶¶ 6, 66, 83. On the merits, Ipsen claims that the FDA's failure to regulate Somatuline Depot as a biological product is arbitrary, capricious, and contrary to law because Somatuline Depot meets the definition of a "protein" or "analogous product." *See* Compl. ¶¶ 69–74. Because InvaGen's product's approval stands to be affected by this action, it intervened as a defendant. *See id.*, Prayer for Relief, ¶¶ B, D; Minute Order of May 12, 2022. All parties have moved for summary judgment. Dkts. 26, 27, 28.

II. LEGAL STANDARD

A court will grant summary judgment if the moving party "shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a); *see also Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 247–48 (1986). A "material" fact is one with potential to change the substantive outcome of the litigation. *See Liberty Lobby*, 477 U.S. at 248; *Holcomb v. Powell*, 433 F.3d 889, 895 (D.C. Cir. 2006). And a dispute is "genuine" if a reasonable jury could determine that the evidence warrants a verdict for the nonmoving party. *See Liberty Lobby*, 477 U.S. at 248; *Holcomb*, 433 F.3d at 895.

In cases arising under the APA, summary judgment "serves as the mechanism for deciding, as a matter of law, whether the agency action is supported by the administrative record and otherwise consistent with the APA standard of review." *Sierra Club v. Mainella*, 459 F. Supp. 2d

76, 90 (D.D.C. 2006). Thus, the Court will "hold unlawful and set aside" agency action that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law," 5 U.S.C. § 706(2)(A), or "in excess of statutory jurisdiction, authority, or limitations, or short of statutory right," *id*. § 706(2)(C). Before reviewing an agency action, however, this Court must first determine whether the party challenging that action has Article III standing. *See Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83, 94–95 (1998).

III. ANALYSIS

A. Standing

Article III of the Constitution limits the "judicial Power" of federal courts to "Cases" and "Controversies." U.S. Const. art. III, § 2, cl. 1. "[T]here is no justiciable case or controversy unless the plaintiff has standing." *West v. Lynch*, 845 F.3d 1228, 1230 (D.C. Cir. 2017). As the Supreme Court has interpreted this requirement, "the irreducible constitutional minimum of standing contains three elements": (1) the plaintiff must have suffered an "injury in fact" that is "concrete and particularized" and "actual or imminent, not conjectural or hypothetical"; (2) there must exist "a causal connection between the injury and the conduct complained of"; and (3) it must be "likely, as opposed to merely speculative, that the injury will be redressed by a favorable decision." *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560–61 (1992) (quotation marks omitted). At the summary judgment stage, the plaintiff must show these elements by "set[ting] forth by affidavit or other evidence specific facts, which for purposes of the summary judgment motion will be taken to be true." *Id.* at 561 (citations and quotation marks omitted). Ipsen has done so.

i. Injury in fact

It is well-settled that "actual or imminent increase in competition" constitutes an injury in fact. *Am. Inst. of Certified Pub. Accts. v. IRS*, 804 F.3d 1193, 1197 (D.C. Cir. 2015) (quoting

Sherley v. Sebelius, 610 F.3d 69, 73 (D.C. Cir. 2010)). Litigants accordingly "suffer an injury in fact when agencies lift regulatory restrictions on their competitors or otherwise allow increased competition against them." *Sherley*, 610 F.3d at 72 (quotation marks and alteration omitted). "The form of that injury may vary; for example, a seller facing increased competition may lose sales to rivals, or be forced to lower its price or to expend more resources to achieve the same sales, all to the detriment of its bottom line." *Id.* Competitive injury that exists even for a short amount of time can still qualify as an injury-in-fact. *See Carpenters Indus. Council v. Zinke*, 854 F.3d 1, 5 (D.C. Cir. 2017) (explaining that "the amount [of economic harm to a business] is irrelevant," for "[a] dollar of economic harm is still an injury-in-fact").

Ipsen has sufficiently shown that it suffered a competitive injury because the FDA's decision to regulate Somatuline Depot as a drug, rather than a biologic, allowed InvaGen to compete with Ipsen using the Drug Act's § 505(b)(2) pathway. That option would not have been available to InvaGen had the FDA instead determined that Somatuline Depot and InvaGen's product were biological products. In that case, InvaGen would have had only two options: file a BLA and conduct its own clinical studies, or file an ABLA and prove that its product is biosimilar to or interchangeable with Ipsen's. Under the Drug Act, however, InvaGen was able to take a "hybrid approach" and rely on Ipsen's clinical studies without qualifying as a biosimilar. "And when the government grants an application to produce [a pharmaceutical], a current manufacturer of the same drugs may challenge that action"—or, here, an antecedent action that made the application possible in the first place—"because 'increased competition represents a cognizable Article III injury.'" *Shays v. FEC*, 414 F.3d 76, 86 (D.C. Cir. 2005) (citing *MD Pharm., Inc. v. DEA*, 133 F.3d 8, 11 (D.C. Cir. 1998)); *see also id.* at 87 ("[W]hen regulations illegally structure

a competitive environment—whether an agency proceeding, a market, or a reelection race—parties defending concrete interests . . . in that environment suffer legal harm under Article III.").

