[PUBLISH]

IN THE UNITED STATES COURT OF APPEALS

FOR THE ELEVENTH CIRCUIT

No. 20-13922

D.C. Docket No. 1:19-cv-22425-BB

CATALYST PHARMACEUTICALS, INC.,

Plaintiff - Appellant,

versus

XAVIER BECERRA, Secretary of Health and Human Services, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, JANET WOODCOCK, Acting Commissioner of the Food and Drug Administration, U.S. FOOD AND DRUG ADMINISTRATION,

Defendants – Appellees,

JACOBUS PHARMACEUTICAL COMPANY, INC.,

Intervenor-Defendant – Appellee.

Appeal from the United States District Court
for the Southern District of Florida

(September 30, 2021)

Before LAGOA, ANDERSON, and MARCUS, Circuit Judges.

LAGOA, Circuit Judge:

This appeal asks us to determine whether the statutory phrase "same disease or condition" contained in the Orphan Drug Act, *see* 21 U.S.C. § 360cc, is ambiguous. It is not. By finding this statutory phrase ambiguous and then deferring to the U.S. Food and Drug Administration's interpretation of it, the district court erred. We therefore reverse the district court's grant of summary judgment in favor of the Defendants[1] and Jacobus, and remand with instructions to grant summary judgment in favor of Catalyst.

I. FACTUAL AND PROCEDURAL HISTORY

A. The Orphan Drug Act

In 1983, Congress enacted the Orphan Drug Act, thereby amending the Federal Food, Drug, and Cosmetic Act ("FDCA"). *See* Pub. L. 97-414, 96 Stat. 2049 (codified as amended at 21 U.S.C. §§ 360aa–360ee). The Orphan Drug Act

[1] Catalyst named Alex Azar, Secretary of Health and Human Services; Norman Sharpless, Acting Commissioner of the FDA; the U.S. Department of Health and Human Services; and the U.S. Food and Drug Administration as the Defendants in its Complaint. During the pendency of this case, the administration changed, and Secretary Azar and Acting Commissioner Sharpless resigned their positions. We therefore have substituted as defendants-appellees the proper individuals in their official capacity. *See* Fed. R. Civ. P. 25(d) ("An action does not abate when a public officer who is a party in an official capacity dies, resigns, or otherwise ceases to hold office while the action is pending. The officer's successor is automatically substituted as a party. Later proceedings should be in the substituted party's name, but any misnomer not affecting the parties' substantial rights must be disregarded. The court may order substitution at any time, but the absence of such an order does not affect the substitution.").

incentivizes pharmaceutical companies to develop "orphan drugs"—drugs for rare diseases that affect such a small portion of the population that there otherwise would be no financial incentive to research and develop treatments. One such incentive is to grant market exclusivity to the manufacturer of an FDA-approved orphan drug for a seven-year period. The framework established by the Orphan Drug Act is fairly straightforward: designation as an orphan drug followed by FDA approval results in market exclusivity. Each of these steps is governed by a separate part of the Orphan Drug Act.

1. Designation

Pursuant to 21 U.S.C. § 360bb(a)(1), a drug manufacturer may request the FDA to designate a drug as an orphan drug—one that "is being or will be investigated for a rare disease or condition." Section 360bb(a)(2) defines a "rare disease or condition" as one that "(A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug." Designation allows the manufacturer to take advantage of certain resulting financial benefits—such as tax credits—while testing for safety and efficacy continues. *See, e.g.*, 26 U.S.C. § 45C.

2. Approval

Before any new drug—orphan or otherwise—can be brought to market, it must be approved by the FDA. *See* 21 U.S.C. § 355(a)–(b). The Orphan Drug Act expressly requires approval pursuant to § 355 before market exclusivity arises. *See id.* § 360bb(a). When the manufacturer files a new drug application ("NDA"), it must include clinical data demonstrating that the drug is safe for use and effective in use. *See id.* § 355(b)(1)(A). The manufacturer must identify the new drug's "proposed indications for use," *see* 21 C.F.R. § 314.50(a)(1), and, if approved by the FDA, *see* § 355(c)(1), the manufacturer may market the drug solely for the specific indications[2] for which the FDA approved it, *see Ironworks Local Union 68 v. AstraZeneca Pharms., LP*, 634 F.3d 1352, 1356 n.5 (11th Cir. 2011). "The process of submitting an NDA is both onerous and lengthy," *Mut. Pharm. Co. v. Bartlett*, 570 U.S. 472, 476–77 (2013), and it involves significant "risk and expense," *Ethypharm S.A. Fr. v. Abbott Labs.*, 707 F.3d 223, 226 (3d Cir. 2013).