ii. Traceability

To fulfill the traceability requirement, a plaintiff must show a "causal nexus between the agency action and the asserted injury." *Freedom Republicans, Inc. v. FEC*, 13 F.3d 412, 418 (D.C. Cir. 1994). For competitive injury, "the causation requirement for constitutional standing is met when a plaintiff demonstrates that the challenged agency action authorize[d] the conduct that allegedly caused the plaintiff's injuries, if that conduct would allegedly be illegal otherwise." *Shays*, 414 F.3d at 92–93 (quoting *Animal Legal Def. Fund, Inc. v. Glickman*, 154 F.3d 426, 440 (D.C. Cir. 1998) (en banc)). The causation requirement of "Article III 'requires no more than *de facto* causality.'" *Dep't of Com. v. New York*, 139 S. Ct. 2551, 2566 (2019) (quoting *Block v. Meese*, 793 F.2d 1303, 1309 (D.C. Cir. 1986) (Scalia, J.)). A plaintiff must show "a genuine nexus between [its] injury and a defendant's alleged illegal conduct," but it need "not . . . show to a scientific certainty" or provide "strict proof of causation to meet [the] threshold jurisdictional requirement." *Friends of the Earth, Inc. v. Gaston Copper Recycling Corp.*, 204 F.3d 149, 161 (4th Cir. 2000) (quotation marks omitted). For "[i]f standing depended on a plaintiff's ability to allege [i]ncontrovertible facts, there would be very few plaintiffs who could establish standing in a lawsuit of any complexity." *Cmty. Nutrition Inst. v. Block*, 698 F.2d 1239, 1248 (D.C. Cir. 1983), *rev'd on other grounds*, 467 U.S. 340 (1984). A plaintiff must make only a reasonable showing "that 'but for' defendant's action the alleged injury would not have occurred." *Id.* at 1247; *see also Attias v. Carefirst, Inc.*, 865 F.3d 620, 629 (D.C. Cir. 2017) (explaining that "Article III standing does not require . . . [showing] proximate caus[ation]").

Ipsen has satisfied this requirement: The FDA's alleged illegal conduct—its refusal to regulate Somatuline Depot under the Biologics Act—was the but-for cause of Ipsen's alleged competitive injury because it allowed InvaGen to get approval for its product under a pathway unique to the Drug Act. While the competitive injury to Ipsen resulted from the FDA's approval of InvaGen under the Drug Act, that injury flowed directly and inextricably from the FDA's decision to regulate Ipsen under the Drug Act. This suffices to causally link the FDA's action to Ipsen's competitive injury.[2] *See Shays*, 414 F.3d at 93 ("[E]conomic competitors may challenge decisions allowing additional entrants into their markets."); *Tel. & Data Sys., Inc. v. FCC*, 19 F.3d 42, 47 (D.C. Cir. 1994) ("[I]njurious private conduct is fairly traceable to the administrative action contested in the suit if that action authorized the conduct or established its legality.").

Establishing that nexus is enough. Ipsen need not further disprove the defendants' assertion that, in the counterfactual world where the FDA transitioned Somatuline Depot to the Biologics Act, InvaGen would have been approved through a BLA or ABLA application. *See* InvaGen Mem. at 17–18; Fed.-Defs.' Mem. in Supp. of Cross-Mot. for Summ. J. (FDA Mem.) at 15–16, Dkt. 29. "Whatever the ultimate accuracy of [that] speculation," InvaGen "now do[es] in fact" compete in the drug market as a drug approved under the § 505(b)(2) pathway. *Duke Power Co. v. Carolina Env't Study Grp., Inc.*, 438 U.S. 59, 77–78 (1978). This could "not have occurred but for" the FDA regulating Somatuline Depot under the Drug Act. *Id*. While it is certainly

[2] That Ipsen "is [it]self an object of the action (or forgone action) at issue" strengthens this conclusion. *Lujan*, 504 U.S. at 561–62. While causation is "substantially more difficult to establish" when "a plaintiff's asserted injury arises from the government's allegedly unlawful regulation (or lack of regulation) of *someone else*," *id.* at 562 (quotation marks omitted), "standing to seek review of administrative action is [often] self-evident" where, as here, a plaintiff is "itself the object of the challenged agency action." *Fund for Animals, Inc. v. Norton*, 322 F.3d 728, 733–34 (D.C. Cir. 2003); *see also Exhaustless Inc. v. FAA*, 931 F.3d 1209, 1212 (D.C. Cir. 2019) ("When a petitioner itself is the object of the challenged agency action, there usually is little doubt of causation.").

possible that InvaGen could have been approved as an ABLA in the hypothetical Biologics Act world, it is not certain, since it has never had to prepare a BLA or ABLA application, and the standard for doing so differs from § 505(b)(2) approval. Indeed, even the FDA stated that it would be "very difficult" for it "to say whether a particular product would or would not have been approved under an alternate scenario with an application the agency hasn't actually received." Hr'g Tr. at 20. Ipsen does not have "to negate [these] kind of speculative and hypothetical possibilities suggested in order to demonstrate" a causal link for standing purposes, *Duke Power*, 438 U.S. at 78, as the defendants argue, *see* InvaGen Mem. at 18; FDA Mem. at 15. *See also Int'l Ladies' Garment Works' Union v. Donovan*, 722 F.2d 795, 810–11 (D.C. Cir. 1983) (explaining that to establish standing plaintiffs need not show that "injurious competition [would have] continue[d]" anyway); *cf. Orange Park Fla. T.V., Inc. v. FCC*, 811 F.2d 664, 672 n.18 (D.C. Cir. 1987) (explaining that "to have standing disappointed bidder for government contract need not show that 'but for' award to competing bidder, appealing bidder would have received award" (citation omitted)).