3. Exclusivity

To incentivize the development of orphan drugs, upon designation and FDA approval of the orphan drug, the manufacturer of the orphan drug is granted market exclusivity for a defined period of time. Specifically, the Orphan Drug Act provides:

Except as provided in subsection (b), if the Secretary--

[2] "Indications" is a term of art that means the drug's "intended use or uses." *United States ex rel. Polansky v. Pfizer, Inc.*, 822 F.3d 613, 615 (2d Cir. 2016).

> (1) approves an application filed pursuant to section 355 of this title, or
>
> (2) issues a license under section 262 of Title 42
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> for a drug designated under section 360bb of this title for a rare disease or condition, the Secretary may not approve another application under section 355 of this title or issue another license under section 262 of Title 42 for ***the same drug for the same disease or condition*** for a person who is not the holder of such approved application or of such license until the expiration of seven years from the date of the approval of the approved application or the issuance of the license.

21 U.S.C. § 360cc(a) (emphasis added). The Orphan Drug Act does not define "same disease or condition," the statutory phrase that is the subject of this dispute.[3]

B. Statutory Exceptions to Market Exclusivity for Orphan Drugs

There are three statutory exceptions to the seven-year period of exclusivity. The first two are found in 21 U.S.C. § 360cc(b).[4] First, the FDA can abrogate the

[3] Through regulation, the FDA has defined "same drug" as "a drug that contains the same active moiety as a previously approved drug and is intended for the same use as the previously approved drug." 21 C.F.R. § 316.3(b)(14)(i). "Moiety," in this context, means the same active ingredient. *See id.* § 316.3(b)(2).

[4] Specifically, § 360cc(b) states:

> During the 7-year period described in subsection (a) for an approved application under section 355 of this title or license under section 262 of Title 42, the Secretary may approve an application or issue a license for a drug that is otherwise the same, as determined by the Secretary, as the already approved drug for the same rare disease or condition if—
>
> (1) the Secretary finds, after providing the holder of exclusive approval or licensure notice and opportunity for the submission of views, that during such period the holder of the exclusive approval or licensure cannot ensure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated; or

manufacturer's exclusivity and approve another manufacturer's NDA if the FDA finds "that during such period the holder of the exclusive approval or licensure cannot ensure the availability of sufficient quantities of the drug." *Id.* § 360cc(b)(1). Second, a drug manufacturer can waive its exclusivity by written consent. *Id.* § 360cc(b)(2).

Third, as part of the 2017 reauthorization and statutory overhaul of the Orphan Drug Act,[5] Congress codified the concept of "clinical superiority" to § 360cc(c) and (e). Under these provisions, during the statutory exclusivity period, a different manufacturer of the same drug can obtain approval of an NDA to use the drug to treat the same disease or condition—effectively abrogating the original manufacturer's exclusivity—if that second manufacturer demonstrates that its drug "provides a significant therapeutic advantage over and above an already approved or licensed drug in terms of greater efficacy, greater safety, or by providing a major contribution to patient care." § 360cc(c)

> (2) the holder provides the Secretary in writing the consent of such holder for the approval of other applications or the issuance of other licenses before the expiration of such seven-year period.

[5] *See* FDA Reauthorization Act of 2017, Pub. L. No. 115-52, § 607, 131 Stat. 1005, 1049–50.

C. LEMS and the Competing Drugs Firdapse and Ruzurgi

Lambert-Eaton Myasthenic Syndrome ("LEMS") is a rare autoimmune disease that causes the immune system to attack the body's own tissues. It is considered an "orphan disease" with less than 0.001% of the population affected—diagnosed cases in the United States range from roughly 950 to 1,300. And the number of pediatric cases is infinitesimal—believed to be a "couple of dozen" nationwide. From all indications in the record evidence, LEMS affects adults and children equally—the disease mechanism, the pathophysiology, the clinical symptoms, the treatment regimens, and even adverse events all point to the same diagnosis, prognosis, and treatment of LEMS for both adults and children.

LEMS is treatable with the chemical amifampridine. Catalyst developed Firdapse (generic name: amifampridine phosphate) for the treatment of LEMS. On November 12, 2009, the FDA designated Firdapse as an orphan drug for the treatment of LEMS pursuant to § 360bb, and there is nothing in the FDA's designation that limits the "rare disease or condition" to subsets of people (e.g., adults or children) suffering from LEMS. Catalyst filed its first NDA in December 2015, which the FDA rejected as "not sufficiently complete to permit a substantive review." In March 2018, Catalyst re-filed its NDA, and the FDA approved Firdapse for the treatment of LEMS "in adults" on November 28, 2018. Consistent with the

Orphan Drug Act, the FDA granted Catalyst exclusivity through November 28, 2025. *See* § 360cc(a).

Jacobus developed its own drug—Ruzurgi (generic name: amifampridine)—for the treatment of LEMS. In fact, the FDA had designated Ruzurgi as an orphan drug to treat LEMS in 1990—nineteen years prior to Catalyst's designation. Like the agency's designation of Firdapse, the FDA's designation of Ruzurgi is not limited to specific groups or subsets of individuals suffering from LEMS, i.e., the "rare disease or condition." While Jacobus continued its development and testing for more than two decades, physicians at the Mayo Clinic and Duke University have used Ruzurgi to treat patients with LEMS for free since at least January 1993 under the FDA's "compassionate use" program. Jacobus submitted its first NDA for Ruzurgi in August 2017, which the FDA rejected. In June 2018, Jacobus re-filed its NDA. In its NDA, Jacobus included the following label for Ruzurgi:

> Safety and effectiveness of RUZURGI have been established in patients 6 to less than 17 years of age. Use of RUZURGI in patients 6 to less than 17 years of age is supported by evidence from adequate and well-controlled studies of RUZURGI in adults with LEMS.

In reviewing Jacobus's NDA, the FDA recognized that Catalyst, through Firdapse, had exclusivity "for the treatment of LEMS in adults that could potentially block approval of amifampridine (Ruzurgi) in that population." Because of this, the FDA "administratively divided" Jacobus's NDA into two parts: one for the treatment of LEMS in pediatric patients, and the other for the treatment of LEMS in adult

patients, "to allow for independent action in these populations." Following its review, the FDA approved Ruzurgi on May 6, 2019 "in patients 6 to less than 17 years of age."

By the FDA's own admission, this was likely the first time it ever "approved an application for a drug with an indication to treat pediatric patients for a certain disease while another sponsor has obtained orphan drug exclusivity for a drug application for the same drug with only an indication to treat adult patients for that disease." Nevertheless, the FDA concluded that approving Ruzurgi did not violate Catalyst's exclusivity because the approval of Ruzurgi for pediatric patients constituted a different "indication or use" from Firdapse's approval for adult patients.

Catalyst contends this decision by the FDA to "administratively divide" Jacobus's NDA was unique for several additional reasons. First, Jacobus never expressed an interest in—much less submitted or requested an NDA based on—pediatric-only approval, and Catalyst contends this would have been "plainly uneconomic," as there are only a couple of dozen pediatric LEMS patients nationwide. Second, Jacobus never conducted any clinical trials in children; every single patient in its clinical trials was an adult. Indeed, Jacobus was able to submit limited data only on pediatric safety, not efficacy—and Jacobus's data came from the expanded access program of compassionate use, not its clinical trials. Pursuant

to 21 U.S.C. § 355(b)(1), however, *both* safety and efficacy data are required for approval of an NDA.

D. Catalyst's Lawsuit Against the FDA and Jacobus's Intervention

Catalyst filed a four-count complaint against the FDA alleging multiple violations of the Administrative Procedure Act ("APA") relating to its approval of Ruzurgi. *See* 5 U.S.C. § 706(2)(A); 21 U.S.C. §§ 355(d), 360cc. Shortly thereafter, Jacobus intervened. Catalyst sought declaratory and injunctive relief, as well as "[a]n order vacating Defendants' approval of Ruzurgi." Catalyst based its claims on two premises. First, Catalyst argued that the plain language of the Orphan Drug Act prohibited the FDA from approving Ruzurgi because it is the "same drug" as Firdapse and treats the "same disease or condition" as Firdapse. Second, Catalyst argued that Ruzurgi could not be approved under the FDCA because it contains "false or misleading" labeling as a matter of law—specifically, because it suggests, in plain violation of an FDA regulation, that "the drug can be used for *adult* patients with LEMS, notwithstanding the fact that Ruzurgi only obtained approval to treat *pediatric* patients."

Each party moved for summary judgment. For purposes of these motions, it was undisputed that: (1) Firdapase and Ruzurgi are the "same drug" under the Orphan Drug Act, and (2) LEMS is "a single disease." The district court referred the motions to the magistrate judge for a report and recommendation. Based on its

application of the *Chevron*-deference doctrine,[6] the magistrate judge determined that the phrase "same disease or condition" in § 360cc(a) of the Orphan Drug Act is ambiguous and that the FDA's interpretation of the phrase was reasonable. The magistrate judge also determined that the FDA's approval of Ruzurgi's labeling did not violate the FDCA. As a result, the magistrate judge recommended granting the Defendants' motions for summary judgment and denying Catalyst's motion for summary judgment.