In the same vein, Ipsen also need not prove that it would have taken InvaGen *longer* to obtain approval under the Biologics Act than it took under the Drug Act, contrary to the defendants' contention. Hr'g Tr. at 23, 31. Ipsen has established all that is necessary to establish standing, namely that "[t]he continuation of the status quo with respect to [all other] behavior, accompanied by classification of [its drug] as a biologic, would ensure" the alleviation of its competitive injury. *Teva Pharms. USA, Inc. v. FDA*, 514 F. Supp. 3d 66, 90 (D.D.C. 2020). For purposes of standing analysis, the Court must assume that Somatuline Depot would have been transitioned in March 2020. *See Comm. on Judiciary of U.S. House of Reps. v. McGahn*, 968 F.3d 755, 762 (D.C. Cir. 2020) (en banc) (requiring the Court to "assume that the [plaintiff] will prevail

on the merits" in the standing analysis). From there, the rest follows because InvaGen did in fact submit a § 505(b)(2) application referencing Somatuline Depot that the FDA would have had to reject, *see* 21 U.S.C. § 355(b)(2) (permitting applications to reference a listed "*drug* for which [other] investigations were conducted" (emphasis added)); *cf.* 21 C.F.R. § 314.101(e)(1) (explaining that the FDA will reject a new drug application if the product is a biologic). The defendants' counterargument, on the other hand, would require the Court to make a series of assumptions: that after Somatuline Depot's transition to a biologic in March 2020, (1) InvaGen would have chosen to submit a BLA or an ABLA instead of a § 505(b)(2) application; (2) it would have satisfied the different standard for such application; and (3) the FDA would have approved it in the same or less time than the § 505(b)(2) application. Ipsen is not required to disprove each of these speculations, and the Court will not credit them. *See Teva Pharms.*, 514 F. Supp. 3d at 90 (rejecting "[d]efendants' theory," which "relie[d] more on a speculative change in prescriber behavior than d[id] [plaintiff's theory]").

Contrary to the defendants' position, *see* FDA Mem. at 14–16; InvaGen Mem. at 17–18, this case is easily distinguished from the prior suit where Ipsen lacked standing to challenge the same agency action. There, Ipsen's competitive injury theory "rest[ed] on the 'highly speculative fear'" that a competitor would submit a drug application, would be approved, and would not have similarly been approved as a biologic—a "'chain of possibilities' [that was] too 'attenuated' to establish Article III standing." *Ipsen*, 2021 WL 4399531, at *4 (quoting *Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 410 (2013)). But this "highly attenuated chain of possibilities," *Clapper*, 568

U.S. at 410, is no longer present, as the first and second links in the chain have since come to pass. With the first two links of the chain present and concrete, the third link falls away in importance.[3]

Take *Clapper* itself. In that case, the Court explained that it was not only speculative whether the plaintiffs would be imminently surveilled (injury-in-fact), but whether such surveillance, were it to occur, "would be under [the challenged statute] § 1881a or some other authority" (traceability). *Clapper*, 568 U.S. at 410–11; *see also Ipsen*, 2021 WL 4399531, at *7 (quoting this passage). In other words, when the injury itself was speculative, it was impossible to pinpoint from what statute such hypothetical injury might arise. *Clapper*, 568 U.S. at 413 ("[B]ecause respondents can only speculate as to whether any (asserted) interception would be under § 1881a or some other authority, they cannot satisfy the 'fairly traceable' requirement."). But had the government in fact surveilled the plaintiffs under § 1881a, both the injury-in-fact and traceability would have been sufficiently concrete—without the plaintiffs having to disprove that the government would have surveilled them regardless under a different statute. *Clapper* holds that a plaintiff must show a sufficiently concrete injury that arises from the challenged source, *id.* at 414, but it does not require a plaintiff to show that the source of the injury is the *only* possible source.

Two cases from this district further illustrate this point. First, in *Braeburn, Inc. v. FDA*, 389 F. Supp. 3d 1 (D.D.C. 2019), pharmaceutical company Braeburn challenged the FDA's determination that its drug could not be marketed until competitor Indivior's statutory right to market exclusivity expired the following year. *Id.* at 14, 16. Indivior argued that Braeburn did not

[3] To the extent the Court's earlier opinion can be read to suggest that the third link was an independent requirement, that reading is incorrect for the reasons explained above. The earlier case rested on the "highly attenuated" "combined chain of possibilities," not simply the third link. *Ipsen*, 2021 WL 4399531, at *10.

have standing because, even if the challenged market exclusivity determination was erroneous, Indivior would have obtained a *different* kind of statutory market exclusivity anyway. *Id.* at 15–16. The Court rejected that argument. It explained that Indivior's entitlement to any other kind of market exclusivity was unresolved by FDA, and Braeburn was not required to prove that such "a hypothesized future event" would not "injure [it] in the same way as the challenged agency decision." *Id.* at 16. So too here: Ipsen's "access to judicial relief does not require that it disprove any speculated alternative source of injury" under the Biologics Act, "but only that it marshal[] evidence of injury, causation, and redressability sufficient for the summary judgment stage" as to the Drug Act. *Id.*

Second, in *Teva Pharmaceuticals*, the court found that Teva had standing to challenge a similar agency action as here: FDA's refusal to transition Teva's product from the Drug Act to the Biologics Act during the March 2020 transition. *See* 514 F. Supp. 3d at 74, 84. The competitive injury there was slightly different. Because it was regulated under the Drug Act, Teva's product was often subject to state laws requiring automatic substitution of its brand name NDA drug for competitors' generic ANDA drugs. *Id.* at 88–89. But if Teva's product had been transitioned to the Biologics Act, the state laws would not permit such automatic substitution unless the FDA made a further finding that the competitor products were "interchangeable" with Teva's—"a heightened requirement separate from [A]BLA approval, with no equivalent in the generic drug context." *Id.* at 89. The defendant contended that it was too "speculative" that the FDA would not have made the interchangeability finding, thus subjecting Teva to automatic substitution anyway under the Biologics Act. *Id.* at 90–91. But the Court rejected that argument, reasoning that "the mere possibility that [this] hypothesized future event . . . might injure a plaintiff in the

same way as the challenged agency decision does not leave a plaintiff without standing." *Id.* at 91–92 (quotation marks and alterations omitted).

The same is true here: Ipsen "need not disprove any speculative harm it may experience as the result of a future [approval of InvaGen's product under the Biologics Act] finding in order to access judicial relief." *Id.* at 92. Simply put, the relevant comparison to *Teva* is this: under the Drug Act, the plaintiff faces a form of competition (*Teva*, automatic substitution of generics; here, competition by a § 505(b)(2) drug) that it would not face under the Biologics Act *unless and until* the FDA made a finding (*Teva*, of interchangeability; here, of BLA or ABLA approval).[4] As in *Teva*, Ipsen need not prove a negative—that the FDA would not have promptly approved InvaGen had it pursued an alternate pathway under the Biologics Act.

iii. Redressability

The third and final prong of standing, redressability, "examines whether the relief sought, assuming that the court chooses to grant it, will likely alleviate the particularized injury alleged by the plaintiff." *Fla. Audubon Soc'y v. Bentsen*, 94 F.3d 658, 663–64 (D.C. Cir. 1996) (footnote omitted). Because an APA case like this one "often presents complex interrelationships between private and government activity that make difficult absolute proof that the harm will be removed . . . , a court should be careful not to require too much from a plaintiff attempting to show redressability." *Cmty. Nutrition Inst.*, 698 F.2d at 1248 (alteration omitted).

[4] Contrary to the defendants' assertion, *see* FDA Mem. at 19; FDA Reply at 5, Dkt. 36, that *Teva* involved automatic substitution does not distinguish it from this case. In *Teva*, the injury was based on the *extent* of competition, since the presence of competition was presumed under either statute. *See, e.g.*, 514 F. Supp. 3d at 89–90 (assuming that all competing products would be simultaneously transitioned to the Biologics Act on March 23, 2020). Here, Ipsen's injury is based on the *presence* of competition, and so the extent is irrelevant. *Cf. Ipsen*, 2021 WL 4399531 at *8 (explaining that substitution "has no bearing on whether Ipsen faces an injury that is certainly impending[,] [i]t merely affects the *magnitude* of any injury that Ipsen could hypothetically suffer" (quotation marks and citation omitted)).

Ipsen's injury is redressable because it would be addressed by the injunctive relief it seeks. If this Court were to grant an injunction vacating the FDA's § 505(b)(2) approval of InvaGen's product, *see* Prayer for Relief, Compl. at 28, InvaGen would then have to seek approval under the Biologics Act by submitting a BLA or ABLA application. Unless and until the FDA approved InvaGen's application, its product would not be able compete in the drug market with Somatuline Depot. Though the scope of that relief "may be limited by an eventual" approval of InvaGen's biologics application, "the clear ability of the requested injunction to redress" Ipsen's "economic harms in the interim is not speculative simply because it may be short-lived." *Teva*, 514 F. Supp. 3d at 91.

The parties dispute the Court's power to vacate the FDA's approval of InvaGen's product, the propriety of doing so, and whether FDA would do so if the Court remanded this case to the agency, *see, e.g.,* InvaGen Mem. at 37–39, but these issues are not relevant at this stage. "[T]he redressability prong of the standing test is not an inquiry into the scope of the court's power to grant relief" and "does not ask whether it is likely that the court's determination would provide the ultimate relief sought." *In re Thornburgh*, 869 F.2d 1503, 1511 (D.C. Cir. 1989) (quotation marks omitted). "Rather, the test assumes that a decision on the merits would be favorable and that the requested relief would be granted; it then goes on to ask whether that relief would be likely to redress the party's injury." *Id.* (emphasis omitted). Assuming that the Court has the authority to vacate the FDA's decision and does so, that remedy would relieve Ipsen of its asserted injury.

B. Merits

On the merits, Ipsen challenges the FDA's determination that Somatuline Depot is not a "biological product" under the Biologics Act as arbitrary, capricious, and contrary to law. In Ipsen's view, the FDA erred in finding that Somatuline Depot does not qualify as a "protein" under

the relevant regulation, and alternatively, that it does not qualify as "analogous" to a protein under the statute. The Court will address each in turn.

i. Whether Somatuline Depot is a "protein" under the regulation

The Biologics Act covers all "biological products" which are defined, as relevant here, to include any "protein . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings." 42 U.S.C. § 262(i)(1). The FDA regulations further define "protein" as

> any alpha amino acid polymer with a specific, defined sequence that is *greater than 40 amino acids in size*. When two or more amino acid chains in an amino acid polymer are *associated with each other in a manner that occurs in nature*, the size of the amino acid polymer for purposes of this paragraph . . . will be based on the total number of amino acids in those chains, and will not be limited to the number of amino acids in a contiguous sequence.

21 C.F.R. § 600.3(h)(6) (emphases added). Ipsen does not challenge the regulation itself; it simply challenges the FDA's determination that Somatuline Depot does not meet the regulation's definition of a "protein." *See* Pl.'s Reply at 2–3; Hr'g Tr. at 50–51.