The district court affirmed and adopted the report and recommendation in full. The district court stated that the crux of the case was "whether the language of section 360cc is ambiguous." Like the magistrate judge, the district court first noted that there was no dispute between the parties that Firdapse and Ruzurgi are the "same drug." The district court focused on the statutory phrase "same disease or condition," finding it ambiguous and quoting with approval the magistrate judge's conclusion that "'it is unclear whether that phrase refers to the use for which the drug is approved after it submits its [NDA]'—here, LEMS for adults—'or the disease or condition for which it . . . received orphan [drug] designation'—LEMS for all patients." The district court also found that because § 360cc was ambiguous it needed to determine whether the FDA's interpretation of the statute was reasonable. As for Catalyst's count alleging Ruzurgi's false or misleading labeling, the district

[6] *See Chevron, U.S.A., Inc. v. Nat. Res. Def. Council, Inc.*, 467 U.S. 837, 842 (1984).

court noted that Catalyst "fail[ed] to present any case law in support of its position . . . [and] present[ed] no authority that would call into question the FDA's interpretation of its regulation under *Chevron*'s highly deferential standard." Catalyst timely appealed.

II. STANDARD OF REVIEW

We review *de novo* the district court's "interpretation and application of statutory provisions, as well as any grant of summary judgment based on that interpretation." *Williams v. Sec'y, U.S. Dep't of Homeland Sec.*, 741 F.3d 1228, 1231 (11th Cir. 2014). In reviewing an order granting summary judgment, we are guided by the well-established rule that summary judgment is appropriate "if the movant 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). Because this case involves a challenge to agency action, our *de novo* review of the district court's grant of summary judgment is, in effect, a direct review of the agency's decision. *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 883 (D.C. Cir. 2004). Under the APA, we must "hold unlawful and set aside agency action . . . found to be . . . arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A); *accord Miami-Dade County v. EPA*, 529 F.3d 1049, 1058 (11th Cir. 2008).

III. ANALYSIS

On appeal, Catalyst raises three issues. First, Catalyst argues that the Orphan Drug Act's language providing exclusivity for "the same disease and condition" is unambiguous, and therefore, the district court erred in determining that the Orphan Drug Act permits the FDA to grant orphan drug exclusivity to the "same drug" based on the drug's "use or indication." Second, Catalyst argues that, even if the Orphan Drug Act is ambiguous, the district court erred in concluding that the FDA's "use or indications" interpretation of the Orphan Drug Act was reasonable. Third, Catalyst argues that the district court erred in concluding that Jacobus's NDA for Ruzurgi did not violate the FDCA's labeling requirements. Because we agree with Catalyst on its first argument and reverse on that basis, we do not reach or address the merits of the remaining issues raised by Catalyst on appeal.

In any question of statutory interpretation, we begin with the language of the statute itself. *CBS Inc. v. PrimeTime 24 Joint Venture*, 245 F.3d 1217, 1225 n.6 (11th Cir. 2001); *Alfaro-Garcia v. U.S. Atty. Gen.*, 981 F.3d 978, 981–82 (11th Cir. 2020) ("The fundamental principle governing any exercise in statutory interpretation is that '[courts] "begin[] where all such inquiries must begin: with the language of the statute itself," and . . . give effect to the plain terms of the statute.'" (second alteration in original) (quoting *In re Valone*, 784 F.3d 1398, 1402 (11th Cir. 2015))).

Section 360cc(a) states, in relevant part:

> [I]f the Secretary--
>
> (1) approves an application filed pursuant to section 355 of this title, or
>
> (2) issues a license under section 262 of Title 42
>
> for a drug designated under section 360bb of this title for a rare disease or condition, *the Secretary may not approve another application* under section 355 of this title or issue another license under section 262 of Title 42 *for the same drug for the same disease or condition* for a person who is not the holder of such approved application or of such license until the expiration of seven years from the date of the approval of the approved application or the issuance of the license. . . .

(emphasis added). The district court found this section of the Orphan Drug Act ambiguous because (1) the statute does not define "same disease or condition" and (2) Congress failed to clarify whether that phrase refers to the use for which the drug is approved after it submits its NDA or for which it received orphan drug designation.