In finding that Somatuline Depot is not a protein under this definition, the FDA first determined that the frame of reference for applying the definition is "the drug substance (i.e., active ingredient) rather than the drug product (finished dosage form)." A.R. 2648. Second, the FDA found that Somatuline Depot's drug substance (*i.e.*, active ingredient) is lanreotide acetate, an "octapeptide"—comprised of 8 amino acids—that does not satisfy the regulatory definition of a protein. A.R. 2648–49. Neither of these findings was contrary to the regulation's plain language, and both reflect rational decision-making.

Importantly, with respect to the FDA's first premise—that a drug's active ingredient is the proper frame of reference for determining whether the drug is a protein—Ipsen agrees. *See* Hr'g Tr. at 51 ("I think we all agree that the important thing to look at is the active ingredient."); Pl.'s Reply at 4 ("In this case, all parties agree that FDA's 'protein' definitional test focuses on the

active ingredient, lanreotide acetate."). Indeed, focusing on the active ingredient is consistent with the approach that the FDA has taken in other contexts. *See, e.g.*, *Sandoz Inc. v. Becerra*, 57 F.4th 272, 280 (D.C. Cir. 2023) (explaining that new chemical entity exclusivity turns on a drug's active ingredient). The FDA also has consistently taken this approach with this regulation. *See* A.R. 2648 n.13 (explaining that "[a]ll of the biological products" FDA transitioned to the Biologics Act in March 2020 "were determined to be a 'protein' . . . based on the drug substance (i.e., active ingredient)").

Ipsen also does not dispute that the active ingredient of Somatuline Depot is lanreotide acetate. *See, e.g.*, Pl.'s Mem. at 11 ("Somatuline Depot is approved for treating several rare diseases through extended-release dosing of its *active ingredient lanreotide acetate*, a synthetic peptide molecule that mimics the naturally occurring hormone somatostatin." (emphasis added)); Pl.'s Reply at 4. Nor could it. Ipsen states in the product labeling for Somatuline Depot that its "[a]ctive ingredient" is "lanreotide acetate." A.R. 1530. And the parties agree that lanreotide acetate—at least standing alone—is an octapeptide, meaning it consists of 8 amino acids. *See, e.g.*, A.R. 1621 (Ipsen's 2019 citizen petition characterizing "lanreotide [a]s a small peptide composed of only eight amino acid residues"); Hr'g Tr. at 4 (Ipsen: "The active ingredient, octapeptide [sic], I think I would be constrained to agree is an octapeptide.").

The FDA's conclusion that Somatuline Depot is not a 40-amino-acid protein naturally follows from these three undisputed premises: that a drug is a protein if and only if its active ingredient is; that Somatuline Depot's active ingredient is lanreotide acetate; and that lanreotide acetate is 8 amino acids in size. Even so, Ipsen insists that the FDA is obligated to look at the active ingredient *as it exists in the finished drug product*, not a theoretical stand-alone form of the active ingredient. *See* Pl.'s Reply at 4; Hr'g Tr. at 60 ("[T]he debate that we're having about active

ingredient isn't whether you look at the active ingredient. It's when you look at the active ingredient."). Under Ipsen's logic, Somatuline Depot is a protein because its finished drug product, lanreotide acetate, is linked together into nanotubes. Because these linkages occur "in a manner that occurs in nature," Ipsen contends that the "size" of lanreotide acetate in Somatuline Depot is determined by the total number of amino acids in the *nanotube* chain, which far exceed 40 and therefore fit the regulatory definition of a protein. Pl.'s Mem. at 23; Pl.'s Reply at 4. In sum, Ipsen challenges two components of the FDA's analysis: one legal—the FDA's decision to consider the size of the active ingredient standing alone, rather than as it appears in the final drug product; and a closely related factual determination—that lanreotide acetate in its stand-alone form *is* the active ingredient of Somatuline Depot. Both challenges fail.

1. Legal challenge

Contrary to Ipsen's position, neither the statute nor the regulatory definition of a "protein" *requires* the FDA to consider the size of the active ingredient as it appears in the final drug product, rather than standing alone. As noted, the parties agree that, even though the term "active ingredient" is not directly invoked in the definitions of "protein" and "biological product," it is proper for the FDA to examine the active ingredient to determine whether a product is a protein. Further, FDA regulations define "active ingredient" (*i.e.*, "drug substance") as "any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease." 21 C.F.R. § 314.3(b). The FDA thus explained that to determine the active ingredient of a drug product, it examines what "confers [its] pharmacologic activity."[5] A.R. 2648. Applied to Somatuline Depot, this definition points to

[5] Despite Ipsen's objection that the pharmacological activity "test comes out of thin air," Pl.'s Reply at 6, this exact language is used to define both "active ingredient" and "drug substance" in the regulations governing new drug applications under the Drug Act. *See* 21 C.F.R. § 314.3.

lanreotide acetate, which is responsible for the drug's pharmacologic activity. *See* A.R. 2649 (explaining that lanreotide acetate confers the drug's therapeutic effect by "bind[ing] to somatostatin receptors to exercise [the drug's] function");[6] *see also* Pl.'s Reply at 4 (not disputing that lanreotide acetate is responsible for Somatuline Depot's therapeutic effect).

The FDA's regulations explicitly distinguish a drug's active ingredient from its "dosage form" (*i.e.*, "drug product")—the "physical manifestation containing the active and inactive ingredients that delivers a dose of the drug product," including "design features that affect frequency of dosing." 21 C.F.R. § 314.3(b). Neither the statutory nor the regulatory text require the FDA to "analyz[e] lanreotide acetate as it appears [this] 'finished dosage form,'" Pl.'s Reply at 4–5. For one, the terms "biological product" and "analogous product" in the statute and regulations, *see* 42 U.S.C. § 262(i)(1); 21 C.F.R. § 600.3(h)(6), do not require the FDA to assess a "finished drug product." Simply because these phrases include the word "product" does not mean that they all refer to the same thing. To the contrary, the Biologics Act defines a "biological product" as something "applicable to the prevention, treatment, or cure of a disease or condition of human beings." 42 U.S.C. § 262(i)(1). This language lends support to the FDA's decision to assess only the active ingredient, which confers the pharmacological activity necessary for the

[6] Ipsen mischaracterizes the FDA's decision as resting on the form the active ingredient takes "in the body after administration," Pl.'s Mem. at 22–24. but the FDA did no such thing. Rather, the FDA considered the drug's effect on the body to determine its active ingredient—an analysis that is consistent with the very definition of "active ingredient." *See* 21 C.F.R. § 314.3 ("any component that is intended to furnish pharmacological activity . . . or to affect the structure or any function of the body of man."). Although the FDA referred to the "released lanreotide octapeptide" when it determined that lanreotide does the pharmacological work in Somatuline Depot, A.R. 2648–49, the FDA did not, as Ipsen suggests, Pl.'s Mem. at 24; Pl.'s Reply at 7, draw any distinction between the active ingredient as it exists inside or outside of the body. *See* FDA Mem. at 26 (explaining that "lanreotide is inherently an 'octapeptide' (eight-amino-acid chain) whether it is within the body or not"). For this reason, *Actavis Elizabeth LLC v. FDA*, 625 F.3d 760 (D.C. Cir. 2010), is inapposite.

"cure, mitigation, treatment, or prevention of disease," but not other effects such as controlling the frequency of dosing. 21 C.F.R. § 341.3(b).

In sum, because the parties agree that the correct frame of reference is the active ingredient and FDA regulations define "active ingredient" as the thing that confers "pharmacological activity," the FDA's decision to analyze just lanreotide acetate (which is responsible for Somatuline Depot's therapeutic effect) and not the nanotubes (which are not) was unambiguously correct. But even if the FDA's regulations were ambiguous on this point, the Court would defer to the FDA's interpretation as reasonable. *See Actavis Elizabeth*, 625 F.3d at 763 ("An agency's interpretation of its own regulations is entitled to judicial deference" unless it is "plainly erroneous or inconsistent with the regulation[.]" (citations and quotation marks omitted)). This is especially so here because "the interpretive issue arises in the context of a complex and highly technical regulatory program" where "judges . . . are least likely to know what they are doing." *Kisor v. Wilkie*, 139 S. Ct. 2400, 2413–14 (2019) (quotation marks omitted); *see also id.* at 2410, 2414, 2417 (repeatedly referring to the FDA regulation defining "active moiety" as a prime example of when courts should defer to the FDA's expertise: "Is there anything to be said for courts all over the country trying to figure out what makes for a new active moiety?"). For the same reasons, the FDA's interpretation to assess Somatuline Depot's active ingredient in its stand-alone rather than its finished dosage form is certainly reasonable, if not unambiguously correct, and does not violate the statutory or regulatory text.

2. Factual challenge

Remaining is Ipsen's challenge that the FDA's scientific judgment—that lanreotide acetate, in its stand-alone form, *is* the active ingredient of Somatuline Depot—was arbitrary and capricious. In Ipsen's view, the FDA cannot look at a "theoretical form [of lanreotide acetate] that

exists on its own," and "the form of lanreotide acetate that appears" in Somatuline Depot's nanotubes is more than 40 amino acids. Pl.'s Reply at 5.

In its most simplistic form, the factual question is whether the lanreotide octapeptide or the nanotube is responsible for Somatuline Depot's pharmacological activity. Fundamentally, this dispute is a scientific one, and the answer falls squarely within the FDA's "area of special expertise"—not this Court's. *Baltimore Gas & Elec. Co. v. Nat. Res. Def. Council, Inc.*, 462 U.S. 87, 103 (1983). "When examining this kind of scientific determination," the "reviewing court must generally be at its most deferential." *Id.*; *see also Fox v. Clinton*, 684 F.3d 67, 75 (D.C. Cir. 2012) ("[A]rbitrary and capricious review is fundamentally deferential—especially with respect to matters relating to an agency's areas of technical expertise." (quotation marks and alteration omitted)). "Meaningful review of the agency's actions does not require [the Court] to step into the FDA's shoes and reassess its scientific judgments—a role that [this Court is] ill-equipped to play under the guise of the APA's arbitrary and capricious standard." *Pharm. Mfg. Rsch. Servs., Inc. v. FDA*, 957 F.3d 254, 265 (D.C. Cir. 2020) (quotation marks omitted); *see also Actavis Elizabeth*, 625 F.3d at 766 ("We are hard pressed to second-guess the FDA's view, especially since it rests on the agency's evaluations of scientific data within its area of expertise." (quotation marks omitted)). The Court thus reviews the FDA's scientific determination only for reasonableness and consistency with the evidence in the record. *See Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983).