We conclude that the district court erred in finding § 360cc of the Orphan Drug Act ambiguous. First, "a statute is not ambiguous merely because it contains a term without a statutory definition." *United States v. Sepulveda*, 115 F.3d 882, 886 n.9 (11th Cir. 1997). Indeed, "Congress is 'not required to define each and every word in a piece of legislation in order to express clearly its will.'" *Id.* (quoting *Newsom v. Friedman*, 76 F.3d 813, 817 (7th Cir. 1996)). As we have recognized, "[w]e interpret words that are not defined in a statute with their ordinary and plain meaning because we assume that Congress uses words in a statute as they are

commonly understood." *Polycarpe v. E&S Landscaping Serv., Inc.*, 616 F.3d 1217, 1223 (11th Cir. 2010) (alteration in original) (defining various terms in the Fair Labor Standards Act using everyday dictionaries). Moreover, courts do not read individual words or terms in isolation, but instead in light of their context within a particular text. *Ruiz v. Wing*, 991 F.3d 1130, 1138 (11th Cir. 2021). Indeed, "[w]hile most words carry more than one dictionary definition, '[o]ne should assume the contextually appropriate ordinary meaning unless there is reason to think otherwise.'" *Id.* (quoting Antonin Scalia & Bryan A. Garner, *Reading Law* 70 (2012)).

Because neither the FDA nor Jacobus disputes that LEMS is a "disease," the issue before us is the meaning of the word "same" as used in the phrase "same disease or condition." "Same," when used as an adjective, has more than one definition (although they are related). Merriam Webster's Collegiate Dictionary defines "same" as: (1) "resembling in every relevant respect; conforming in every respect (used with "as")"; (2) "being one without addition, change, or discontinuance: identical; being the one under discussion or already referred to"; (3) "corresponding so closely as to be indistinguishable"; and (4) "equal in size, shape, value, or importance (usually used with *the* or a demonstrative (such as *that*, *those*)." *Same*, *Merriam-Webster's Collegiate Dictionary*, https://unabridged.merriam-webster.com/collegiate/same.

As noted earlier, § 360cc(a) provides that if the FDA approves an "application filed pursuant to section 355 of this title . . . for a drug designated under section 360bb . . . for a rare disease or condition, the Secretary may not approve another application under section 355 . . . for the same drug for the same disease or condition" until the expiration of seven years. Here, the word "same" is being used in the sense of "being the one under discussion or already referred to." The only "disease or condition" already referred to in § 360cc(a) is the "rare disease or condition" for which the drug was "designated under § 360bb." The ordinary and plain meaning of "same drug or condition" read in the context of this sentence yields only one result—the term unambiguously refers to the "rare disease or condition" designated under § 360bb. Thus, the scope of exclusivity under § 360cc(a) is determined by what has been designated under § 360bb.

As it relates to the facts here, pursuant to § 360bb, the FDA designated Catalyst's Firdapse as an orphan drug for treating the "rare disease or condition" of LEMS. As discussed earlier, LEMS is the same disease in all people suffering from it, regardless of their age, and there is nothing in the record to suggest that the FDA qualified its § 360bb designation with an age-restriction or that the designation of Firdapse applied to anything other than LEMS for all people suffering from the disease. The active ingredient in Firdapse is amifampridine. Under § 360cc(a), the FDA could not approve another manufacturer's NDA seeking approval of

amifampridine to treat LEMS, i.e., the "same disease or condition" that was designated under § 360bb, for a seven-year period. Because the active ingredient in Jacobus's Ruzurgi is also amifampridine, § 360cc(a) therefore temporarily barred the FDA from approving Jacobus's NDA to use Ruzurgi to treat LEMS.

In determining that the statutory phrase "same disease or condition" as used in § 360cc(a) was ambiguous, the district court looked to another section of the FDCA—21 U.S.C. § 355—which governs NDAs for many drugs, including orphan drugs. The district court noted that § 360cc(a) expressly refers to § 355 and that § 355 requires a drug manufacturer, as part of its NDA, to provide evidence that the drug is safe and effective for its intended use.[7] The district court further noted that the FDA's approval of Catalyst's NDA under § 355 was for the treatment of LEMS "in adults." The district court concluded that it was not clear whether "same disease or condition" refers to the "use" approved by the FDA to treat a disease or condition pursuant to § 355 or to the "rare disease or condition" designated by the FDA pursuant to § 360bb of the Orphan Drug Act. Because it concluded that either interpretation was reasonable, the district court deferred to the FDA's interpretation under the *Chevron*-deference doctrine.