The FDA's conclusion that lanreotide acetate itself, regardless of its association in any particular structure, is the active ingredient of Somatuline Depot is sufficiently supported by the record. The FDA concluded that lanreotide acetate is what "binds to somatostatin receptors to exercise [the drug's] function," A.R. 2649, based on Ipsen's own product labeling describing

Somatuline Depot as "*contain[ing] the drug substance lanreotide acetate, a synthetic octapeptide* with a biological activity similar to naturally occurring somatostatin, water for injection and acetic acid (for pH adjustment)." A.R. 2648–49 (emphasis in original) (quoting Somatuline Depot Labeling, Section 11); *see also* A.R. 1526 (Somatuline Depot Labeling stating: "Lanreotide, *the active component* of SOMATULINE DEPOT is an *octapeptide* analog of natural somatostatin." (emphasis added)).[7] Further, the FDA cited scientific studies concluding that "the lanreotide cyclic octapeptide furnishes the same pharmacological activity" no matter whether administered in an "extended release" formulation (*e.g.*, in nanotubes) or "administered by daily injections or continuous infusion" (*e.g.*, not in nanotubes). A.R. 2649–50.

In contrast, the FDA found that the nanotube structures are a "formulation property" of Somatuline Depot "that act[] to control the release rate of the lanreotide drug substance"—but do not themselves confer any pharmacological activity. A.R. 2649; *see* Pl.'s Reply at 4 (not disputing that the "nanotubes control the distribution of lanreotide acetate in the patient's body, effectively keeping it from taking effect all at once after it is administered to the patient"). Ipsen itself has explained that the nanotubes are responsible for the drug's "semi-solid," "viscous gel"-like property that "forms a depot" "under the skin" which, in turn, "diffuses specific amounts of lanreotide into circulation" in the body "over an extended period of time." Compl. ¶¶ 47–48. The FDA thus concluded that the nanotubes in Somatuline Depot are a "formulation change [that] alters the pharmacokinetics"—movement of the drug, including distribution and absorption—"but does

[7] That the labeling was written before the regulatory definition of a "protein" was promulgated, *see* Pl.'s Mem. at 24–25, has no impact on the labeling's relevance here. The labeling's description of Somatuline Depot is not dispositive as to whether the drug is a protein. Rather, it is relevant because it accurately identifies, in Ipsen's own words, the drug substance (*i.e.*, active ingredient) and the makeup of that active ingredient. Ipsen does not argue that its labeling's description is inaccurate—and so the fact that Ipsen did not "ha[ve] front of mind" the protein test when writing the description, *id.* at 25, is irrelevant.

not change the active ingredient that is intended to furnish pharmacological activity." A.R. 2649. Accordingly, applying the definition of "active ingredient" in the regulations, the nanotube structures are not the active ingredient—only lanreotide acetate is. The nanotubes instead fit more naturally into the regulatory definition of "dosage form" which, as noted above, is distinguished from active ingredient in the Drug Act regulations. *See* 21 C.F.R. § 314.3(b) (defining "dosage form" to include "design features that affect frequency of dosing").

These justifications reflect the FDA's reasoned "scientific analysis," which deserves "a high level of deference." *Pharm. Mfg. Rsch. Servs.*, 957 F.3d at 262 (quotation marks omitted). It is pure scientific judgment that lanreotide acetate confers Somatuline Depot's pharmacological activity by itself, regardless of its association into nanotubes, and that it can therefore be assessed in its stand-alone octapeptide form. "A court is ill-equipped to second-guess that kind of agency scientific judgment under the guise of the APA's arbitrary and capricious standard." *Cytori Therapeutics, Inc. v. FDA*, 715 F.3d 922, 927 (D.C. Cir. 2013). Instead, the Court's review is limited to whether the "FDA's assessment [is] both reasonable and reasonably explained." *Id.* Because the FDA's choice was rational, carefully explained, and consistent with the record evidence, the Court will not "unduly second-guess[]" its "scientific judgment[]." *Pharm. Mfg. Rsch. Servs.*, 957 F.3d at 262 (quotation marks omitted).

Finally, it is irrelevant whether, in forming the nanotubes, lanreotide acetate associates in a manner that occurs in nature. *See* 42 C.F.R. § 600.3(h)(6). Either way, under the FDA's rational interpretation of the regulations, it would not consider the number of amino acids in a nanotube as a whole. As explained, whether a drug is a protein centers on its active ingredient (the thing that confers the pharmacological activity). Because the FDA reasonably determined that Somatuline Depot's nanotube formulation has nothing to do with the drug's pharmacological activity, it also

reasonably concluded that it need not assess whether the nanotubes are formed in a manner that occurs in nature.[8] A.R. 2652.

ii. Whether Somatuline Depot is "analogous" to a protein under the statute

In the alternative, Ipsen argues that even if Somatuline Depot does not meet the regulatory definition for "protein," it is at least "analogous" to a protein. As noted, the Biologics Act defines "biological product" to include any "virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, *protein, or analogous product* . . . ." 42 U.S.C. § 262(i)(1) (emphasis added). The FDA regulations define what counts as "analogous" to a virus, therapeutic serum, toxin, and antitoxin. *See* 21 C.F.R. § 600.3(h)(5). But the regulations are silent as to what qualifies as "analogous" to a protein. *See generally id.* § 600.3(h).