[7] *See* § 355(b)(1)(A) (stating that drug manufacturer must provide the FDA with "full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use."

The district court's determination that the phrase "same disease or condition" is ambiguous, however, is not supported by the statutory text. First, the provisions of § 355, which apply generally to all NDAs and not solely those for orphan drugs, use different, more limited language, e.g., "safe" and "effective" for "use," rather than the broader, disease-specific language found in § 360cc(a). We must presume that Congress acts intentionally when it omits language included elsewhere in the same statute, *see Dep't of Homeland Sec. v MacLean*, 574 U.S. 383, 392 (2015) (explaining the interpretive canon that Congress acts intentionally when it omits language included elsewhere); *Jian Le Lin v. U.S. Att'y Gen.*, 681 F.3d 1236, 1240 (11th Cir. 2012) ("[An] inference may be drawn from the exclusion of language from one statutory provision that is included in other provisions of the same statute." (quoting *Hamdan v. Rumsfeld*, 548 U.S. 557, 578 (2006))), and we must give meaning to Congress's choice. Indeed, "[c]ourts have no authority to alter statutory language." *CBS Inc.*, 245 F.3d at 1228 (alteration in original). And "we are not allowed to add or subtract words from a statute; we cannot rewrite it." *Friends of the Everglades v. S. Fla. Water Mgmt. Dist.*, 570 F.3d 1210, 1224 (11th Cir. 2009). If Congress wanted to make the "use or indication" inquiry relevant to a holder's market exclusivity for an orphan drug, it could have done so by including such language in § 360cc(a). The fact that Congress did not include that language counsels against an interpretation that finds an ambiguity in § 360cc(a)'s language.

And, as we have already discussed, the "same disease or condition" already referred to in § 360cc(a) is the "rare disease or condition" for which the drug was "designated under § 360bb."

Second, while it is certainly true that § 366cc(a) refers to approval of applications submitted pursuant to § 355, it also refers to issuance of licenses pursuant to 42 U.S.C. § 262:

> if the Secretary—
>
> > (1) approves an application filed pursuant to section 355 of this title, or
> >
> > (2) issues a license under section 262 of Title 42
>
> for a drug designated under section 360bb of this title for a rare disease or condition, the Secretary may not approve another application under section 355 of this section or issue another license under section 262 of Title 42 for the same drug for the same disease or condition . . . .

The references to § 355 and § 262 simply identify what must occur to trigger market exclusivity (approval of an application under § 355 or issuance of a license under § 262) and what the FDA is prohibited from doing once both the designation and approval conditions are met (approve another application under § 355 or issue another license under § 262.) There is nothing in the express language of § 360cc that incorporates by reference the substantive provisions, requirements, or limitations of either § 355 or § 262, nor does the context in which the language appears or the structure of § 360cc(a) suggest that be done.

Third, although Congress did not define "same disease or condition," it did define "rare disease or condition"—the first phrase used and then referred back to in § 360cc—elsewhere in the Orphan Drug Act. As already noted, a manufacturer may request the FDA designate its drug "as a drug for a rare disease or condition." § 360bb(a)(1). Congress defined "rare disease or condition" as:

> any disease or condition which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug.

§ 360bb(a)(2). The statutory definition depends solely upon the modifier "rare." In other words, a disease or condition is "rare" under the Orphan Drug Act if it meets one of the two statutory conditions relating to how many people it affects. And while Congress could have included an additional use-specific definition for the words "disease or condition," it chose not to do so. By defining the term "rare disease or condition" in this manner—"rare" being defined, but the words "disease" and "condition" left without a statutory-specific definition—Congress left to the courts the obligation to interpret those words and apply the ordinary and plain meaning of those words as they are commonly understood. *See Polycarpe*, 616 F.3d at 1223. Moreover, "reasonable statutory interpretation must account for both 'the specific context in which . . . language is used' and 'the broader context of the statute as a whole.'" *Util. Air Regul. Grp. v. EPA*, 573 U.S. 302, 321 (2014) (quoting *Robinson*

v. Shell Oil Co., 519 U.S. 337, 341 (1997)). The Orphan Drug Act addresses drugs developed and designated for rare diseases or conditions. By its express language, § 360cc provides exclusivity and protection from others marketing the same drug for the rare disease or condition for which the orphan drug was designated pursuant to § 360bb.

Fourth, the district court's reliance on *Spectrum Pharmaceuticals, Inc. v. Burwell*, 824 F.3d 1062 (D.C. Cir. 2016), and *Sigma-Tau Pharmaceuticals, Inc. v. Schwetz*, 288 F.3d 141 (4th Cir. 2002), in support of its finding of ambiguity was misplaced. In *Spectrum*, the question before the court was whether intended off-label use mattered for purposes of § 360cc(a)'s exclusivity. *See* 824 F.3d at 1067. Spectrum first obtained orphan drug designation and FDA approval for a drug to treat liver damage, with its market exclusivity expiring in 2015. *Id.* at 1064. Spectrum then obtained orphan drug designation and FDA approval for the same drug to treat a different condition—pain management for patients with advanced colorectal cancer, with its market exclusivity expiring in 2018. *Id.* After exclusivity for the liver damage treatment expired, another manufacturer obtained FDA approval to sell a generic version of Spectrum's drug to treat liver damage. *Id.* Spectrum filed suit, asserting that the generic manufacturer intended to market the drug for off-label use for pain management, thereby infringing on Spectrum's remaining exclusivity period for that condition. *Id.* The district court granted

summary judgment against Spectrum, and the D.C. Circuit affirmed, stating that "the words 'for such disease or condition' suggest that Congress intended to make section 360cc 'disease-specific, not drug-specific,' and the rest of the statutory language focuses on protecting approved indications, not intended off-label uses." *Id.* at 1067 (quoting *Sigma-Tau*, 288 F.3d at 145).[8]

Like *Spectrum*, the issue in *Sigma-Tau* dealt with the scope of market exclusivity in the context of off-label use. Sigma-Tau first obtained orphan drug designation and FDA approval for a drug to treat carnitine deficiency in people with inborn metabolic disorders, with its market exclusivity expiring in 1999. 288 F.3d at 143. Sigma-Tau then obtained orphan drug designation and FDA approval for the same drug to treat a different condition—carnitine deficiency in patients suffering with end-stage renal disease ("ESRD"), with its market exclusivity expiring in 2006. *Id.* After exclusivity for the treatment of inborn metabolic disorders expired, two manufacturers obtained FDA approval to sell a generic version of Sigma-Tau's drug to treat carnitine deficiency in people with inborn metabolic disorders. *Id.* Like the manufacturer in *Spectrum*, Sigma-Tau sued, arguing that the generic manufacturers intended to market the drug for ESRD-related treatment and that the market

[8] Both *Spectrum* and *Sigma-Tau Pharmaceuticals* involved claims arising under the prior version of § 360cc, which used the term "such disease or condition." That language was amended as part of the 2017 overhaul of the Orphan Drug Act to the current term "same disease or condition." *See* 131 Stat. at 1049–50.

exclusivity Sigma-Tau still held for ESRD-related treatment precluded FDA approval. *Id.* at 143–44. The Fourth Circuit concluded that the Orphan Drug Act allowed for the approval of a generic version of a drug "for an indication that was no longer protected by market exclusivity." *Id.* at 143. The court noted that the Orphan Drug Act is *disease*-specific and stated, "[i]n other words, the statute as written protects uses, not drugs for any and all uses." *Id.* at 145. While the Fourth Circuit in *Sigma-Tau* certainly used the terms "uses" and "indications," to read that language as supportive of the FDA's interpretation, or as supportive of ambiguity in general, is to take the court's language out of context, as it is clear that the Fourth Circuit is comparing use of the same drug to treat *different* diseases and is using those terms to refer to that situation. Nothing in either *Spectrum* or *Sigma-Tau Pharmaceuticals* supports the notion that § 360cc incorporates the substantive provisions, requirements, or limitations of either § 355 or § 262.

Indeed, we agree that § 360cc(a) is "disease-specific, not drug-specific." But *Spectrum* and *Sigma-Tau Pharmaceuticals* both addressed the application of market exclusivity in the context of the treatment of different diseases; neither court was asked to address whether the phrase "same disease or condition" referred to designation under § 360bb or to the terms and conditions for approving an application under § 355 or issuing a license under § 262. We hold therefore that the

disease referred to in the phrase "same disease or condition" is the "rare disease or condition" for which the drug received designation under § 360bb.

We further hold that the phrase "same disease or condition" in § 360cc of the Orphan Drug Act is not ambiguous, as it plainly refers back to the term—"rare disease or condition"—used earlier in the same statutory provision. Additionally, the references in § 360cc(a) to § 355 and § 262 simply identify what agency actions satisfy the approval condition and what actions cannot occur once both designation and approval occurs. In this case, § 360cc prohibits the approval of subsequent NDAs for amifampridine to treat LEMS—the "rare disease or condition" designated under § 360bb—while Catalyst holds its seven-year exclusivity. Unless one of the three statutory exemptions applies—and there is no record evidence to suggest that any do apply—it is irrelevant if the subsequent NDA is intended to address only a subset of the population for LEMS. The district court therefore erred in finding that the statutory phrase "same disease or condition" in § 360cc was ambiguous.