Under the statute, the FDA determined that Somatuline Depot is not an "analogous product" to a protein. A.R. 2657–58. While it found "the term 'analogous' . . . ambiguous," the FDA explained, it did not consider Somatuline Depot to be analogous "because it would not be appropriate to interpret the statutory term 'analogous product' (with reference to a 'protein') in a way that would include amino acid polymers that are specifically excluded by the interpretation of the term 'protein' set forth in the FDA's [regulation]." A.R. 2657. The FDA explained that the 40-amino-acid size requirement is a "critical characteristic" of a protein, and to be analogous to a protein "a product must share [that] critical characteristic[]." A.R. 2657–58. Because the active ingredient of Somatuline Depot, lanreotide acetate, is only 8 amino acids, it "is specifically

[8] Because the Court accepts the FDA's finding that the lanreotide acetate alone, and not the nanotube, is the relevant unit for the protein definition, the Court need not assess the FDA's alternative finding that the nanotubes do not associate in a manner that occurs in nature. And even if it did, it would reach same conclusion because the Court is not equipped to second-guess the FDA's scientific judgment on this point either. *See Cytori Therapeutics*, 715 F.3d at 927.

excluded from the category of 'protein'" and thus cannot be considered "analogous" to one. A.R. 2658.

That conclusion was not contrary to the statute.[9] Ipsen argues that the FDA's interpretation cannot be correct because it requires a product to have all of the characteristics of a protein to be "analogous" to one, and therefore effectively reads the term "analogous product" out of the statute. *See* Pl.'s Reply at 15–16. But as an initial matter, even if Ipsen were correct that FDA's interpretation leaves empty the set of products that are analogous to but not actually proteins, the Court fails to see how that would render the statutory term "analogous product" superfluous. The statutory term would still include those products that the FDA has explicitly defined as analogous to a virus, therapeutic serum, toxin, or antitoxin. 21 C.F.R. § 600.6(h)(5). And Ipsen has provided no reason why "analogous product" must include at least one product analogous to each and every discrete type of biological product in the statute's list. *Cf. United States v. Turkette*, 452 U.S. 576, 583 n.5 (1981) ("Language in a statute is not rendered superfluous merely because in some contexts that language may not be pertinent.").

In any event, Ipsen has not established that the FDA's interpretation leaves empty the category of products analogous to but not themselves proteins. The FDA has identified at least one product in this category—namely, drugs with active ingredients that are comprised of certain "naturally derived mixtures" that include one or more protein(s) "as well as one or more non-biological product component(s) (e.g., lipids)." A.R. 2658. In these products, non-biological products such as lipids (as well as proteins) "contribute to the product's activity" and "to their

[9] Ipsen does not contend that the term "analogous" has an unambiguous meaning under the statute, *see* Pl.'s Reply at 17, and consequently does not appear to dispute that *Chevron* comes into play, *see id.* at 15 n.11. Rather, Ipsen argues that the Court should not defer to the FDA's interpretation under *Chevron* because it is unreasonable and "negates the plain meaning of the statute." *Id.* The Court thus addresses only this objection.

therapeutic effect"—*i.e.*, make up the active ingredient. *Id.* Looking at the active ingredient as a whole, it is by definition not a protein: a protein "*is* an[] alpha amino acid polymer," 21 C.F.R. § 600.3(h)(6), and an active ingredient that is comprised not only of amino acids but rather includes non-protein molecules does not fit this bill. Contrary to Ipsen's assertion, *see* Pl.'s Reply at 16, that these mixtures contain a protein does not make the mixtures as a whole proteins. A biological product is not defined as any product that contains a protein; nor is a protein defined as anything that contains a protein. Thus, such naturally derived mixtures would not fit the definition of "protein," yet the FDA considers them analogous to one. Ipsen has failed to show that this interpretation of "analogous product" is contrary to statute.

Finally, the FDA's conclusion that Somatuline Depot is not a product analogous to a protein was not otherwise arbitrary, capricious, or unreasonable. Ipsen argues that to be "analogous," a product must be "similar or comparable to something else either in general or in some specific detail." Pl.'s Reply at 14 (quoting *Analogous*, Merriam-Webster Dictionary, https://tinyurl.com/y49khdfa (last visited May 8, 2023)). Fair enough. But in no way is the lanreotide acetate octapeptide similar or comparable to a protein. While Ipsen would again prefer that the FDA assess the nanotube structures rather than the lanreotide acetate on its own, *see* Pl.'s Reply at 14, for the above-stated reasons, this result is not compelled by the statute or the regulations. And it would be anomalous for the FDA to use two different frames of reference for analyzing whether something is a "protein" or is "analogous" to one. *Cf.* A.R. 2648 n.13 (noting that the FDA consistently looks to a drug's active ingredient to determine if it is a biological product). Thus, in the Court's view, the FDA's assessment properly centered on whether Somatuline Depot's active ingredient, lanreotide acetate, is analogous to a protein—without considering other features of the product, such as its nanotube structures. *See* A.R. 2657. Because

lanreotide acetate is only 8 amino acids in size, this was not a close question. It is in no way comparable or "analogous" to a protein, which is 40 or more amino acids in size. For all of the above reasons, the "FDA's assessment [was] both reasonable and reasonably explained." *Cytori Therapeutics*, 715 F.3d at 927.

* * *

In sum, the FDA's conclusion that Somatuline Depot is a drug, rather than a biological product, was not contrary to the relevant statute or the regulations. Further, the agency's factual determinations were well-reasoned, consistent with the evidence, and addressed Ipsen's objections. "In Administrative Procedure Act cases alleging arbitrary and capricious agency action, courts must be careful not to unduly second-guess an agency's scientific judgments. That basic principle of administrative law controls this case." *Cytori Therapeutics*, 715 F.3d at 923.

CONCLUSION

For the foregoing reasons, the defendants' motions for summary judgment are granted, and the plaintiff's motion for summary judgment is denied. A separate order accompanies this memorandum opinion.

DABNEY L. FRIEDRICH
United States District Judge

May 8, 2023