And because the statutory phrase "same disease or condition" in § 360cc is not ambiguous, we also conclude that the district court erred in treating this as a *Chevron*-deference case and deferring to the FDA's interpretation of the statutory language. "When a court reviews an agency's construction of the statute which it administers, it is confronted with two questions." *Nat'l Ass'n of State Util. Consumer Advocs. v. FCC*, 457 F.3d 1238, 1253 (11th Cir. 2006) (quoting *Chevron,*

U.S.A., Inc. v. Nat. Res. Def. Council, Inc., 467 U.S. 837, 842 (1984)), *modified on denial of reh'g*, 468 F.3d 1272 (11th Cir. 2006). We first consider whether Congress has directly spoken to the precise question at issue in the case, and, if Congress's intent is clear, we "must give effect to the unambiguously expressed intent of Congress." *Id.* (quoting *Chevron*, 467 U.S. at 843). Where a statute is silent or ambiguous with respect to the specific issue, however, we must determine "whether the agency's answer is based on a permissible construction of the statute." *Id.* (quoting *Chevron*, 467 U.S. at 843).

Because the statute here is unambiguous, "that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Wilderness Watch & Pub. Emps. for Env't Resp. v. Mainella*, 375 F.3d 1085, 1091 (11th Cir. 2004). Courts "do not defer to an agency's interpretation of a statute when the text is clear." *Villarreal v. R.J. Reynolds Tobacco Co.*, 839 F.3d 958, 970 (11th Cir. 2016). And here, the FDA's interpretation of Orphan Drug Act is contrary to the clear statutory language enacted by Congress.

We now address the parties' cross-motions for summary judgement. Our review is *de novo*, and the parties agree that no genuine issues of material fact exist. The undisputed record evidence establishes that: (1) LEMS is a rare disease as defined in § 360bb(a)(2); (2) Firdapse was designated as an orphan drug to treat LEMS pursuant to § 360bb; (3) the FDA's designation of Firdapse to treat LEMS

was not for a specific category of patients suffering from LEMS; (4) Firdapse was granted approval by the FDA pursuant to § 355 and was granted market exclusivity pursuant to § 360cc prior to the FDA's approval of Jacobus's NDA for Ruzurgi; (5) the active ingredient in both Firdapse and Ruzurgi is amifampridine; (6) Ruzurgi is the "same drug" as Firdapse; (7) Firdapse and Ruzurgi both treat LEMS; and (8) Firdapse's exclusivity had not expired at the time the FDA approved Ruzurgi. Additionally, none of the three statutory exceptions to market exclusivity apply here: (1) the parties agree that Catalyst can ensure sufficient quantities of Firdapse, *see* § 360cc(b)(1); (2) there is no record evidence that Catalyst waived its exclusivity by written consent, *see* § 360cc(b)(2); and (3) there is no record evidence that Jacobus filed its NDA based on the representation that Ruzurgi is clinically superior to Firdapse, *see* § 360cc(c), (e).

Based on these undisputed facts and record evidence, the FDA's approval of Ruzurgi was contrary to the unambiguous language of the Orphan Drug Act. Catalyst Pharmaceuticals, Inc., held the exclusive right to market, Firdapse, an orphan drug, for a period of seven years in order to treat the rare autoimmune disease, LEMS. Because it is undisputed that none of the statutory exceptions to Catalyst's market exclusivity apply, the FDA was prohibited from approving for sale the same drug manufactured by Jacobus Pharmaceutical Company, Inc., to treat the same autoimmune disease during the period of Catalyst's market exclusivity. As a result,

the FDA's agency's action was arbitrary, capricious, and not in accordance with law, and its approval of Ruzurgi must be set aside. *See* 5 U.S.C. § 706(2)(A); *Miami-Dade County*, 529 F.3d at 1058.

IV. CONCLUSION

Because it is undisputed that Catalyst held the exclusive right to market Firdapse, i.e., amifampridine, to treat LEMS and that none of the statutory exceptions to market exclusivity apply here, we conclude that Catalyst is entitled to summary judgment in its favor. The district court's grant of summary judgment in favor of Defendants and Jacobus is reversed, and on remand, the district court shall enter summary judgment in favor of Catalyst.

REVERSED and REMANDED.